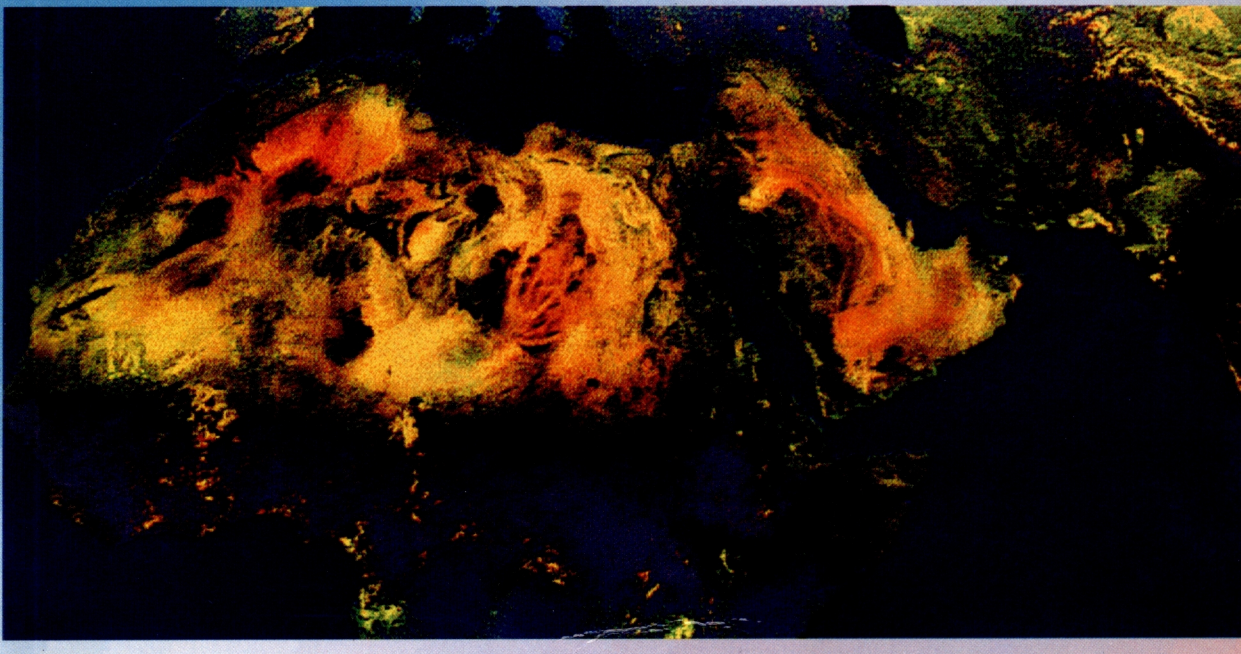
ISSN 1020-3397

المجلة الصحية لشرق المتوسط

Eastern Mediterranean Health Journal

La Revue de Santé de la Méditerranée orientale

Vol. 10 Nos 4/5 July/Juillet September/Septembre 2004 المجلد العاشر، العددان ٤ / ٥ تموز / يوليو ايلول / سبتمبر



منظمة الصحة العالمية
World Health Organization
Organisation mondiale de la Santé

المكتب الإقليمي لشرق المتوسط
Regional Office for the Eastern Mediterranean
Bureau régional de la Méditerranée orientale

المجلة الصحية لشرق المتوسط

هي المجلة الصحية الرسمية التي تصدر عن المكتب الإقليمي لشرق المتوسط بمنظمة الصحة العالمية. وهي منبر لتقديم السياسات والمبادرات الجديدة في الخدمات الصحية والترويج لها، ولتبادل الآراء والمفاهيم والمعطيات الوبائية ونتائج الأبحاث وغير ذلك من المعلومات، وخاصة ما يتعلق منها بإقليم شرق المتوسط. وهي موجهة إلى كل أعضاء المهن الصحية، والكليات الطبية وسائر المعاهد التعليمية، وكذا المنظمات غير الحكومية المعنية، والمراكز المتعاونة مع منظمة الصحة العالمية والأفراد المهتمين بالصحة في الإقليم وخارجه.

EASTERN MEDITERRANEAN HEALTH JOURNAL

IS the official health journal published by the Eastern Mediterranean Regional Office of the World Health Organization. It is a forum for the presentation and promotion of new policies and initiatives in health services; and for the exchange of ideas, concepts, epidemiological data, research findings and other information, with special reference to the Eastern Mediterranean Region. It addresses all members of the health profession, medical and other health educational institutes, interested NGOs, WHO Collaborating Centres and individuals within and outside the Region.

LA REVUE DE SANTE DE LA MEDITERRANEE ORIENTALE

EST une revue de santé officielle publiée par le Bureau régional de l'Organisation mondiale de la Santé pour la Méditerranée orientale. Elle offre une tribune pour la présentation et la promotion de nouvelles politiques et initiatives dans le domaine des services de santé ainsi qu'à l'échange d'idées, de concepts, de données épidémiologiques, de résultats de recherches et d'autres informations, se rapportant plus particulièrement à la Région de la Méditerranée orientale. Elle s'adresse à tous les professionnels de la santé, aux membres des instituts médicaux et autres instituts de formation médico-sanitaire, aux ONG, Centres collaborateurs de l'OMS et personnes concernés au sein et hors de la Région.

The Eastern Mediterranean Health Journal is abstracted/indexed in the Index Medicus and MEDLINE (Medical Literature Analysis and Retrieval Systems on Line) and the ExtraMed-Full text on CD-ROM, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), CAB International, Lexis Nexis™ and the Index Medicus for the WHO Eastern Mediterranean Region (IMEMR).
EMHJ is also available on the World Wide Web: http://www/emro.who.int/emhj.htm

ALL ARTICLES ARE PEER REVIEWED

ISSN 1020-3397

COVER: Remote sensing image of the area of the world that includes the Eastern Mediterranean Region. Cover image produced by the Canada Centre for Remote Sensing, Ottawa, Canada. (NOAA AVHRR Composite) Reproduced with permission

Cover designed by Ahmed Hassanein, EMRO
Printed on acid-free paper
Printed by Dar Mourad for Printing Cairo, Egypt

المجلة الصحية لشرق المتوسط

Eastern Mediterranean Health Journal

La Revue de Santé de la Méditerranée orientale

Vol. 10 Nos 4/5 July/Juillet September/Septembre 2004 المجلد العاشر، العددان ٤/٥ تموز/ يوليو ايلول/سبتمبر

Contents

Eastern Mediterranean Health Journal

Letter from the Editor

The ongoing conflict in Darfur, western Sudan has been of grave concern lately with increasing numbers of internally displaced people. Thus in July, Dr LEE Jong-wook, WHO Director-General, and Dr Hussein Gezairy, WHO Regional Director for the Eastern Mediterranean, visited camps and hospitals in south and west Darfur to asses the situation. While joint action by the Ministry of Health and many aid and humanitarian organizations has resulted in improvements, there still remains a wide gap between the needs of the people and available relief. WHO is working closely with the Ministry of Health and other partners to tackle the urgent problems, to prevent communicable disease outbreaks and to rehabilitate hospitals. A worrying turn of events was the reporting of 3 new cases of poliomyelitis in Sudan in the Darfur Region, indicating the urgent need to immunize and the potential difficulty posed by the civil unrest in Darfur. On a brighter note, despite the security situation in Iraq, 4.3 million children under 5 were reached in a campaign spearheaded by the Ministry of Health, Iraqi Red Crescent, WHO and UNICEF, an achievment which will help keep Iraq free of poliomyelitis. Included in this issue of EMHJ are four papers from Sudan concerning malaria and a paper on poliomyelitis from Pakistan investigating factors for persistent transmission in certain regions of the country.

WHO has also acted in Afghanistan with its partners the Massoud Foundation and HealthNet International to tackle the current epidemic of leishmaniasis. Distribution of insecticide impregnated bed nets and provision of drug treatment are the focus of the initiative to try and control the situation. This debilitating and disfiguring disease is also endemic in the Islamic Republic of Iran, a neighbouring country, and we present here a paper from the Islamic Republic of Iran studying leishmaniasis vectors.

Other communicable disease papers published here are a review on SARS and papers on childhood pneumonia, streptococcus infection, measles and cryptosporidiosis. As regards noncommunicable diseases, there are, among others, submissions on prenatal screening for chromosomal abnormality, hypertension, renal disease and smoking. We also present a comprehensive study in Arabic into handicap among children in Saudi Arabia.

The issue contains a good representation of the countries of the Region with 13 of the 22 member countries included. As always we welcome feedback on the Journal, and we respectfully remind our readers that our online evaluation form can be accessed at: http://www.emro.who.int/publications/emhj/evaluationform.asp

رسالة من المحرِّر

لقد أضحى الصراع المستمر في دارفور، غربي السودان مصدر قلق واهتمام كبيرين مؤخراً، إثر تزايد أعداد المهجَّرين داخل البلاد، ولذا فقد قام الدكتور لي يونغ ووك، المدير العام لمنظمة الصحة العالمية والدكتور حسين عبد الرزاق الجزائري، المدير الإقليمي لشرق المتوسط بزيارة للمخيمات وللمستشفيات في جنوب وغرب دارفور لتقييم الوضع. ورغم ما أحرز من تقدم نتيجة عمل مشترك لوزارة الصحة مع العديد من منظمات المساعدة الإنسانية، فإن الفجوة المتبقية من احتياجات السكان وبين الإغاثة المتاحة لاتزال واسعة. وتعمل منظمة الصحة العالمية بتعاون وثيق مع وزارة الصحة والشركاء الآخرين لمعالجة المشكلات الملحة واتِّقاء حدوث الفاشيات من الأمراض السارية ولإعادة المستشفيات إلى ما كانت عليه سابقاً. ومما يدعو للقلق الإبلاغ عن ثلاث حالات مستجدة من شلل الأطفال في السودان، في دارفور. مما يشير إلى الحاجة الملحة لحملات التطعيم، وإلى الصعوبات التي قد يواجهها الناس بسبب القلاقل المدنية في دارفور. ومما يدعو للفخر في المقابل، أنه تم الوصول إلى 4.3 مليون طفل دون سن خمس سنوات في العراق، رغم ما آل إليه الوضع الأمني هذه الأيام، وذلك عبر حملة قادتها وزارة الصحة العراقية والهلال الأحمر العراقي ومنظمة الصحة العالمية واليونيسف، وهو إنجاز سيساعد على إبقاء العراق خالياً من شلل الأطفال. ويتضمَّن هذا العدد من المجلة الصحية لشرق المتوسط أربع وَرَقات بحثية من السودان حول الملاريا، وورقة أخرى حول شلل الأطفال في باكستان، تم فيها استقصاء العوامل التي أدت إلى استمرار سرايته في بعض المناطق الباكستانية.

وقد كان لمنظمة الصحة العالمية ولشركائها في أفغانستان، ولاسيما مؤسسة مسعود والشبكة الصحية الدولية، دور هام في مواجهة الوباء الحالي لداء الليشمانيات. وقد كان توزيع الناموسيات المشبعة بمبيدات الحشرات وتوفير الأدوية محور اهتمام الجهود المبذولة لمكافحة الوباء، ويعد هذاء المنهك والمشوِّه متوطناً في إيران، البلد المجاور لأفغانستان، ويتضمن هذا العدد ورقة مقدمة من إيران لدراسة العوامل الناقلة لداء الليشمانيات.

وتستعرض الورقات الأخرى من هذا العدد بعض الأمراض السارية ولاسيما الالتهاب الرئوي الحاد الوخيم (سارس) والالتهاب الرئوي لدى الأطفال، والعدوى بالعقديات، والحصبة، وداء خفيات الأبواغ. أما الأمراض غير السارية فسنجد حولها مواضيع متعددة، منها تحرِّي الشذوذات الصبغية قبل الولادة، وارتفاع ضغط الدم، وأمراض الكلية والتدخين، كما تستعرض إحدى الوَرَقات التي كتبت بالعربية دراسة شاملة للإعاقة والعجز في المملكة العربية السعودية.

ويعد هذا العدد تمثيلاً صادقاً لبلدان الإقليم، إذ ضم بين دفتيه دراسات من 13 بلداً من بين بلدان الإقليم الاثنين والعشرين. ونحن، كما كنا دائماً، نرحب بتلقي المعلومات حول المجلة، ونذكِّر قراءنا باستمارة التقييم المتاحة على الإنترنت:

http://www/emro.who.int/publication/emhj/evaluationform.asp

Prevalence of measles antibody in children of different ages in Shiraz, Islamic Republic of Iran

A. Karimi,[1] A. Arjomandi,[1] A. Alborzi,[1] M. Rasouli,[1] M.R. Kadivar,[1] B. Obood[1] and B. Pourabbas[1]

معدل انتشار أضداد الحصبة لدى الأطفال من مختلف الأعمار في شيراز، جمهورية إيران الإسلامية

عبد الله كريمي، آرمان أرجمندي، عبد الوهاب البرزي، منوجهر رسولي، محمد رحيم كديور، برات عبودي، بهمن بورعباس

الخلاصة: دفعنا إلى إجراء هذا البحث حصول فاشية من الحصبة ناجمة عن فشل ثانوي في اللقاح، وذلك للتعرُّف على معدل انتشار أضداد الحصبة لدى الأطفال. فقمنا بدراسة 608 من الأطفال في سبع مجموعات عمرية مختلفة هي 6 أشهر، و9 أشهر، و14 شهراً، و18 شهراً، و6 سنوات، و10 سنوات، و15 سنة. و لم يكن الأطفال في سن 6 أشهر و9 أشهر قد تلقّوا أي تطعيم ضد الحصبة، أما بقية المجموعات فقد تلقّت جرعتَيْن من اللقاح في عمر 9 أشهر و15 شهراً. في حين تلقّى أفراد مجموعة 15 عاماً جرعة إضافية. وقد لوحظ أن أضداد الحصبة العابرة للمشيمة قد نقصت من 10٪ في عمر ستة أشهر إلى صفر بالمئة في عمر تسعة أشهر. وأصبحت أضداد الحصبة إيجابية في 52.9٪ في عمر 14 شهراً، و89.4٪ في عمر 18 شهراً، ثم 60.8٪ في عمر 6 سنوات، و45٪ في عمر 10 سنوات، لتعود فتصبح 96.8٪ في عمر 15 عاماً. وهكذا فلكي تزداد مستويات أضداد الحصبة يُوصَى بإعطاء جرعة تعزيزية من التطعيم، إما مع الجرعة المعزِّزة للّقاح الثلاثي (الخناق والشاهوق والكزاز) أو قبل دخول المرحلة الثانوية.

ABSTRACT An outbreak of measles due to secondary vaccine failure prompted this investigation into the prevalence of measles antibody in children. We studied 608 children in 7 different age groups: 6, 9, 14 and 18 months and 6, 10 and 15 years. Children in the 2 youngest groups received no vaccination; the rest were vaccinated at 9 months and 15 months. The 15-year-old age group received an additional vaccination. Transplacental measles antibody (Ab) decreased from 10.0% at 6 months to 0% at 9 months. Measles Ab was positive in 52.9% (14 months), 89.4% (18 months), 60.8% 96 years), 45.0% (10 years) and 96.8% (15 years). To increase Ab levels, a booster vaccination is recommended, administered either with the second DPT booster or at pre-high school age.

Prévalence des anticorps antirougeoleux chez des enfants de différents âges à Chiraz (République islamique d'Iran)

RÉSUMÉ Une flambée de rougeole due à l'échec de la vaccination secondaire a conduit à effectuer une étude de la prévalence des anticorps antirougeoleux chez les enfants. Nous avons étudié 608 enfants dans sept groupes d'âge différents : 6, 9, 14 et 18 mois et 6, 10 et 15 ans. Les enfants des deux groupes d'âge les plus jeunes n'avaient pas été vaccinés ; le reste des enfants avaient été vaccinés à l'âge de 9 et 15 mois. Le groupe des enfants de 15 ans avait eu une vaccination supplémentaire. Les anticorps transplacentaires diminuaient, passant de 10,0 % à l'âge de 6 mois à 0 % à l'âge de 9 mois. Dans les groupes d'âge étudiés, la proportion des enfants présentant des anticorps antirougeoleux par âge était de 52,9 % (14 mois), 89,4% (18 mois), 60,8 % (6 ans), 45,0 % (10 ans) et 96,8 % (15 ans). Afin d'augmenter les taux d'anticorps, une vaccination de rappel est recommandée, à administrer soit avec le deuxième rappel DTC soit à l'âge correspondant au cycle d'enseignement pré-secondaire.

[1]Clinical Microbiology Research Centre, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran.

Received : 10/10/02; accepted: 21/09/03

Introduction

Prevention of measles using vaccination is still the most important task in developing countries. The disease is a substantial cause of mortality and morbidity in children. It is highly contagious but preventable [*1*]. Mortality has declined dramatically since the introduction of a live attenuated vaccine. Despite an 85% decrease in mortality, however, outbreaks of measles have been reported due to secondary vaccine failure in older age groups (10–24 years), e.g. in a study of measles epidemiology by the Iranian Minister of Health and Medical Education in 1998 [*2*]. This has led some countries, including the United States of America, to introduce an additional dose of vaccine in school-age children. In the Islamic Republic of Iran, the decline in measles incidence due to the vaccination programme has been noticed in children; cases in older age groups are, however, still emerging. This might be due to immigration from neighbouring countries such as Afghanistan and Pakistan, which have a vaccine coverage of less than 80% (unpublished report, Ministry of Health and Medical Education, 1988).

Our study was conducted to disclose the prevalence of measles antibodies in different age groups and to evaluate the necessity of administering additional doses of vaccine. The study was prompted by an outbreak of measles in our country in 1997.

Methods

Over the period 2001–02 we enrolled 608 children into the study in 7 different age groups. Details of the groups and their vaccination history are given in Table 1. The children were selected by random cluster sampling of children referred to the Motahhari out-patient clinic or from primary schools in Shiraz. The epidemiological data including sex, age, socioeconomic status, number of family members and vaccination history were obtained. For antibody (Ab) testing, 5 mL of blood was drawn and serum was separated and frozen at –20 °C. The sera were examined using an enzyme-linked immunosorbent assay IgG kit (Morbillio, Radim SpA, Pomezia, Italy). Samples with optical density (OD) lower than the cut-off control (OD < 0.200) were considered non-reactive for measles IgG antibodies. Samples with OD higher than the cut-off control (OD > 0.700) were considered reactive for measles IgG antibodies. Samples with absorbance values ± 10% of the cut-off (OD 0.200 to 0.700) control were considered questionable and were retested for confirmation.

Results

We enrolled 608 children, 52% male and 48% female, in the study. Table 2 shows

Table1 **Vaccination history for children in seven different age groups**

Group	No.	Age	Vaccination history
1	70	6 m	No vaccination
2	62	9 m	No vaccination
3	70	14 m	Vaccinated at 9 m
4	66	18 m	Vaccinated at 9 m and 15 m
5	97	6 y	Vaccinated at 9 m and 15 m
6	149	10 y	Vaccinated at 9 m and 15 m
7	94	15 y	Vaccinated at 9 m, 15 months and 9 m prior to the study

m = months. ***y = years.***

Table 2 **Prevalence of measles antibody (Ab) in children in seven different age groups in Shiraz**

Age	Total No.	Ab positive No.	%	Ab negative No.	%	*P*-values between different age groups	
6 m	70	7	10.0	63	90.0		
9 m	62	0	–	62	100.0	6 m and 9 m	0.014
14 m	70	37	52.9	33	47.1	9 m and 14 m	0.00001
18 m	66	59	89.4	7	10.6	18 m and 6 y	0.00006
6 y	97	59	60.8	38	39.2	6 y and 10 y	0.016
10 y	149	67	45.0	82	55.0	10 y and 15 y	0.00001
15 y	94	91	96.8	3	3.2	All age groups	0.00001
Total	608	320	50.7	288	49.3		

m = months. ***y = years.***

the frequency of measles Ab prevalence in each age group. Antibody prevalence was higher in girls, although the result was not statistically significant. The Ab prevalence was significantly different in all consecutive age groups ($P = 0.00001$). The *P*-values for the different age groups are shown in Table 2. Number of family members, socioeconomic status and literacy of parents were not significant (data not shown).

Transplacental IgG from mothers declined from 10.0% at 6 months to 0% at 9 months of age in non-vaccinated children. Although this is unusual and we do not have good explanation for it, it is possible the titre of measles Ab in our pregnant women was very low due to low contact with wild measles viruses. However, in infants more than 9 months old, the prevalence of Ab increased owing to vaccination at 9 months and 15 months of age, and declined over time thereafter.

Primary vaccine failure is defined as a no detectable antibody after vaccination. It can be caused by interaction of maternal antibody to the vaccine by immunological response, technical problems, and so on. Primary vaccine failure in our study was 47.1% in the 14-month-old group, reducing to about 10.6% in the 18-month-old group due to the second dose of vaccine given at 15 months. Primary vaccine failure was 55% at age 10, reducing to 3.2% at 15 due to the third vaccine administration.

Discussion

Measles is a highly contagious, preventable disease. The incidence has shown a remarkable decline in our county over recent years due to routine administration of live, attenuated vaccine at the ages of 9 months and 15 months, but several reports of disease outbreak in older age groups have been documented [*2*,*3*]. The presence of measles Ab indicates previous infection, active immunization or, at ages below 9 months, maternal Ab transmission, all of which offer immunity.

Our study was conducted to determine the pattern of Ab prevalence in different age groups of children. In this study, transplacental Ab was detected in only 10.0% of 6-month-old infants, declining to 0% at 9 months. This finding is in accord with pre-

vious studies from Iran [*4,5*]. The decline of maternal antibody in infants in different geographic areas is dependent on socioeconomic states, catabolism of antibody, amount of antibody transmission to fetus, level of maternal antibody, and so on. In some studies it was shown to be between 0% and 10% at about 11 months of age [*2,4*]. Therefore, a high percentage of children at 6 months of age are also susceptible in an outbreak of the disease. It has been documented that the Schwarz type vaccine that is used in the Islamic Republic of Iran is not so effective for 6-month-old infants [*6,7*]. The absence of Abs during outbreaks was 47.1% at 14 months, 1 month before the second vaccination and 10.6% 3 months afterwards. This finding was in accordance with previous studies [*8–10*]. High primary vaccine failure at 9 months of age might be related to trans-placental Ab from mothers [*8*].

Other possible factors responsible for this high primary vaccine failure include nutritional status of children [*11*], acute disease during vaccination [*12–14*] and concomitant administration of gamma globulin [*15*], race, environmental factors [*16,17*], sex [*18*] and immunity status of those being vaccinated [*19,20*]. In our study, sex and literacy were not statistically important factors in primary vaccine failure. Measles Ab was positive in 89.4% of the 18-month-old children and 60.8% at 6 years of age, which was statistically significant ($P < 0.001$). In the 10-year-old group, only 45.0% of the children were positive for measles Ab ($P = 0.016$). This Ab-waning phenomenon is reported to be about 2%–20% in several studies [*21–24*]. The presence of Ab may be due to the vaccine effect or to previous infection with wild virus. The waning of Ab titre is greater in subjects who produce lower initial Ab titres. Accordingly, a single vaccination produces more significant Ab waning [*25*]. An important observation was the significant rise in the Ab titre of the 15-year-old age group following the administration of an additional booster dose of the vaccine, compared to the 10-year-old age group ($P < 0.00001$) (Table 2). The necessity for an additional immunization is also emphasized in a report from Singapore [*26*] and in other countries [*27,28*]. Therefore, an additional dose of measles vaccine is recommended for Iranian children around high-school age.

Acknowledgement

The authors wish to thank Dr A. Japoni for his help in preparing the manuscript.

References

1. Issacs D, Menser M. Modern vaccines, measles, mumps, rubella, and varicella. ***Lancet***, 1990, 335:1384–7.

2. ***Study of measles epidemiology in Iran during 1991 to 1998***. ***Annual report of the Minister of Health and Medical Education.*** Tehran, Ministry of Health and Medical Education, 1998.

3. ***Health picture***. ***Annual report of the Minister of Health and Medical Education.*** Tehran, Ministry of Health and Medical Education, 2002.

4. Mirchamsy H et al. Age of measles immunization in tropics. ***Developments in biological standardization***, 1978, 41: 191–4.

5. Mokhtariazad T. ***Evaluation of measles vaccination in 6-month infants*** [thesis]. Tehran, Tehran University of Medical Sciences, 1982.

6. Markowitz LE et al. Immunization of six-month-old infants to different doses of Edmonston–Zagreb and Schwarz measles vaccine ***New England journal of medicine***, 1990, 322:580–7.

7. Tidjani O et al. Serological effects of Edmonston–Zagreb, Schwarz and AIK-C measles vaccine strains given at ages 4–5 or 8–10 months. ***Lancet***, 1989, 11: 1357–60.

8. Shelton JD et al. Measles vaccine efficacy: Influence of age at vaccination vs duration of time since vaccination. ***Pediatrics***, 1978, 62:961–4.

9. Mirchamsy H et al. Comparative field trial of five measles vaccines produced in human diploid cell, MRC-S. ***Journal of biological standardization***, 1977, 5:1–18.

10. Mirchamsy H et al. Mass immunization of children in Iran with live attenuated Sugiyama virus adapted to calf kidney cell cultures. ***Japanese journal of experimental medicine***, 1971, 41:39–40.

11. Wesley A, Coovadia HM, Henderson L. Immunological recovery after measles. ***Clinical and experimental immunology***, 1978, 32:540–4.

12. Krober MS, Stracener CE, Bass JW. Decreased measles antibody response after measles–mumps–rubella vaccine in infants with colds. ***Journal of the American Medical Association***, 1991, 265(16): 2095–6.

13. Halsey NA et al. Response to measles vaccine in Haitian infants 6 to12 months old. ***New England journal of medicine***, 1985, 313(9):544–9.

14. Ndikuyeze A et al. Immunogenicity and safety of measles vaccines in ill African children. ***International journal of epidemiology***, 1988, 17(2):448–55.

15. Krugman S. Present studies of measles and rubella immunization in the United States: a medical program report. ***Pediatrics***, 1971, 78:1–16.

16. Black FL et al. Geographic variation in infant loss of maternal measles antibody and in prevalence of rubella antibody. ***American journal of epidemiology***, 1986, 124(3):442–52.

17. Neiburg P, Dibley MJ. Risk factors for fatal measles infection. ***International journal of epidemiology***, 1980, 15(3): 309–11.

18. Bromberg K et al. Maternal immunity to measles and infant immunity at less than twelve months of age relative to maternal place of birth. ***Journal of pediatracs***, 1994, 125(4):579–81.

19. Dai B et al. Duration of immunity following immunization of live measles vaccine. ***Bulletin of the World Health Organization***, 1991, 69(4):415–23.

20. Markowitz LE et al. Persistence of measles antibody after revaccination. ***Journal of infectious diseases***, 1992, 166(1):205–8.

21. Climie A, Andre FE. Field trial of heat-stable measles vaccine in Papua New Guinea. ***Journal of tropical medicine and hygiene***, 1984, 87(6):249–55.

22. Zhuji Measles Vaccine Study Group. Epidemiologic examination of immunity period of measles vaccine. ***Chinese medical journal***, 1987, 67:19–22 [in Chinese].

23. Xiang JZ, Chen AH. Measles vaccine in the People's of Republic of China. ***Reviews of infectious diseases***, 1983, 5(3): 506–10.

24. Gdalevich M et al. Measles epidemic in Israel—successful containment in the military. ***Preventive medicine***, 2000, 31(6):469–51.

25. Smith FR et al. Reported measles in persons immunologically primed by prior

vaccination. ***Journal of pediatrics***, 1982, 101(3):391–3.

26. Goh D et al. Resurgence of measles in Singapore: profile of hospital cases. ***Journal of paediatrics and child health***, 1999, 35(5):493–6.

27. Christenson B, Bottiger M. Measles antibody comparison of long-term vaccination titer, early vaccination titers and naturally acquired immunity. ***Vaccine***, 1994, 12(2):129–33.

28. Olsha M et al. Measles immunity in Israeli young adults. ***Israel journal of medical sciences***, 1994, 30:596–9.

Measles mortality reduction

Measles remains a leading cause of death among young children, despite the availability of a safe and effective vaccine for the past 40 years. More than half a million people, the majority of them children, died from measles in 2003; in the Eastern Mediterranean Region (EMR) there were an estimated 69 000 deaths from measles. WHO and UNICEF have developed a joint Strategic Plan for Measles Mortality Reduction and Regional Elimination 2001–2005. The overriding goal of this plan is to reduce the number of global measles deaths (from the 1999 level) by 50% by the end of 2005. The priority countries in EMR are Afghanistan, Djibouti, Pakistan, Somalia and Sudan. The four-pronged strategy for sustainable measles mortality reduction is based on: providing strong routine immunization; providing a "second opportunity" for measles immunization to all children; surveillance; improvement in the clinical management of measles cases. Thus, from 1999 to 2003, more than 350 million children globally received measles vaccine through supplementary immunization activities. Moreover, improvements were made in routine immunization over this period. These accelerated activities have resulted in a significant reduction in estimated global measles deaths. Overall, global measles mortality decreased by 39% between 1999 and 2003. Given the progress made to date, it is expected that the 2005 global measles mortality reduction goal will be achieved.

Source: WHO Fact sheet No. 286
Available at: http://www.who.int/mediacentre/factsheets/fs286/en/

Évaluation de la réponse vaccinale contre la poliomyélite et la rougeole chez les enfants malnutris au Maroc

H. Caidi, [1] F. Bennis, [2] N. Mouan [2] et R. El Aouad [1]

تقييم الاستجابة للتلقيح ضد شلل الأطفال والحصبة في الأطفال المصابين بسوء التغذية في المغرب

حياة قايدي، فاطمة بنيس، نزهة معان، رجاء العواد

الخلاصة: أجرى الباحثون دراسة سيرولوجية مسحيَّة للمقارنة بين أضداد لقاح شلل الأطفال (النمط الأول والنمط الثاني والنمط الثالث) وأضداد لقاح الحصبة في الأطفال المصابين بسوء التغذية في المغرب ممَّن تلقّوا تطعيماتهم كاملة. وقد شملت الدراسة 37 طفلاً من هؤلاء إلى جانب 34 طفلاً شاهداً، وتراوحت أعمارهم بين 10 أشهر و5 سنوات. وقد دلّت الدراسة على أن معدل التمنيع كان منخفضاً جداً لدى الأطفال المصابين بسوء التغذية بالبروتين والطاقة بالنسبة لكلا اللقاحَيْن. ففي حين كانت معدلات الانتشار المصلي في المجموعة الشاهدة للنمط الأول لشلل الأطفال 94.1٪، وللنمط الثاني لشلل الأطفال 97.1٪، وللنمط الثالث لشلل الأطفال 91.2٪، وللقاح الحصبة 82.4٪. فإن معدّلات الانتشار هذه في الأطفال المصابين بسوء التغذية كانت أخفض بكثير، إذْ بَلَغَتْ (بمُعامل دقة 0.001)، 40.5٪ بالنسبة لأضداد النمط الأول لشلل الأطفال، و59.5٪ بالنسبة لأضداد النمط الثاني، و40.5٪ بالنسبة لأضداد النمط الثالث، و35.1٪ بالنسبة لأضداد لقاح الحصبة. وقد استنتج الباحثون أن سوء التغذية يمثِّل محدِّداً رئيسياً للاستجابة الخلطية للقاحات شلل الأطفال والحصبة، ويجب أن يولى ما يستحقه من اهتمام لاتِّقاء فشل التطعيم.

RÉSUMÉ Il s'agit d'une étude comparative de la séroprévalence des anticorps anti-poliovirus type 1, anti-poliovirus type 2, anti-poliovirus type 3 et des anticorps anti-rougeole chez les enfants malnutris (37) et complètement vaccinés et les enfants dont l'état nutritionnel est normal (34). L'âge est compris entre 10 mois et 5 ans. Les enfants souffrant d'une malnutrition protéino-calorique présentaient un taux d'immunisation vis-à-vis du vaccin poliomyélitique et du vaccin antirougeoleux très faible en comparaison avec les enfants témoins. En effet, 94,1 % des enfants témoins sont immunisés contre le poliovirus type 1, 97,1 % contre le poliovirus type 2 et 91,2 % contre le poliovirus type 3. Chez les enfants malnutris, ces taux étaient dans certains cas significativement plus faibles : 40,5 % ($p = 0,001$), 59,5 % ($p = 0,001$) et 40,5 % respectivement. La même baisse de la réponse vaccinale a été notée concernant le vaccin antirougeoleux: le taux d'immunisation est de 82,4 % chez les enfants témoins contre 35,1 % chez les enfants malnutris. La malnutrition est le facteur majeur de l'échec de la réponse vaccinale qui nous interpelle pour adopter les attitudes adéquates en vue d'éviter les échecs de vaccination.

Evaluation of the response to vaccination against poliomyelitis and measles in malnourished children in Morocco

ABSTRACT We made a comparative survey of the poliovirus antibodies (anti-poliovirus type 1, anti-poliovirus type 2 and anti-poliovirus type 3) and the measles antibodies in malnourished but completely vaccinated children (37) and control children (34). The age range was 10 months to 5 years. Immunization in children with protein–energy malnutrition was low for both vaccines. Seroprevalence rates of the polio 1, polio 2, polio 3 antibodies and the measles antibodies in the control group were 94.1%, 97.1%, 91.2% and 82.4% respectively. In malnourished children the respective rates were in some cases significantly lower being: 40.5% ($P = 0.001$), 59.5% ($P = 0.001$), 40.5% and 35.1%. Malnutrition is a major determinant of the humoral response to oral polio and measles vaccines and must be given due consideration to prevent vaccination failure.

[1]Département d'Immuno-Virologie, Institut national d'Hygiène, Rabat (Maroc).
Courriel : hcaidi@mailcity.com.
[2]Service de Pédiatrie III, C.H.U. Avicenne, Rabat (Maroc).
Reçu : 07/02/02 ; accepté : 26/10/03

Introduction

La malnutrition protéino-calorique (MPC) représente dans les pays en développement l'un des principaux problèmes de santé publique, responsable d'une forte mortalité infantile [*1,2*]. D'après des analyses récentes des causes de décès chez l'enfant, la malnutrition, mesurée par les paramètres anthropométriques, serait associée au décès dans près de la moitié des cas dans les pays en développement [*1*]. Elle est par ailleurs fréquemment associée sous une forme grave ou modérée à de très nombreuses affections où elle intervient comme facteur aggravant [*1,2,3*].

Plusieurs mécanismes immunitaires sont défaillants chez les enfants malnutris qui, de ce fait, sont victimes de sévères infections et du cycle vicieux infection-malnutrition [*4*]. La malnutrition constitue un problème majeur de l'échec des programmes de vaccination dans les pays où la malnutrition est répandue.

Des études ont montré la faible réponse au vaccin vivant atténué contre la rougeole et la poliomyélite en comparaison avec les enfants témoins [*5,2,6,7*].

L'objectif de notre étude consiste à évaluer la séroprévalence des anticorps anti-poliovirus type 1, anti-poliovirus type 2 et anti-poliovirus type 3 ainsi que des anticorps anti-rougeole chez les enfants malnutris, complètement vaccinés. La prévalence de ces mêmes anticorps est déterminée en parallèle chez les enfants complètement vaccinés et dont l'état nutritionnel est normal.

Méthodes

Enfants malades et enfants témoins

L'étude est réalisée sur 37 enfants (20 garçons et 17 filles) âgés de 10 mois à 5 ans auprès du service de Pédiatrie III, Hôpital d'enfants du Centre hospitalier universitaire (C.H.U.) de Rabat. Tous ces enfants sont vaccinés contre la poliomyélite (vaccin antipoliomyélitique oral trivalent ; fabricants *: Bucham & Clyron*) et la rougeole (vaccin antirougeoleux ; fabricants *: Serum Institut of India et* Aventis) et remplissent les critères de malnutrition qui sont vérifiés au préalable grâce à un questionnaire validé par le clinicien. Ils sont alors classés selon l'âge (Tableau 1), le type de malnutrition (Tableau 2) et le degré de maigreur (Tableau 3).

Le calendrier vaccinal au Maroc prévoit une première dose de vaccin poliomyélitique oral à la naissance et 3 doses de rappel à un intervalle d'un mois, et une dose de vaccin antirougeoleux à 9 mois.

Le groupe témoin a été recueilli également auprès du même service. Il s'agit de 20 garçons et 14 filles (34 enfants) âgés de 10 mois à 5 ans. Ces enfants sont tous vaccinés contre la poliomyélite et la rougeole et ne présentent aucun signe de malnutrition. Le prélèvement sanguin est fait dans le cadre d'un bilan destiné à l'exploration de la pathologie qui a motivé leur hospitalisation.

Tableau 1 **Répartition des enfants malnutris et des enfants témoins en fonction de l'âge et du sexe**

Variable	*Enfants malnutris*		*Enfants témoins*	
	Nombre	%	Nombre	%
Âge (mois)				
10-12	16	34,2	14	41,1
13-15	10	27,0	9	26,4
16-24	7	18,9	6	17,6
>24	4	10,8	5	14,7
Sexe				
Masculin	20	54,0	20	58,8
Féminin	17	45,9	14	41,1

Tableau 2 **Répartition des enfants malnutris en fonction du type de malnutrition**

Type de malnutrition	Garçons	Filles	Total (%)
Kwashiorkor	2	2	4 (10,8)
Marasme	6	0	6 (16,2)
Autres hypotrophies	12	15	27 (27,9)
Syndromes anémiques	3	0	3
Vomissements associés à une béance du cardia	1	1	2
Infections parasitaires	2	0	2
Infections mycobactériennes	0	1	1
Avitaminose	2	0	2
Maladie cœliaque	4	3	7
Cardiopathie congénitale	1	0	1
Diarrhées avec déshydratation	6	4	10
Total (%)	20 (54)	17 (45,9)	37 (100)

Prélèvement sanguin

Un prélèvement sanguin (5 ml) veineux est recueilli dans un tube sec pour chaque enfant. Le sang est centrifugé (500 g pendant 10 minutes) et le sérum est stocké congelé à - 80 °C jusqu'à son utilisation.

Tableau 3 **Répartition des enfants malnutris en fonction du degré de maigreur**

Degré de maigreur (%)	Nombre de cas	%
< 60	14	37,8
70	10	27,0
80	8	21,6
90	5	13,5

Titrage des anticorps anti-polio 1, 2 et 3 et des anticorps anti-rougeole

Le titrage des anticorps anti-poliovirus 1, 2 et 3 ainsi que des anticorps anti-rougeole est réalisé par réaction de séroneutralisation sur cultures cellulaires. Deux lignées sont utilisées : la lignée HEp-2 pour le titrage des anticorps anti-poliovirus 1, 2 et 3, et la lignée Vero pour le titrage des anticorps anti-rougeole. Le choix de ces techniques était justifié par leur grande maîtrise dans notre laboratoire.

Pour le poliovirus, le titre du sérum est donné par la plus forte dilution sérique qui neutralise 50 % des cultures cellulaires contre 100 DI_{50} de virus d'épreuve. Les résultats des titres d'anticorps sont normalement exprimés par leur réciproque *(Manual for the virological investigation of the poliomyelitis).*

La DCP 50 % est calculée par la méthode de Reed et Munch.

Log DCP 50% = log (dilution 50 % d'effet cytopathogène) + DP corrigé

Pour le titrage du taux d'anticorps contre le vaccin antirougeoleux, le titre du sérum est calculé par la méthode de Kärber *(Manual for the laboratory diagnosis of measles virus infection).*

Log_{10} (inverse) de la plus grande dilution - (somme des moyennes des plages de lyse *(UFP)* ÷ titre inverse du virus contrôle - 0,5) × log_{10} du facteur de dilution.

Résultats

La tranche d'âge la plus touchée par la carence nutritionnelle se situe entre 9 mois et 2 ans et touche aussi bien le sexe masculin que le sexe féminin.

Les résultats de séroneutralisation pour le vaccin antipoliomyélitique chez les enfants témoins montrent qu'après trois doses de vaccin antipoliomyélitique oral trivalent (VPOT), la proportion d'enfants témoins présentant des titres ≥ 8 est de 94,1 % (32/34) pour le type 1, de 97,1 % (33/34) pour le type 2 et de 91,2 % (31/34) pour le type 3.

Chez les 37 enfants de notre étude souffrant d'une malnutrition protéino-calorique et en comparaison avec le groupe témoin, le taux d'immunisation est beaucoup plus faible aussi bien pour le poliovirus type 1 que pour le poliovirus type 2 et le poliovirus type 3. En effet, la séroconversion est de 40,5 % (15/37) pour le poliovirus type 1, 59,5 % (22/37) pour le poliovirus type 2 et 40,5 % (15/37) pour le poliovirus type 3. Le pourcentage d'enfants triple positifs est de 37,8 % (14/37) seulement (Tableau 4).

Pour le vaccin antirougeoleux, les résultats de la séroneutralisation ont révélé que malgré une couverture vaccinale de 100 % chez les enfants témoins, le taux de séroconversion contre le vaccin est de 82,4 % (28/34) ; 70 % présentent un taux d'anticorps compris entre 120 et 899 UFP et seulement 12,4 % des enfants présentent un titre supérieur à 900 UFP. Le taux de séroconversion négatif chez ce groupe d'enfants est de 17,6 % (6/34).

Chez les enfants malades, le taux d'immunisation contre la rougeole est beaucoup plus abaissé par rapport au groupe témoin. Ainsi, la présence d'anticorps neutralisant le virus de la rougeole révélé par la réaction de séroneutralisation est notée chez seulement 35,1 % (13/37) des enfants, le titre des anticorps étant entre 120 et 899 UFP. La majorité des enfants de ce groupe sont séronégatifs (24/34), soit un pourcentage de 64,8 % ; le titre des anticorps neutralisants est inférieur à 8 UFP. Par ailleurs, aucun enfant ne présente un taux d'anticorps supérieur à 900 UFP.

On a également pu comparer le taux d'immunisation contre la poliomyélite et la rougeole chez les enfants malnutris en fonction de deux paramètres : le type de malnutrition et le degré de maigreur.

Chez les cas de kwashiorkor (4 cas) et de marasme (6 cas), le taux d'immunisation est nul aussi bien pour les trois types de poliovirus que pour le virus de la rougeole. Pour les autres hypotrophies (27 cas), 12 présentent un statut immunitaire normal pour le vaccin antipoliomyélitique et le vaccin antirougeoleux avec un pourcentage de 44,4 % et 13 enfants ont des tests négatifs pour la poliomyélite et la rougeole, soit un pourcentage de 48,1 %. Les deux hypotrophes restants ont des tests positifs pour la poliomyélite et négatifs pour la rougeole (7,4 %).

L'immunisation la plus défaillante est celle trouvée chez les enfants avec un degré de maigreur < 60 % et un degré de maigreur de 90 % : 3 enfants seulement sur 14 (21,4 %) avec un degré de maigreur < 60 % présentent une séroconversion vis-à-vis du vaccin antipoliomyélitique contre 2 cas (14,2 %) pour le vaccin antirougeoleux ; un seul cas sur 5 (20,0 %) avec un degré de maigreur de 90 % (les enfants avec un degré de maigreur de 90 % sont

Tableau 4 **Taux d'immunisation contre le poliovirus et le virus de la rougeole chez les enfants témoins et les enfants malnutris**

Immunisation contre	Enfants témoins %	Enfants malnutris %	p
Poliovirus			
Type 1	94,0	40,5	< 0,001
Type 2	97,0	59,0	< 0,001
Type 3	91,0	40,5	< 0,001
Virus de la rougeole	82,3	35,1	< 0,001

tous des formes œdémateuses où le degré de maigreur n'est pas un bon indicateur de l'état nutritionnel du malade) est séropositif aussi bien pour le virus poliomyélitique que pour le virus de la rougeole.

Trois cas sur 10 (30,0 %) avec un degré de maigreur de 70 % montrent une séroconversion positive vis-à-vis du poliovirus et 4 enfants sur 10 (40,0 %) une séroconversion positive vis-à-vis du virus de la rougeole ; 7 enfants sur 8 ayant un degré de maigreur de 80 % sont séropositifs pour le poliovirus (87,5 %) contre 6 cas (75,0 %) pour le virus de la rougeole.

Discussion

Comme déjà mentionné, la tranche d'âge la plus touchée par la carence nutritionnelle se situe entre 10 mois et deux ans ; cette prédilection trouve son explication dans le sevrage de l'allaitement au sein et la grande fréquence des maladies associées à cet âge [*2,3*]. Par ailleurs, la malnutrition touche aussi bien les garçons (54 %) que les filles (45,9 %), la différence n'étant pas statistiquement significative (p = 0,48). Pour les résultats de séroneutralisation, notre étude montre que le taux d'immunisation aussi bien pour le vaccin antipoliomyélitique que pour le vaccin antirougeoleux chez les enfants malnutris est plus faible en comparaison avec les enfants dont l'état nutritionnel est normal. Pour le vaccin antipoliomyélitique, le taux de séroconversion pour le type 1 est de 94 % chez les enfants témoins, alors que chez les enfants malades il est de 40,5 %, la différence étant statistiquement très significative (p = 0,001). Pour le poliovirus type 2, la proportion d'enfants présentant des titres d'anticorps ≥ 8 est de 97 % chez les enfants témoins contre 59 % chez les enfants malades (p = 0,001). Il n'en reste pas moins que l'immunité contre le poliovirus type 1 constitue un atout majeur dans la lutte contre la poliomyélite antérieure aiguë puisqu'il s'agit à la fois du type le plus fréquent et le plus pathogène. La même différence est notée pour le poliovirus type 3 : 91 % pour les témoins contre 40,5 % pour les enfants souffrant d'une malnutrition protéino-calorique (p = 0,001). Ces résultats sont tout à fait comparables à ceux rapportés par d'autres auteurs, le poliovirus type 3 étant connu pour sa faible immunogénicité [*8*].

En effet, les carences en protéines et en apport énergétique ont une influence directe sur l'immunité et plus particulièrement sur la production d'anticorps qui sont des glycoprotéines [*4*]. Ainsi l'absence de réponse immunitaire vaccinale, plus particulièrement dans les formes œdémateuses (kwashiorkor) où le taux d'immunisation est nul aussi bien pour le vaccin antipoliomyélitique que pour le vaccin antirougeoleux, trouve son explication dans le défaut de protéosynthèse. Dans ces formes œdémateuses, la protidémie est très basse, elle atteint 38 g/L ; l'électrophorèse des fractions protéiques a révélé une hypoalbuminémie (< 18 g/L) et une hypogammaglobulémie (< 3 g/L).

Dans la malnutrition protéino-énergétique, le système du complément, surtout la fraction C3, est déficiente et par conséquent la production d'anticorps est déficiente elle aussi. Cette déficience en production des anticorps aussi bien pour le vaccin trivalent oral (VPOT) que pour le vaccin antirougeoleux est beaucoup plus marquée chez les cas de kwashiorkor et de marasme [*9*] ; ceci explique la susceptibilité sinon la confirmation d'une réinfection par la poliomyélite et par la rougeole chez les enfants souffrant de MPC.

D'autres facteurs peuvent expliquer la faible réponse vaccinale antipoliomyélitique, comme les diarrhées chroniques et

l'interférence des entérovirus non poliomyélitiques qui sévissent pendant la période sèche. Deux études ont permis d'illustrer le rôle de ces deux facteurs. Ainsi, une étude menée en Tunisie en 1997 sur 121 enfants ayant reçu 3 doses du vaccin VPOT a montré que les taux de séroconversion pour le poliovirus type 1, le poliovirus type 2 et le poliovirus type 3 sont de 94,7 %, 100 % et 89,5 % respectivement. Le faible taux de séroconversion a été noté surtout pour le poliovirus 3 comparé à celui du poliovirus 2 et du poliovirus 1. L'interférence virale avec les entérovirus a été notée dans 50 % de la non-réponse à un type de poliovirus ou à un autre. L'étude a montré que la faible réponse vaccinale peut aussi être associée à d'autres facteurs comme la présence d'anticorps maternels et la malnutrition [*10*].

Une étude menée en Chine (province de Guangdong) a permis d'illustrer le rôle de la saison de vaccination dans la séroconversion vaccinale antipoliomyélitique chez 82 enfants vaccinés en été et 106 enfants vaccinés en hiver. Le dosage des anticorps a été testé avant et après vaccination. Le taux de séroconversion est de deux à sept fois plus important en hiver qu'en été. L'interférence virale avec les entérovirus non poliomyélitiques a été notée dans 75,6 % et 38 % des cas en été et en hiver respectivement ; ceci laisse apparaître que la fréquence des infections à entérovirus pendant la période sèche, période où l'incidence de la malnutrition est à son pic, peut être la cause principale de l'échec de la réponse vaccinale antipoliomyélitique. Une suggestion proposée par l'auteur de l'étude est de donner une dose de vaccin supplémentaire en dehors de la période sèche, surtout chez les enfants à risque de malnutrition [*11*]. Ceci donc laisse comprendre que l'infection par des virus autres que le poliovirus pourra diminuer la réponse vaccinale vis-à-vis du vaccin contre la poliomyélite, surtout chez les enfants à risque pour la malnutrition où l'infection par d'autres virus est plus fréquente [*12*].

La malnutrition et les maladies diarrhéiques très fréquentes dans les pays en développement sont les causes majeures de l'échec vaccinal. Une étude similaire a été réalisée en 1996 aux Philippines sur l'évaluation de la réponse vaccinale vis-à-vis du vaccin poliomyélitique oral chez les enfants dénutris suite à des diarrhées chroniques. Les résultats montrent que le taux d'immunisation chez les enfants est diminué de 26 à 34 % en comparaison avec le groupe témoin ($p < 0,002$) [*13*]. En effet, les diarrhées fréquentes chez les enfants souffrant de MPC peuvent expliquer la non-fixation du virus dans la paroi intestinale, soit par un phénomène d'inférence virale avec les anticorps en réponse au VPOT (l'adénovirus, l'entérovirus et le rotavirus), bactérienne ou parasitaire, soit en favorisant une élimination trop rapide du virus [*10,14*].

Pour le vaccin antirougeoleux comme pour le vaccin antipoliomyélitique, la séroconversion vis-à-vis du virus de la rougeole est bien plus diminuée dans le cas d'une dénutrition sévère. Ainsi, le taux d'immunisation chez les témoins est de 82,3 % (28/34) ; ce taux est abaissé à 35,1 % (13/37) chez les enfants malnutris ($p = 0,001$).

Une étude sur la réponse vaccinale vis-à-vis du vaccin vivant atténué de la rougeole a été réalisée au Soudan chez 35 enfants malnutris en comparaison avec 35 enfants témoins dont l'état nutritionnel est normal. Un prélèvement sanguin a été effectué avant et après vaccination, et le dosage des anticorps a été réalisé par réaction d'inhibition d'hémagglutination. Le taux de séroconversion chez les enfants malnutris et les enfants témoins est de 92 % et 96 % respectivement ($p < 0,02$) ;

le faible taux de séroconversion a été noté chez les cas de kwashiorkor [*15*].

La baisse de la réponse vaccinale est la conséquence d'un état nutritionnel défaillant. Des études ont rapporté que le taux d'immunisation ou de séroconversion vis-à-vis du virus de la rougeole est beaucoup plus abaissé chez les enfants malnutris [*16*] en comparaison avec les enfants dont l'état nutritionnel est normal. Ainsi, une bonne couverture vaccinale ne garantit pas une bonne immunité sérologique chez les enfants souffrant de MPC.

La supplémentation en vitamine A chez les mères après l'accouchement et les nouveau-nés pourra remédier à ce problème et pourra augmenter la production des anticorps en réponse à la vaccination. Une étude menée en Inde consistait à donner de la vitamine A (60 mg de rétinol) aux mères ainsi qu'à leur bébé (7,5 mg) à chaque administration d'une dose de VPO. Cette supplémentation a amélioré le taux d'immunisation vis-à-vis du vaccin de la poliomyélite, surtout pour le poliovirus de type 3 [*17*].

Conclusion

Au vu de ces résultats qui démontrent les faibles taux de séroconversion vis-à-vis du vaccin poliomyélitique oral et du vaccin antirougeoleux chez les enfants malnutris comparés à des enfants témoins, il nous paraît urgent de discuter d'une conduite pour améliorer l'état vaccinal de ces enfants et de s'assurer que les taux satisfaisants de couverture vaccinale (> 95 % pour la poliomyélite et 92 % pour la rougeole à l'échelle nationale) permettront d'atteindre les objectifs assignés, à savoir l'éradication de la poliomyélite d'ici l'an 2005 et l'élimination de la rougeole d'ici 2010. Si la malnutrition protéino-calorique a légèrement reculé ces dernières années au Maroc (de 28 % à 24 %), il n'en reste pas moins que les cas de malnutrition que l'on continue à enregistrer constituent un obstacle qui ralentit, voire compromet, le succès des programmes d'éradication de la poliomyélite et d'élimination de la rougeole.

L'évaluation de l'importance de la malnutrition protéino-calorique au Maroc permettrait de proposer une attitude adaptée pour prévenir ces échecs de la vaccination. L'impact de la supplémentation en vitamine A, qui est actuellement intégrée dans les activités du programme de vaccination, sur la séroconversion vis-à-vis du VPO et du vaccin antirougeoleux chez les enfants malnutris doit être apprécié lorsque l'administration d'une dose supplémentaire de vaccin antipoliomyélitique et antirougeoleux, une fois la malnutrition protéino-calorique jugulée, pourrait être une alternative pour prévenir ces échecs de vaccination. Ceci suppose néanmoins qu'un dépistage ciblé de la malnutrition protéino-calorique dans les régions à risque doit être entrepris, ce qui pourrait être d'une grande importance à la phase finale d'éradication de la poliomyélite et d'élimination de la rougeole.

Remerciements

Nous tenons à remercier tout le personnel du service de Pédiatrie III pour leur aide précieuse. Nous tenons à remercier également nos collègues du laboratoire de virologie de l'Institut national d'Hygiène à Rabat.

Références

1. Rice AL et al. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. ***Bulletin of the World Health Organization***, 2000, 78(10): 1207–21.
2. El Khaier A. Etude épidémiologique étiologique clinique évolutive et thérapeutique des malnutritions protéinocaloriques de l'enfant. Thèse n° 376 ; 1987
3. Bhaskaram P. Nutritional modulation of immunity to infection. ***Indian journal of pathology and microbiology***, 1992, 35(4):392–40.
4. Pastoret PP. Nutrition et réponse immune. In : Pastoret PP, Govaerts A, Bazin H. ***Immunologie animale***. Paris, Flammarion Médecine Sciences, 1990.
5. Bhaskaram P. Measles and malnutrition. ***Indian journal of medical research***, 1995, 102:195–9
6. Powell GM. Response to live attenuated measles vaccine in children with severe kwashiorkor. ***Annals of tropical paediatrics***, 1982, 2(3):143–5.
7. Chandra RK. Reduced secretory antibody response to live attenuated measles and poliovirus vaccines in malnourished children. ***British medical journal***, 1975, 2(5971):583–5.
8. Jody R et al. Sabin inactivated trivalent poliovirus vaccine : first clinical trial and seroimmunity survey. ***Pediatric infectious diseases journal***, 1988, 7:760–5.
9. Hafez M et al. Antibody production and complement system in protein energy malnutrition. ***Journal of tropical medicine and hygiene***, 1977, 80(2):36–9
10. Triki H, Abdallah MV, Ben Aissa R. Influence of host related factors on the antibody response to trivalent oral polio vaccine in Tunisian infants. ***Vaccine***, 1997, 15(10):1123–9.
11. Wu CM, Zheng HY, Ren YL. [Immune interference of enteroviruses to immune response of TOPV in subtropical areas.] ***Zhonghua liu xing bing Xne za zhi***, 1996, 17(4): 233–5 [In Chinese].
12. Faden H, Duffy L. Effect of concurrent viral infection on systemic and local antibody response to live attenuated and enhanced-potency inactivated poliovirus vaccines. ***American journal of diseases of children***, 1992, 146(11): 1320–3
13. Yoon PW, Black RE, Moulton LH. The effect of malnutrition on the risk of diarrheal and respiratory mortality in children < 2 years of age in Cebu, Philippines. ***American journal of clinical nutrition***, 1997, 65(4):1070–7.
14. Myaux JA et al. Effect of diarrhea on the humoral response to oral polio vaccination. ***Pediatric infectious diseases journal***, 1996, 15(3):204–9.
15. Idriss S, El Seed AM. Measles vaccination in severely malnourished Sudanese children. ***Annals of tropical pediatrics***, 1983, 3(2):6–7.
16. Halsey NA et al. Response to measles vaccine in Haitian infants 6 to 12 months old. Influence of maternal antibodies, malnutrition and concurrent illnesses. ***New England journal of medicine***, 1985, 313(9):544–9.
17. Bahl R et al. Effect of vitamin A administered at Expanded Programme on Immunization contacts on antibody response to oral polio vaccine. ***European journal of clinical nutrition***, 2002, 56(4):321–5.

Detection of pneumonia among children under six years by clinical evaluation

H. Shamo'on,[1] A. Hawamdah,[1] R. Haddadin[1] and S. Jmeian[2]

كشف الالتهاب الرئوي بين الأطفال دون ست سنوات بالتقييم السريري

هيام شمعون، علي حوامدة، رانيا حدادين، سامي جميعان

الخلاصة: قمنا بدراسة سريرية (إكلينيكية) استباقية في مستشفى الملكة علياء في عمَّان، الأردن، لتحديد العلامات والأعراض السريرية الأكثر فائدة في كشف الالتهاب الرئوي لدى الأطفال، وقد شملت الدراسة 147 طفلاً أدخلوا المستشفى في الفترة بين شهرَيْ آب/أغسطس 2002 وكانون الثاني/يناير 2003 لإصابتهم بالالتهاب الرئوي. وقد وجد أن أكثر العلامات والأعراض حساسية للتنبؤ بالالتهاب الرئوي هي السعال وسرعة التنفس التي تزيد على 50 مرة في الدقيقة، والانسحاب الداخلي لجدار الصدر. وقد لاحظنا أن وجود سرعة التنفس والانسحاب الداخلي لجدار الصدر يمكن كشفها في معظم حالات الالتهاب الرئوي، أما إذا كانت جميع العلامات السريرية سلبية فإن من غير المحتمل أن تكون صورة الصدر الشعاعية إيجابية الموجودات.

ABSTRACT To determine the most useful clinical symptoms and signs for detection of pneumonia in children, we carried out a prospective clinical study at Queen Alia Hospital, Amman, on 147 children admitted between August 2002 and January 2003 with clinical pneumonia. All the children had chest X-rays, which were read by the same radiologist. The most sensitive and specific signs and symptoms for prediction of pneumonia were coughing, tachypnoea (respiratory rate > 50/min) and chest wall indrawing. We found that presence of tachypnoea and lower chest wall indrawing can detect most cases of pneumonia. If all clinical signs are negative, chest X-ray findings are unlikely to be positive.

Dépistage de la pneumonie chez des enfants de moins de six ans par évaluation clinique

RÉSUMÉ Afin de déterminer les symptômes et les signes cliniques les plus utiles pour le dépistage de la pneumonie chez l'enfant, nous avons réalisé une étude clinique prospective à l'hôpital Reine Alia d'Amman chez 147 enfants hospitalisés entre août 2002 et janvier 2003 pour un épisode de pneumonie avec diagnostic clinique. Tous les enfants ont eu des radiographies pulmonaires interprétées par le même radiologue. La toux, la tachypnée (rythme respiratoire > 50/min) et le tirage respiratoire étaient les signes et les symptômes les plus sensibles et les plus spécifiques pour prédire une pneumonie. Nous avons trouvé que la présence de tachypnée et d'un tirage sous-sternal permet de dépister la plupart des cas de pneumonie. Si tous les signes cliniques sont négatifs, il est peu probable que les résultats de la radiographie pulmonaire soient positifs.

[1]Department of Paediatrics; [2]Ear, Nose and Throat Department, Queen Alia Military Hospital, Royal Medical Services, Amman, Jordan.
Received: 09/12/03; accepted: 17/03/04

Introduction

Acute lower respiratory tract illness (ALRI) is common among children seen in primary care [*1*], and accounts for slightly less than 50% of deaths in children under 1 year and about 20% of deaths in all hospitalized children under 15 years [*2*].

The physical differences between the chests of children and adults account for some of the differences in physical signs [*3*]. Small children find it difficult to take large breaths, so crackles and wheezes which may be expected only during such a manoeuvre will not be heard. In ALRI, when the history and physical examination suggest the same diagnosis, chest radiography is rarely necessary; when the 2 are inconsistent, then a radiograph may be helpful [*4*]. The identification of signs such as rapid breathing and chest retraction is very important in deciding who needs expensive treatment and who does not [*5*]. Also important is the decision to refer a child to hospital, which may be many miles away for many people living in rural areas in developing countries.

Our aim was to emphasize the importance of using simple clinical signs such as respiratory rate and chest wall indrawing in detecting ALRI, especially pneumonia, in children.

Methods

We did a prospective clinical observation study at Queen Alia Military Hospital, Amman, Jordan over a 6-month period (August 2002–January 2003) for all children below 6 years of age admitted with clinical pneumonia (most cases admitted were below this age). All patients were admitted via the outpatient clinic at Marqa, which is about 20 km from the hospital. This clinic sees patients from areas surrounding Amman (suburban areas) but does not always have radiology facilities available. The paediatrician admitted all cases on a clinical basis according to World Health Organization criteria: cough with tachypnoea (respiratory rate > 50/min in infants or > 40/min in older children), indrawing or wheezing. The respiratory rate was counted for a full minute after lowering the temperature (using cold compresses or paracetamol) to < 38 °C rectally or 37.5 °C axillary and before the routine extraction of blood.

All children admitted were examined by a specialist in paediatrics and the same ear, nose and throat specialist to exclude severe upper respiratory tract infection and all had chest X-rays which were assessed by the same radiologist. No clinical findings were written on the X-ray request.

Exclusion criteria from the study were children with immune deficiency, those known to have asthma, history of foreign body aspiration or chemical pneumonitis, children with failure to thrive and malnutrition, and children with severe upper respiratory tract infection. Malnourished children were excluded because tachypnoea and lower chest wall indrawing are not sufficiently sensitive as predictors of pneumonia in these children [*6*].

The 147 patients in our study were divided into 2 groups according to the chest X-ray findings: those having lobar pneumonia or bronchopneumonia in 1 or more lobes, and those having normal or hyperinflated chest X-rays. The clinical signs and symptoms of the 2 groups were analysed and compared with the radiological evidence of pneumonia (gold standard) and their sensitivity and specificity calculated.

Results

Our study included 147 children admitted with clinical pneumonia, 72 (49%) male

and 75 (51%) female. The ages of the children were: 1–12 months 92 (63%), 13–36 months 47 (32%) and 37–72 months 8 (5%). Mean duration of admission was 5 days for the first and second age groups and 2 days for the third age group.

From the chest X-ray findings, 40 children (27%) had lobar pneumonia in 1 or 2 lobes and 50 children (34%) had bronchopneumonia, a total of 90 children (61%) with pneumonia diagnosed on a radiological basis. Fifty-seven children (39%) had normal or hyperinflated chest X-rays. A family history of bronchial asthma or allergy was discovered in 15 children (10%).

Table 1 shows the overall frequency of symptoms and signs of pneumonia and Table 2 shows their sensitivity and specificity compared with radiology results (gold standard). Cough, fever, tachypnoea and chest indrawing were the most frequently observed signs and symptoms, while tachypnoea was both the most sensitive (99%) and most specific (88%) sign of pneumonia and cough the most sensitive (98%) symptom. Most of the children (146) received antibiotics; 2 patients needed a respirator (1 developed pneumothorax) and 3 had pleural effusion. There were no deaths.

Table 1 **Frequency of symptoms and signs in children with pneumonia (*n* = 147)**

Clinical sign or symptom	No.	%
Cough	105	71
Fever	103	70
Tachypnoea	96	65
Chest indrawing	92	63
Poor feeding	79	54
Grunting	79	54
Diminished air entry	58	40
Crepitation	52	35
Wheezes	49	33

Discussion

In developing countries, the case fatality rate from ALRI in children could to be reduced if the most serious forms of ALRI were identified and dealt with appropriately.

Our study showed that the most sensitive symptom was cough 98%, with 70% specificity. The most sensitive signs in decreasing order were: tachypnoea (99%), chest wall indrawing (88%), and fever (78%), while the most specific were tachypnoea (88%) followed by chest wall indrawing (77%).

Anadol found that tachypnoea had a specificity of 99% and a sensitivity of 61% and was the most important sign in diagnosing pneumonia [*7*]. Another study showed that the best screen for pneumonia was the presence of fever along with tachypnoea [*8*]. A study done in China showed that tachypnoea was more reliable than auscultation in predicting pneumonia [*9*].

Most of our children were infants, so in our study clinical signs appear to predict pneumonia in infants more reliably than in older children. A study done by Redd et al. comparing the clinical and radiological diagnosis of pneumonia found that children with a radiographic diagnosis tended to have been ill longer and to be older because mothers may have tended to take febrile children with mild ALRI to the health centre or hospital more often than non-febrile children with mild ALRI [*10*]. In the absence of respiratory signs, febrile infants are unlikely to have abnormal chest radiography [*11,12*].

Wheezing was found in 33% of the children in our study and was not a useful sign

Table 2 **Sensitivity and specificity of clinical symptoms and signs at presentation for predicting pneumonia**

Clinical sign or symptom	Chest X-ray		Sensitivity (%)	Specificity (%)
	Pneumonia detected (*n* = 90) No. positive for symptom/sign	Normal or hyperinflated (*n* = 57) No. positive for symptom/sign		
Tachypnoea	89	7	99	88
Cough	88	17	98	70
Chest indrawing	79	13	88	77
Fever	70	33	78	42
Poor feeding	52	27	58	53
Grunting	52	27	58	53
Diminished air entry	30	28	33	51
Crepitation	27	25	30	56
Wheezes	20	29	22	49

for determining pneumonia in children. This is in agreement with a study done by Mahabee-Gittens et al., who found that in wheezy infants and toddlers, grunting along with oxygen saturation is highly specific and can be used to help diagnose pneumonia in wheezing infants and toddlers [*13*].

We did not differentiate ALRI from bronchial asthma so it is possible that children were overtreated for ALRI and undertreated for asthma. In regions where wheezing illness is prevalent, the specificity of the World Health Organization pneumonia algorithm is reduced and this may lead to unnecessary use of antibiotics or underutilization of bronchodilators [*14*]. Simple physical signs that require minimal expertise to recognize can be used to determine oxygen therapy and to aid in screening for referral [*15–17*].

There may be poor agreement, even among experienced physicians, on the presence of rales in young children, and this was the case in our study. Subcostal or intercostal recessions (difficulty in breathing) are generally more often seen in infants than in older children because the chest wall is more compliant than that of the older child.

The most useful single factor for ruling out pneumonia in an infant is the absence of tachypnoea [*18*]. We found that tachypnoea and chest wall indrawing in the presence of cough can help the clinician to determine the need for chest radiography in the paediatric emergency clinic. A study done in Brazil showed that the clinical symptoms taken together contribute more than the signs and are on a par with X-ray in importance [*19*]. Another study found that age-specific respiratory rate (recommended by the World Health Organization, with or without chest wall indrawing) is a sensitive and specific indicator of pneumonia in almost all age groups [*20*]. Careful attention to specific clinical factors and use of adjunct radiographs and laboratory tests

should guide physicians in selection of antibiotics and decisions regarding hospitalization [*21*].

The employment of simple clinical criteria gives a good indication of pneumonia and can decrease unnecessary referral and admissions to hospital and thus result in cost-savings.

Most of the children in our study received antibiotics, which appear to be used in a high percentage of cases, even if inappropriate for the condition, because these clinical signs do not distinguish viral from bacterial pneumonia, nor do chest X-ray, temperature measurement or duration of fever [*22*].

Our study justifies the premise that pneumonia case detection does not require auscultation, chest X-ray or laboratory testing, and that observation of the respiratory rate and lower chest wall indrawing are the key elements of assessment in young children.

Conclusions

Initial observation of the infant may be the most critical component for the diagnosis of pneumonia.

Tachypnoea is the most valuable of the individual clinical signs for prediction of radiological pneumonia and can be a sensitive and reasonably specific indicator of respiratory infection.

The absence of tachypnoea and chest wall indrawing can safely be used to reduce the number of chest X-rays ordered for children under investigation. These findings have relevance for assessment protocols and resulting treatment decisions when chest X-ray is not routinely available.

These methods for pneumonia case detection could be taught to primary care physicians, nurses and even mothers, allowing them to seek medical advice early. This would lead to a decrease in the pneumonia mortality rate in children.

References

1. Margolis P, Gadomski A. Does this infant have pneumonia? ***Journal of the American Medical Association***, 1998, 279(4): 308–13.
2. Larsen GL et al. Respiratory tract and mediastinum. In: Hay WW et al., eds. ***Current pediatric diagnosis and treatment***, 13th ed. Stamford City, Appleton & Lange, 1997:420–74.
3. Helms P, Henderson J, eds. Respiratory disorders. In: Campbell AGM, McIntosh N, eds. ***Forfar and Arneil's textbook of pediatrics***, 5th ed. London, Churchill Livingstone, 1998, 12:489–583.
4. Alario AJ et al. Usefulness of chest radiographs in children with acute lower respiratory tract disease. ***Journal of pediatrics***, 1987, 111(2):187–93.
5. Cherian T et al. Evaluation of simple clinical signs for the diagnosis of acute lower respiratory tract infections. ***Lancet***, 1988, 2(8603):125–8.
6. Falade AG et al. Use of simple clinical signs to predict pneumonia in young Gambian children: the influence of malnutrition. ***Bulletin of the World Health Organization***, 1995, 73(3):299–304.
7. Anadol D, Aydin YZ, Gocmen A. Overdiagnosis of pneumonia in children. ***Turkish journal of pediatrics***, 43(3):205–9.
8. Zukin DD et al. Correlation of pulmonary signs and symptoms with chest radiographs in the pediatric age group. ***Annals of emergency medicine***, 1986, 15(7):792–6.

9. Dai Y et al. Respiratory rate and signs in roentgenographically confirmed pneumonia among children in China. ***Pediatric infectious disease journal***, 1995, 14 (1):48–50.

10. Redd SC et al. Comparison of the clinical and radiographic diagnosis of paediatric pneumonia. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1994, 88(3):307–10.

11. Crain EF et al. Is a chest radiograph necessary in the evaluation of every febrile infant less than 8 weeks of age? ***Pediatrics***, 1991, 88(4):821–4.

12. Taylor JA et al. Establishing clinically relevant standards for tachypnea in febrile children younger than 2 years. ***Archives of pediatrics & adolescent medicine***, 1995, 149(3):283–7.

13. Mahabee-Gittens EM et al. Clinical factors associated with focal infiltrates in wheezing infants and toddlers. ***Clinical pediatrics***, 2000, 39(7):387–93.

14. Nascimento-Carvalho CM et al. Childhood pneumonia: clinical aspects associated with hospitalization or death. ***Brazilian journal of infectious diseases***, 2002, 6(1):22–8.

15. Margolis PA et al. Accuracy of the clinical examination in detecting hypoxemia in infants with respiratory illness. ***Journal of pediatrics***, 1994, 124(4):552–60.

16. Usen S et al. Clinical predictors of hypoxaemia in Gambian children with acute lower respiratory tract infection: prospective cohort study. ***British medical journal***, 1999, 318(7176):86–91.

17. Weber MW et al. Predictors of hypoxaemia in hospital admission with acute lower respiratory tract infection in a developing country. ***Archives of disease in childhood***, 1997, 76(4):310–4.

18. Bloomfield D. Tachypnea. ***Pediatrics in review***, 2002, 23(8):294–5.

19. Pereira JC, Escuder MM. The importance of clinical symptoms and signs in the diagnosis of community-acquired pneumonia. ***Journal of tropical pediatrics***, 1998, 44(1):18–24.

20. Singhi S et al. Validity of clinical signs for the identification of pneumonia in children. ***Annals of tropical paediatrics***, 1994, 14(1):53–8.

21. Lichenstein R, Suggs AH, Campbell J. Pediatric pneumonia. ***Emergency medicine clinics of North America***, 2003, 21(2):437–51.

22. Korppi M et al. Comparison of radiological findings and microbial aetiology of childhood pneumonia. ***Acta paediatrica***, 1993, 82(4):360–3.

Group A streptococci in children with acute pharyngitis in Sousse, Tunisia

R. Mzoughi,[1] O. Bouallègue,[1] H. Selmi,[2] H. Ben Said,[3] A.S. Essoussi[2] and M. Jeddi[1]

العقديات من الزمرة A في الأطفال المصابين بالتهاب البلعوم الحادّ في سوسة، تونس

رضا مازوغي، بوعلاّق، سالمي، بن سعيد، عسوسي، جدي

الخلاصة: أجرى الباحثون دراسة استباقية لمدّة سنة واحدة في عيادتَيْن خارجيتَيْن للأطفال في سوسة، تونس، بهدف كشف وجود العقديات من الزمرة A في الأطفال المصابين بالتهاب حاد في البلعوم وبين حَمَلَة الجرثوم، ومعرفة توزُّع الأنماط المصلية والبيولوجية. وقد تم العثور على النمط A من العقديات، في 9٪ من المسحات البلعومية التي جمعت من 155 من الشواهد، وفي 17.7٪ من المسحات البلعومية التي جمعت من 474 من المرضى، وذلك بعامل دقة ($P < 0.05$). ومن بين الذراري الثلاث والأربعين التي استُفردت من المرضى، وعُيِّنَتْ أنماطها، تم كشف 15 نمطاً مختلفاً. وكان أكثر الأنماط شيوعاً النمط M75 فقد كشف في 14 ذرية وهو ما يشكّل نسبة 32.5٪، والنمط M9 الذي كشف في ست من الذّراري وهو ما يشكّل نسبة 14.0٪، والنمط M76 الذي كُشف في خمس من الذّراري وهو ما يشكّل نسبة 11.6٪، والنمط M12 الذي كُشف في أربع من الذّراري وهو ما يشكّل نسبة 9.3٪. وقد تعذَّر تعيين نمط ثلاث من الذّراري، وهو ما يشكّل نسبة 7.0٪. وقد أظهر تعيين النمط البيولوجي ثلاثاً من الأنماط البيولوجية السائدة وهي النمط البيولوجي الثالث في 14 ذرية والنمط البيولوجي الثاني في 11 ذرية والنمط البيولوجي الأول في 7 من الذّراري.

ABSTRACT A 1-year prospective study in 2 paediatric outpatient clinics in Sousse, Tunisia, aimed to determine the presence of group A streptococci in acute pharyngitis cases and carriers, and the distribution of the serotypes and biotypes. Group A streptococci were found in 9.0% of throat swabs from 155 controls and 17.7% from 474 patients ($P < 0.05$). Of 43 strains isolated from patients and submitted for typing, 15 different types were identified, the most common being M75 (14 strains; 32.5%), M9 (6 strains; 14.0%), M76 (5 strains; 11.6%) and M12 (4 strains; 9.3%). Three strains were non-typeable (7.0%). Biotyping of the strains showed 3 predominant biotypes: biotype 3 ($n = 14$), biotype 2 ($n = 11$), and biotype 1 ($n = 7$).

Les streptocoques du groupe A chez des enfants atteints de pharyngite aiguë à Sousse (Tunisie)
RÉSUMÉ Une étude prospective sur un an réalisée dans deux services de consultations externes pédiatriques à Sousse (Tunisie) avait pour objectif de déterminer la présence de streptocoques du groupe A dans les cas de pharyngite aiguë et chez les porteurs, ainsi que la répartition des sérotypes et biotypes. On a trouvé des streptocoques du groupe A dans 9,0 % des prélèvements de gorge de 155 sujets témoins et chez 17,7 % des 474 patients ($p < 0,05$). Parmi les 43 souches isolées chez les patients et soumises au typage, 15 types différents ont été identifiés, les plus courants étant M75 (14 souches ; 32,5 %), M9 (6 souches ; 14,0 %), M76 (5 souches ; 11,6 %) et M12 (4 souches ; 9,3 %). Trois souches étaient non typables (7,0 %). Le biotypage des souches a montré trois biotypes prédominants : le biotype 3 (n = 14), le biotype 2 (n = 11) et le biotype 1 (n = 7).

[1]Microbiology Laboratory; [2]Paediatric Service, Farhat Hached Hospital, Sousse, Tunisia.
[3]Centre de Protection Maternelle et Infantile (Centre PMI), Erriadh, Sousse, Tunisia.
Received: 16/01/03; accepted: 07/10/03

Introduction

Streptococcus pyogenes (group A streptococcus) is still the most frequent cause of pharyngitis in children and can lead to severe post-infection sequelae including rheumatic fever and glomerulonephritis [*1*]. The incidence of rheumatic fever has declined rapidly in developed countries where improved living conditions and systematic antibiotic therapy with penicillin have limited the spread of bacterial strains in the population [*2–4*]. However, unexpected outbreaks of rheumatic fever have occurred in the United States of America [*5*]. The changing epidemiology of group A streptococci and rheumatic fever is said to be related to changes in the distribution of serotypes [*6,7*], where certain virulent M types have been associated with invasive disease [*5,8–10*]. Thus, it is important to establish the epidemiological patterns of group A streptococci in different countries and regions, and especially to serotype the strains that have been isolated. This knowledge will be important for the development and use of vaccines [*11*].

In Tunisia, rheumatic fever remains an important health problem in children, with an incidence of 57 cases per 100 000 inhabitants in 2001 [*12*]. As a part of the national effort to clarify the epidemiological pattern of group A streptococci in our country the present study was conducted to determine the presence of group A streptococci in acute pharyngitis cases and in carriers in the city of Sousse, and the distribution of serotypes and biotypes.

Methods

A 1-year prospective study, between 1 October 1994 and 20 September 1995, was conducted in 2 paediatric outpatient clinics in Sousse: Farhat Hached Hospital and Centre de Protection Maternelle et Infantile (Centre PMI) Erriadh. Samples were collected from patients with acute pharyngitis, diagnosed on the basis of fever over 38 °C, sore throat, pharyngeal exudates and acute inflammatory tonsillitis.

A total of 474 patients, age 2 to 8 years, living in a populous district around Sousse were monitored by 3 general practitioners and 1 paediatrician. Samples were also collected from 155 healthy paediatric patients who were attending for vaccination. A swab was applied over both tonsils and the posterior pharynx and was transferred to the Microbiology Laboratory of Farhat Hached Hospital as soon as possible (2 to 3 hours after sampling). Samples were collected from patients before any antibiotic therapy.

All swabs were inoculated onto 5% horse blood agar plates, with nalidixic acid and colistin and incubated in a CO_2-enriched atmosphere for 24 hours at 37 °C. The cultures negative for beta-haemolytic streptococci were incubated during 24 hours under the same conditions. The positive beta-haemolytic colonies were isolated and applied to a 0.04 U bacitracin disk, the halo was measured and the strains were identified by latex agglutination (Streptokit, bioMérieux, France). Forty-three (43) strains of group A streptococci isolated from the patients were serotyped by standard methods [*13*] at the Institut Für Experimentelle Mikrobiologie, Jena, Germany. The biotypes were determined with a commercially available identification system (rapid ID 32 STREP, bioMérieux, France), using the classification of Bouvet et al. [*14*].

Statistical analysis was carried out using chi-squared tests.

Results

Streptococcal strains were found in 12.9% of the controls and 20.7% of the patients. Group A streptococci had a frequency of 9.0% and 17.7% in the controls and the patients respectively (significant difference, $P < 0.05$) (Table 1).

The isolation rates of group A streptococci peaked twice during the year from October to December and in June (Figure 1).

Of the 43 strains analysed, 93.0% were typeable. Fifteen different types were identified, the most common being M75 (32.5% of strains), M9 (14.0%), M76 (11.6%), and M12 (9.3%) (Figure 2). The remaining serotypes (< 3% each) were: M1, M14, M25, M2, M3, M11, M28, M8 and M49. Only 3 strains (7.0%) were nontypeable.

Three biotypes were predominant: biotype 3, biotype 2 and biotype 1 (Table 2).

Table 1 **Throat swab culture results in patients with acute pharyngitis and healthy controls**

Patient group	No. of patients	Group A streptococci		Group C, G, F streptococci		Positive culture	
		No. of strains	%	No. of strains	%	No. of strains	%
Acute pharyngitis	474	84	17.7	14	3.0	98	20.7
Controls (carrier state)	155	14	9.0	6	3.9	20	12.9

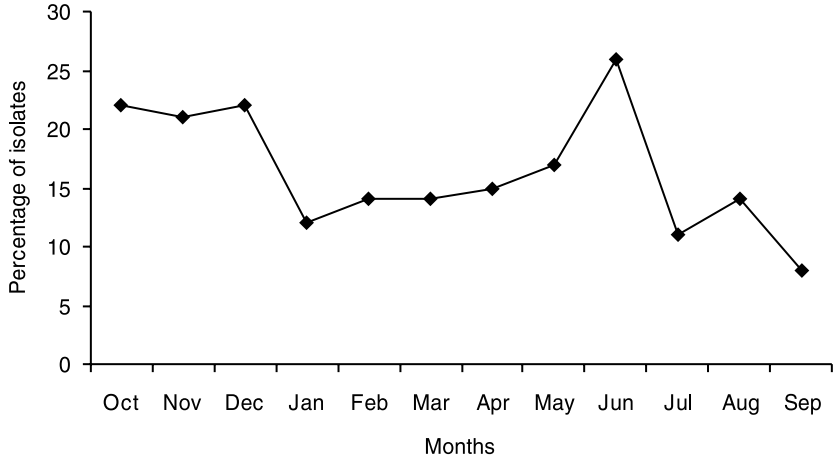


Figure 1 **Monthly isolation rates of group A streptococci in patients with pharyngitis**

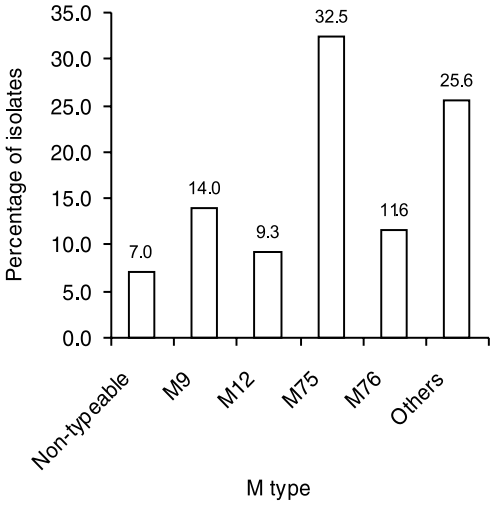


Figure 2 **Distribution of M types of group A streptococci associated with acute pharyngitis (*n* = 43 strains)**

Discussion

Little is known about the group A streptococci serotypes circulating in the Maghreb area and North Africa. To the best of our knowledge, the present study is the first Tunisian report of the serotypes of group A streptococci isolated from children with pharyngitis.

M serotyping might not adequately reflect the clonal diversity of bacterial strains, as suggested by the finding that isolates expressing the same M serotype can be distinguished by genetic methods [*15–17*]. Our results suggest that streptococcal pharyngitis is caused by a wide variety of strains, although 4 serotypes predominated (M75, M9, M76 and M12). Continued study may help define the epidemiology of group A streptococci in Tunisia.

Most isolates of group A streptococci described in developing countries, especially in the Middle East region, are untypeable [*7,18*]. Among typeable strains, M type 1 is usually one of the predominant serotypes, as it was reported in Kuwait [*7*], Islamic Republic of Iran [*18*], and the United Arab Emirates [*19*].

In contrast, the high rate of typeable isolates in our study (93.0%) suggests that group A streptococci strains in our city are similar but not necessarily related to those commonly found in Europe and North America. Furthermore, our findings highlight the low rate (< 3%) of M type 1, which has been associated with serious diseases such as rheumatic fever, a recognized problem in Tunisia, and toxic shock syndrome [*9,20*], which has not yet been reported from our area.

Although the number of isolates was not sufficient to make any epidemiological conclusions, this data could be useful for further understanding the epidemiology of group A streptococcal infections, and for the development and use of a vaccine.

Table 2 **Biotype distribution of group A streptococci associated with acute pharyngitis (*n* = 43 strains)**

Biotype	1	2	3	4	5	8	10
No. of strains	7	11	14	5	4	1	1

Acknowledgements

This work was supported by the Tunisian Ministry of Scientific Research. We thank Drs E. Günther and E. Straube (Institut Für experimentelle Mikrobiologie, Jena, Germany) for their help in serotyping the strains.

References

1. Bisno AL. Group streptococcal infections and acute rheumatic fever. ***New England journal of medicine***, 1991, 325:783–93.
2. Bach JF et al. 10-year educational programme aimed at rheumatic fever in two French Caribbean islands. ***Lancet***, 1996, 347:644–8.
3. Markowitz M, Gerber MA, Kaplan EL. Treatment of streptococcal pharyngotonsillitis: reports of penicillin's demise are premature. ***Journal of pediatrics***, 1993, 123:679–85.
4. Massel BF et al. Penicillin and the marked decrease in morbidity and mortality from rheumatic fever in the United States. ***New England journal of medicine***, 1988, 318:280–6.
5. Veasy LG et al. Resurgence of acute rheumatic fever in the intermountain area of the United States. ***New England journal of medicine***, 1987, 316:421–7.
6. Kaplan EL, Wotton JT, Johnson DR. Dynamic epidemiology of group A streptococcal serotypes associated with pharyngitis. ***Lancet***, 2002, 358:1334–7.
7. Majeed HA et al. The concurrent associations of group A streptococcal serotypes in children with acute rheumatic fever or pharyngitis-associated glomerulonephritis and their families in Kuwait. ***Zentralblatt für Bakteriologie, Mikrobiologie, und Hygiene. Series A***, 1986, 262:346–56.
8. Bryant AE, Hayes-Schroer SM, Stevens DL. M type 1 and 3 group A streptococci stimulate tissue factor-mediated procoagulant activity in human monocytes and endothelial cells. ***Infection and immunity***, 2003, 71:1903–10.
9. Schwartz B, Facklam RR, Breiman RF. Changing epidemiology of group A streptococcal infection in the USA. ***Lancet***, 1990, 336:1167–71.
10. Stollerman GH. Rheumatic group A streptococci and the return of rheumatic fever. ***Archives of internal medicine***, 1990, 35:1–26.
11. Olive C et al. Protection of mice from Group A streptococcal infection by intranasal immunisation with a peptide vaccine that contains a conserved M protein B cell epitope and lacks a T cell epitope. ***Vaccine***, 2002, 20:2816–25.
12. ***Bulletin épidémiologique. Direction des soins de santé de base.*** Tunis, Ministère de la Santé Publique, 2001.
13. Johnson DR et al. ***Laboratory diagnosis of group A streptococcal infections***. Geneva, World Health Organization, 1997.
14. Bouvet A et al. Restricted association between biotypes and serotypes within group A streptococci. ***Journal of clinical microbiology***, 1994, 32:1312–7.
15. Muotiala A et al. Molecular comparison of group A streptococci of T1M1 serotype from invasive and non invasive infections in Finland. ***Journal of infectious diseases***, 1997, 175:392–9.
16. Nguyen L et al. Molecular epidemiology of ***streptococcus pyogenes*** in an area where acute pharyngotonsillitis is endemic. ***Journal of clinical microbiology***, 1997, 35:2111–4.
17. Murase T et al. Characteristics of ***Streptococcus pyogenes*** serotype M1 and M3 isolates from patients in Japan from 1981 to 1997. ***Journal of clinical microbiology***, 1999, 37:4131–34.
18. Fazeli MR et al. Group A streptococcal serotypes isolated from healthy school children in Iran. ***European journal of clinical microbiology and infectious diseases***, 2003, 22:475–8.

19. Ameen AS et al. Serotypes of group A streptococci isolated from healthy schoolchildren in the United Arab Emirates. ***Bulletin of the World Health Organization***, 1997, 75(4):355–9.

20. Johnson DR, Stevens DL, Kaplan EL. Epidemiologic analysis of group A streptococcal serotypes associated with severe systemic infections, rheumatic fever, or uncomplicated pharyngitis. ***Journal of infectious diseases***, 1992, 166:374–82.

Correction

Knowledge, attitudes and practices survey among health care workers and tuberculosis patients in Iraq. D.S. Hashim, W. Al Kubaisy and A. Al Dulayme. *Eastern Mediterranean Health Journal,* 2003, Vol. 9 No. 4, pages 718–31.

The authors' names in Arabic should read:

ظافر سلمان هاشم، وقار الكبيسي، عايد موحان منعم الدليمي

The affiliation of Professor Al Kubaisy should read: College of Medicine, Al Nahrain University, Baghdad, Iraq.

Active tuberculosis among Iraqi schoolchildren with positive skin tests and their household contacts. W. Al Kubaisy, A. Al Dulayme and D.S. Hashim. *Eastern Mediterranean Health Journal,* 2003, Vol. 9 No. 4, pages 675–88.

The authors' names in Arabic should read:

وقار الكبيسي، عايد موحان منعم الدليمي، ظافرسلمان هاشم

The affiliation of Professor Al Kubaisy should read: College of Medicine, Al Nahrain University, Baghdad, Iraq.

Cryptosporidiosis in children in a north Jordanian paediatric hospital

E.S. Mahgoub,[1] A. Almahbashi[2] and B. Abdulatif[3]

خفيات الأبواغ لدى الأطفال في مستشفى للأطفال شمال الأردن

الشيخ محجوب، أنس المحبشي، بهاء عبد اللطيف

الخلاصة: استقصى الباحثون معدل حدوث العدوى بخفيات الأبواغ القصيرة لدى الأطفال منذ ولادتهم حتى بلوغهم 12 عاماً، ممن راجعوا مستشفى الأميرة رحمة التعليمي في إربد، الأردن، وقاموا بتقييم طرق مختلفة للتشخيص، فجمعوا نماذج برازية وحيدة من 300 طفلاً، علماً بأن 7 من هذه النماذج قد أخذت من أطفال يعالجون كيميائياً لإصابتهم بالسرطان. وقد كانت الطرق التشخيصية التي استُخدمت لكشف العدوى، هي المستحضرات الرطبة المباشرة، والتركيز للطفاوة، والتلوين البارد بملوّن كينيون تسيل نيلسون، والتألق المناعي المباشر. وقد كشف الباحثون الكيسات البيضية لخفيات الأبواغ لدى 112 نموذجاً (37.3٪) باستخدام التألق المناعي المباشر، وهو ما أبدى أعلى معدل من الحساسية. ويبدو أن مصدر مياه الشرب تمثّل عاملاً من عوامل الاختطار الهامة لانتشار العدوى. وقد سجّل معدل أكثر ارتفاعاً للعدوى في الفصل المطير، بين شهرَيْ كانون الثاني/يناير وأيار/مايو.

ABSTRACT We investigated the rate of infection by ***Cryptosporidium parvum*** among children from birth to 12 years attending Princess Rahma Teaching Hospital in Irbid, Jordan and evaluated various diagnostic methods. We collected single stool specimens from 300 children; 7 specimens were from children undergoing chemotherapy treatment for cancer. Diagnostic methods used for detection of infection were direct wet mount preparation, flotation concentration, cold Kinyoun Ziehl–Neelsen stain and direct immunofluorescence. We detected ***C. parvum*** oocysts in 112 samples (37.3%) using direct immunofluorescence, which showed the highest sensitivity. Source of drinking water appeared to be an important risk factor for transmission of infection. A higher incidence of infection was recorded during January–May, the rainy season.

La cryptosporidiose chez l'enfant dans un hôpital pédiatrique du nord de la Jordanie

RÉSUMÉ Nous avons étudié le taux d'infection par ***Cryptosporidium parvum*** chez des enfants de la naissance à l'âge de 12 ans consultant à l'hôpital universitaire Princesse Rahma d'Irbid (Jordanie) et évalué diverses méthodes diagnostiques. Nous avons recueilli un échantillon unique de selles chez 300 enfants ; 7 échantillons provenaient d'enfants sous chimiothérapie anticancéreuse. Les méthodes de diagnostic utilisées pour le dépistage de l'infection était l'examen direct de préparation à l'état frais, la concentration par flottation, la coloration de Ziehl-Neelsen, la coloration de Kinyoun à froid et l'immunofluorescence directe. Nous avons détecté des oocystes de ***C. parvum*** dans 112 échantillons (37,3 %) par immunofluorescence directe, méthode qui a montré la plus forte sensibilité. La source d'eau de boisson semblait être un important facteur de risque de transmission de l'infection. Une incidence plus élevée de l'infection a été enregistrée entre janvier et mai, la saison des pluies.

[1]Department of Microbiology, Faculty of Medicine; [2]Faculty of Applied Medical Science; [3]Faculty of Veterinary Science, Jordan University of Science and Technology, Irbid, Jordan.
Received: 27/10/02; accepted: 14/09/03

Introduction

Cryptosporidium parvum is a coccidian protozoan parasite found in the brush-border of the enterocytes of the small intestine in many vertebrates, including humans [*1*]. Cryptosporidiosis is recognized as a cause of diarrhoeal illness in man and several mammalian species [*2*]. The first cases of human cryptosporidiosis were reported in 1976, and there are increasing numbers of reports of patients with documented infection with *C. parvum*. It is now considered a common enteric pathogen in humans and domestic animals worldwide [*3*]. Cryptosporidiosis can induce self-limiting diarrhoea in immunocompetent people or severe and prolonged diarrhoea in immunocompromised patients, such as those with AIDS, transplant recipients, those receiving chemotherapy for cancer, institutionalized patients, and patients with immunosuppressive infectious disease [*4*].

A study in the same area of Jordan in 1994 reported that the rate of infection among elementary-school children was 7% [*5*].

Diagnosis of the infection generally requires the observation of the infective stage (oocysts 4–6 μm). Owing to the small size of the oocysts, the routine wet mount preparation and concentration methods have limited value for detection of *C. parvum* in faecal samples, where oocysts can easily be confused with other materials present in the sample [*6*].

We conducted this study because of the increasing international documentation of infection by *C. parvum* and the fact that it is under-diagnosed in most Jordanian hospital laboratories. We also wanted to compare the different methods used for the diagnosis of *C. parvum* including the direct immunofluorescence test which was used for the first time in Jordan in this study. In addition, we tried to focus on some epidemiological factors that lead to infection in children.

Methods

Patients

Over a period of 11 months, 300 single stool specimens were collected from children attending outpatient clinics as well as inpatients in Princess Rahma Teaching Hospital. Requests for stool examinations were made by paediatricians who deemed it necessary for diagnosis and follow-up of their patients. Princess Rahma Teaching Hospital is the hospital for medical care of children under 12 years of age. Faecal samples were taken from children with diarrhoea who were sent to the laboratory for investigation. Seven of the children were undergoing chemotherapy for cancer. There were no exclusion criteria.

The purpose of the study was verbally explained to the parents who agreed to give samples from their children. Paeditricians filled in the clinical information and supplied data on drugs as well as chemotherapeutic agents used for treatment. Additional information about the children was obtained by means of a questionnaire filled in with the assistance of the parents. Information requested included name, age, sex and residence (urban/rural). The source of drinking water was also ascertained (well, spring, tap, filtered, boiled). Parents were also asked whether they kept animals in the home.

Laboratory tests

Stool specimens were collected in the laboratory facilities at Princess Rahma Teaching Hospital and transported in a cool box to the laboratory in the Department of Microbiology at Jordan University of Science

and Technology in Irbid. Each sample, whether liquid, semi-solid or formed, was divided in 4 aliquots and processed according to each of the 4 methods described here. In all methods used, a positive slide was read by at least 2 of the investigators.

Direct wet mount
The direct wet mount preparation was used according to the World Health Organization *Bench aids for the diagnosis of intestinal parasites* [*7*]. Lugol's 1% iodine was used to differentiate *C. parvum* oocysts from yeast cells: *C. parvum* oocysts do not accept the iodine stain, so they appear transparent; yeast cells accept the stain and appear deep yellow.

Sugar flotation concentration method
Sheather's sugar flotation technique was used (specific gravity of solution 1.20–1.25). The high specific gravity allows the oocysts to float on the top of the solution in the test tube. Briefly, a suspension of stool in sugar solution was made in a test tube filled to the brim with Sheather's sugar solution. A cover slip was put on top of the test tube in contact with the solution for 15 minutes. The cover slip was placed downwards on a microscope slide and the oocysts were visualized microscopically at × 400 magnification [*8,9*].

Cold Kinyoun staining
Differential staining using a modified Ziehl–Neelsen technique, the cold Kinyoun technique (TCS Biosciences Limited, Buckingham, United Kingdon), was employed to differentiate *C. parvum* oocysts from other cells and artefacts. The oocysts are acid-fast so they accept the stain and appear pink to red in colour (4–6 mm) against a blue background of debris.

Direct immunofluorescent antibody staining
MeriFluor™ *Cryptosporidium/Giardia* (Meridian Diagnostic Incorporated, Cincinnati, United States of America) is an in vitro direct immunofluorescence kit for the simultaneous detection of *Cryptosporidium* oocysts and *Giardia* cysts in faecal material. The detection reagent contains a mixture of fluorescein isothiocynate-labelled monoclonal antibodies directed against cell wall antigens of *Cryptosporidium* oocysts. Positive and negative controls were provided with the kit by the manufacturing company and manufacturer's instructions were followed.

Statistical analysis
Statistical analysis was performed using *SPSS*.

Results

Of 300 stool samples, 112 (37.3%) were positive for *C. parvum*. According to the consistency of the sample, oocysts were detected in 27.2% of liquid samples, 51.1% of semi-solid samples and 12.5% of formed samples. Among the 7 children who were on chemotherapy for cancer, *C. parvum* was detected in the stools of 4 (57.1%).

The monoclonal direct immunofluorescence method gave the highest rate of positive samples (37.3%) (Table 1) and was statistically the most sensitive compared with the other 3 methods (Table 2). In addition, under ultraviolet light, the direct immunofluorescence slide showed clear, oval, fluorescent green oocysts against an orange to dark background.

When the results were examined according to the children's age, the highest

Table 1 **Comparison of four methods for diagnosis of *Cryptosporidium parvum***

Method	Samples positive, *n* = 300	
	No.	%
Direct wet mount	52	17.3
Sheather's flotation	68	22.6
Cold Kinyoun stain	92	30.6
Direct immunofluorescence	112	37.3

rate of infection (57%) was noted among those in the age group 5–< 7 years (Figure 1).

The relation of infection to locality, sex, presence of animals in the home and source of drinking water is illustrated in Table 3. There was no significant difference in the distribution of cases between males and females. Out of 138 samples from children who lived in rural areas, 60 (43.5%) were positive for *C. parvum* oocysts, whereas of the 162 samples from children who lived in urban areas only 52 (32.1%) were positive. In regard to the presence of animals, the infection rate was 36.2% among children who lived in compounds with no animals in comparison with 45.0% among those who lived in association with animals. In the children who drank tap water, the infection rate was 35.3%. In those who drank well water or spring water, however, infection rates were 48.4% and 42.9% respectively.

The seasonal pattern of *C. parvum* infection showed that a higher rate of incidence was recorded in the periods from January to July 2001, the first 5 months of which represent the rainy months for that year (Figure 2).

Table 2 shows the comparative results between the 4 methods usually used for diagnosis of *C.parvum* in stools. Comparison of the various methods revealed the superiority of immunofluorescence followed by the modified Ziehl–Neelsen, sugar flotation and the direct methods.

Discussion

Our findings showed a high incidence of cryptosporidiosis in the 300 children whose stools we examined. Oocysts of *C. parvum* were detected in 37.3% of samples using the immunofluorescence technique. This is the first time the immunofluores-

Table 2 **Specificity, sensitivity and efficiency of the 4 diagnostic methods used for the detection of *Cryptosporidium parvum* oocysts in stool samples from children in Irbid**

Method	Specificity (%)	Sensitivity (%)	Efficiency (%)
Direct wet mount	95	47	81
Sheather's flotation	96	61	85
Cold Kinyoun stain	100	82	94
Direct immunofluorescence	100	98	99

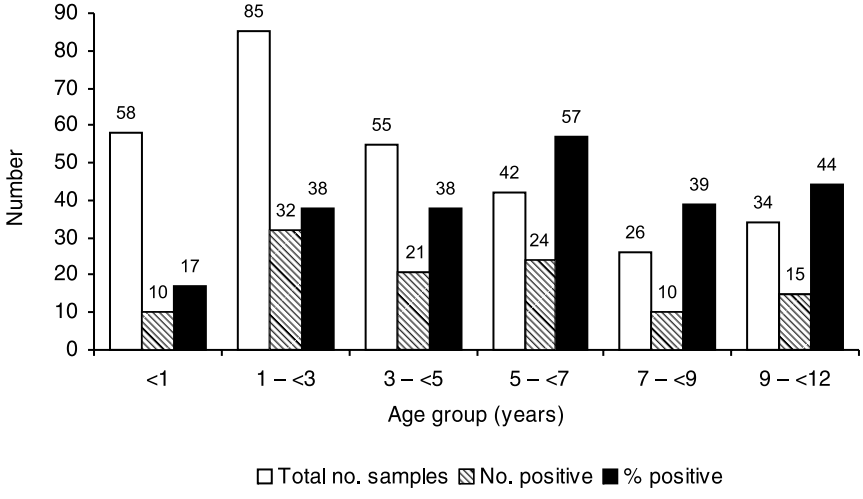


Figure 1 **Incidence of cryptosporidiosis according to age**

Table 3 **The rate of infection by *Cryptosporidium parvum* in relation to sociodemographic characteristics and source of drinking water**

Variable	Positive	
	No.	%
Sex[a]		
Male	72/186	38.7
Female	40/114	35.1
Locality[b]		
Rural	60/138	43.5
Urban	52/162	32.1
Animals at residence[c]		
With	18/40	45.0
Without	94/206	36.2
Source of drinking water[d]		
Well water	31/64	48.4
Spring water	3/7	42.9
Tap water	73/207	35.3
Filtered water	4/14	28.6
Boiled water	0/7	–

[a] $P = 0.529$, degrees of freedom = 1, $\chi^2 = 0.40$.
[b] $P = 0.042$, degrees of freedom = 1, $\chi^2 = 4.12$.
[c] $P = 0.282$, degrees of freedom = 1, $\chi^2 = 1.16$.
[d] $P = 0.425$, degrees of freedom = 3, $\chi^2 = 1.71$.

cence test has been used in Jordan. Although this figure is higher than the one reported before from Jordan [*10*], it is similar to high figures from other countries as cited below. It is also worth noting that previous workers from Jordan took specimens from healthy schoolchildren while ours were sick children reporting to a paediatric hospital. Our colleagues used a single method, namely the modified Ziehl–Neelsen, while we used 4 methods.

A number of other studies on prevalence of cryptosporidiosis have been reported from different parts of the world. The incidence rates vary according to sample collection, which depends on clinical judgement; diagnostic tests, where some methods are better than others; availability of facilities; and reporting systems. Incidence rates of 13.5% to 19.5% have been reported from Egypt [*11,12*], and 10% in Kuwaiti children [*13*]. Very high rates have been reported in Israeli children 48% [*14*], from the Texas–Mexico border 70.2% [*15*] and from the Republic of Korea 57% [*16*].

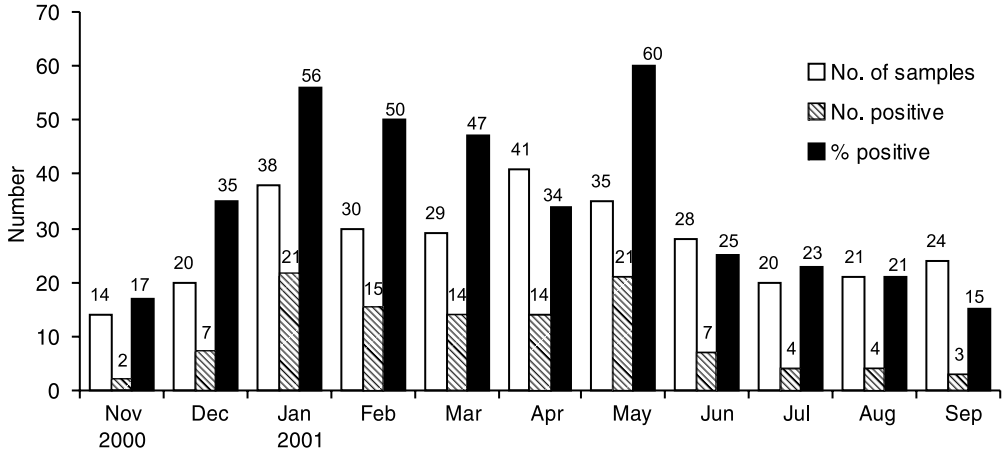


Figure 2 **Seasonal variation of cryptosporidiosis, November 2000 to September 2001**

A review of several human population-based studies, especially on immunocompromised patients in less-developed countries, reported prevalence ranging from 9% to 48% in Africa and Asia [*17*].

In this study, 4 different methods were used to detect and identify *C. parvum* oocysts in children's stool samples. The direct wet mount with iodine identified the lowest number of samples, 52 (17.3%), positive for oocysts. The *C. parvum* oocyst is very small in size and can easily be mistaken in stool debris for artefacts. Also, it is easy to confuse with other oocysts, such as those of *Cyclospora* spp., and cells, especially yeast cells, which resemble *C. parvum* oocysts in size and morphology [*18*].

The number of oocysts detected increased to 68 (22.6%) using the flotation concentration method. This procedure showed a clear slide picture during microscopic examination yet the oocysts did not appear pink and refractile, and other parasites cannot be detected by this method. Also, this procedure necessitated reading the results within 15 minutes of preparation because the oocysts tend to collapse and disappear if left for a long time. Moreover, the presence of Sheather's sugar solution inhibits the staining procedure [*19*].

The cold Kinyoun acid-fast staining technique yielded a higher rate of oocyst identification, 92 (30.6%). Using this method we could differentiate between *C. parvum* oocysts, which take a red to pink colour, and other faecal components, especially yeast cells, which take the colour of the counterstain, i.e. blue if using methylene blue, or green using malachite green.

The direct immunofluorescence method gave the highest number of positive samples, 112 (37.3%). In comparison with other methods, this method showed high sensitivity so we were able to detect oocysts even when present in low numbers in the samples and large numbers of samples could be scanned.

Our findings support and agree with other studies which reported that using fluorescent monoclonal reagents increased the sensitivity and specificity of the detection of *C. parvum* oocysts. It provides an excellent screening method and offers a useful technique for epidemiological studies, and hence, control of the parasite [*20–22*]

Source of drinking water plays an important role in the transmission of infection. Many people in Irbid depend on untreated rainwater collected directly from the roof, then stored in metal or cement tanks. This is why most of our cases were diagnosed during April–May, during the rainy season. Some families use wells or spring water for drinking. The results showed that the rate of infection among those who drink from wells was 48.4%, compared to those who use only tap water, 35.3%. We know that the oocysts of *Cryptosporidium* spp. can survive in concentrations of chlorine used for water treatment, let alone untreated water [*23*].

Considering the locality, we found that the infection rate in children who lived in rural areas was 43.5% whereas in children in urban areas it was 32%.

Seasonal or temporal trends associated with increased incidence vary from country to country. Our result agrees with other studies from Central America, South Africa, and India that reported a high peak incidence in rainy season [*24*]. Also, our findings were similar to those of another study conducted in Kuwait to detect the incidence and seasonality of cryptosporidiosis in Kuwaiti children. The results of that study showed that the maximum numbers of cases were recorded during the months January to April [*13*].

Acknowledgement

This study was supported by the Deanship of Research, Jordan University of Science and Technology.

References

1. Tzipori S. Cryptosporidiosis in animals and humans. ***Microbiological reviews***, 1983, 47(1):84–96.

2. Fayer R, Ungar BL. ***Cryptosporidium*** spp. and cryptosporidiosis. ***Microbiological reviews***, 1986, 50(4):458–83.

3. Meisel JL et al. Overwhelming watery diarrhea associated with a cryptosporidium in an immunosuppressed patient. ***Gastroenterology***, 1976, 70(6):1156–60.

4. Fayer R, Morgan U, Upton SJ. Epidemiology of ***Cryptosporidium***: transmission, detection and identification. ***International journal for parasitology***, 2000, 30(12–13):1305–22.

5. Nemri LF and Hijazi SS. Cryptosporidium a cause of gastroenteritis in preschool children in Jordan. ***Journal of clinical gastroenterology***, 1994, 19(4): 288–91.

6. Weber R et al. Threshold of detection of ***Cryptosporidium*** oocysts in human stool specimens: evidence for low sensitivity of current diagnostic methods. ***Journal of clinical microbiology***, 1991, 29(7): 1323–7.

7. O'Donoghue JP. Cryptosporidium and cryptosporidiosis in man and animals. ***International journal for parasitology***, 1995, 25(2):139–95.

8. ***Bench aids for the diagnosis of intestinal parasites***. Geneva, World Health Organization, 1994.

9. Garcia LS. ***Practical guide to diagnostic parasitology***. Washington DC, ASM Press, 1999.

10. Nimri LF, Batchoun R. Prevalence of ***Cryptosporidium*** species in elementary school children. ***Journal of clinical microbiology***, 1994, 32(4):1040–2.

11. Stazzone AM et al. Frequency of ***Giardia*** and ***Cryptosporidium*** infections in Egyptian children as determined by conventional and immunofluorescence methods. ***Pediatric infectious disease journal***, 1996, 15(11):1044–6.

12. Abdel-Maboud AI et al. Cryptosporidiosis in Benha; study of some modalities in diagnosis and treatment. ***Journal of the Egyptian Society of Parasitology***, 2000, 30(3):717–25.

13. Iqbal J et al. Cryptosporidiosis in Kuwaiti children: seasonality and endemicity. ***Clinical microbiology and infection***, 2001, 7(5):261–6.

14. Robin G et al. ***Cryptosporidium*** infection in Bedouin infants assessed by prospective evaluation of anticryptosporidial antibodies and stool examination. ***American journal of epidemiology***, 2001, 153(2):194–201.

15. Leach CT et al. Prevalence of ***Cryptosporidium parvum*** infection in children along the Texas–Mexico border and associated risk factors. ***American journal of tropical medicine and hygiene***, 2000, 62(5):656–1.

16. Cha JY et al. High prevalence and seasonality of cryptosporidiosis in a small rural village occupied predominantly by aged people in the Republic of Korea. ***American journal of tropical medicine and hygiene***, 2001, 65:518–22.

17. Ungar BLP. Cryptosporidium. In: Mandell GL, Bennett JE, Dolin R, eds. ***Mandell, Douglas and Bennett's principles and practice of infectious diseases***, 5th ed. Philadelphia, Churchill Livingstone, 1999:2903–15.

18. Fayer R, Speer SA, Dubey JP. The general biology of Cryptosporidium. In: Fayer R, ed. ***Cryptosporidium and cryptosporidiosis***. Boca Raton, Florida, CRC Press, 1997:1–41.

19. Weber R et al. Threshold of detection of ***Cryptosporidium*** oocysts in human stool specimens: evidence for low sensitivity of current diagnostic methods. ***Journal of clinical microbiology***, 1991, 29(7):1323–7.

20. Garcia LS, Brewer TC, and Bruckner DA. Fluorescence detection of ***Cryptosporidium*** oocysts in human fecal specimens by using monoclonal antibodies. ***Journal of clinical microbiology***, 1987, 25(1):119–21.

21. Xiao L, Herd RP. Quantitation of ***Giardia*** cysts and ***Cryptosporidium*** oocysts in fecal sample by direct immunofluorescence assay. ***Journal of clinical microbiology***, 1993, 31(11):2944–6.

22. Alles AJ et al. Prospective comparison of direct immunofluorescence and conventional staining methods for detection of ***Giardia*** and ***Cryptosporidium*** spp. in human fecal specimens. ***Journal of clinical microbiology***, 1995, 33(6):1632–4.

23. Korich DJ et al. Effects of ozone, chlorine and monochloromine on ***Cryptosporidium parvum*** oocyst viability. ***Applied and environmental microbiology***, 1990, 56:1423–8.

24. Casemore DP, Wright SE, Coop RL. Cryptosporidiosis—human and animal epidemiology. In: Fayer R, ed. ***Cryptosporidium and cryptosporidiosis***. Boca Raton, Florida, CRC Press, 1997.

الإعاقة بين الأطفال في المملكة العربية السعودية: معدل الانتشار، والتوزُّع، والأنماط، والعوامل المسبِّبة لها

محسن بن علي فارس الحازمي، عبد الرحمن بن عبد العزيز السويلم، ناصر بن علي الموسى*

الخلاصة: تناولت هذه الدراسة معدل انتشار الإعاقة، وتوزُّعها الجغرافي، والعوامل المسبِّبة لها بين الأطفال في المملكة العربية السعودية. واشتملت الدراسة على مسح ميداني في الفترة 1417هـ–1420هـ، (1997–2000م) شمل 60 630 طفلاً دون سن السادسة عشرة، تم اختيارهم من جميع مناطق المملكة بطريقة الانتقاء الطبقي التجمُّعي العشوائي. وتم جمع معلومات عن جميع الأطفال باستخدام استبيان، وتمت إحالة حالات الإعاقة والحالات المشتبه بها لإجراء فحوصات التشخيص التأكيدي. ومن بين إجمالي العيِّنة بلغ عدد الأطفال المعاقين 3838 طفلاً (6.33٪). وكانت أعلى نسبة إعاقة في منطقة جيزان (9.9٪)، وأقل نسبة في الرياض (4.36٪). وكانت الإعاقة الحركية هي النمط الأكثر شيوعاً (3٪ من إجمالي العيِّنة)، تليها إعاقة صعوبات التعلُّم (1.8٪). وتبيِّن ارتفاع نسبة الإعاقة لدى الأطفال المولودين لأمهات أو آباء لديهم إعاقات، أو المولودين لأمهات كبار السن أو لم يتلقَّيْن الرعاية الطبية والتلقيحات (التطعيمات) اللازمة أثناء الحمل.

Handicap among children in Saudi Arabia: prevalence, distribution, type, determinants and related factors

ABSTRACT We determined the prevalence, distribution and determinants of handicap among children in Saudi Arabia. A field survey was carried out from 1417 to 1420 AH (1997–2000 AD) of 60 630 children under 16 years selected from all regions of the country. Information was collected by questionnaire for all children and those with a handicap, or suspected of having a handicap, were referred for confirmatory diagnosis. Of the total sample, 3838 (6.33%) were recorded as handicapped. The region with the highest proportion of handicapped children was Jazan (9.90%); Riyadh had the lowest (4.36%). Motor disability was the commonest kind of handicap (3.0% of the total sample), followed by learning disability (1.8%). The highest proportion of disability was found among children with handicapped parents, those whose mothers were older at the time of their birth and those whose mothers had not had medical care and necessary vaccination during pregnancy.

Le handicap chez l'enfant en Arabie saoudite : prévalence, répartition, type, déterminants et facteurs associés

RÉSUMÉ Cette étude a déterminé la prévalence, la répartition et les déterminants du handicap chez l'enfant en Arabie saoudite. Une enquête sur le terrain a été réalisée de 1417 à 1420 de l'Hégire (1997-2000) auprès de 60 630 enfants de moins de 16 ans sélectionnés dans toutes les régions du pays. Des informations ont été recueillies à l'aide d'un questionnaire pour tous les enfants, et ceux ayant un handicap ou suspectés d'avoir un handicap ont été adressés à un laboratoire pour diagnostic de confirmation. Dans l'échantillon total, 3838 enfants (6,33 %) ont été recensés comme handicapés. La région ayant le plus fort pourcentage d'enfants handicapés était Jazan (9,90 %) ; Riyad avait le plus faible pourcentage (4,36 %). Le handicap moteur était le type d'handicap le plus courant (3,0 % de l'échantillon total), suivi par les troubles de l'apprentissage (1,8 %). Le pourcentage d'incapacités le plus élevé a été constaté chez les enfants de parents handicapés, chez ceux dont la mère était plus âgée à leur naissance et ceux dont la mère n'avait pas bénéficié d'une surveillance médicale ni reçu les vaccinations nécessaires pendant la grossesse.

M.B. Al-Hazmy,[1] B. Al Sweilan[2] and N.B. Al-Moussa[3]
[1]Department of Medical Biochemistry, Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia.
[2]Red Crescent Society, Riyadh, Saudi Arabia.
[3]Special Education, Ministry of Health, Riyadh, Saudi Arabia.
Received: 25/02/03; accepted: 23/02/04

مقدمة: بعد أن نجح الناس في مكافحة الأمراض المعدية باكتشاف المضادات الحيوية خلال القرن الماضي ظهرت إلى الوجود أمراض لم تكن شائعة ساهمت إلى حد كبير في حدوث الإعاقات المختلفة لدى الأطفال، وبعض مسببات تلك الأمراض ناتج عن عوامل وراثية والأخرى عن عوامل مكتسبة، ويهدف هذا البحث إلى دراسة مختلف العوامل المؤثرة ذات الصلة بحدوث الإعاقة والتي تشمل:

(أ) عوامل مؤثرة أثناء حمل الطفل:

مثل الأمراض الوراثية، الأمراض المعدية (السارية)، تعرض الأم للأشعة، أمراض المشيمة .. الخ.

(ب) عوامل مؤثرة أثناء الولادة:

مثل إصابة رأس الطفل، النزيف المخي، تعرض الطفل للاختناق، نقص سكر الدم الخ.

(ج) عوامل مؤثرة بعد الولادة:

مثل أمراض الجهاز العصبي، والأمراض المعدية (السارية)، التسمم، الحوادث ... الخ.

ونظراً للقصور في المعلومات وقلة الدراسات حول الإعاقة بالمملكة، فقد تم تنفيذ دراسة شاملة من خلال مركز الأمير سلمان لأبحاث الإعاقة للتعرف على مشكلة الإعاقة لدى الأطفال بالمملكة بعنوان «البحث الوطني لدراسة الإعاقة لدى الأطفال بالمملكة العربية السعودية» [1] نتج عنها مؤشرات جيدة عن حجم مشكلة الإعاقة وأنواعها وتوزُّعها بمختلف مناطق المملكة، وكذلك العوامل المؤثرة المتعلقة بحدوث الإعاقات بين الأطفال والتي نسلط عليها الضوء في هذا البحث، وذلك بهدف اقتراح وتنفيذ برامج للحد من حدوث وانتشار الإعاقات بين المواليد والأطفال [2].

مواد وطرق البحث:

اعتمد الباحثون في إعداد البحث على طبيعة المشكلة المراد دراستها [3]، فقد صممت طريقة البحث بهدف تحديد العوامل المؤثرة (في الطفل والأسرة) المتعلقة بحدوث الإعاقة بمختلف مناطق المملكة العربية السعودية (الشكل - 1) واشتملت على الجوانب التالية:

(أ) مجتمع الدراسة وطريقة جمع العينة:

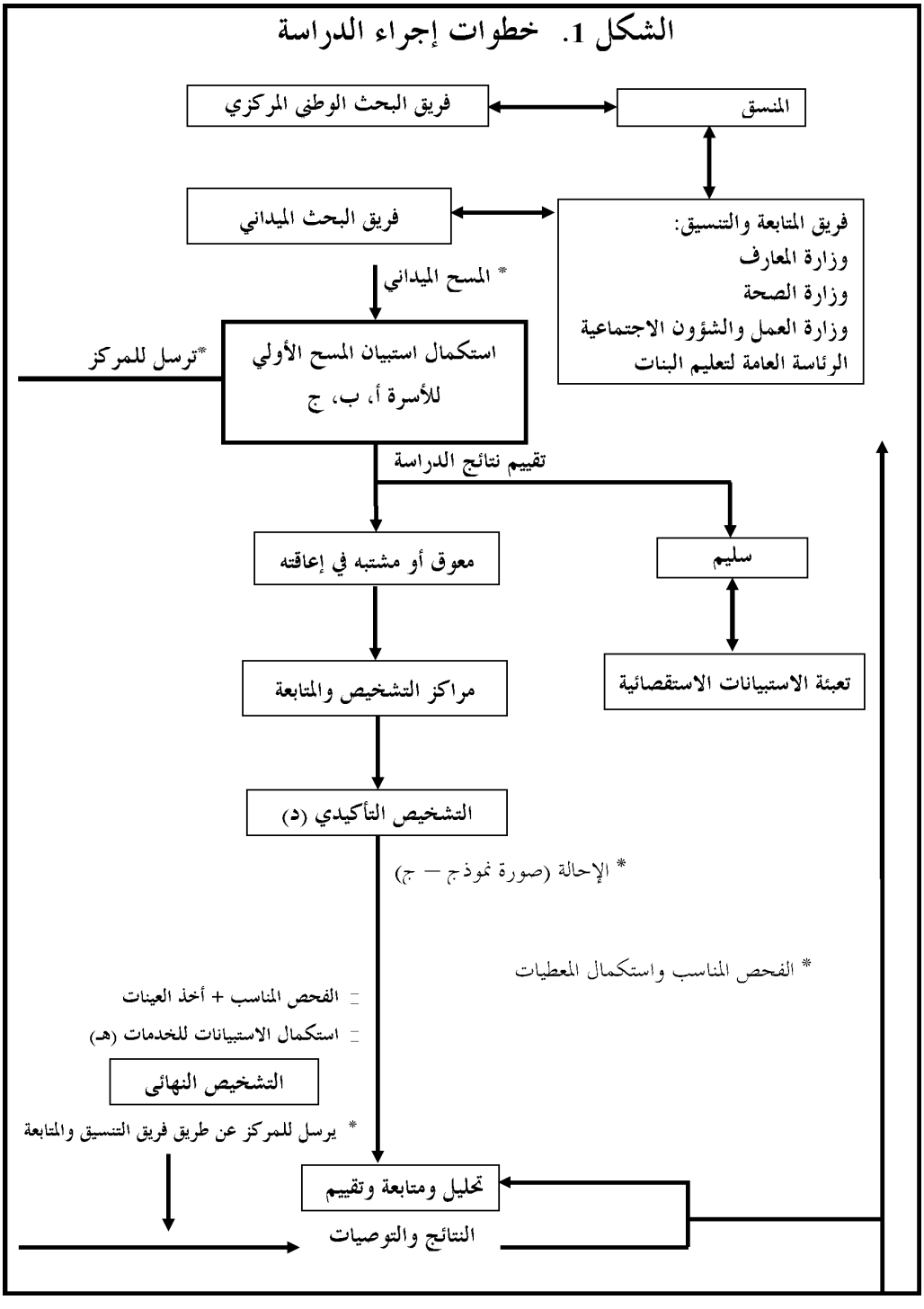
شملت العينة التي تمت دراستها الأطفال السعوديين دون سن السادسة عشرة من مختلف مناطق المملكة العربية السعودية، خلال فترة الدراسة من 1417-1420 للهجرة.

واعتمد الباحثون على جمع العينات العنقودية العشوائية المطبقة[4 و5] بهدف تقليل التحيز وإعطاء صورة ممثلة لمختلف مناطق المملكة، آخذين في الاعتبار عدة عوامل من أهمها مكان الإقامة (الحاضرة أو الريف).

(ب) أدوات الدراسة:

1. الاستبيان: وتشمل استبيانات جمع المعطيات الأولية عن الأسرة والطفل، ونموذج الإحالة إلى الأخصائي لإعداد التشخيص النهائي للحالات المشتبه بها.
2. الوثائق: وتشمل الوثائق ذات الصلة المتوفرة بالجهات الحكومية المشاركة في الدراسة.
3. دراسة المتغيرات (العمر، الجنس، مكان الإقامة، معلومات عن الوالدين والأسرة ، مسببات الإعاقة، تاريخ الإصابة ...) وغير ذلك.

الشكل 1. خطوات إجراء الدراسة



(ج) حجم العينة:

بلغ حجم العينة التي تم جمعها من مختلف مناطق المملكة 60800 طفلٍ دون سن السادسة عشرة، أخذاً في الاعتبار عوامل جغرافية وإدارية وعملية. وقد تم تقدير هذا العدد استناداً على التوزيع الجغرافي والكثافة السكانية في المحافظات والمدن والمراكز والقرى والهجر.

(د) الدراسة الميدانية:

استغرقت هذه المرحلة 24 شهراً، تم خلالها تنفيذ عملية المسح الميداني بجميع أنحاء المملكة بمشاركة عدة فرق بحث ميدانية، تحت إشراف منسق لجنة الإشراف والمتابعة بالمنطقة، حيث قامت الفرق بزيارة الأُسَر التي شملتها الدراسة وتعبئة الاستبيانات المعدة لهذا البحث لكل طفل بالأسرة دون سن السادسة عشرة، ومن ثَـمَّ تم إرسال حالات الإعاقة والحالات المشتبه بها إلى المختصين لإجراء الفحوصات التأكيدية، وصولاً إلى التشخيص التأكيدي لها.

(هـ) أسلوب المعالجة الإحصائيــة

تم تجميع الاستبيانات المستكملة بالمعطيات من المناطق المختلفة، وتدقيقها وترميزها وتصنيفها من قِبَل فريق مركزي مختص بمركز الأمير سلمان لأبحاث الإعاقة بالرياض، حيث تم تصميم برنامج حاسوبي لإدخالها في الحزمة الإحصائية *Epi-Info* في الإصدار السادس والأخير، وتم تعريب جزء كبير من الأجزاء المختلفة للبرنامج حتى يتسنى لمدخلي المعطيات أداء عملهم في يسر وبطريقة موحدة[*6, 7*]. وتم ترجمة وتجميع الحالات المدخلة من الاستبيانات من *Epi-Info* إلى برنامج *SPSS* في الإصدار التاسع والأخير [*8*].

وقد اشتملت خطة المعالجة الإحصائية التي تم تنفيذها من قبل فريق متخصص على: استخراج الجداول المركبة لكل متغير على حدة، واستخراج النسب المئوية للتوزيعات التكرارية لمتغيرات الدراسة، وحساب التوزيعات التكرارية المركبة بين بعض المتغيرات ومعدل الإعاقة.

النتائج والمناقشة:

من خلال التحليل الإحصائي للمعطيات المتوفرة من الدراسة الميدانية، تم الحصول على مؤشرات نتائج عن العوامل المختلفة المتعلقة بحدوث الإعاقات في كلٍّ من أطفال الدراسة وأُسَرِهم، والتي قد تلعب دوراً في حدوث الإعاقة، ومقارنة نسبة حدوثها لدى المعوقين والأصحاء في عينة الدراسة (الجداول من1– 9) وبدراسة النتائج يمكن الوصول إلى الاستنتاجات التالية:

أولاً: الإعاقة العقلية (التخلف العقلي):

- 5.2٪ من أمهات الأطفال المصابين بالتخلف العقلي كُنَّ يعانين من فقر الدم مقارنة بـ 2.2٪ من أمهات غير المصابين بالتخلف العقلي، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 21.4 ، ومعامل الترابُط = 0.019) .
- 2٪ من أمهات الأطفال المصابين بالتخلف العقلي أصبن بارتفاع في درجة الحرارة أثناء الحمل مقارنة بـ 0.8٪ من أمهات الأطفال غير المصابين بالتخلف العقلي، وكانت العلاقة الإحصائية هامة وطردية (خي مربع =10.6، ومعامل الترابُط = 0.013).
- 85.5٪ من أمهات الأطفال المصابين بالتخلف العقلي أصبن بالقيء الشديد أثناء الحمل مقارنة بـ 70٪ من أمهات الأطفال غير المصابين بالتخلف العقلي، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 60.5، ومعامل الترابُط = 0.032).

- 8.7٪ من أمهات الأطفال المصابين بالتخلف العقلي تعرضن للأشعة أثناء الحمل مقارنة بـ 6.3٪ من أمهات الأطفال غير المصابين بالتخلف العقلي، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 5.1، ومعامل الترابُط = 0.009).
- 13.5٪ من الأطفال المصابين بالتخلف العقلي أصيبوا بالشلل المخي مقارنًة بـ 0.2٪ من الأطفال الأصحاء، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 3360، ومعامل الترابُط = 0.32).
- 8٪ من الأطفال المصابين بالتخلف العقلي أصيبوا بالصرع مقارنةً بـ 0.3٪ من الأطفال الأصحاء، وكانت العلاقة الإحصائية هامة و طردية (خي مربع = 927، ومعامل الترابُط = 0.12).
- 20.6 ٪ من الأطفال المصابين بالتخلف العقلي لم تتح لهم فرصة الرضاعة من الثدي، و33.6٪ كانت رضاعتهم مختلطة مقارنةً بنسبة 6.1٪ من الأطفال غير المصابين بالتخلف العقلي و لم تتح لهم فرصة الرضاعة من الثدي و28.9٪ في الأطفال غير المصابين بالتخلف العقلي، مِمَّنْ كانت رضاعتهم مختلطة وكانت العلاقة الإحصائية هامة (خي مربع = 217، ومعامل الترابُط = 0.06).

جدول (1): العلاقة بين العوامل المتعلقة بالإعاقات والإعاقة العقلية

م	العامل المتعلق بحدوث الإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	إصابة الأم بفقر الدم أثناء الحمل	5.2	2.2	21.4	0.019
2	إصابة الأم بالحميات أثناء الحمل	2.0	0.8	10.6	0.013
3	معاناة الأم من القيء الشديد أثناء الحمل	85.5	70.0	60.5	0.032
4	تعرض الأم للأشعة أثناء الحمل	8.7	6.3	5.1	0.009
5	إصابة الطفل بالشلل المخي	13.5	0.2	3360	0.32
6	إصابة الطفل بالصرع	8.0	0.3	927	0.12
7	إصابة الطفل بأمراض الدم الوراثية	0.9	0.3	6.3	0.019
8	إطعام الطفل لا يعتمد على الإرضاع من الثدي	20.6	6.1	217	0.06
9	رضاعة الطفل كانت مختلطة	33.6	28.9		

ثانياً: الإعاقة الحركية:

- 0.8٪ من الأطفال المصابين بالإعاقة الحركية أصيبوا بشلل بالأطراف بعد الولادة مقارناً بـ 0.1 ٪ في غير المعوقين، وكانت العلاقة الإحصائية هامة (خي مربع = 153.3، ومعامل الترابُط = 0.05).
- 0.7٪ من الأطفال المصابين بالإعاقة الحركية أصيبوا بكسر بالأطراف عند الولادة مقارناً بـ 0.1٪ في غير المعوقين، وكانت العلاقة الإحصائية طردية (خي مربع = 124.0، ومعامل الترابُط = 0.045).
- 98.7٪ من الأطفال المصابين بالإعاقة الحركية تلقوا التطعيم ضد شلل الأطفال مقارناً بنسبة 97.6٪ لدى غير المصابين بالإعاقة، وكانت العلاقة الإحصائية عكسية (خي مربع = 13.8، ومعامل الترابُط = - 0.015) أي أن التطعيم ضد شلل الأطفال يقلل من فرص احتمال الإصابة به ومن ثم بالإعاقة الحركية.
- 1.7 ٪ من الأطفال المصابين بالإعاقة الحركية كانوا يعانون من الصرع مقارناً بـ 0.3 ٪ لدى غير المصابين بالإعاقة، وكانت العلاقة الإحصائية طردية (خي مربع = 164.1، ومعامل الترابُط = 0.052).

- 1.8 ٪ من الأطفال المصابين بالإعاقة الحركية كانوا يعانون من الشلل المخي مقارناً بـ 0.2 ٪ لدى غير المصابين بالإعاقة، وكانت العلاقة الإحصائية قوية وطردية خاصة في الأطفال دون سن الخامسة عشرة (خي مربع = 224.7، ومعامل الترابُط = 0.06).

جدول (2): العلاقة بين العوامل المتعلقة بحدوث الإعاقات والإعاقة الحركية

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ*
1	تعرض الطفل لكسر بالأطراف عند الولادة	0.7	0.1	153.3	0.05
2	تعرض الطفل لشلل بالأطراف بعد الولادة	0.8	0.1	124	0.045
3	إصابة الطفل بالصرع	1.7	0.3	164.1	0.052
4	إصابة الطفل بالشلل المخي	1.8	0.2	224.7	0.06
5	تطعيم الطفل ضد شلل الأطفال	98.7	97.6	13.8	0.015 -

* إذا تجاوزت قيمة (خي مربع) 11.6 كانت ذات دلالة إحصائية قوية، وإذا اقتربت قيمة معامل الترابُط من الصفر كانت العلاقة ضعيفة وإذا اقتربت من الواحد الصحيح كانت العلاقة قوية جداً، أمّا إذا كانت قيمة معامل الترابُط موجبة دلّت على وجود علاقة طردية وإذا كانت سالبة كانت العلاقة عكسية.

ثالثاً: الإعاقة الكلامية:

- 18.6٪ من المصابين بالإعاقة الكلامية كانت أمهاتهم قد تناوَلْنَ أدوية علاج الضغط أثناء الحمل مقارنةً بنسبة 25.8٪ من غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية عكسية ، أي أن تناول الأم لأدوية الضغط أثناء الحمل يقلل احتمال إصابة الطفل بالإعاقة الكلامية (خي مربع = 22.5، ومعامل الترابُط = - 0.019).
- 8.8٪ من المصابين بالإعاقة الكلامية كانت أمهاتهم قد تعرضن للأشعة أثناء الحمل مقارنةً بـ 6.3٪ من غير المصابين بالإعاقة، وكانت العلاقة الإحصائية هامة فيمن تعرضن للأشعة على البطن (خي مربع = 8.4، ومعامل الترابُط = 0.012).
- 9.8٪ من أمهات الأطفال المصابين بالإعاقة الكلامية قد أصبن بمرض السكري أثناء الحمل مقارنةً بـ 5.7٪ من أمهات الأطفال غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية هامة (خي مربع = 25.8، ومعامل الترابُط = 0.021).
- 2.5٪ من أمهات الأطفال المصابين بالإعاقة الكلامية قد أصبن بمرض ارتفاع ضغط الدم أثناء الحمل مقارناً بـ 0.9٪ من أمهات الأطفال غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية هامة (خي مربع = 25.2، ومعامل الترابُط = 0.020).
- 4٪ من الأطفال المصابين بالإعاقة الكلامية كانت ولادتهم بالسحب تحت تخلية بالهواء (بالمحجم السويدي أو الفانتوز)، مقارنةً بنسبة 1.4 ٪ من غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية هامة (خي مربع = 91.7، ومعامل الترابُط = 0.04).
- 3.9٪ من المصابين بالإعاقة الكلامية تعرضوا لنقص مستوى سكر الدم مقارنةً بنسبة 0.1 ٪ في غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية هامة (خي مربع = 940، ومعامل الترابُط = 0.13).

جدول (3): العلاقة بين العوامل المتعلقة بحدوث الإعاقة والإعاقة الكلامية

م	العامل المتعلق بحدوث الإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	تناول الأم لأدوية الأمراض النفسية أثناء الحمل	1.1	0.3	13	0.015
2	تناول الأم لأدوية الصرع أثناء الحمل	0.8	0.3	10	0.013
3	تناول الأم لأدوية ضغط الدم أثناء الحمل	18.6	25.8	22.5	0.019 -
4	تناول الأم لأدوية السكري أثناء الحمل	10.3	6.0	28	0.021
5	تعرض الأم للأشعة أثناء الحمل	8.8	6.3	8.4	0.012
6	إصابة الأم بالسكري أثناء الحمل	9.8	5.7	25.8	0.021
7	إصابة الأم بارتفاع ضغط الدم أثناء الحمل	2.5	0.9	25.2	0.02
8	ولادة الطفل عن طريق السحب بملقط الجنين	4.0	1.4	91.7	0.04
9	تعرض الطفل لنقص سكر الدم	3.9	0.1	940	0.13
10	تعرض الطفل لانخفاض في حرارة الجسم	0.9	0.1	101	0.04
11	إصابة الطفل باليَرَقان (الصفراء) بعد الولادة	19.0	4.0	470	0.12
12	رضاعة الطفل كانت طبيعية	53.0	65.0		
13	تغذية الطفل من الزجاجة	17.0	6.0	175	0.054
14	رضاعة الطفل كانت مختلطة	30.0	29.0		
15	تطعيم الطفل ضد النكاف	86.7	89.7	7.9	0.011 -
16	تطعيم الطفل ضد الحصبة	93.0	97.0	13.5	0.015 -
17	تطعيم الطفل ضد السل	77.5	68.4	26.4	0.023
18	إصابة الطفل بالصرع	6.3	0.3	883.5	0.12
19	إصابة الطفل بالشلل المخي	8.1	0.2	1820	0.17
20	ارتفاع حرارة الطفل بعد الولادة	15.0	2.1	630	0.102
21	تعرض الطفل للحوادث داخل المنزل	3.7	1.3	36	0.024
22	وجود قرابة بين الأبوين بدرجات مختلفة	64.0	58.0	12	0.014

- 0.9٪ من المصابين بالإعاقة الكلامية تعرضوا لنقص في درجة الحرارة مقارنةً بنسبة 0.1 ٪ لدى غير المصابين بالإعاقة الكلامية، وكانت العلاقة ذات دلالة إحصائية (خي مربع = 101، ومعامل الترابُط = 0.04).
- 19٪ من المصابين بالإعاقة الكلامية كانوا قد تعرضوا للإصابة باليرقان بعد الولادة مقارنةً بنسبة 4 ٪ من غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية هامة (خي مربع = 470، ومعامل الترابُط = 0.12).
- 53٪ من المصابين بالإعاقة الكلامية كانت رضاعتهم طبيعية من الثدي و17٪ كانت تغذيتهم بالمستحضرات وبدائل الحليب، و30٪ كانت تغذيتهم مختلطة، مقارنة بنسبة 65٪ في الحالات السليمة كانت رضاعتهم طبيعية من الثدي و6٪ كانت تغذيتهم بالمستحضرات وبدائل الحليب، و29٪ كانت تغذيتهم مختلطة،

وكانت العلاقة بين نوع الرضاعة ووجود الإعاقة الكلامية ذات دلالة إحصائية هامة (خي مربع = 175، ومعامل الترابُط = 0.054).

جدول (4): العلاقة بين العوامل المتعلقة بحدوث الإعاقة والإعاقة السمعية

م	العامل المتعلق بحدوث الإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	أحد أفراد الأسرة يعاني من الإعاقة السمعية	18.6	2.4	611	0.101
2	وجود قرابة بين الأبوين من الدرجة الأولى	35.2	27.2	21	0.019
3	تطعيم الأم ضد الحصبة الألمانية أثناء الحمل	53.8	58.4	14	0.016 -
4	إصابة الأم بالحميات أثناء الحمل	3.4	0.8	51.1	0.029
5	سقوط الطفل أثناء الولادة	43.7	31.2	41.9	0.026
6	إصابة الطفل بالتهاب السحايا أو التهاب المخ	40.3	27.6	46.3	0.028
7	تعرض الطفل للتسمم بالأدوية أو الكيماويات	7.5	2.6	52.8	0.03
8	إصابة الطفل بأمراض الدم	2.7	0.3	107.8	0.042

جدول (5): العلاقة بين العوامل المتعلقة بحدوث الإعاقة والإعاقة البصرية

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	وجود قطط وكلاب بمنزل الطفل	5.9	3.2	11	0.014
2	وجود قرابة بين الأبوين من الدرجة الأولى	35.2	27.2	18	0.017
3	تطعيم الأم ضد الحصبة الألمانية قبل الحمل	56.0	58.5	35.2	0.024 -
4	إصابة الطفل أثناء الولادة	0.4	0.0	30.7	0.012
5	سقوط الطفل أثناء الولادة	47.7	31.2	63.5	0.024
6	انخفاض حرارة الطفل بدرجة كبيرة بعد الولادة	0.4	0.1	8.4	0.006
7	انخفاض مستوى السكر بدم الطفل بعد الولادة	6.9	0.1	1810	0.24
8	إصابة الطفل بالتهاب السحايا	42.2	27.6	52.9	0.011
9	نقل الطفل للعناية المركزة بعد الولادة	11.9	2.3	279.5	0.02
10	إصابة الطفل بارتفاع شديد في درجة الحرارة	9.7	2.2	126.6	0.02

- 86.7٪ من المصابين بالإعاقة الكلامية تم تطعيمهم ضد النكاف مقارنةً بنسبة 89.7٪ في غير المصابين بالإعاقة الكلامية، وكانت العلاقة الإحصائية عكسية (خي مربع = 7.9، ومعامل الترابُط = - 0.011)، أي أن التطعيم يقلل من احتمال إصابة الطفل بالإعاقة الكلامية.

جدول(6): العلاقة بين العوامل المتعلقة بالإعاقات والإعاقة بالاضطرابات السلوكية والانفعالية

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	*Φ
1	الآباء غير متعلمين	32.0	19.8	61.2	0.02
2	الأمهات غير متعلمات	55.6	46.2	23.7	0.014
3	وجود قرابة بين الأبوين	65.0	58.0	8.2	0.012
4	وجود قرابة من الدرجة الأولى بين الأبوين	36.5	27.5	18	0.017
5	ارتفاع المستوى الاجتماعي والاقتصادي	27.9	37.1	14.84	0.016 -
6	وجود إعاقة لدى أحد أفراد الأسرة من أي نوع	26.7	11.6	89.3	0.038
7	وجود إعاقة سلوكية وعقلية لدى أحد أفراد الأسرة	4.7	2.8	5.01	0.009
8	وجود إعاقة سلوكية لدى الأب	0.7	0.1	18.4	0.017
9	مدة حمل الطفل طبيعية (9 شهور)	62.3	68.8	28.7	0.019 -
10	ولادة الطفل غير طبيعية	16.9	12.8	10	0.013
11	وزن الطفل عند الولادة أقل من 2.5 كغ	13.7	2.8	194.1	0.02
12	إصابة الطفل باختلاجات بعد الولادة	15.4	1.3	572	0.097
13	إصابة الطفل بالتهاب السحايا	32.6	27.7	4.8	0.009
14	إصابة الطفل بالصرع	8.8	0.3	864.1	0.119
15	تَعرُّض الطفل لحادث داخل المنزل	5.4	1.3	51.8	0.029
16	تَعرُّض الطفل لحادث خارج المنزل	2.5	0.8	24.3	0.001
17	التحاق الطفل بالمدرسة	35.5	44.7	13.8	0.015-

- 93٪ من الأطفال المصابين بالإعاقة الكلامية تلقوا التطعيم ضد الحصبة مقارنةً بـ 97٪ من غير المصابين بها، وكانت العلاقة الإحصائية عكسية (خي مربع = 13.5، ومعامل الترابُط = - 0.015)، أي أن تلقي التطعيم يقلل من احتمال إصابة الطفل بالإعاقة الكلامية.
- 6.3٪ من الأطفال المصابين بالإعاقة الكلامية كانوا يعانون من الصرع مقارنةً بنسبة 0.3 ٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية (خي مربع = 883.5، ومعامل الترابُط = 0.12).
- 8.1٪ من الأطفال المصابين بالإعاقة الكلامية كانوا قد تعرضوا إلى شلل مخي مقارنةً بنسبة 0.2 ٪ من غير المصابين بها، وكانت العلاقة الإحصائية قوية جداً (خي مربع = 1820، ومعامل الترابُط = 0.17).
- 15٪ من الأطفال المصابين بالإعاقة الكلامية كانوا قد تعرضوا لارتفاع في درجة الحرارة مقارنةً بنسبة 2.1٪ من غير المصابين بها، وكانت العلاقة الإحصائية قوية جداً (خي مربع = 630، ومعامل الترابُط = 0.102).
- 3.7٪ من الأطفال المصابين بالإعاقة الكلامية تعرضوا لحادث داخل المنزل مقارنةً بنسبة 1.3 ٪ من غير المصابين بها، وكانت العلاقة الإحصائية هامة (خي مربع = 36، ومعامل الترابُط = 0.024).
- 64٪ من والدي الأطفال المصابين بالإعاقة الكلامية كانوا أقارب بدرجات مختلفة مقارنةً بنسبة 58٪ من والدي الأطفال غير المصابين بهـا، وكانت العلاقة الإحصائية (خي مربع = 12، ومعامل الترابُط = 0.014)،

مع ارتفاع قوة هذه العلاقة عند وجود قرابة من الدرجة الأولى، وانحصار هذه العلاقة الإحصائية بعد إجراء التحليل حسب طبيعة المكان في المدن والمحافظات فقط وعدم ظهورها في القرى والهجر.

جدول (7): العلاقة بين العوامل المتعلقة بالإعاقة وإعاقة صعوبات التعلم

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	الآباء غير متعلمين	35.7	19.6	222	0.20
2	الأمهات غير متعلمات	62.9	45.9	134	0.02
3	تَعرُّض الأم للأشعة أثناء حمل الطفل	2.9	0.7	47.7	0.01
4	تناول الأم أدوية الضغط أثناء الحمل	10.6	6.1	37	0.014
5	تناول الأم أدوية السكري أثناء الحمل	9.7	6.0	25.9	0.014
6	تناول الأم أدوية الصرع أثناء الحمل	0.8	0.3	9.5	0.012
7	تلقّي الأم عناية طبية أثناء الحمل	61.8	75.6	186.9	0.2 -
8	عمر الأم أكبر من 40 عاماً عند ولادة الطفل	26.3	20.3	14	0.01
9	تعرُّض الطفل لحادث داخل المنزل	2.2	0.8	25	0.012
10	تعرُّض الطفل لحادث خارج المنزل	3.4	1.3	34	0.014
11	تغذية الطفل من الزجاجة	11.1	6.1	47.9	0.012
12	وجود قرابة بين الأبوين بأي درجة	66.6	57.9	32	0.023
13	وجود قرابة بين الأبوين من الدرجة الأولى	38.4	27.1	70.6	0.034

رابعاً: الإعاقة السمعية:

- 18.6٪ من الأطفال المصابين بالإعاقة السمعية كان أحد أفراد أسرته يعاني من نفس الإعاقة مقارناً بنسبة 2.4٪ فقط في الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 611، ومعامل الترابُط = 0.101).
- 35.2٪ من والدي الأطفال المصابين بالإعاقة السمعية كان بينهما قرابة من الدرجة الأولى مقارناً بنسبة 27.2٪ من والدي الأطفال غير المصابين بها، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 21، ومعامل الترابُط = 0.019).
- 53.8 ٪ من أمهات الأطفال المصابين بإعاقة سمعية تَلَقَّيْنَ التطعيم ضد الحصبة الألمانية أثناء الحمل مقارناً بنسبة 58.4 ٪ من أمهات الأطفال غير المعوقين، وكانت العلاقة ذات دلالة إحصائية عكسية (خي مربع = 14، ومعامل الترابُط = - 0.016)، أي أن عدم تطعيم الأم الحامل ضد الحصبة الألمانية يزيد من احتمال إصابة الطفل بالإعاقة السمعية.

جدول (8): العلاقة بين العوامل المتعلقة بالإعاقات والإعاقة بالصرع

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	تعرض الطفل لحادث داخل المنزل	5.2	1.3	37.6	0.025
2	تطعيم الطفل ضد النكاف	85.6	89.7	5.7	0.01 -
3	إصابة الطفل باختلاجات في الشهر الأول من عمره	18.7	1ر3	692	0.107
4	إصابة الطفل بارتفاع في حرارته في الشهر الأول	14.1	2.2	206	0.058
5	إصابة الطفل باليرقان الولادي في الشهر الأول	19.0	4.2	175	0.054
6	إصابة الطفل بزرقة في الجلد بعد الولادة	25.7	17.0	17.6	0.017
7	إصابة الطفل بأمراض معدية	4.0	0.4	106	0.042
8	ولادة الطفل بملقط الجنين	4.0	1.4	58.3	0.031
9	ولادة الطفل عن طريق الجراحة (القيصرية)	13.1	11.4		
10	وجود قرابة بين الأبوين	64.2	58.0	5.2	0.009
11	وجود قرابة بين الأبوين ولديهما صرع في الأسرة	11.0	1.2	158	0.067
12	وجود صرع في أسرة الأبوين بدون قرابة بينهما	8.5	1.2	54.2	0.046
13	تلقي الأم لمتابعة طبية أثناء الحمل	48.9	52.3		
14	تلقي الأم للتطعيمات أثناء الحمل	9.2	10.2	16.9	0.017 -
15	تلقي الأم للعلاج الطبي أثناء الحمل	5.8	10.1		

- 3.4٪ من أمهات الأطفال المصابين بإعاقة سمعية أُصِبْنَ بالحميات أثناء الحمل مقارناً بنسبة 0.8٪ من أمهات الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 51.08، ومعامل الترابُط = 0.029).
- 43.7٪ من الأطفال المصابين بإعاقة سمعية أصيبوا أثناء الولادة بسقوط مقارناً بنسبة 31.2٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 41.9، ومعامل الترابُط = 0.026).
- 40.3٪ من الأطفال المصابين بإعاقة سمعية أصيبوا بالتهاب السحايا (بالحمى الشوكية) أو التهاب المخ في العام الأول من العمر مقارناً بنسبة 27.6٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 46.3، ومعامل الترابُط = 0.028).

خامساً: الإعاقة البصرية:

- كان الأبوان من ذوي القرابة من الدرجة الأولى في نسبة 35.2٪ من الأطفال المصابين بإعاقة بصرية مقارناً بنسبة 27.2٪ من أبوي الأطفال غير المصابين بإعاقة بصرية، وكانت العلاقة ذات دلالة إحصائية طردية وقوية (خي مربع = 18، ومعامل الترابُط = 0.017).

جدول (9): العلاقة بين العوامل المتعلقة بالإعاقات والإصابة بالأمراض المزمنة أو الوراثية

م	العامل المتعلق بالإعاقة	٪ لدى المعوقين	٪ لدى الأصحاء	X^2	Φ^*
1	اقتناء الأسرة للطيور المنزلية	8.6	5.6	11.87	0.014
2	وجود أشخاص لديهم إعاقة بالأسرة	28.4	11.5	190	0.056
3	وجود أشخاص لديهم إعاقة بمرض مزمن بالأسرة	13.7	2.4	351	0.076
4	إصابة الأب بنفس الإعاقة	13.3	4.7	109.1	0.04
5	إصابة الأم بنفس الإعاقة	9.1	2.2	148	0.049
6	إصابة أخوة الطفل بنفس الإعاقة	1.4	0.1	80.3	0.036
7	وجود قرابة بين الأبوين من الدرجة الأولى	33.4	27.2	15.3	0.015
8	الفوارق العمرية بين أخوة الأطفال غير منتظمة	39.6	32.4	16.9	0.017
9	عمر الأم أكبر من 40 عاماً	32.7	20.3	82.6	0.037
10	إصابة الأم بالسكري أثناء الحمل	39.9	30.4	29.6	0.022
11	تلقّي الأم لأدوية السكري أثناء الحمل	17.3	5.9	158	0.051
12	إصابة الأم بارتفاع ضغط الدم أثناء الحمل	17.0	6.0	144	0.049
13	إصابة الأم بنزيف شديد أثناء الحمل	2.3	0.5	38.3	0.025
14	ولادة الطفل غير طبيعية	20.0	13.6	58.2	0.031
15	وزن الطفل أقل من 2.5 كيلو غرام عند الولادة	7.4	2.8	122	0.045
16	وزن الطفل أكثر من 4.0 كيلو غرام عند الولادة	1.6	0.8		
17	إصابة الطفل بالتهاب السحايا (بالحمى الشوكية)	37.0	27.5	36.37	0.025
18	إصابة الطفل بالتهاب في المخ	38.0	27.6		
19	إصابة الطفل بزرقة الجلد بعد الولادة	35.7	16.8	175	0.054
20	إصابة الطفل بانخفاض السكر بالدم	3.4-3.0	0.5-0.1	447	0.087
21	إصابة الطفل بحادث داخل المنزل	2.3	1.3	4.9	0.009
22	رضاعة الطفل طبيعية	60.8	65.0	54.1	0.03
23	فترة رضاعة الطفل أقل من شهرين	39.8	31.4	47.7	0.028
24	تعرض الطفل للتسمم بالأدوية أو الكيماويات	5.4	2.6	20.4	0.018

- 56٪ من أمهات الأطفال المصابين بإعاقة بصرية تَلَقَّيْنَ التمنيع بلقاح مضادٍّ للحصبة الألمانية قبل الحمل مقارناً بنسبة 58.5٪ من أمهات الأطفال غير المصابين بها، وكانت العلاقة الإحصائية هامة وعكسية (خي مربع = 35.2، ومعامل الترابُط = - 0.024).
- 0.4٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بها أثناء الولادة بينما لم يصب أحد من الأطفال الآخرين أثناء الولادة من غير المصابين بها، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 30.7، ومعامل الترابُط = 0.012).

- 47.7٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بسقوط أثناء الولادة مقارناً بنسبة 31.2٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية هامة وطردية (خي مربع = 63.5، ومعامل الترابُط = 0.024).
- 6.9٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بانخفاض مستوى السكر بالدم بعد الولادة مقارناً بنسبة 0.1٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية طردية وقوية (خي مربع = 1810، ومعامل الترابُط = 0.24).
- 42.2٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بالتهاب السحايا (الحمى الشوكية) مقارناً بنسبة 27.6٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية (خي مربع = 52.9، ومعامل الترابُط = 0.011).
- 11.9٪ من الأطفال المصابين بإعاقة بصرية نقلوا إلى العناية المركزة بعد الولادة مقارناً بنسبة 2.3٪ من الأطفال غير المصابين بالإعاقة البصرية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 279.5، ومعامل الترابُط = 0.02).
- 9.7٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بارتفاع شديد في درجة الحرارة مقارناً بنسبة 2.2٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية (خي مربع = 126.6، ومعامل الترابُط = 0.02).
- 7.5٪ من الأطفال المصابين بإعاقة بصرية تعرضوا للتسمم بالأدوية أو الكيماويات مقارناً بنسبة 2.6٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 52.8، ومعامل الترابُط = 0.03).
- 2.7٪ من الأطفال المصابين بإعاقة بصرية أصيبوا بأمراض الدم مقارناً بنسبة 0.3 ٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 107.8، ومعامل الترابُط = 0.042).

سادسًا: الاضطرابات السلوكية والانفعالية:

- 32٪ من آباء الأطفال المصابين بالاضطرابات السلوكية والانفعالية غير متعلمين مقارناً بنسبة 19.8٪ من آباء الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 61.2، ومعامل الترابُط = 0.02).
- 55.6٪ من أمهات الأطفال المصابين بالاضطرابات السلوكية والانفعالية كن غير متعلمات مقارناً بنسبة 46.2٪ من أمهات الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 23.7، ومعامل الترابُط = 0.014).
- 65٪ من والدي الأطفال المصابين بالاضطرابات السلوكية والانفعالية كانوا أقارب مقارناً بنسبة 58٪ من والدي الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 8.2، ومعامل الترابُط = 0.012)، وكان 36.5٪ من والدي الأطفال المصابين بالاضطرابات السلوكية والانفعالية أقارب من الدرجة الأولى مقارناً بنسبة 27.5 ٪ من والدي الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، (خي مربع = 18، ومعامل الترابُط = 0.017).
- 27.9٪ من أسر الأطفال المصابين بالاضطرابات السلوكية والانفعالية كانوا من المستوي الاجتماعي والاقتصادي المرتفع مقارناً بنسبة 37.1٪ من أسر الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وعكسية (خي مربع = 14.84 ، ومعامل الترابُط = ـ 0.016) أي أنه كلما ارتفع المستوى الاجتماعي والاقتصادي للأسرة انخفضت فرصة احتمال إصابة الأطفال بالإعاقات السلوكية والانفعالية.

- 26.7٪ من أسر الأطفال المصابين بالاضطرابات السلوكية والانفعالية كانوا معوقين بأي نوع من الإعاقات مقارناً بنسبة 11.6٪ من أسر الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 89.3، ومعامل الترابُط = 0.038).
- 0.7٪ من آباء الأطفال المصابين بالاضطرابات السلوكية والانفعالية كانت لديهم إعاقة سلوكية وانفعالية مقارناً بنسبة 0.1٪ من آباء الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 18.4، ومعامل الترابُط = 0.017).
- 62.3٪ من الأطفال المصابين بالاضطرابات السلوكية والانفعالية أتموا مدة حملهم 9 شهور مقارناً بنسبة 68.8٪ من الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية هامة وعكسية (خي مربع = 28.7، ومعامل الترابُط = ـ 0.019)، أي أنه كلما كانت مدة حمل الطفل طبيعية انخفضت فرصة احتمال إصابته بهذه الإعاقة .
- 13.7٪ من الأطفال المصابين بالاضطرابات السلوكية والانفعالية كان وزنهم عند الولادة أقل من 2.5 كيلو غرام مقارناً بنسبة 2.8٪ من الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 194.1، ومعامل الترابُط = 0.02).
- 15.4٪ من الأطفال المصابين بالاضطرابات السلوكية والانفعالية أصيبوا باختلاجات (بتشنجات) بعد الولادة مقارنةً بنسبة 1.3٪ من الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية جداً وطردية (خي مربع = 572، ومعامل الترابُط = 0.097).
- 8.8٪ من الأطفال المصابين بالاضطرابات السلوكية والانفعالية كانوا يعانون من الصرع مقارناً بنسبة 0.3٪ من الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية جداً وطردية (خي مربع = 864.1، ومعامل الترابُط = 0.119).
- 5.4٪ من الأطفال المصابين بالاضطرابات السلوكية والانفعالية تعرضوا لحادث داخل المنزل مقارناً بنسبة 1.3٪ من الأطفال غير المصابين بالاضطرابات السلوكية والانفعالية، وكانت العلاقة الإحصائية قوية جداً وطردية (خي مربع = 51.8، ومعامل الترابُط = 0.029).
- 35.5 ٪ من الأطفال المصابين بإعاقة سلوكية وانفعالية كانوا ملتحقين بالمدارس مقارناً بنسبة 44.7٪ من الأطفال غير المصابين بها، وكانت العلاقة الإحصائية قوية وعكسية (خي مربع = 13.8، ومعامل الترابُط = ـ 0.015) أي أن زيادة نسبة الإعاقة السلوكية بين الأطفال تقلل من فرص التحاقهم وانتظامهم بالمدارس.

سابعًا: صعوبات التعلم:

- 35.7٪ من آباء الأطفال الذين يعانون من صعوبات التعلم كانوا غير متعلمين مقارناً بنسبة 19.6٪ في الأطفال الذين لا يعانون من صعوبات التعلم، وكانت العلاقة ذات دلالة إحصائية قوية (خي مربع = 222، ومعامل الترابُط = 0.20).
- 62.9٪ من أمهات الأطفال الذين يعانون من صعوبات التعلم كن غير متعلمات بأي درجة مقارنةً بنسبة 45.9٪ من أمهات الأطفال الذين لا يعانون من صعوبات التعلم، وكانت العلاقة الإحصائية قوية (خي مربع = 134، ومعامل الترابُط = 0.02).
- 94.5٪ من أمهات الأطفال الذين يعانون من صعوبات التعلم كن ربات بيوت مقارنة بنسبة 91.2٪ من أمهات الأطفال الذين لا يعانون من صعوبات التعلم، وكانت العلاقة الإحصائية قوية (خي مربع = 17، ومعامل الترابُط = 0.014).
- 2.9٪ من أمهات الأطفال الذين يعانون من صعوبات التعلم تعرضن للأشعة أثناء الحمل مقارناً بنسبة 0.7٪ من أمهات الأطفال الذين لا يعانون من صعوبات التعلم، وكانت العلاقة الإحصائية قوية (خي مربع = 47.7، ومعامل الترابُط = 0.01).

- 10.6٪ من أمهات الأطفال الذين يعانون من صعوبة التعلم تناولن أدوية علاج الضغط أثناء الحمل مقارنة بنسبة 6.1 ٪ من أمهات الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية (خي مربع = 37، ومعادل الترابُط = 0.014).
- 9.7٪ من أمهات الأطفال الذين يعانون من صعوبة التعلم تناولن أدوية علاج السكري أثناء الحمل مقارناً بنسبة 6 ٪ من أمهات الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية هامة (خي مربع = 25.9 ، ومعامل الترابُط = 0.014).
- 61.8٪ من أمهات الأطفال الذين يعانون من صعوبة التعلم تلقين عناية طبية أثناء الحمل مقارناً بنسبة 75.6٪ من أمهات الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية عكسية (خي مربع = 186.9، ومعامل الترابُط = ـ 0.2)، أي أن زيادة العناية الصحية بالأم أثناء الحمل تقلل من فرص احتمال إصابة الطفل بإعاقة صعوبة التعلم.
- 26.3٪ من الأطفال الذين يعانون من صعوبة التعلم كان سن الأمهات عند ولادتهم أكبر من 40 سنة مقارناً بـ 20.3٪ لأمهات الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية هامة (خي مربع = 14، ومعامل الترابُط = 0.01).
- تعرّض 2.2٪ ، 3.4٪ من الأطفال الذين يعانون من صعوبة التعلم لحوادث داخل المنزل وخارجه على التوالي، مقارناً بنسبة 0.8٪، 1.3٪ في الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية لكلا الحالتين هامة (خي مربع = 25، 34، ومعامل الترابُط = 0.012، 0.014).
- 11.1٪ من الأطفال الذين يعانون من صعوبات التعلم كانت تغذيتهم تعتمد على مستحضرات بدائل لبن الأم مقارنة بنسبة 6.1٪ من الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية قوية (خي مربع = 47.9، ومعامل الترابُط = 0.012).
- 38.4٪ من والدي الأطفال الذين يعانون من صعوبة التعلم كانوا أقارب من الدرجة الأولى مقارنةً بنسبة 27.1٪ في الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية قوية (خي مربع = 70.6، ومعامل الترابُط = 0.034).
- 66.6٪ من الأطفال الذين يعانون من صعوبة التعلم، كان أبواهم ذوي قرابة بأي درجة مقارنةً بنسبة 57.9٪ في الأطفال الذين لا يعانون من صعوبة التعلم، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 32، ومعامل الترابُط = 0.023)، والخطر النسبي يبلغ 1.4 (1.2 ـ 1.6).

امناً: الإعاقة بالصرع:

- 5.2٪ من المعوقين لإصابتهم بالصرع تعرضوا لحادث داخل المنزل مقارنةً بنسبة 1.3٪ من غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 37.6، ومعامل الترابُط = 0.025).
- 85.6٪ من المعوقين لإصابتهم بالصرع تلقوا تطعيماً ضد النكاف مقارنةً بنسبة 89.7٪ من غير المعوقين، وكانت العلاقة الإحصائية عكسية (خي مربع = 5.7، ومعامل الترابُط = – 0.01) أي أن عدم التطعيم يزيد من فرص احتمال حدوث الصرع.
- 18.7٪ من المعوقين لإصابتهم بالصرع أصيبوا باختلاجات (بتشنجات) بعد الولادة (خلال الشهر الأول) مقارنةً بنسبة 1.3٪ من غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 692، ومعامل الترابُط = 0.107).
- 14.1٪ من المعوقين لإصابتهم بالصرع أصيبوا بارتفاع في درجة الحرارة (خلال الشهر الأول) مقارنةً بنسبة 2.2٪ من غير المعوقين لإصابتهم بالصرع، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 206، ومعامل الترابُط = 0.058).

- 19٪ من المعوقين لإصابتهم بالصرع أصيبوا باليرقان في الشهر الأول مقارنةً بنسبة 4.2٪ من غير المعوقين لإصابتهم بالصرع، وكانت العلاقة ذات دلالة إحصائية قوية وطردية (خي مربع = 175، ومعامل الترابُط = 0.054).
- 25.7٪ من المعوقين لإصابتهم بالصرع أصيبوا بزرقة في الجلد بعد الولادة مقارنةً بنسبة 17٪ من غير المعوقين، وكانت العلاقة ذات دلالة إحصائية قوية وطردية (خي مربع = 17.6، ومعامل الترابُط = 0.017).
- 4٪ من المعوقين لإصابتهم بالصرع أصيبوا بأمراض معدية خلال طفولتهم مقارنةً بنسبة 0.4٪ من غير المعوقين لإصابتهم بالصرع، وكانت العلاقة ذات دلالة إحصائية قوية وطردية (خي مربع = 106، ومعامل الترابُط = 0.042).
- 4٪ من المعوقين لإصابتهم بالصرع تمت ولادتهم بالسحب بالمحجم السويدي (الفانتوز) مقارنةً بنسبة 1.4٪ من غير المعوقين، ونسبة 13.1٪ من المعوقين لإصابتهم بالصرع تمت ولادتهم بالقيصرية مقارنةً بنسبة 11.4٪ من غير المعوقين لإصابتهم بالصرع، وكانت العلاقة الإحصائية بين الولادة التدخلية والصرع قوية وطردية (خي مربع = 58.3، ومعامل الترابُط = 0.031).
- 11٪ من والدي الأطفال المعوقين لإصابتهم بالصرع كانوا أقارب، ولديهم سوابق صرع في الأسرة، مقارنةً بنسبة 1.2٪ من والدي الأطفال غير المعاقين لإصابتهم بالصرع (خي مربع = 158، ومعامل الترابُط = 0.067).
- 8.5٪ من والدي الأطفال المعوقين لإصابتهم بالصرع لديهم سوابق صرع في الأسرة، ولا توجد بينهم قرابة مطلقاً، مقارنةً بنسبة 1.2٪ من غير المعوقين لإصابتهم بالصرع وكانت العلاقة الإحصائية هامة (خي مربع = 54.2، ومعامل الترابُط = 0.046)، أي أن وجود صرع في أسرة الأبوين يزيد من احتمال حدوث الإعاقة للإصابة بالصرع، ويزيد هذا الاحتمال إذا وجدت قرابة بأية درجة.
- 48.9٪ من أمهات المعوقين للإصابة بالصرع تَلَقَّيْنَ متابعة أثناء الحمل مقارنةً بنسبة 52.3٪ من أمهات الأطفال غير المعوقين لإصابتهم بالصرع، ونسبة 9.2٪ من أمهات الأطفال المعوقين للإصابة بالصرع تلقين التطعيمات أثناء الحمل مقارنةً بنسبة 10.2٪ من أمهات الأطفال غير المعوقين لإصابتهم بالصرع، ونسبة 5.8٪ من الأمهات تَلَقَّيْنَ علاجاً طبياً أثناء الحمل مقارنة بنسبة 10.1٪ من أمهات الأطفال غير المعوقين للإصابة بالصرع، وكانت العلاقة الإحصائية للمتابعة، والتطعيمات، والعلاج الطبي أثناء الحمل هامة وعكسية (خي مربع = 16.9، ومعامل الترابُط = ـ 0.017)، أي أن العناية بهذه الأمور يقلل من فرص احتمال حدوث الإعاقة بالصرع.

تاسعاً: الإعاقة من الأمراض الوراثية والمزمنة:

- 28.4٪ من الأطفال المعوقين بأمراض وراثية ومزمنة كان يوجد في أسرهم أشخاص مصابون بالإعاقة مقارنةً بنسبة 11.5٪ من أسر الأطفال غير المصابين بالإعاقة، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 190 ومعامل الترابُط = 0.056).
- 13.7٪ من الأطفال المعوقين بأمراض وراثية ومزمنة كان في سوابق أسرهم شخص مصاب بإعاقة من مرض مزمن أو وراثي مقارنةً بنسبة 4ر2 ٪ من أُسَر الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 351 ومعامل الترابُط = 0.076).
- 13.3٪ من آباء الأطفال المعوقين بأمراض وراثية ومزمنة كانوا مصابين بنفس المرض مقارنةً بنسبة 4.7٪ من آباء الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 109.1 = ومعامل الترابُط 0.04).

- 9.1٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة كُنَّ مصابات بنفس الإعاقة مقارنة بنسبة 2.2٪ من أمهات الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 148 ومعامل الترابُط = 0.049).
- 1.4٪ من أخوة الأطفال المعوقين بأمراض وراثية ومزمنة كانوا مصابين بنفس الإعاقة مقارنةً بنسبة 0.1٪ من أخوة الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 80.3 ومعامل الترابُط = 0.036).
- 33.4٪ من والدي الأطفال المعوقين بأمراض مزمنة أو وراثية كانا أقارب من الدرجة الأولى مقارنةً بنسبة 27.2٪ من آباء الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية.
- 39.6٪ من الأطفال المعوقين بالأمراض المزمنة والوراثية كانت الفوارق العمرية بينهم غير منتظمة مقارنةً بنسبة 32.4٪ من الأطفال غير المعوقين، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 16.9 ومعامل الترابُط = 0.017).
- 32.7٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة كان عمرهُنَّ فوق 40 سنة مقارنةً بنسبة 20.3٪ من أمهات الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 82.6 ومعامل الترابُط = 0.037).
- 17.3٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة كُنَّ يتعاطين أدوية السكر أثناء الحمل مقارنةً بنسبة 5.9٪ من أمهات الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 158 ومعامل الترابُط = 0.051).
- 39.9٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة أُصِبْنَ بالسكري أثناء الحمل مقارنةً بنسبة 30.4٪ من أمهات الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 29.6 ومعامل الترابُط = 0.022).
- 17٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة أُصِبْنَ بارتفاع ضغط الدم أثناء الحمل مقارنةً بنسبة 6 ٪ من أمهات الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية (خي مربع = 144 ومعامل الترابُط = 0.049).
- 2.3٪ من أمهات الأطفال المعوقين بأمراض وراثية ومزمنة أُصِبْنَ بنزيف شديد أثناء الحمل مقارنةً بنسبة 0.5٪ من أمهات الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية (خي مربع = 38.3 ومعامل الترابُط = 0.025).
- 20٪ من الأطفال المعوقين بأمراض وراثية ومزمنة كانت ولادتهم غير طبيعية مقارنة بنسبة 13.6٪ من الأطفال غير المعوقين بأمراض وراثية ومزمنة، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 58.2 ومعامل الترابُط = 0.031).
- 37٪ من الأطفال المعوقين بأمراض وراثية ومزمنة أصيبوا بالتهاب السحايا (الحمى الشوكية)، 38٪ منهم أصيبوا بالتهاب في المخ مقارنةً بنسبة 27.5٪، 27.6٪ من الأطفال الأصحاء، وكانت العلاقة الإحصائية قوية وطردية (خي مربع = 36.37 ومعامل الترابُط = 0.025).
- 35.7٪ من الأطفال المعوقين بأمراض مزمنة أو وراثية أصيبوا بزرقة في الجلد بعد الولادة مقارنةً بنسبة 16.8٪ من الأطفال غير المعوقين بأمراض مزمنة أو وراثية، وكانت العلاقة الإحصائية طردية وهامة (خي مربع = 175، ومعامل الترابُط = 0.054).
- 3٪ ـ 3.4٪ من الأطفال المعوقين بأمراض وراثية ومزمنة أصيبوا بانخفاض أو نقص في مستوى السكر في الدم مقارنةً بنسبة 0.1٪ ـ 0.5٪ من الأطفال غير المعوقين بأمراض مزمنة أو وراثية، وكانت العلاقة الإحصائية طردية وهامة (خي مربع = 447، ومعامل الترابُط = 0.087).

- 60.8٪ من الأطفال المعوقين لإصابتهم بأمراض وراثية ومزمنة كانت رضاعتهم طبيعية من الثدي مقارنةً بنسبة 65 ٪ من الأطفال غير المعوقين بأمراض مزمنة أو وراثية، وكانت العلاقة الإحصائية قوية (خي مربع =54.1، ومعامل الترابُط = 0.030).
- 39.8٪ من الأطفال المعوقين لإصابتهم بأمراض وراثية ومزمنة كانت رضاعتهم أقل من شهرين مقارنة بنسبة 31.4 ٪ من الأطفال غير المعوقين بأمراض مزمنة أو وراثية، وكانت العلاقة الإحصائية هامة (خي مربع = 47.7، ومعامل الترابُط = 0.028).
- 5.4٪ من الأطفال المعوقين لإصابتهم بأمراض وراثية ومزمنة تعرضوا للتسمم بالأدوية أو الكيماويات مقارنةً بنسبة 2.6٪ من الأطفال غير المعوقين بأمراض مزمنة أو وراثية، وكانت العلاقة الإحصائية قوية وطردية خاصة مع التسمم بالأدوية (خي مربع = 20.4، ومعامل الترابُط = 0.018).

مؤشرات عامة على النتائج:

- وجود إعاقة لدى الأم أو الأب وبخاصة الإعاقات الوراثية التي يمكن أن تنتقل من أحد الأبوين أو كليهما للطفل.
- صغر سن الأم أو كبره عند الإنجاب (أقل من 16 سنة أو أكبر من 35 سنة) قد يؤدي إلى قصر فترة الحمل (الطفل الخديج أو المبتسر)، أو حدوث صعوبات عند الولادة سواء لعدم اكتمال نضج عظام الحوض لدى الأم الصغيرة أو ارتخاء عضلات الرحم لدى الأم الكبيرة، مما يتسبب في اختناق الطفل أو نقص الأكسجين لديه، والذي قد يؤدي بدوره إلى الإعاقات العقلية.
- زيادة عدد مرات الحمل لأكثر من خمس مرات قد يؤدي إلى قصور في الرعاية المقدمة للطفل خلال مرحلة الطفولة.
- عدم اهتمام الأم بتلقي التطعيم ضد الكزاز (التيتانوس) قبل أو أثناء الحمل يساهم في زيادة احتمال تعرض الطفل للإصابة بالكزاز ومضاعفاته.
- إصابة الأم بمرض أثناء الحمل يؤثر على صحتها بصفة عامة، وقد ينتقل المرض بدوره إلى الجنين ويسبب له مضاعفات خطيرة .
- تناول الأم لبعض الأدوية أثناء الحمل قد يتسبب في حدوث بعض التشوهات الخلقية للجنين.
- عدم اهتمام الأم بتناول الحديد والفيتامينات أثناء الحمل يضعفها ويؤثر بدوره على نمو الجنين وتكوينه.
- نقص الرعاية الطبية المقدمة للأم أثناء الحمل وعدم متابعتها بمراكز الرعاية الصحية يلعب دوراً هاماً في حدوث بعض الإعاقات.
- قِصَر فترة حمل الطفل (الطفل الخديج أو المبتسر) قد يؤدي إلى حدوث بعض الإعاقات مثل الإعاقات الحركية والعقلية.
- الولادة غير الطبيعية للطفل بالسحب بالمحجم السويدي (الفانتوز) أو بعملية جراحية (القيصرية) له علاقة بحدوث إصابات برأس الطفل والتي قد تؤدي إلى حدوث الإعاقة العقلية أو السمعية أو البصرية أو غيرها.
- قصر الفوارق العمرية بين الأبناء والتي تقلل من مستوى العناية بهم.
- الوضع غير الطبيعي للطفل عند الولادة مثل المجيء بالقدمين أو المجيء المقعدي والذي قد ينتج عنه إصابات بالرأس والعمود الفقري وضيق في التنفس.
- حدوث انسداد أو صعوبة في التنفس للطفل أثناء الولادة مما يؤدي إلى زرقة بالجلد نتيجة نقص الأكسجين والذي يؤثر بدوره على المخ وحدوث إعاقة عقلية أو كلامية أو صرع أو صعوبات تعلم.

- إصابة الطفل أثناء الولادة بسقوط أو كسر ، وكذلك تعرضه لنقص في مستوى السكر في الدم أو ارتفاع في درجة حرارته، وإصابته باختلاجات بعد الولادة أو بأمراض معدية أو بالتهاب في المخ أو التهاب السحايا (الحمى الشوكية) أو بنزلات معوية وغيرها مما قد يساهم في حدوث الإعاقة العقلية أو الحركية، وتتضح زيادة نسبة هذه العوامل لدى الأطفال المعوقين مقارنة بالأصحاء.
- انخفاض نسبة تلقي الطفل للتطعيمات بعد الولادة وأثناء مرحلة الطفولة يعرضه للإصابة بالأمراض المعدية المسببة للإعاقة مثل شلل الأطفال.
- قصر فترة الرضاعة للطفل بصفة عامة قد يعرض الطفل لأمراض سوء التغذية والإعاقة، مع عدم تأثير نمط الإطعام أو الرضاعة على حدوث الإعاقة.

الاقتراحات:

بدراسة النتائج التي تم الحصول عليها من المعلومات المتوافرة من هذه الدراسة التي شملت مختلف العوامل المؤثرة المتعلقة بالأسرة والطفل، ونتائج التحاليل الإحصائية للعوامل المتعلقة بحدوث الإعاقات، أمكن صياغة الاقتراحات التالية من واقع نتائج البحث:

(1) التركيز على ضرورة إجراء الفحص قبل الزواج والتوسع في خدماته (تم البدء بتنفيذه على المستوى الوطني بموجب قرار مجلس الوزراء الموقر) للحد من حدوث الأمراض الوراثية المسببة للإعاقات وبخاصة أمراض الدم الوراثية.

(2) الاهتمام بإجراء برامج توعية للأمهات الحوامل حول ضرورة أخذ التطعيمات اللازمة قبل وأثناء الحمل ضد الأمراض المعدية المسببة لبعض الإعاقات.

(3) تعميم إعطاء الفيتامينات والحديد للأمهات الحوامل بمختلف القطاعات الصحية ومراكز رعاية الأمومة للحد من حدوث أمراض سوء التغذية وكذا التشوهات الخلقية مثل عيوب القناة العصبية والتي تسبب الإعاقة.

(4) إجراء الفحوصات الطبية والمخبرية والوراثية ذات العلاقة أثناء الحمل وعند الولادة للاكتشاف المبكر ومن ثم وضع استراتيجيات للتدخل المبكر.

(5) إعداد برامج توعية للأمهات الحوامل للتأكيد على أهمية الولادة في المستشفيات والعمل على توفير الإمكانيات اللازمة للعناية بالمواليد الطبيعيين والخدَّج أو المُبْتَسَرين.

(6) التوسع في التطعيمات الخاصة بالأمراض المعدية للأطفال في مرحلة ما بعد الولادة وفي سن دخول المدرسة على مستوى الهجر والقرى والمراكز والمدن والمحافظات.

(7) إجراء الفحص الدوري الشامل على أطفال المدارس الابتدائية والمتوسطة والثانوية وتقييم حالاتهم الصحية ومستوى تحصيلهم الدراسي لاكتشاف حالات الإعاقة ومن ثمّ التدخل المبكر.

(8) الاهتمام ببرامج التوعية للمواطنين لتغيير نظرتهم تجاه المعوقين ـ وبخاصة من قدّر الله عليهم الإعاقة في أحد أبنائهم ـ عن طريق النشرات والمحاضرات والبرامج الإذاعية والمرئية ومعاملتهم كأفراد عاديين لهم من الحقوق مثل ما للأصحاء ، ومشاركتهم آلامهم وآمالهم.

References المراجع

1. الحازمي، م ع ف، وآخرون، 2000م التقرير الفني النهائي لمشروع البحث الوطني لدراسة الإعاقة لدى الأطفال بالمملكة العربية السعودية، الرياض.

2. ***WHO Expert Committee on Disability Prevention and Rehabilitation***. Geneva, World Health Organization, 1981 (Technical Report Series No. 668):1–39.

3. Hutchison T, Nicoll A. Developmental screening and surveillance. ***British journal of hospital medicine***, 1988, 39(1):22–9.

4. Cochran WG. ***Sampling techniques***, 3rd ed. New York, John Wiley, 1977.

5. Wilson JM, Jungner G. ***Principles and practice of screening for disease***. Geneva, World Health Organization, 1968 (Public Health Papers, No. 34):11.

6. Fleiss JL. ***Statistical methods for rates and proportions***, 2nd ed. New York, John Wiley, 1981.

7. SPSS ***6.0 for Windows***. Chicago, SPSS Inc., 1995.

8. Schneiderman ED et al. A PC program for computing confidence band for average and individual growth curves. ***Computers, biology and medicine***, 1994, 24(2):119–27.

ملحوظة من المحرِّر:

نرجو أن نحيط قراءنا علماً بأن موضوع العدد الخاص من المجلة الصحية لعام 2005 (المجلد الحادي عشر) هو *صحة الأم والطفل*.

Attitudes of a high-risk group of pregnant Saudi Arabian women to prenatal screening for chromosomal anomalies

Z.A. Babay[1]

مواقف الحوامل السعوديات المعرَّضات لخطر مرتفع من تحرِّي الشذوذات في الصبغيات قبل الولادة

زينب أحمد باباي

الخلاصة: قامت الباحثة بدراسة مواقف 550 من الحوامل السعوديات اللاتي تتجاوز أعمارهن 35 عاماً من عملية تحرِّي الشذوذات في الصبغيات قبل الولادة. وقد قبلت 336 منهن (61.1٪) الفكرة العامة للتحرِّي قبل الولادة، و لم تقبل بذلك 160 منهن (29.1٪) وبقي 54 منهن (9.8٪) دون اتخاذ قرار بشأن ذلك. وقد كان معدل القبول مرتفعاً للطرق غير الباضعة مثل الفحص بالأمواج فوق الصوتية (61.3٪) والتحرِّي الكيمياوي الحيوي (53.0٪)، في حين كان معدل القبول متدنياً للطرق الباضعة (34.2٪). أما السبب الرئيسي لرفض التحرِّي فهو عدم تقبُّل فكرة إنهاء الحمل كأحد الخيارات العلاجية. وقد كان هناك فرق إحصائي واضح بين اللواتي قَبِلْنَ فكرة التحرِّي وبين من لم يَقْبَلْنَها فيما يتعلق بمدى وَعْيِهِنَّ لتوافُر التحرِّي قبل الولادة؛ ولرفضهن إنهاءَ الحمل، وللشك في صحة الاختبارات، وفي اعتقادهن أن الشذوذاتَ الصبغية لا تحتاج للتحرِّي. وتوصي الباحثة بإذكاء الوعي العام حول القضايا المتعلقة بالشذوذات في الصبغيات وحول التحرِّي السابق للولادة.

ABSTRACT The attitude of 550 pregnant Saudi Arabian women aged > 35 years to prenatal screening for chromosomal anomalies was investigated. A total of 336 women (61.1%) accepted the general idea of prenatal screening while 160 (29.1%) did not; 54 women (9.8%) were undecided. There was a high acceptance of non-invasive methods such as ultrasound (61.3%) and biochemical screening (53.0%) but a low acceptance of invasive methods (34.2%). The main reason for refusal of screening was the unacceptability of termination of pregnancy as a treatment option. There were statistically significant differences between those who accepted the idea of screening and those who did not with regard to their awareness of the availability of prenatal screening, their rejection of pregnancy termination, their doubt of the accuracy of the tests and in their belief that chromosomal abnormalities need no be screened for.

Attitudes d'un groupe de femmes enceintes saoudiennes à haut risque vis-à-vis du dépistage prénatal des anomalies chromosomiques

RÉSUMÉ On a examiné l'attitude de 550 femmes enceintes saoudiennes âgées de plus de 35 ans vis-à-vis du dépistage prénatal des anomalies chromosomiques. Au total, 336 femmes (61,1 %) acceptaient l'idée générale du dépistage prénatal tandis que 160 (29,1 %) ne l'acceptaient pas ; 54 femmes (9,8 %) étaient indécises. Il y avait une forte acceptation des méthodes noninvasives telles que l'échographie (61,3 %) et le dépistage biochimique (53,0 %) mais une faible acceptation des méthodes invasives (34,2 %). La raison principale du refus du dépistage était l'inacceptabilité de l'interruption de grossesse comme option thérapeutique. Il y avait des différences statistiquement significatives entre les femmes qui acceptaient l'idée du dépistage et celles qui ne l'acceptaient pas pour ce qui concerne la connaissance de l'existence du dépistage prénatal, leur rejet de l'interruption de grossesse, leur doute au sujet de l'exactitude des tests et leur opinion concernant le fait que les anomalies chromosomiques ne nécessitent pas de dépistage.

[1]Department of Obstetrics and Gynaecology, King Saud University, King Khaled University Hospital, Riyadh, Saudi Arabia.

Received: 30/04/03; accepted: 14/01/04

Introduction

Genetic diseases affect all populations and have been apparent since antiquity. In recent years many advances have been made in the field of prenatal screening for chromosomal anomalies. Techniques now available for such screening include second trimester biochemical screening (α-fetoprotein, β human chorionic gonadotropin (HCG) and unconjugated estrogen), first trimester biochemical screening (pregnancy associated plasma protein A (PAPPA), and β HCG), ultrasound fetal nuchal translucency measurement, in addition to the older invasive techniques such as amniocentesis and chorionic villus sampling. Some of the non-invasive methods have high sensitivity, especially if combined with ultrasound nuchal translucency measurement (90% sensitivity and 3.1% false positive rate) [*1*] in addition to causing no harm to the fetus. The use of these tests has resulted in a significant decrease in the prevalence of children with chromosomal abnormalities [*2*].

The incidence of Down syndrome in Saudi Arabia is 1.8 per 1000 live births [*3*], which is similar to the reported incidence in Hawaii but higher than the rest of the United States of America (10 per 10 000 live births) [*4*]. Some modern Islamic opinion and rulings have accepted prenatal diagnosis and approved severe congenital anomalies and malformations per se as a reason for termination of pregnancy before ensoulment (120 days from conception or 134 days from last menstrual period) [*5,6*]. However, in spite of the availability of these screening tests, there are no reports in literature about their use in Saudi Arabia nor the awareness of Saudi Arabian women of such tests and their attitudes to them. Therefore, this study was carried out to assess the awareness and acceptance of such screening methods among pregnant Saudi Arabian women.

Methods

King Khalid University Hospital (KKUH) Riyadh, Saudi Arabia is the largest teaching hospital in the central region in Saudi Arabia, with an average delivery rate of 4500 babies per month. All pregnant women aged 35 years or older attending the Saturday afternoon antental clinic at KKUH between October 2002 and January 2003 were included in the study and were administered a questionnaire devised by the author. The questionnaire was conducted verbally and it included information on age, parity, personal or family history of a child with chromosomal anomalies, awareness of the availability of prenatal screening for such conditions and their acceptance of such screening in the next pregnancy, in addition to reasons for non-acceptance. None of the women refused to participate. Statistical analysis was done using *SPSS*, version 10. The Student *t*-test was used to compare between variables and a *P*-value of ≤ 0.01 was considered significant.

Results

A total of 1680 pregnant women attended the antental clinic during the study period. Of those, 550 (32.7%) women were aged 35 years or older and were included in the study. The mean age and standard deviation (SD) was 37 (2.34) years (range 35–44 years) and mean parity was 4 (3.23) (range 1–7). In all, 284 women (51.6%) knew about the availability of prenatal screening, 28 women (5.1%) had a positive family history of a child with chromosomal anomalies and 13 women (2.4%) had a history of giving birth to an affected child. A total of

336 women (61.1%) accepted the general idea of prenatal screening in the next pregnancy while 160 women (29.1%) did not and 54 women (9.8%) could not decide (Table 1). Among the women who accepted the idea of screening, 53.0% accepted the idea of biochemical screening, 61.3% accepted the idea of ultrasound screening and 34.2% accepted the idea of invasive procedures such as amniocentesis and chorionic villus sampling.

Further questioning of the women who did not accept the idea of screening showed that 76% did not accept termination of pregnancy as an option in the event of an abnormal result, 22% did not accept screening in general as they doubted the accuracy of the tests, 19% did not believe that they would have an abnormal child and 6% did not believe chromosomal anomalies were an abnormality that should be screened for (Table 2).

Table 3 shows a comparison between those who accepted the idea of screening in pregnancy versus those who did not. There was a statistically significant difference between the 2 groups in their awareness of the availability of prenatal screening (57.7% versus 42.1%) (P = 0.0005), in their rejection of pregnancy termination (65.5% versus 92.5%) (P = 0.001), in their doubt of the accuracy of the tests (8.9% versus 42.5%) (P = 0.001) and in their belief that chromosomal abnormalities were not an abnormality that should be screened for (0.3% versus 15.0%) (P = 0.001). There was no significant difference in acceptance or rejection of prenatal screening between those who had a positive family history of a child with chromosomal anomalies, those who had positive personal history of having a child with chromosomal anomalies, and those who believed that they would not have a child with chromosomal anomalies.

A comparison was made between the women who had positive family history of a child with a chromosomal anomaly, those with a positive personal history of having a child with a chromosomal anomaly, and those who did not have any such history (Table 4). There was a statistically significant difference between the 3 groups in acceptance of termination of pregnancy (75.0%, 69.2% and 76.2% respectively) (P = 0.001), in the belief in the possibility

Table 1 **Characteristics of the study sample**

Charactersitic	No. (n = 550)	%
Had a positive personal history of a child with chromosomal anomaly	13	2.4
Had a positive family history of a child with chromosomal anomaly	28	5.1
Was aware of the availability of prenatal screening	284	51.6
Found screening:		
Acceptable	336	61.1
Unacceptable	160	29.1
Undecided	54	9.8

Table 2 **Reasons for finding prenatal screening unacceptable**

Reason	%
Did not accept termination of pregnancy as an option	76
Doubted the accuracy of the tests	22
Did not believe that they would have a child with chromosomal anomalies	19
Did not believe chromosomal abnormality was an abnormality that should be screened for	6

Table 3 **Comparison of women who accepted the idea of prenatal screening for chromosomal abnormalities and those who did not**

Variable	Accepted screening (*n* = 336)		Did not accept screening/was undecided (*n* = 214)		Odds ratio	95% CI	*P*-value
	No.	%	No.	%			
Had a positive family history of a child with chromosomal anomaly	20	6.9	8	3.7	1.63	0.67–4.11	0.3407
Had a positive personal history of a child with chromosomal anomaly	8	2.4	5	2.3	1.02	0.29–4.02	0.7992
Was aware of the availability of prenatal screening	194	57.7	90	42.1	1.88	1.31–2.70	0.0005**
Did not accept termination of pregnancy as an option	220	65.5	198	92.5	0.15	0.08–0.28	0.001**
Doubted the accuracy of prenatal screening tests	30	8.9	91	42.5	0.13	0.08–0.22	0.001**
Did not believe that they would have a child with chromosomal anomalies	56	16.7	49	22.9	0.67	0.43–1.06	0.0889
Did not believe chromosomal anomaly was an abnormality that should be screened for	1	0.3	32	15.0	0.02	0.0–0.1	0.001**

*****Statistically significant at*** P ≤ ***0.01.***
CI = confidence interval.

of delivering a child with chromosomal anomalies (64.3%, 84.6% and 14.9% respectively) (P = 0.001), in the acceptance of chromosomal anomalies as an abnormality that should be screened for (7.1%, 38.5% and 5.1% respectively) (P = 0.001), in the acceptance of biochemical screening during pregnancy (71.4%, 53.8% and 29.7% respectively) (P = 0.001), in the acceptance of ultrasound screening during pregnancy (71.4%, 61.5% and 25.5% respectively) (P = 0.001), and in the acceptance of an invasive investigation (25.0%, 100.0%, 43.4% respectively) (P = 0.001).

Discussion

The old adage that prevention is better than cure applies as much to genetic as to acquired diseases. Primary prevention of abnormal genotypes would need to act prior to conception. Prenatal diagnosis with selective termination (secondary prevention) alters the birth frequency of the condition but is really only a holding measure pending the development of primary prevention of genetic disease. Currently the only primary prevention available is pre-implantation genetic diagnosis which requires *in vitro*

Table 4 **Comparison of the women with a positive family history, those with a positive personal history and those with no history of a child with a chromosomal anomaly**

Variable	Positive family history (*n* = 28)		Positive personal history (*n* = 13)		No history (*n* = 509)		*P*-value
	No.	%	No.	%	No.	%	
Accepted the idea of prenatal screening	20	71.4	8	61.5	308	60.5	0.263
Was aware of the availability prenatal screening	15	53.6	10	76.9	259	50.9	0.0639
Did not accept termination of pregnancy as an option	21	75.0	9	69.2	388	76.2	0.0019**
Doubted the accuracy of prenatal screening tests	5	17.9	3	23.1	113	22.2	0.86
Did not believe that they would have a child with chromosomal anomalies	18	64.3	11	84.6	76	14.9	0.001**
Did not believe chromosomal anomaly was an abnormality that should be screened for	2	7.1	5	38.56	26	5.1	0.001**
Accepted the idea of biochemical screening	20	71.4	7	53.8	151	29.7	0.001**
Accepted the idea of ultrasound screening	20	71.4	8	61.5	130	25.5	0.001**
Accepted the idea of invasive screening (aminocentesis and chorionic villus sampling	7	25.0	13	100.0	221	43.4	0.001**

***Statistically significant at** $P \leq 0.01$.

fertilization and this is not suitable as a screening test. The principle for any test to be used for screening populations is that it should be sensitive, relatively specific and harmless. In addition, the disorder screened for should be of appreciable frequency and early diagnosis should be an advantage. In our study almost two-thirds (61.1%) of the women questioned accepted the idea of screening. Of those accepting the idea of screening, all accepted ultrasound screening, probably because it is part of the antenatal care in Saudi Arabia and is therefore familiar to them and does not carry any risk of abortion. The acceptance rate for biochemical screening was lower (53.0%). This rate is similar to the reported acceptance rate in other parts of the world [*7,8*]. The acceptance rate of invasive procedures was much lower (34.2%) probably because as it carries the risk of abortion. On the other hand, 29.1% of the women did not accept the idea of screening; the main reason was that they did not accept termination of pregnancy as a treatment option.

Factors such as socioeconomic structure, education and religion affect the

acceptability of prenatal diagnosis. These factors are very important in Saudi Arabia as all Saudi Arabians are Muslims and high parity is a characteristic feature of the community. At the same time, the physician's attitude towards such tests is important as they share the same religious background.

Public awareness of the risks and difficulties facing a child with chromosomal anomalies and the effect on their future health and living is of great importance for acceptance of prenatal screening. In our study 19% of the women believed that they would not have a child with chromosomal anomalies although, because of their age (> 35 years), this was a high-risk population for certain such conditions. In addition, the difference between those who accepted screening and those who did not was statistically significant in regards to their awareness of the availability of prenatal screening and in their belief in the accuracy of the tests (Table 3), which reflects a lack of health knowledge.

From this study we conclude that combined biochemical screening and ultrasound nuchal translucency are the most acceptable prenatal genetic screening tests for Saudi Arabian women bearing in mind the religious and social background. Prenatal diagnosis of such anomalies is important for both the parents and physicians even if termination is not undertaken. Physicians should be encouraged to offer these test and to give appropriate counseling as this high-risk group constituted 32.7% of the women attending the antental clinic. Public awareness should also be raised about the issues of genetic abnormalities and prenatal screening until suitable primary prevention is available.

References

1. Benn PA et al. Combined second trimester biochemical and ultrasound screening for Down syndrome. ***Obstetrics and gynecology***, 2002, 100(6):1168–76.
2. Cheffins T et al. The impact of maternal serum screening on the birth prevalence of Down syndrome and the use of amniocentesis and chorionic villus sampling in south Australia. ***British journal of obstetrics and gynaecology***, 2000, 107(12):1453–9.
3. Niazi MA et al. Down's syndrome in Saudi Arabia: incidence and cytogenetics. ***Human heredity***, 1995, 45(2):65–9.
4. Forrester MB, Merz RD. Epidemiology of Down syndrome (trisomy 21) in Hawaii, 1986–97. ***Teratology***, 2002, 65(5):207–12.
5. Ghanem I. [Abortion as a necessity]. ***Al Faisal medical journal***, 1984, 9:6–15 [in Arabic].
6. [***Regarding termination of pregnancy for congenital abnormality*** (No. 4)]. Twelfth Session of the Moslem World League Conference of Jurists, Mecca 10–17 February 1990 [In Arabic].
7. DeGraaf IM et al. Women's preference in Down syndrome screening. ***Prenatal diagnosis***, 2002, 22(7):624–9.
8. Lam YH et al. Acceptability of serum screening as an alternative to cytogenetic diagnosis of Down syndrome among women 35 years or older in Hong Kong. ***Prenatal diagnosis***, 2000, 20(6): 487–90.

Validity of vision screening by school nurses in seven regions of Oman

R. Khandekar,[1] S. Al Harby,[1] T. Abdulmajeed,[1] S.A. Helmi[2] and I.S. Shuaili[3]

مدى الصحة في عملية تحرِّي ممرضات المدارس للقدرة البصرية في سبع مناطق في عُمان

راجيف خانديكار، صالح الحربي، طلعت عبد المجيد، سحر عبد الحليم، عيسى شويلي

الخلاصة: درس الباحثون مدى صلاحية قيام الممرضات العاملات في المدارس بتَحَرِّي القدرة البصرية للتلاميذ في سبع مناطق في عُمان عام 2003. وقد فحص باحثان 1719 تلميذاً ممن تم اختيارهم عشوائياً من المرحلة الدراسية الرابعة وذلك باستخدام اختبار القدرة البصرية بحسب شنين E. وقد سبق لممرضات المدارس المتدرِّبات أن تحرّوا 233 182 تلميذاً. فأُجريت مقارنة للحالة الإبصارية في الدراستَيْن. وقد تبيَّن أن حساسية التحرِّي لدى الممرضات بلغت 68.34٪ (67.30 - 96.38) وبفاصلة ثقة مقدارُها 95٪. في حين بَلَغَت النوعية 99.23٪ (99.19 - 99.27) وبفاصلة ثقة مقدارُها 95٪، وكانت القيمة التنبؤية الإيجابية 85.42٪ (84.63 - 86.21) بفاصلة ثقة مقدارُها 95٪ والقيمة التنبؤية السلبية 97.93٪ (97.87 - 98.00) بفاصلة ثقة مقدارُها 95٪. وقد كانت حساسية اختبار الإبصار أعلى بشكل ملحوظ عند الإناث وكبار التلاميذ، وفي المنطقة الشرقية الشمالية. وبشكل عام فإن تحرِّي الإبصار لتلاميذ المدارس في عُمان يتمتَّع بدرجة من الصحة تبعث على الرضى. ويرى الباحثون أن التدريب الدوري للممرضات والإشراف على إجراءات التحرِّي يمكن أن تحسِّن من الحساسية، أما الأسباب الكامنة وراء الأعداد المرتفعة للحالات السلبية عند الإناث فتحتاج لمزيد من الاستقصاءات.

ABSTRACT We tested the validity of vision screening in schools in 7 regions of Oman in 2003. Two researchers tested 1719 randomly selected students in 4 school grades using the Snellen E acuity test. Trained school nurses had previously screened 182 233 students. The visual status recorded in the 2 screenings was compared. Sensitivity of screening by nurses was 68.34% (95% CI: 67.30–69.38) and specificity 99.23% (95% CI: 99.19–99.27). The positive predictive value was 85.42% (95% CI: 84.63–86.21) and negative predictive value was 97.93% (95% CI: 97.87–98.00). The sensitivity of the vision test was significantly higher in females, older students and in North Sharqiya region. In general, the vision screening of school students in Oman has satisfactory validity. Periodic training of nurses and supervision of the screening procedures could improve its sensitivity. Underlying causes of the high numbers of false negative cases should be further investigated.

Validité du dépistage visuel réalisé par des infirmières scolaires dans sept régions d'Oman

RÉSUMÉ Nous avons testé la validité du dépistage visuel dans des écoles de sept régions d'Oman en 2003. Deux chercheurs ont testé 1719 élèves choisis de manière aléatoire dans quatre classes à l'aide du test de Snellen (test du E). Des infirmières scolaires formées avaient examiné auparavant 182 233 élèves. Le bilan visuel noté lors des deux examens a été comparé. La sensibilité de l'examen visuel réalisé par les infirmières était de 68,34 % (IC 95 % : 67,30-69,38) et la spécificité de 99,23 % (IC 95 % : 99,19-99,27). La valeur prédictive positive était de 85,42 % (IC 95 % : 84,63-86,21) et la valeur prédictive négative était de 97,93 % (IC 95 % : 97,87-98,00). La sensibilité du test de vision était significativement plus élevée chez les filles, chez les élèves plus âgés et dans la région septentrionale de Sharqiya. De manière générale, le dépistage visuel des écoliers et écolières à Oman avait une validité satisfaisante. La formation périodique des infirmières et le contrôle des procédures d'examen pourraient améliorer sa sensibilité. Les causes sous-jacentes du nombre élevé de cas faux négatifs devraient faire l'objet d'études approfondies.

[1]Eye and Ear Health Care Department; [2]School Health Department, Directorate General of Health Affairs; [3]Department of Noncommunicable Diseases, Ministry of Health, Muscat, Oman.
Received: 23/06/03; accepted: 20/10/03

Introduction

Despite the widespread acceptance of vision screening programmes as a means of detecting ocular disorders in children, there has been little formal assessment of their validity and reliability [*1*]. This is more challenging as different methods are used for vision screening, e.g. the Snellen letter acuity and Modified Clinical Technique vision screening kits, the Random Dot E stereogram and the hand-held autorefractor [*2*].

A study to assess the predictive ability of school screening programmes suggested the need for a detailed prospective study to review predictability of both test-positive and test-negative findings [*3*]. In our study, the validity of the school vision screening programme was evaluated using specificity and sensitivity parameters. First level screening was performed by trained nurses and was compared with screening by practising optometrists. Validating vision screening by estimating the number of false negatives was also done [*4*].

In Oman, the eye health care programme is aimed at the early detection of common and blinding eye diseases. Hence, trained nurses conduct vision screening annually, targeting students in 4 grades in all schools in Oman. Refractionists in each region recheck the students shortlisted with defective vision, refract them in schools and prescribe visual aids [*5*]. In 2002, the number of students with defective vision referred by nurses and subsequently found to be normal was high for 1st primary students but lower for 1st secondary students [*6*]. Rapid turnover of the health staff involved in this activity has raised serious doubts concerning the quality of the screening procedures. The programme therefore evaluated the validity of vision screening using sensitivity and specificity parameters, reviewed the predictability of vision screening for detection of refractive error and recommended steps to further strengthen the vision screening activities.

Methods

We carried out a cross-sectional agreement study on 182 233 students in 7 regions of Oman during school year 2002–2003. The study population was from 4 school grades: 1st primary (6–7 years), 4th primary (9–10 years), 1st preparatory (12–13 years) and 1st secondary (16–17 years).

The list of schools in each region and the number of students in each grade were provided by the Ministry of Education. The visual status of a randomly selected sample was examined by the study investigators. The visual status of the same students that had been noted by the school nurses during school year 2002–2003 was recovered from school health records.

Hypothesis: the vision screening done by school health staff matched the supervisor's screening in 90% or more of students. Null hypothesis: the vision screening done by school health staff does not match the supervisor's screening in 90% or more of the students.

The study aimed to achieve a goal of 90% power of the study and 95% significance level among a study population which ranged from 15 000 to 45 000 per region. With an acceptable error of 7%, the sample required was 137. To compensate for the clustering effect of students in selected schools and to cover loss of data, the sample was multiplied by a factor of 1.8. Thus, the minimum sample in each region was 250.

The list of schools was used to randomly select 4–6 schools in each region. Since the proportion of male and female students is almost equal, equal numbers of boys' and girls' schools were selected. In each

school, 1 class from each grade was randomly selected. If the class had less than 50 students, an additional sample was enrolled from another randomly selected class of the same grade. The aim was to enrol and examine 50 students in all 4 grades in 1 region and give an equal opportunity to all students of that grade in the school to participate in the study.

The field staff comprised 2 national eye health care supervisors who had at least 5 years of experience of vision screening.

The vision testing procedure and method of response were explained to all students. Each student then was called according to his or her serial number. The Snellen distant vision E chart was placed 6 metres away from the student. The vision of the right eye was tested first followed by the left and the results immediately noted on a standard form. Personal details of the students such as age, sex, area of residence and visual status of each eye with and without visual aids were collected. History of check-ups by an optician or ophthalmologist was obtained from students who had defective vision.

The school nurse had tested vision 3 months prior to the study and the visual status of each student had been recorded in the student's health booklet. These records were referred to after the vision testing was completed by the supervisors.

Definitions: if vision screening in 1 eye was found to have no more than 1 line difference in the 2 screenings, it was defined as being in agreement. If vision screening in 1 eye differed by more than 1 line in the 2 screenings, the vision screening of that student was defined as being in disagreement. The disagreement was further graded according to the difference in visual status. Sensitivity was defined as ability of vision screening by the nurse to correctly identify the students with defective vision. Specificity was defined as ability of vision screening by the nurse to correctly identify the students without defective vision. Positive predictive value was defined as ability of vision screening to correctly predict cases of defective vision among students with suspected defective vision. Negative predictive value was defined as ability of the test to correctly predict students without defective vision among those declared to have normal vision.

The data was computed using *EpiData*. Univariate analysis was conducted using *SPSS*, version 11. Agreement and disagreement rates per student were calculated. The sensitivity, specificity, false positives, false negatives, positive predictive and negative predictive values of the vision screening were estimated. The rates of validity parameters were projected for the study population. They were also adjusted by sex, school grade and region using indirect standardization. The determinants of these parameters by sex, school grade and region of residence were also evaluated. The frequencies, percentage proportions, odds ratios and 95% confidence intervals were estimated to validate the results.

To ensure a high and uniform quality of the study, a standardization workshop was conducted for the field staff. A pilot study was carried out in schools not selected for the study; on the basis of the pilot study, the methodology, data collection form and data entry format were revised. Field staff having at least 5 years experience in vision screening and supervision work were selected for the study. The study was supervised by the study investigators at various stages. During the pilot study, inter-observer variation was evaluated and was found to be minimal. The supervisors' skills in vision screening were also compared to those of optometrists and were found to match.

The authorities in the Department of School Health, Ministry of Health and Ministry of Education were approached and their consent was obtained for the study. Verbal consent of school principals was also taken. The results of the study were used to improve the vision screening of students. The results were also distributed to regional health authorities and health managers of related health programmes.

Due to logistic problems, the study could not be conducted in Dhofar, Musundam and Al Wousta regions of Oman. Hence, the result of the study should be extrapolated to the whole of Oman with caution. There was a gap of around 3 months between the vision screening done by the nurse and that done by the supervisors. It is assumed that vision status between the 2 screenings had not changed in most of the students. However, a marginal increase in refractive error or progress in pathology causing further deterioration of visual status in a limited number of cases cannot be ruled out.

Results

The profile of the study population and the sample we examined is given in Table 1. The total study population comprised 182 233 students in 4 school grades in 7 regions of Oman during the school year 2002–2003. We enrolled a sample of 1720 students as participants in our study. One student did not complete the vision testing as he had to leave the school. Of the 1719 students examined, 861 (50.1%) were male and 858 (49.9%) were female. The sample was evenly distributed between the 4 grades and the 7 health regions. The proportion of the study population and the sample differed by region so adjusted rates should be used for comparison.

Table 1 **Profile of the study population and the sample**

Variable	Study population (*N* = 182 233)		Sample (*n* = 1719)	
	No.	%	No.	%
Sex				
Male	94 276	51.7	861	50.1
Female	87 957	48.3	858	49.9
School grade				
1st primary	40 437	22.2	415	24.1
4th primary	48 396	26.6	416	24.2
1st preparatory	51 043	28.0	479	27.9
1st secondary	42 357	23.2	409	23.8
Region				
Muscat	34 056	18.7	250	14.5
Dhakhiliya	29 101	16.0	237	13.8
North Sharqiya	14 542	8.0	255	14.8
South Sharqiya	15 750	8.6	228	13.3
North Batinah	45 280	24.8	235	13.7
South Batinah	26 621	14.6	259	15.1
Dhahirah	16 883	9.3	255	14.8

The vision of 1599 students (93.0%) was 6/6 in both eyes in both screenings. In 74 (4.30%) students, vision was impaired in at least 1 eye. In 13 (0.76%) students, the screening by the nurse suggested impaired vision but screening by the supervisor showed 6/6 vision. In 33 (1.92%) students the screening by the nurse suggested either 6/6 or 6/9 vision, but on rescreening by a supervisor, these students were found to have a higher grade of defective vision. Based on these findings, we calculated validity parameters for the sample and for the study population as a whole. For the statistical validation, 95% confidence intervals were also estimated (Table 2).

The validity parameters of vision screening by sex are given in Table 3. The specificity of screening was high for both sexes. However, the sensitivity of vision

Table 2 **Parameters of validity**

Parameter	No.	Crude OR	Adjusted OR	95% CI
True positives	74	4.30	4.24	3.79–4.69
False positives	13	93.02	93.07	92.95–93.19
False negatives	33	0.76	0.72	0.26–1.18
True negatives	1599	1.92	1.96	1.51–2.41
		%	%	
Sensitivity		69.16	68.34	67.30–69.38
Specificity		99.19	99.23	99.19–99.27
Positive predictive value		85.06	85.42	84.63–86.21
Negative predictive value		97.98	97.93	97.87–98.00

Rates are adjusted for sex, school grade and region.
The false positive rate was 13/1719 × 100 = 0.76%.
The false negative rate was 33/1719 × 100 = 1.92%.
OR = odds ratio; CI = confidence interval.

screening was significantly higher in female than in male students.

The agreement and disagreement rates for 1st primary and 4th primary were determined and compared to those for 1st preparatory and 1st secondary students (Table 4). The screening of students in higher grades by school nurses had significantly higher specificity than that for primary students.

Table 3 **Validity of vision screening by sex**

Variable	Males (*n* = 861)		Females (*n* = 858)	
	No.	%	No.	%
True positives	32	4.0	42	4.5
False positives	2	0.3	11	1.2
False negatives	18	2.2	15	1.7
True negatives	809	93.5	790	92.6
	% (95% CI)		% (95% CI)	
Sensitivity	64.87 (63.35–66.39)		72.09 (70.68–73.49)	
Specificity	99.73 (99.69–99.76)		98.69 (98.62–98.77)	
Positive predictive value	94.02 (93.29–94.75)		78.46 (77.32–79.60)	
Negative predictive value	97.72 (97.62–97.81)		98.17 (98.08–98.26)	

Rates are adjusted for school grade and region.
CI = confidence interval.

The validity parameters (adjusted for sex and school grade) for each region were compared (Table 5). Sensitivity ranged from 57.29% in Dhahirah to 80.08% in North Sharqiya.

Discussion

After 10 years of annual vision screening in schools, a review was needed. Our study tested the validity of vision screening. On the basis of our results, the programme would be able to strengthen the strategy for reducing eye strain in schoolchildren. Thus, the study was crucial for the eye care programme.

Since the sample was evenly distributed in all regions and the number of school students varied in different regions and grades, the study results were adjusted before outcomes of variants were compared. This also helped to minimize the confounding effects of school grade, sex, region and other related confounders on the validity.

The cooperation of students could be the effect modifiers in such a study [*7*]. Proper explanation of the procedures along with help from teachers ensured the full cooperation of all participants.

The vision screening done by the nurses had a specificity of 99.23%. Thus, vision screening by nurses could accurately identify students who did not have vision defects. The test had 68.34% sensitivity. Thus, the vision screening procedures missed a substantial proportion of students with defective vision.

In a study in New York State in the United States of America (USA), using a vision screening battery, the Snellen test was 100% specific but it missed 75.5% of the children found to have vision problems when given a complete visual examination [*8*]. Although the methodology is different in the 2 studies, our study had a higher rate of specificity and a relatively low sensitivity. The World Health Organization has recommended that vision screening should

Table 4 **Validity of vision screening by school grade**

Variable	1st & 4th primary (*n* = 831)		Preparatory and secondary (*n* = 888)	
	No.	%	No.	%
True positives	14	1.67	60	6.68
False positives	4	0.53	9	0.91
False negatives	11	1.36	22	2.54
True negatives	802	96.43	797	89.87
	% (95% CI)		**% (95% CI)**	
Sensitivity	55.08 (52.55–57.61)		72.49 (71.39–73.60)	
Specificity	99.45 (99.40–99.50)		99.00 (98.93–99.07)	
Positive predictive value	75.87 (73.97–77.76)		88.06 (87.30–88.81)	
Negative predictive value	98.61 (98.53–98.68)		97.26 (97.15–97.36)	

Rates are adjusted for sex and region.
CI = confidence interval.

Table 5 **Validity of vision screening by region**

Region	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)
Muscat	67.64	98.92	84.21	97.30
Dhakhiliya	75.84	99.19	84.23	98.55
North Sharqiya	80.08	97.83	73.22	98.51
South Sharqiya	67.38	98.52	74.00	97.97
North Batinah	62.71	98.72	75.25	97.71
South Batinah	74.78	99.98	99.61	98.29
Dhahirah	57.29	99.97	99.09	97.53

Rates are adjusted for sex and school grade.

have at least 80% specificity and sensitivity for it to be cost-effective (A. Choudhury, unpublished data, 2003).

Vision screening of 652 elementary students by lay volunteers was compared to that of optometrists in the USA. The Modified Clinical Technique was used in this study. It showed 5.5% false positives and 4.3% false negatives [*9*]. Our study had a very low number of false positives (0.76%) and false negatives (1.92%). Considering a difference of 1 line as normal in our study could be a lenient criterion resulting in these low rates.

There is no evidence to suggest that a more complex protocol would improve the detection of ocular disorders in screening. Rather, a more effective implementation of the current screening procedure gives better results [*1*]. In our study, simple vision testing methods were used and still had valid outcomes. This is in agreement with the observations of earlier studies [*1*,*9*].

In view of the shortage of qualified opticians, it would be impossible to screen the large number of children in the present school population. Wong found that following an educational programme and collaboration with optometrists, nurses were able to correctly refer a high percentage of children [*10*]. Therefore, first level screening should be conducted by nurses or other school staff trained in such procedures. Oman has adopted a similar model of using simple vision screening tools, annual training of nurses and active supervision by opticians. This has resulted in a reasonable quality of screening. Countries with limited resources should focus on strengthening vision screening procedures using similar models and strategies instead of investing in costly equipment and using complicated screening methods.

Bailey compared vision screening procedures done by optometric students with those done by licensed opticians using the Modified Clinical Technique. They were found to have less satisfactory validity. It was proposed that the limited experience of the first level vision screeners was mainly responsible for the low predictive ability of this test [*3*]. The staff involved in our study had been trained in vision screening frequently. This could have accounted for the high validity in our study.

Vision screening of schoolchildren in many states of the USA has suggested that even if different procedures and criteria are used, school screening may show a false positive rate of 30% or more [*11*,*12*]. In

our study, the rate for false positives and false negatives was less than 2%. The low rate of refractive error and the high quality of vision screening in our study could account for these observations.

The vision screening carried out by nurses could accurately predict the presence of refractive error in almost 70% of the students with this problem. The number of students declared as having normal vision by a nurse after vision screening was almost 98% accurate. This high rate could be due to the large number of students in our study sample who did not have defective vision.

Refractive errors, which often become manifest during school age, rarely carry any serious prognostic implications. Experts disagree on whether an uncorrected refractive error that would be detected by screening has any adverse effects on academic performance in school-age children [*13,14*]. Hence, the 1.92% asymptomatic refractive error cases that were missed in schools might be of minimal importance.

The sensitivity of vision screening in our study was significantly higher for female than for male students. Differences in the attitudes of male and female students to cooperating with female nurses and male supervisors could be responsible for this observation.

Refractive error may be marginal in children of primary-school age compared to students in preparatory and secondary grades. Difference in prevalence in these 2 groups of students and differential understanding of vision screening procedures may have resulted in high specificity in students of higher grades.

Differences in the training of the nurses as well as in the quality of vision screening by different nurses could account for the regional variation in the validity.

Vision screening by nurses and second level screening performed by school refractionists in Oman is similar to the model proposed in the USA [*15*]. This would certainly reduce unnecessary referrals to the ophthalmologist.

Vision screening in schools by trained nurses in a large part of Oman has very high validity. However, false negative cases observed in this study could be further reduced through vigilant screening. Further operational research is needed to determine yield and efficiency for the low rate of refractive error cases in 1st primary grade.

Recommendations

Vision screening in schools is an important strategy in many countries to detect and manage defective vision in the early stages. The use of primary staff for first level screening needs to be validity tested. In Oman, screening sensitivity was 68.3% and specificity 99.2.% The large number of false negative cases compromised the quality of vision screening. The underlying causes of low sensitivity should be identified and addressed. Further training and periodic supervision of vision screening by nurses could improve the validity of the vision test. The sensitivity of vision screening in primary school and validity was lower than in preparatory and secondary students. It could be improved through training and more thorough screening

Vision screening of school students in Oman has satisfactory validity. Its low sensitivity needs to be improved. Periodic training of nurses and supervision of the screening procedures could improve the quality of vision screening. Because of the low yield, vision screening of primary-school students should perhaps be discon-

tinued and replaced by preschool vision screening. Determinants of low sensitivity such as being male and of young age, as well as regional variation, should be further investigated to strengthen the quality of screening.

References

1. Macfarlane DJ, Fitzgerald WJ, Stark DJ. Assessment of the Queensland School Health Service vision screening programme. ***Australian and New Zealand journal of ophthalmology***, 1987, 15(3): 175–80.
2. Hammond RS, Schmidt PP. A Random Dot E stereogram for the vision screening of children. ***Archives of ophthalmology***, 1986, 104(1):54–60.
3. Bailey RN. Assessing the predictive ability of the test-positive findings of an elementary school vision screening. ***Optometry and vision science***, 1998, 75(9): 682–91.
4. Robinson B et al. Measurement of the validity of a preschool vision screening program. ***American journal of public health***, 1999, 89(2):193–8.
5. ***Eye health care manual***, 1st ed. Muscat, Oman, Ministry of Health and United Nations Children's Fund, 1995:55–7.
6. ***Annual health report year 2002***. Muscat, Oman, Ministry of Health, 2003:1–41.
7. ***Elimination of avoidable visual disability due to refractive errors***. Geneva, World Health Organization, 2000 (WHO/PBL/00.79).
8. Lieberman S et al. Validation study of the New York State Optometric Association (NYSOA) vision screening battery. ***American journal of optometry and physiological optics***, 1985, 62(3):165–8.
9. Wick B, O'Neal M, Ricker P. Comparison of vision screening by lay and professional personnel. ***American journal of optometry and physiological optics***, 1976, 53(9 Pt 1):474–8.
10. Wong SG. Comparison of vision screening performed by optometrists and nurses. ***American journal of optometry and physiological optics***, 1978, 55(6): 384–9.
11. Appelboom TM. A history of vision screening. ***Journal of school health***, 1985, 55(4):138–41.
12. Romano PE. Summary and conclusions. Symposium on preschool/school vision and eye screening: current techniques and future trends. ***American orthoptic journal***, 1988, 38:73–80.
13. Halveston EM et al. Visual function and academic performance. ***American journal of ophthalmology***, 1985, 99(3):346–55.
14. Rosner J, Rosner J. Comparison of visual characteristics in children with and without learning difficulties. ***American journal of optometry and physiological optics***, 1987, 64(7):531–3.
15. Donaldson LA et al. Pediatric community vision screening with combined optometric and orthoptic care: a 64-month review. ***Ophthalmic and physiological optics***, 2002, 22(1):26–31.

Schoolteachers' knowledge of common health problems in Bahrain

F.A. Alnasir[1] and J.H. Skerman[2]

معارف معلّمي المدارس حول المشكلات الصحية الشائعة في البحرين

فيصل الأنصاري، جوناثان شيرمان

الخلاصة: يُعَدُّ المعلّمون مصدراً مفيداً للمعلومات الصحية يَسْتَقي منه الطلاب، مما ينبغي معه أن يكون لدى المعلّمين معارف دقيقة عن القضايا الصحية. وقد قام الباحثان بتقييم معارف معلّمي المدارس حول المشكلات الصحية الشائعة، باستخدام استبيان مصمم ومختبر مُسْبَقاً، عن المعلومات المتعلقة بالمعطيات الديموغرافية الخاصة بمعلّمي المدارس ومعارفهم حول خمس مشكلات شائعة في البحرين، وهي الربو القصبي، وفقر الدم المنجلي، وفرط ضغط الدم، والسكّري، وخطر التدخين. ثم قام الباحثان بتحليل المعطيات المجموعة من 1140 من المستجيبين للدراسة ممن تم اختيارهم عشوائياً من بين المعلّمين في جميع مدارس البحرين. وقد أحرز معلّمو المدارس ما يقرب من 50٪ من معدل المعارف حول المشكلات الصحية الشائعة، مما يدل على الحاجة إلى تثقيف معلّمي الدارس حول الصحة، لتحسين معارفهم وقدراتهم على نشر المعارف والمعلومات الصحية بين تلاميذهم.

ABSTRACT Schoolteacher could be a useful source of health information for students but that they themselves would have to possess adequate and accurate knowledge of health issues. We assessed Bahraini schoolteachers' knowledge of some common health problems using a pre-tested, structured questionnaire which requested information on schools, teachers' demographic data, and knowledge about 5 common health problems in Bahrain: bronchial asthma, sickle-cell anaemia, hypertension, diabetes mellitus and the dangers of smoking. We analysed the data on 1140 respondents from a random selection of teachers in all schools in Bahrain. The schoolteachers scored only around 50% on average for knowledge about common health problems which indicates a need to educate schoolteachers about health in order to improve their knowledge and their capability to disseminate health knowledge and information to students.

Connaissance des problèmes de santé courants par les enseignants scolaires à Bahreïn

RÉSUMÉ Les enseignants scolaires pourraient représenter une source utile d'information sur la santé pour les élèves mais il devraient eux-mêmes posséder des connaissances suffisantes et exactes sur les questions de santé. Nous avons évalué les connaissances des enseignants scolaires Bahreïnites concernant des problèmes de santé courants à l'aide d'un questionnaire structuré, testé au préalable, qui cherchait à recueillir des informations sur les écoles, des données démographiques concernant les enseignants et la connaissance de cinq problèmes de santé courants à Bahreïn : l'asthme bronchique, la drépanocytose, l'hypertension, le diabète sucré et les dangers du tabagisme. Nous avons analysé les données de 1140 répondants dans une sélection aléatoire d'enseignants de toutes les écoles de Bahreïn. Les enseignants n'ont obtenu qu'un score d'environ 50 % en moyenne pour les connaissances concernant ces problèmes de santé courants, ce qui indique une nécessité d'éduquer les enseignants en matière de santé afin d'améliorer leurs connaissances et leur capacité à diffuser des connaissances et des informations sur la santé aux élèves.

[1]Department of Family and Community Medicine, College of Medicine and Medical Sciences, Arabian Gulf University, Bahrain.
[2]Department of Anaesthesia and Intensive Care, College of Medicine and Medical Sciences, Arabian Gulf University and Salmaniya Medical Complex, Bahrain.
Received: 01/07/03; accepted: 29/10/03

Introduction

Schoolteachers form a group with great potential for influencing the health knowledge and attitudes of students and other population groups. Schoolteachers' perceptions of health, their attitudes and practices, and their knowledge of common health problems could be essential factors in optimizing their roles as health educators in society.

Many adult behaviour patterns and attitudes develop in early childhood. In addition there is a growing acceptance of the need for health education at primary school age. For example, it has been found that various interventions such as improving teachers' awareness of cancer education issues and providing appropriate cancer education resources might increase the level of primary school-based cancer education [*1*].

Schoolteachers are expected to be role models so that students can emulate and adopt their behaviour and attitudes. In Sweden, the majority of school pupils thought that schoolteachers were the best sources of information for sexually transmitted infections and sexuality [*2*]. Schoolteachers are also considered the major source of information for their students and would appear to be suitable as health educators [*3*]. In Australia, teachers and the clergy have been identified as "gatekeepers" who might serve as a first line of assistance for distressed young people [*4*].

Since current emphasis in health education is on prevention of serious illness through lifestyles that promote wholeness, teachers are well placed professionally to carry out health education at school [*5,6*]. Teachers' education is considered a major factor in the effective implementation of comprehensive school health [*7*]. Attitudes, behaviour and general knowledge are disseminated to the students from the teachers, either deliberately or unconsciously. In order to raise students' health knowledge and improve their attitudes toward health, they should be placed in an appropriate environment that is based on 3 main determining factors: teachers, school and society (including home).

School and health professionals should continue to advocate school-wide policies and programmes that support both students and teachers if the goal of an integrated healthy school environment is to be realized [*8*]. Ministries of education and health should organize seminars on health education [*9*]. Educational health packages could be developed with collaboration between teachers who have an understanding of the principles of curriculum design and health professionals who are fully aware of health problems [*10*]. Development efforts by teachers, including training and ongoing reinforcement to increase their sense of preparedness, have significant effects in the classroom [*11*]. In Nigeria, most teachers felt that health education was important and should be an integral part of the curriculum [*12*]. Multicultural attitudes and knowledge on the part of teachers changed in a positive direction when candidates attended a teacher preparation programme [*13*].

It is reported that the formation of a population's healthy lifestyle, which is one of the main tasks of Soviet medicine, can be accomplished with the help of school health education teams [*14*]. It has been documented, however, that in Bahrain school health education is not included in the curriculum [*15*]. Few states in the United States of America include health education in their state tests, and elementary school teachers often do not feel it is an important subject and therefore spend insufficient time on health instruction in the classroom [*16*].

It was our goal to study teachers' awareness about common health problems in Bahrain. We hypothesized that the teachers were well informed about these problems and hence would be able to disseminate information to others, specifically students.

Methods

Information was collected about the schools in Bahrain and permission for conducting the study was obtained from the Ministry of Education, who sent out an information circular to all schools in the country. The study was carried out during 1997–1998. The target population was all Bahraini teachers of all disciplines in 49 randomly selected schools.

Schools in the 5 geographic regions of Bahrain (Muharraq, Manama, Northern area, Central area and Western area) were selected for this study. The total number of schools in these areas is 152, with a total of 3360 teachers. A random sample of 49 schools was selected. Stratified random sampling was done, giving appropriate representation to the 5 regions, and taking into account the number of Bahraini teachers in each school, the type of school, and the locality. All 1248 Bahraini teachers in those schools were included in the study.

The study tool for this investigation was a questionnaire. Based on a comprehensive review of the literature, a 4-item survey was designed. Items addressed each of the following areas: information about the school, teachers' demographic characteristics, teachers' health perceptions, and health knowledge. The questionnaire was adapted to the local language and designed in a simple way to make it easy for the selected teachers to read and complete. The face value and content validity of the questionnaire were tested by distributing it to doctors in various specialties and obtaining their feedback. It was also tested for repeatability by sending it again to the same doctors after a 1-week lapse. A pilot study was done to test the various areas of the questionnaire.

The health information portion of the questionnaire was aimed at collecting information about the teachers' health status and their experiences of illness. Five common health problems in Bahrain (asthma, sickle-cell anaemia, hypertension, diabetes mellitus and the dangers of smoking) were chosen because of their high prevalence among Bahrainis. The teachers were asked questions (a total of 48: 8 questions for the smoking problem and 10 for each of the others) related to signs, symptoms and complications of those problems. Some untrue information for each problem was included to test the teachers' knowledge. The teachers were asked to give their response to the pre-set questions by writing "Yes" (agree), "No" (do not agree) or "Do not know" to the answer. Each blank space was considered a missing value (i.e. teachers did not respond to it).

After analysing the responses, a score of 1 was given for the correct answer and 0 for other answers (wrong, missing or "Do not know" answers).

No questions inquiring about whether the teachers had received any formal training or special education about common health problems were included.

The head teacher of each school was given complete information on the study, either by telephone or through direct contact. The questionnaires were delivered to the teachers in the selected schools in the morning and collected at the end of the same day or after a maximum of 2 days. An accompanying letter was written to the teachers giving them information on the study, its aims, how to complete the questionnaire and requesting their cooperation.

Data were analysed using *SPSS*. Results were cross-tabulated and chi-squared calculated. The knowledge portions of the data were scored and assessed as percentage scores.

Results

Of the 1254 teachers included in the sample, 1140 (91%) responded and 114 (9%) did not. Efforts were made to obtain the questionnaire from the non-respondents, but without success. The general characteristics of these non-respondents, such as age, sex and type of school, were investigated and were not found to differ from those of the respondents. There were 679 (60%) female respondents and 461 (40%) male. Age range was 20–58 years (mean 32.7 years, median 32 years, standard deviation [SD] 6.17). Only 15% of the teachers stated they were above 40 years of age. Of the 220 teachers who did not wish to disclose their ages (19%), the majority (94%) were female. Of the responding teachers, 78% were married, 20% were single and 2% were either divorced or widowed. There were 774 teachers who were married and had children (range 1–16 children, mean 3). More male teachers than female teachers had children (65% compared to 35%).

Of the 1091 who responded to the question related to the teachers' level of education, 19% had only high school education and 81% had higher education, which includes a Diploma or Bachelor's degree. Teachers in primary and intermediate schools were younger (≤ 32 years) ($P < 0.01$) and more of them had degres than secondary school teachers. More females than males had higher education. Of the total, 29% taught science subjects, including mathematics, and 71% taught arts subjects. There were 1068 responses (94%) to the question about the duration of occupation. Duration ranged from 1 year to 35 years (mean 12.3 years, SD 7.3). Only 6% of the teachers were smokers, of whom the majority (94%) were male, while 4% were ex-smokers. Regarding alcohol consumption, since it is not usual in an Islamic country, not all who drink admit to it, and the others may find the question offensive. Of the 98% who responded to this question, only 14 (1%), all of whom were male, admitted to drinking alcohol. Some 40% of the teachers were the heads of the household, and 35% said they shared that responsibility.

Table 1 shows the teachers' responses to questions on their own health and health-related attitudes. The health status of the teachers was satisfactory as only 16% had any acute illness during the past 6 months.

The total scores for each teacher, which represented correct answers, ranged between 0 and 41 (mean 21.9, median 24, SD 9.3). Only 1 teacher obtained the highest score, but there were 39 teachers (3%) who scored 0, i.e. no knowledge at all. Table 2 shows the scores for each health problem. The total scores for knowledge, after categorizing into 2 groups (group 1 = ≤ 24, group 2 = > 24) according to the median, were studied in relation to all other variables in the study (Table 3). There were a large number of missing values on the topics of sickle-cell anaemia and asthma, while there were no missing values on knowledge related to hypertension, diabetes mellitus or the dangers of smoking.

A higher percentage of females than males were teaching science, 23% compared with 16% (chi-squared 7.225, $P < 0.5$). More of the younger teachers (≤ 32 years) were teaching science subjects (46%), while more of the older teachers (> 32 years) were teaching arts subjects (77%) (chi-squared 20.81, $P < 0.001$).

Table 1 **Health and health-related attitudes of teachers**

Variable	Yes		No		Did not respond	
	No.	%	No.	%	No.	%
Suffered from any acute illness during the past 6 months	179	16	936	82	25	2
Any chronic illness	344	30	759	67	37	3
Family illness	322	28	785	69	33	3
Doing exercise	191	17	862	76	87	8
Hospital admissions[a]	137	12	963	85	40	4
	Good		**Unsatisfactory**		**No knowledge**	
Teachers' perception of their general health[b]	930	82	100	9	68	6
Perception of health services in Bahrain	762	67	265	23	113	10

[a]More females (72%) than males (28%) reported having been admitted to hospital.
[b]42 (4%) teachers did not respond.

In general, teachers who had no chronic illness had better health knowledge for each category of health knowledge (chi-squared 15.8, $P < 0.001$). Of the 93% of teachers who had not had any recent illness, 88% perceived their general health as satisfactory (chi-squared 67.1, $P < 0.001$).

With regard to the dangers of smoking, surprisingly, it was found that there was no relationship between the smoking habit and knowledge about smoking ($P < 0.9$). However knowledge about smoking increased as the number of years of occupation increased (chi-squared 11.673, $P < 0.001$).

Table 2 **Teachers' scores on knowledge of five common health problems in Bahrain**

Health problem	Respondents (n = 1140)		No. of questions	Score			SD
	No.	%		Range	Mean	Median	
Sickle-cell anaemia	1053	92	10	0–10	4.88	5	1.980
Smoking	1067	94	8	0–8	5.28	6	1.852
Asthma	1029	90	10	0–10	5.16	5	2.185
Hypertension	969	85	10	0–10	3.00	3	1.899
Diabetes mellitus	1064	93	10	0–10	5.34	6	2.133

SD = standard deviation.

Table 3 **Correlation of some characteristics of teachers to better knowledge of five common health problems in Bahrain**

Characteristic	Better knowledge	*P*-value
Duration of occupation as a teacher	Fewer years > more years	< 0.05
Type of school	Primary + intermediate > secondary	< 0.02
Sex	Female > male	< 0.001
Marital status	Married > single	< 0.02
Teaching discipline	Science > arts	< 0.02
Recent illness	No recent illness > having recent illness	< 0.05
Chronic illness	No chronic illness > having chronic illness	< 0.001
Family size	Smaller family size > larger family size	< 0.01

Table 4 shows some characteristics that were found to have a significant relationship with teachers having adequate knowledge (≥ mean) about diabetes mellitus. Knowledge of other health problems was found not to be related to the teachers' characteristics.

There was no relationship between suffering from chronic illness and knowledge about asthma, sickle-cell anaemia or the

Table 4 **Relationship between characteristics of teachers and having adequate (≥ mean) knowledge about diabetes**

Characteristic	Teachers with adequate knowledge, %	*P*-value	χ^2
Sex			
Male	90	< 0.001	33.927
Female	77		
Discipline taught			
Science	90	< 0.05	4.505
Art	84		
Family illness			
Yes	89	< 0.05	5.240
No	83		
Perception of own health			
Satisfactory	84	< 0.05	3.897
Unsatisfactory	93		
Drinking alcohol			
Yes	76	< 0.002	5.040
No	85		

dangers of smoking. There was a significant relationship between suffering from chronic illness and knowledge about diabetes mellitus (chi-squared 9.2, $P < 0.02$) and knowledge about hypertension (chi-squared 6.4, $P < 0.001$)

Discussion

The majority of the teachers who participated in this study were young adults, and most had a university degree, either a Diploma or Bachelor degree. Most of the teachers were female, and we found they had better health knowledge than the males. A study done in the United States of America indicated that students' attitudes improved if their teachers were more educated and older. It was reported that the students' perception and attitude regarding adolescent homosexuality varied with the teacher's sex, age, educational level and teaching status [*17*].

The overall knowledge of the schoolteachers was found to be average in the areas related to sickle-cell anaemia, asthma and diabetes mellitus. While it was poor (< mean) in the area of hypertension, they had a good (≥ mean) knowledge of the dangers of smoking. Considering that the prevalence of these problems is high in Bahrain and the surrounding areas (3%–5% for sickle-cell anaemia, 25% for diabetes mellitus, 5% for bronchial asthma and approximately 15% for hypertension) [*18*], it is alarming that schoolteachers are not more aware of the problems. It is not surprising therefore if students lack information about such problems.

Teachers who had personal experience of illness, i.e. chronic or acute illness, either at the time of the study or earlier in life, or who had a family member with a significant illness, knew more in the areas of diabetes mellitus and hypertension. Both of these are chronic conditions and are very common in our community. This could explain why teachers were more informed in these 2 areas than the other areas

There was no relationship between teachers' perceptions regarding their own health or the health services in Bahrain and their knowledge of common health problems. This finding was supported by results of another study which found that teachers' health beliefs are not linked to whether teachers teach health generally [*19*].

Surprisingly, primary and intermediate school teachers had better knowledge than secondary school teachers. This could be explained by the fact that they may be younger and more of them have university degrees. Such findings regarding knowledge about common diseases are supported by studies in other parts of the world. A study in Brazil found that in areas where helminthic diseases are known to have been present for a long time, teachers and pupils still had little information on them, nor were they aware of the mechanism of transmission [*20*].

Another barrier to quality health instruction is when little or no in-service training is available for teachers. Several conditions are necessary for the development of learning opportunities allowing teachers freedom to develop new understandings of teaching and learning. Poor knowledge of health can be attributed to the fact that health education is not a priority at many schools, and can also be related to the fact that health education questions are usually absent from end of year examinations [*16*]. Most teachers in our study were self-taught with regard to health education as there is no formal training, and relied primarily on traditional teacher-centred instruction methods. In order to deliver effective health education in schools,

teachers require a substantial body of knowledge and a variety of skills [*21*,*22*]. The type of training programme offered usually has a marked influence on the length and type of programme they offer to their students [*23*].

Our findings are in agreement with those of several other reports which indicated that teachers' health knowledge is deficient and this may ultimately affect their ability either to deliver health education or to manage acute health problems in school. In one study it was found that the majority of teachers encounter child abuse among their students although they did not receive sufficient education on how to address it [*24*]. In another study it was reported that teachers needed more knowledge regarding head lice and were significantly more knowledgeable as teaching experience increased [*25*]. In an Indian study about sex education, pupils in one school were reassessed after a health talk and distribution of a handout. Despite having had no formal sex education, most respondents were reasonably well informed about the transmission of HIV. Media teachers and health workers were quoted as the main sources of knowledge [*26*]. In a Canadian study on the effectiveness of school-based sexual health education, it was found that it depended in part on the preparation of the teachers [*24*]. The delivery of consistently high quality sexual health education in schools requires that all teachers of sexual health education are adequately prepared and acquire a substantial body of knowledge.

Conclusion

We found that there was a deficiency in teachers' health knowledge and therefore there is a need to educate schoolteachers about health, particularly about health problems prevailing in the society. There should be regular pre-service and in-service training regarding such problems. Health and education ministries in Bahrain should organize joint seminars for schoolteachers on health education to improve their level of health awareness. This would help teachers to develop health education packages in collaboration with the curriculum designers and health professionals to tackle current knowledge about health-related problems.

References

1. Carey P et al. Cancer education and the primary school teacher in England and Wales. ***Journal of cancer education***, 1995, 10(1):48–52.
2. Persson E, Sandstrom B, Jarlbro G. Sources of information, experiences and opinions on sexuality, contraception and STD protection among young Swedish students. ***Advances in contraception***, 1992, 8(1):41–9.
3. McGovern M, Barry MM. Death education: knowledge, attitudes and perspectives of Irish parents and teachers. ***Death studies***, 2000, 24(4):325–33.
4. Leane W, Shute R. Youth suicide: the knowledge and attitudes of Australian teachers and clergy. ***Suicide and life-threatening behaviour***, 1998, 28(2):165–73.
5. Mull, SS. The role of the health educator in development of self-esteem. ***Journal of health education***, 1991, 22:349–51.
6. Masvidal RM et al. La educación sanitaria en la escuela [Health education in school]. ***Atención primaria*** 1995, 15(6): 369–70, 372.

7. Wood DN. ***Teacher credential candidates' perceptions of the need for pre-service training in comprehensive health education***. Paper presented at the annual meeting of the American School Health Association, Milwaukee, Wisconsin, 1995.

8. Kubik MY et al. Food-related beliefs, eating behavior, and classroom food practices of middle school teachers. ***Journal of school health***, 2002, 72(8):339–45.

9. Brook U. Teachers' attitudes towards AIDS: an explorative study in Israel. ***Patient education and counseling***, 1994, 24(3):337–40.

10. Henry RL et al. Integrated health and education input in the development of educational resources about asthma for schools. ***Journal of paediatric and child health***, 1994, 30(6):492–6.

11. Hausman AJ, Ruzek SB. Implementation of comprehensive school health education in elementary schools: focus on teacher concerns. ***Journal of school health***, 1995, 65(3):81–6.

12. Fabiyi AK, Blumenthal DS. Health education in Nigerian secondary schools. ***Journal of community health***, 1991, 16(3):151–8.

13. Capella-Santana N. Voices of teacher candidates: positive changes in multicultural attitudes and knowledge. ***Journal of educational research***, 2003, 96(3):182–92.

14. Tsurikov VT, Gavriushenko VV. Iz opyta organizatsii smotra-konkursa shkol'nykh sanprosvetagitbrigad. [Experience in organizing competition of school health education teams]. ***Sovetskoe zdravookhranenie***, 1991, (5): 54–6.

15. Roemer R. ***Legislative action to combat the world tobacco epidemic***, 2nd ed. Geneva, World Health Organization, 1993:210.

16. Telljohann SK et al. Effects of an inservice workshop on the health teaching self-efficacy of elementary school teachers. ***Journal of school health***, 1996, 66(7):261–5.

17. Telljohann SK et al. Teaching about sexual orientation by secondary health teachers. ***Journal of school health***, 1995, 65(1):18–22.

18. Health Information Directorate. ***Health statistics report – 2003***. Bahrain, Ministry of Health, 2003.

19. Carey P et al. Is health locus of control related to health education activity? ***Psychological reports***, 1995, 76(3 pt 2): 1389–90.

20. Dos Santos MG et al. Educacao em saúde em escolas públicas de 1 grau da periferia de Belo Horizonte, MG, Brasil. II - Conhecimentos, opinioes e prevalencia de helmintiases entre alunos e professors. [Health education in 1st grade public schools at the periphery of Belo Horizonte, Brazil. II. Knowledge, opinion and prevalence of helminthiasis among students and teachers]. ***Revista do Instituto de Medicina Tropical de São Paulo***, 1993, 35(6):573–9.

21. Gingiss PL, Basen-Engquist K. HIV education practices and training needs of middle school and high school teachers. ***Journal of school health***, 1994, 64(7): 285–90.

22. McKay A, Barrett M. Pre-service sexual health education training of elementary, secondary, and physical health education teachers in Canadian faculties of education. ***Canadian journal of human sexuality***, 1999, 8(2):91–101.

23. Sequier A, Demarteau M, Pereira M. L'analyse des représentations: un moyen d'évaluer la formation des enseignants en éducation pour la santé. [Representational analysis: a means to

evaluate teacher training in health education]. ***Promotion & education***, 1994, 1(3):14–8.

24. Abrahams N, Casey K, Daro D. Teachers' knowledge, attitudes and beliefs about child abuse and its prevention. ***Child abuse and neglect***, 1992, 16(2):229–38.

25. Kirchofer GM, Price JH, Telljohann SK. Primary grade teachers' knowledge and perceptions of head lice. ***Journal of school health***, 2001, 71(9):448–52.

26. Agrawal KH et al. Knowledge of and attitudes to HIV/AIDS of senior secondary school pupils and trainee teachers in Udupi District, Karanataka, India. ***Annals of tropical paediatrics***, 1999, 19(2):143–9.

Note from the Editor

We would like to inform our readers that the next issue of EMHJ (Volume 10 No. 6) will be a Special Issue on Nutrition.

Comparison of prostaglandin E_2 tablets or Foley catheter for labour induction in grand multiparas

M.I. Al-Taani[1]

مقارنة بين البروستاغلاندين E_2 وبين قثطرة فولي في تحريض المخاض لدى من زاد لديهن عدد الولادات عن خمسة

محمد الطعاني

الخلاصة: قارن الباحث بين كفاءة وسلامة وحصائل استخدام البروستاغلاندين E_2، واستخدام قثطرة فولي في تحريض المخاض لدى من ولدت أكثر من خمس مرات. ففي إحدى المستشفيات الأردنية درست 147 امرأة ممن كانت لديهن أَحْراز بيشوب تساوي أو تقل عن 5 بإعطاء 3 ميلي غرام من البروستاغلاندين E_2 على شكل أقراص مهبليَّة عند 75 منهن، أو باستخدام قثطرة فولي بضخ 50 ميلي لتر فيها لدى 72 امرأة أخرى. وقد لوحظ أن التغيُّر في أَحْراز بيشوب أعلى بكثير لدى من استخدم لديهن البروستاغلاندين E_2 بالمقارنة مع من استخدم لديهن قثطار فولي، كما كان الزمن المنقضي بين بدء التحريض وبين الولادة أقصر بكثير عند من استخدم لديهن البروستاغلاندين E_2. كذلك كان عدد اللواتي احتَجْنَ للأوكسيتوسين لتقوية المخاض أكبر في مَن استخدمت لديهن قثطرة فولي ممَّن استخدم لديهن البروستاغلاندين E_2. وكانت الضائقة الجنينية أكثر تكراراً من الناحية الإحصائية. وهكذا تدلّ الدراسة على أن من الأفضل استخدام أقراص مهبلية من البروستاغلاندين E_2 لإنضاج عنق الرحم ولتحريض المخاض.

ABSTRACT The efficacy, safety and outcome of prostaglandin (PG)E_2 was compared with Foley catheter for labour induction in grand multiparous women. At a hospital in Jordan, 147 women with Bishop score ≤ 5 were randomized to receive 3 mg PGE_2 vaginal tablets (***n*** = 75) or 50 mL intracervical Foley catheter (***n*** = 72). The change in Bishop score was significantly higher in the PGE_2 group than the catheter group, and time from induction to delivery was significantly shorter in the PGE_2 group. Significantly more women needed oxytocin for labour augmentation in the catheter than the PGE_2 group and fetal distress was significantly more frequent. For grand multiparas, PGE_2 vaginal tablets may be preferable for ripening the cervix as well as for labour induction.

Comparaison des ovules de prostaglandine E_2 et de la sonde de Foley pour le déclenchement du travail chez des grandes multipares

RÉSUMÉ L'efficacité, l'innocuité et l'effet de la prostaglandine (PG) E_2 ont été comparés avec la sonde de Foley pour le déclenchement du travail chez des grandes multipares. Dans un hôpital en Jordanie, 147 femmes dont le score de Bishop était inférieur ou égal à 5 ont été randomisées pour recevoir des ovules vaginaux de PGE_2 de 3 mg (n = 75) ou une sonde de Foley intracervicale de 50 mL (n = 72). La modification du score de Bishop était significativement plus importante dans le groupe de la PGE_2 que dans le groupe de la sonde, et le temps entre le début du travail et l'accouchement était significativement plus court dans le groupe de la PGE_2. Un nombre significativement plus important de femmes a eu besoin d'ocytocine pour augmenter le travail dans le groupe de la sonde que dans le groupe de la PGE_2 et la souffrance foetale était significativement plus fréquente. Chez les grandes multipares, les ovules vaginaux de PGE_2 peuvent être préférables pour la maturation cervicale ainsi que pour l'induction du travail.

[1]Department of Obstetrics and Gynaecology, Queen Alia Military Hospital, Royal Medical Services, Amman, Jordan.

Received: 04/05/03; accepted: 23/10/03

Introduction

The process of cervical ripening usually commences before labour begins; the cervix undergoes significant biochemical changes over a period lasting from 12 hours to 6–8 weeks [*1*]. It is believed to be controlled by certain hormones (in particular prostaglandin E_2) that play a role in triggering uterine contractile activity [*2*]. So the state of the cervix has been suggested to be the most important factor in predicting the success rate of labour induction [*3–5*].

Calder et al. reported an increasing maternal and neonatal morbidity when labour induction begins with a Bishop score ≤ 3 [*6*]. Trofatter in 1992 reported a decrease in induction failure when using a variety of methods to ripen the cervix [*7*]. The use of prostaglandins for cervical ripening administered by any route has been reported to improve the rate of vaginal delivery and decrease the rate of caesarean section and instrument deliveries [*8*]. In addition, the use of a cervical catheter has been shown effective for cervical priming and leads to a favourable outcome [*9*].

Grand multiparity is considered a risk factor for maternal and neonatal morbidity. However, the subject is still under debate, with several authors reporting conflicting results as to whether a pregnancy is high risk or not because of its associated medical and obstetric complications [*10–13*]. Labour induction using prostaglandins in this high parity group has been viewed as a stressful and potentially dangerous procedure. Other reports on the use of prostaglandins in grand multiparas contradict this notion and have yielded a safe and effective method of labour induction [*14–16*].

Grand multiparity is common in Jordan. The total number of deliveries conducted in Queen Alia Military Hospital during the study period (12 months) was 3684 and 1547 (42%) of these were to grand multiparous women. The number of inductions of labour conducted was 590 (16%). It is therefore important to study the efficacy, safety and outcome of vaginal prostaglandin (PG)E_2 tablet compared with intracervical Foley catheter insertion for induction of labour in this high parity group.

Methods

This prospective randomized study was carried out at Queen Alia Military Hospital, Amman, Jordan. Between September 2001 and August 2002, 147 grand multiparous women who had a clinically unfavourable cervix and indications for labour induction were recruited for the study. Patients were eligible for inclusion if they had a singleton pregnancy at term, vertex presentation, intact membranes, reassuring fetal heart tracings and Bishop score ≤ 5. Women with previous caesarean section, ruptured membranes, contraindications for vaginal birth, suspected cephalopelvic disproportion or unexplained antepartum haemorrhage were excluded.

After written informed consent was obtained, patients were randomized to one of the 2 methods, using a random number table. For the first method, 75 women were given PGE_2 3 mg vaginal tablet, inserted in the posterior vaginal fornix. This was repeated at 6-hour intervals, if needed. For the second method, 72 women were given a size 18 Foley catheter, inserted intracervically in order to pass the internal os using a sterile speculum technique. This was inflated with 50 mL distilled water and taped to the inner side of the thigh to produce a small traction.

For all women, vital signs were recorded on admission and blood was drawn for

complete blood count and cross-matching. General and systemic examinations followed by pelvic examination were performed. A fetal heart rate tracing was obtained upon admission and after the initiation of the induction method for a minimum time of 45 minutes. Abdominal and cervical examinations were performed at 4–6 hour intervals to diagnose the start of labour and to measure Bishop score changes, unless these were indicated at earlier times. Amniotomy was performed within 1–2 hours of the diagnosis of labour or as soon as clinically feasible.

The progress of labour was monitored every 2 hours. Labour abnormalities were defined by Friedman's criteria [*16*]. For these cases, oxytocin infusion was started for augmentation of labour, administered in the manner outlined by O'Driscoll and Meagher [*17*]. Intrapartum continuous fetal heart rate monitoring was performed.

The primary outcome measures were the route of delivery and the time required from beginning of the induction method to delivery. The secondary outcome measures were the change in Bishop score, intrapartum complications or the need for oxytocin for labour augmentation.

Comparison of continuous variables was made with Student *t*-test. Categorical variables were compared using the chi-squared or Fisher exact test. $P < 0.05$ was considered to indicate a significant difference.

Results

There were no significant differences in presenting characteristics between the 2 study groups (Table 1) and both groups had similar indications for labour induction (Table 2). Postdates and pre-eclampsia were the most frequent indications in both groups. The frequency of postdate pregnancies was significantly higher in the cather group than the PGE_2 group ($P = 0.029$).

Table 1 **Presenting characteristics of grand multiparas treated with Foley catheter or prostaglandin E_2 (PGE_2) vaginal tablet for induction of labour**

Characteristic	Catheter group (*n* = 72)	PGE_2 group (*n* = 75)	*P*-value
Maternal age (years)	27.7 (5.5)	27.1 (5.7)	0.438
Gestational age (weeks)	39.4 (1.9)	39.5 (1.7)	0.721
Parity (No.)	7.7 (2.1)	7.4 (1.9)	0.176
Initial Bishop score	2.56 (1.40)	2.61 (1.30)	0.873

Values are shown as mean (standard deviation).
n ***= number of patients.***

As shown in Table 3, the change in Bishop score was statistically significantly higher in the PGE_2 group than the Foley catheter group (mean 3.95 ± SD 2.20 versus 3.10 ± 1.10) ($P < 0.01$). Significantly more women in the catheter group (49%) needed oxytocin for labour augmentation than in the PGE_2 group (20%) ($P < 0.001$).

The time from initiation of the induction method to delivery was significantly shorter in the PGE_2 group compared with the catheter group (16.5 ± 2.2 versus 20.5 ± 3.9 hours) ($P < 0.01$). Of women that were randomized to use PGE_2, 61% delivered within 16 hours after initiation of induction compared with 42% of those randomized to use the Foley catheter. This was a statistically significant difference ($P < 0.01$). There were 21 women who delivered after 24 hours in the catheter group, compared with 5 women in the PGE_2 group. This difference was highly statistically significant ($P < 0.001$).

Table 2 **Indications for induction of labour in grand multiparas treated with Foley catheter or prostaglandin E_2 (PGE_2) vaginal tablet for induction of labour**

Indication	Catheter group (*n* = 72)		PGE_2 group (*n* = 75)		*P*-value
	No.	%	No.	%	
Postdates	29	40	23	31	0.029
Pre-eclampsia	20	28	24	32	0.164
Diabetes	8	11	12	16	0.118
Suspected IUGR	10	14	11	15	0.693
Suspected macrosomia	5	7	5	7	0.999

IUGR = intrauterine growth restriction.
n = number of patients.

Table 3 **Labour and delivery outcomes of grand multiparas treated with Foley catheter or prostaglandin E_2 (PGE_2) vaginal tablet for induction of labour**

Outcome	Catheter group (*n* = 72)		PGE_2 group (*n* = 75)		*P*-value
	No.	%	No.	%	
Change in Bishop score					
Mean (SD)	3.10 (1.10)		3.95 (2.20)		< 0.01
Oxytocin required	35	49	15	20	< 0.001
Time from induction to delivery					
< 16 hours	30	42	46	61	< 0.01
16–24 hours	21	29	24	32	0.228
> 24 hours	21	29	5	7	< 0.001
Mean (SD)	20.5 (3.9)		16.5 (2.2)		< 0.01
Intrapartum complications					
Fetal distress	11	15	6	8	0.01
Pyrexia	0	0	1	1	0.105
Failure to progress	6	8	7	9	0.617
Haemorrhage	3	4	5	7	0.91
Delivery type					
Spontaneous vaginal	52	72	57	76	0.166
Forceps	3	4	2	3	0.581
Vacuum	5	7	6	8	0.611
Caesarean section	12	17	10	13	0.147

SD = standard deviation.
n = number of patients.

There were no significant differences between the groups in intrapartum complications or in type of delivery but the frequency of fetal distress was significantly higher in the catheter group than the PGH_2 group (P = 0.01) (Table 3). In addition, there were no statistically significant differences in fetal outcomes (Apgar scores at 5 minutes, birth weight, admissions to the neonatal intensive care unit or meconium aspiration) between the 2 groups (Table 4). No more than 2 × 3 mg PGE_2 vaginal tablets were needed to achieve a clinically feasible cervix for amniotomy. No woman needed a blood transfusion. All women and their babies were discharged home in good condition.

Discussion

This study demonstrates that cervical ripening as well as labour induction in grand multiparas is safe using either PGE_2 or Foley catheter. Both methods were effective, but use of PGE_2 3 mg vaginal tablets appeared to be superior to the intracervical insertion of a Foley catheter, in view of the higher change in Bishop score, shorter interval from initiation to delivery and less need of oxytocin for labour augmentation. The current study agrees with other reports regarding the use and safety of PGE_2 vaginal tablets for labour induction in grand multiparas [*14,18,19*].

These findings contradict Sciscione et al. [*9*] who used PGE_2 intracervical gel compared with intracervical insertion of Foley catheter; however this gel is not readily available in our hospital. It is well known that some factors might affect the safety, absorption and efficacy of PGE_2, such as the vehicle, oily lubrication, humidity and possibly vaginal pH [*20,21*]. The difference in results may be attributed to the type of PGE_2 used, as the main effect of PGE_2 gel is cervical ripening and its contractile effect is considered to be small [*22,23*].

The most hazardous major complication of labour induction in grand multiparas is rupture of the uterus. Suggested risk factors for uteruine rupture include multiparity, oxytocin use and the state of the cervix. The present study revealed no major complications. Comparison of intrapartum complications between groups showed no

Table 4 **Fetal outcomes of grand multiparas treated with Foley catheter or prostaglandin E_2 (PGE_2) vaginal tablet for induction of labour**

Outcome	Catheter group (n = 72)		PGE_2 group (n = 75)		P-value
	No.	%	No.	%	
Mean (SD) birth weight (g)	3503 (575)		3452 (530)		0.319
Apgar score < 6 at 5 min	5	6.9	3	4.0	0.094
Admission to NICU	6	8.3	5	6.7	0.259
Meconium present	13	18.1	15	20.0	0.293

NICU = neonatal intensive care unit.
SD = standard deviation.
n = number of patients.

significant differences except for fetal distress which was significantly higher in the catheter group. Oxytocin was needed for labour augmentation in 48.6% and 20.0% of the Foley and PGE_2 groups, respectively. Outcome of labour and delivery compared favourably well in both groups. This demonstrates an equivalent safety of both methods, a finding that has been confirmed by others [*14*,*24*].

Furthermore, labour induction in grand multiparas with previous caesarean section has been reported to be safe, so too is the use of oxytocin when there is no contraindication for repeating the caesarean section [*25*,*26*]. However, in the current study there were no cases of previous caesarean section. This might eliminate grand multiparity as a risk factor in the genesis of rupture of the uterus and in the increasing incidence of intrapartum complications as other studies indicate [*12*,*13*,*27*].

In the view of these findings, it can be concluded that cervical priming as well as labour induction in grand multiparous women is safe and effective when using either PGE_2 tablets or Foley catheter, together with the use of oxytocin if needed for labour augmentation, but in the absence of any contraindications to induction. The use of PGE_2 3 mg vaginal tablets is preferred to the intracervical Foley catheter.

References

1. Steiner AL, Creasy RK. Methods of cervical ripening. ***Clinical obstetrics and gynecology***, 1983, 26:37–46.
2. Garfield RE. Cellular and molecular bases for dystocia. ***Clinical obstetrics and gynecology***, 1987, 30:3–18.
3. Garrett WJ. Prognostic signs of surgical induction of labour. ***Medical journal of Australia***, 1960, 49:29.
4. Bishop EH. Pelvic scoring for elective induction. ***Obstetrics and gynecology***, 1964, 24:266–8.
5. Anderson AM, Turnbull AC. Relationship between the length of gestation and cervical dilatation, uterine contractility and other factors during pregnancy. ***American journal of obstetrics and gynecology***, 1969, 105:1207–14.
6. Calder AA, Embrey MP, Tait T. Ripening of the cervix with extra-amniotic prostaglandin E_2 in viscous gel before induction of labour. ***British journal of obstetrics and gynaecology***, 1977, 84:264–8.
7. Trofatter KF. Cervical ripening. ***Clinical obstetrics and gynecology***, 1992, 35: 476–85.
8. Keirse MJ N. Prostaglandins in preinduction cervical ripening. Meta-analysis of worldwide clinical experience. ***Journal of reproductive medicine***, 1993, 38 (1 suppl.):89–100.
9. Sciscione AC et al. A prospective randomized comparison of Foley catheter insertion versus intracervical prostaglandin E_2 gel for preinduction cervical ripening. ***American journal of obstetrics and gynecology***, 1999, 180(1 Pt 1):55–60.
10. Mwambingu FT, Al-Meshari AA, Akiel A. The problem of grandmultiparity in current obstetric practice. ***International journal of gynaecology and obstetrics***, 1988, 26(3):355–9.
11. Evaldson GR. The grandmultipara in modern obstetrics. ***Gynecologic and obstetric investigation***, 1990, 30(4):217–23.
12. Babinszki A et al. Perinatal outcome in grand and great-grand multiparity: effects of parity on obstetric risk factors. ***American journal of obstetrics and gynecology***, 1999, 181(3):669–74.

13. Goldman GA et al. The grandmultipara. ***European journal of obstetrics, gynecology, and reproductive biology***, 1995, 61(2):105–9.

14. Abou el-Leil LA, Nasrat AA, Fayed HM. Prostaglandin E2 vaginal pessaries in the grandmultipara with an unripe cervix, a comparison of different parity groups. ***International journal of gynaecology and obstetrics***, 1993, 40(2):119–22.

15. Yamani TY, Rouzi AA. Induction of labor with vaginal prostaglandin-E2 in grand multiparous women. ***International journal of gynaecology and obstetrics***, 1998, 62(3):255–9.

16. Friedman EA. The labour curve. ***Clinics in perinatology***, 1981, 8(1):15–25.

17. O'Driscoll K, Meagher D. ***Active management of labour. The Dublin experience***, 2nd ed. London, Baillière Tindall, 1986.

18. Sobande AA, Al-Bar HM, Archibong EI. A comparison of spontaneous labor with induced vaginal tablets prostaglandin E2 in grand multiparae. ***Saudi medical journal***, 2001, 22(8):698–701.

19. Yamani TY, Rouzi AA. Induction of labor with vaginal prostaglandin-E2 in grand multiparous women with one previous cesarean section. ***International journal of gynaecology and obstetrics***, 1999, 65(3):251–3.

20. Lyrenas S, Clason I, Ulmsten U. ***In vivo*** controlled release of PGE2 from a vaginal insert (0.8 mm, 10 mg) during induction of labour. ***British journal of obstetrics and gynaecology***, 2001, 108(2):169–78.

21. Ramsey PS et al. Effect of vaginal pH on efficacy of the dinoprostone gel for cervical ripening/labor induction. ***American journal of obstetrics and gynecology***, 2002, 186(4):843–6.

22. Seeras RC. Induction of labor utilizing vaginal vs. intracervical prostaglandin E2. ***International journal of gynaecology and obstetrics***, 1995, 48(2):163–7.

23. Nuutila M, Kajanoja P. Local administration of prostaglandin E2 for cervical ripening and labor induction: the appropriate route and dose. ***Acta obstetricia et gynecologica scandinavica***, 1996, 75(2): 135–8.

24. St Onge RD, Connors GT. Preinduction cervical ripening: a comparison of intracervical prostaglandin E2 gel versus the Foley catheter. ***American journal of obstetrics and gynecology***, 1995, 172(2 Pt 1):687–90.

25. Abu-Heija AT, Ali AM. Induction of labor in grand multiparous women and previous cesarean section: is it safe? ***Gynecologic and obstetric investigation***, 2002, 53(2):121–4.

26. Ben-Aroya Z et al. Oxytocin use in grandmultiparous patients: safety and complications. ***Journal of maternal–fetal medicine***, 2001, 10(5):328–31.

27. Toohey JS et al. The "dangerous multipara": fact or fiction? ***American journal of obstetrics and gynecology***, 1995, 172(2 Pt 1):683–6.

Low-dose quinine for treatment of chloroquine-resistant falciparum malaria in Sudanese pregnant women

I. Adam,[1] M.H. Ibrahim,[1] I.A. A/elbasit[2] and M.I. Elbashir[2]

الكينين بجرعات منخفضة لمعالجة الملاريا المنجلية المقاومة للكلوروكين لدى الحوامل في السودان

إسحق آدم، محمد حامد إبراهيم، إشراقة الطيب عبد الباسطَ، مصطفى إدريس البشير

الخلاصة: تم توزيع الحوامل السودانيات اللاتي يراجعن إحدى المستشفيات في شرق السودان لإصابتهن بالملاريا المنجلية المقاومة للكلوروكين توزيعاً عشوائياً في أحد النظامَيْن العلاجيَيْن التاليَيْن: 18 مريضة تتلقّى جرعات منخفضة (10 ميلي غرام من الكينين لكل كيلوغرام من الوزن مرتَيْن يومياً)، 24 مريضة تتلقّى النظام العلاجي المعياري (10 ميلي غرام من الكينين لكل كيلوغرام من الوزن ثلاث مرات يومياً). واستمرت المعالجة سبعة أيام، في حين استمرت المتابعة 28 يوماً. وقد كان عدد من عانَيْنَ من الأقياء والألم البطني ممن تلقّيْنَ الجرعات المنخفضة أقل وبشكل ملحوظ من عدد من عانى منهما ممن تلقّى الجرعات المعيارية. في حين كان كلٌّ من نقص سكر الدم والولادة قبل الأوان والانتكاس أعلى بقليل لدى من تلقّيْنَ ثلاث جرعات يومياً مما كان لدى من تلقّيْنَ جرعتَيْن يومياً. ولم يكن هناك فرق يذكر بين المجموعتَيْن في الفترة الوسطية بين الإدخال في المستشفى وبين زوال الحمى واختفاء الطفيليات من الدم. ويشجِّع الدارسون في الوقت الحاضر استخدام جرعتَيْن يومياً من الكينين، لإنقاص التأثيرات الجانبية، ولتحسين امتثال المرضى للمعالجة.

ABSTRACT Pregnant Sudanese women who presented at a hospital in eastern Sudan with chloroquine-resistant falciparum malaria were randomly allocated to one of two quinine regimens: low-dose (10 mg/kg 2 times/day) (18 patients) or standard (10 mg/kg 3 times/day) (24 patients). Treatment was for 7 days and follow-up for 28 days. Significantly fewer patients in the low-dose group reported vomiting and abdominal pain than the standard regimen group. Hypoglycaemia, preterm labour and recrudescence were slightly but not significantly higher in patients in the standard group than low-dose group. There were no significant differences between the groups in the mean time from admission to remission of fever and parasite clearance. We tentatively advocate the use of quinine 2 times/day to reduce side-effects and improve compliance.

Quinine à faible dose pour le traitement du paludisme à falciparum chloroquino-résistant chez des femmes enceintes soudanaises

RÉSUMÉ Des femmes enceintes soudanaises atteintes de paludisme à falciparum chloroquino-résistant qui ont consulté dans un hôpital du Soudan oriental ont été réparties de manière aléatoire entre les deux schémas thérapeutiques de quinine suivants : faible dose, 10 mg/kg 2 fois/jour (18 patientes), ou standard, 10 mg/kg 3 fois/jour (24 patientes). Le traitement durait 7 jours et le suivi 28 jours. Un nombre significativement moindre de patientes dans le groupe du traitement à faible dose a signalé des vomissements et des douleurs abdominales par rapport aux patientes recevant le traitement standard. L'hypoglycémie, le travail prématuré et la recrudescence étaient légèrement, mais non significativement, plus élevés chez les patientes du groupe du traitement standard que dans le groupe du traitement à faible dose. Il n'y avait aucune différence significative entre les deux groupes pour ce qui est du temps moyen entre l'admission, la rémission de la fièvre et l'élimination du parasite. Nous recommandons provisoirement l'utilisation de la quinine deux fois par jour pour réduire les effets secondaires et améliorer l'observance du traitement.

[1]New Halfa Hospital, New Halfa, Sudan.
[2]Faculty of Medicine, University of Khartoum, Khartoum, Sudan.
Received: 14/07/03; accepted: 28/10/03

Introduction

In Sudan, falciparum malaria has been reported to cause a number of adverse maternal and fetal outcomes, such as maternal anaemia, low birth weight, preterm labour and perinatal mortality [*1–6*]. It is the leading cause of maternal mortality [*5,6*].

The treatment of falciparum infection remains the main means available to limit the impact of malaria on pregnancy [*7*]. The spread of chloroquine and sulfadoxine–pyrimethamine resistance in Sudan [*8–10*] necessitates the use of alternative drugs for the treatment of falciparum infections, such as quinine which is the second most prescribed antimalarial drug in Sudan [*11*]. Quinine is the treatment of choice for severe and chloroquine-resistant falciparum malaria.

The standard dose of quinine is 10 mg/kg, 3 times per day for 7 days [*12*]. This dose has been reduced effectively in children without impairing its efficacy, and with marked improvement in compliance with drug use [*13*]. The side-effects of quinine treatment that can lead to poor compliance are tinnitus, nausea, vomiting, diarrhoea, hypoglycaemia and acute hypersensitivity. Physicians in central and eastern Sudan are now also giving quinine to pregnant women 2 times daily rather than 3 times, with apparently good outcomes. The present study was carried out to verify the efficacy and safety of this ongoing clinical practice.

Methods

We performed a prospective clinical trial in New Halfa Hospital in eastern Sudan from the period November 2002 to March 2003. After verbal consent, all pregnant women presenting with failure of chloroquine therapy for the treatment of falciparum malaria were successively enrolled to the study. Those with one or more manifestations of severe falciparum malaria were excluded [*14*].

For both groups, quinine (Laboratoires Renaudin, France) was given under strict supervision, first by intravenous infusion in 5% dextrose solution over 2–4 hours, and when the patient could tolerate it, therapy was continued orally in the form of tablets. For this phase of the study, patients were randomized into 2 treatment groups: quinine 10 mg/kg 2 times/day for 7 days (BD group) and quinine 10 mg/kg 3 times/day for 7 days (TDS group).

A detailed record was made for each patient, including: personal data, medical and obstetric history, physical examination and use of antimalarials in the 3 weeks before entry to the study. During the follow-up, all patients were asked daily about the expected side-effects of quinine (tinnitus, vomiting and abdominal pain). Axillary temperature was recorded every 8 hours until it fell to normal (37.5 °C), and then daily until day 7. All patients were kept in the hospital for at least 7 days and then followed up weekly in the antenatal clinic for 28 days.

Laboratory investigations

Using finger prick blood samples, thick and thin blood smears were prepared from each patient in both groups, stained with Giemsa (pH 7.0, diluted in phosphate-buffered saline) and counted against 200 white blood cells assuming that the number of cells is 6000/mm^3 of blood. Thin blood films, fixed in methanol and Giemsa-stained were made when the parasite species was doubtful. The blood films were repeated every 8 hours until 2 consecutive films were negative, then daily until day 7 and then on days 14, 21 and 28. Haemoglobin concentration and capillary blood glucose level were determined on presentation. Capillary blood

glucose was estimated 2 hours after administration of the drug.

All patients were resident in the same area during the follow-up period. Therefore, the possibility of re-infection or recrudescence could not be ruled out. Three spots of blood were taken on filter paper initially and later if parasites reappeared microscopically during the follow-up period. Primers from 3 polymorphic *Plasmodium falciparum* antigens; merozoite surface protein-1 and 2 (MSP-1 and MSP-2) and glutamate-rich protein (GLURP) were used in polymerase chain reaction analysis (PCR) to differentiate between true recrudescence and re-infection as described previously [*15*].

Evaluation criteria

The efficacy and side-effects of the 2 regimens of quinine were assessed according to parasite clearance time, fever clearance time, occurrence of side-effects (tinnitus, vomiting, abdominal pain and hypoglycaemia) and recrudescence. Parasite clearance time was defined as the time between start of treatment until 2 consecutive negative blood smears were obtained. Fever remission time was defined as the time between admission and achievement of normal body temperature.

Statistics

Data was entered into the computer using *SPSS/PC* batching for data analysis. Simple frequency distribution cross-tabulation, descriptive statistics, mean, *t*-test and chi-squared with probability ≤ 0.05 was used for testing the hypotheses.

Ethics

Informed consent was obtained from the women who participated in the study. Ethical clearance for the study was obtained from the Faculty Research Board, Faculty of Medicine, University of Khartoum and the National Ethical Committee at the Sudanese Federal Ministry of Health.

Results

Sixty-five pregnant women presented to New Halfa hospital with manifestations of chloroquine-resistant falciparum malaria during the study period. After confirmation of the infection, 14 patients were excluded from the study because they had severe manifestations of the disease. Initially, 25 patients were enrolled in the BD group, and 26 patients in the TDS group. However, 7/25 of the BD and 2/26 of the TDS group ($P = 0.05$) were excluded from the follow-up and evaluation as they chose to leave hospital and continue the treatment at home after the first or the second dose of quinine.

Table 1 shows the major characteristics of the remaining women on presentation. There were no significant differences between the 2 groups in age, parity, weight, temperature, haemoglobin level, parasite count and random blood glucose level at presentation.

A slightly higher proportion of women in the BD group presented with vomiting than the TDS group—4/18 (22.2%) versus 3/24 (12.5%)—but this was not statistically significant. On day 1, vomiting was recorded in more BD patients; 7/18 (38.9%) versus 4/24 (16.7%) but this was not statistically significant ($P > 0.05$). On day 2, significantly fewer patients in the BD than the TDS suffered from vomiting; 29/18 (50.0%) versus 9/24 (79.2%) ($P < 0.05$).

Tinnitus was reported slightly less frequently by patients who received quinine BD, than in those who received it TDS; 12/18 (66.7%) versus 19/24 (79.2%) ($P > 0.05$). Significantly fewer patients reported abdominal pain in the BD group than in the

Table 1 **Characteristics on admission and outcomes of treatment for pregnant women treated with quinine 10 mg/kg 2 times/day (BD) or 10 mg/kg 3 times/day (TDS)**

Variable	BD regimen (n = 18)		TDS regimen (n = 24)		P-value
	Mean	SD	Mean	SD	
On admission					
Age (years)	25.2	6.0	25.5	6.9	0.4
Parity (No.)	2.6	1.9	2.6	2.2	0.3
Weight (kg)	59.3	15.9	52.2	9.3	0.09
Gestational age (weeks)	26.1	9.9	26.1	8.9	0.4
Axillary temperature (°C)	38.1	0.9	37.8	1.0	0.8
Haemoglobin level (g/L)	89.0	5.6	86.0	9.0	0.08
Parasite count (rings/µL)	5837	8361	4207	12325	0.6
Random blood sugar level (mg/dL)	117.6	30.1	106.5	25.7	0.9
Treatment outcomes					
Fever remission time[a] (hours)	25.5	12.1	21.0	16.9	0.13
Parasite clearance time[b] (hours)	27.7	12.9	33.7	12.7	0.63

[a]Fever remission time was defined as the time between admission and achievement of normal body temperature (37.5 °C).
[b]Time from admission and start of treatment until 2 consecutive negative blood smears were obtained.
SD = standard deviation.

TDS group, 1/18 (5.6%) versus 7/24 (29.2%) (P = 0.05). Some of the TDS group developed hypoglycaemia; 4/24 (16.7%), but this was not recorded in any patient in the BD group (0/18); this difference was not significant (P > 0.05).

While none of the patients in the BD delivered prematurely (< 37 weeks), 2/24 (8.3%) patients in the TDS group delivered prematurely at 29 and 30 weeks gestational age and their babies died immediately (P > 0.05).

True recrudescence was confirmed by parasite genotyping on days 21 and 28 in 2/18 (11.1%) patients among the BD group. They were successfully treated with sulfadoxine–pyrimethamine. There was no detectable parasitaemia during follow-up in the TDS group, but this difference was not significant (P > 0.5).

The mean (SD) parasite clearance time was lower in the BD than in the TDS group, but this did not reach the level of significance: 27.2 (12.9) versus 33.7 (12.7) hours.

Discussion

This is the first study of the efficacy of low-dose quinine in the treatment of chloroquine-resistant falciparum malaria during pregnancy in an area of high chloroquine resistance in eastern Sudan [*8*].

The study showed that significantly more patients chose to continue the quinine treatment at home in the BD than in the TDS group and this may reflect the simplicity of this regimen. Moreover, quinine side-effects were reported more frequently

in the TDS group than in the BD group; significantly more patients suffered from vomiting and abdominal pain in the TDS group than in the BD group. Although these side-effects were more frequent in the TDS than in the BD group, they might be considered a subjective assessment of these 2 regimens of quinine. Nevertheless, even objective side-effects were more frequent in the TDS than in the BD group. For example, hypoglycaemia was seen in more of the patients in the TDS group than the BD group (16.7% versus 0%) although the different not significant. However, hypoglycaemia was reported in around 50% of pregnant women at one stage or another of severe falciparum malaria treated with quinine 3 times/day for 7 days [*16*], therefore, hypoglycaemia may be dose related. In a recent study, a low dose of quinine was used in children in a community-based study but hypoglycaemia was not assessed [*13*].

Two patients in the TDS group delivered prematurely and their babies died immediately, but there was no premature delivery in the BD group. In a previous study where we were testing the efficacy of quinine 3 times/day in the treatment of severe falciparum malaria during pregnancy in central Sudan, 3/33 (9%) patients delivered prematurely, and only 1 patient delivered during quinine therapy [*4*]. This comparison should be viewed with caution because in the previous study we used quinine for severe illness, while such patients were excluded in the present study. However, no preterm labour was reported by McGready et al. in 1998 [*17*]. Malaria can cause abortion and preterm labour as well, and in central Sudan it was found to be the leading cause of low birth weight as a result of preterm labour [*3*]. However, the oxytocic effect of quinine on the pregnant uterus cannot be excluded totally. Previously, quinine was used as a labour-inducing agent but in high doses [*18*].

The parasite clearance time was shorter but not significantly so in the BD group than in the TDS group. However, 2 patients (11.1%) in the BD group showed true parasite recrudescence during the follow-up, compared with none of the patient in the TDS group. This difference was not statistically significant and it should be viewed with caution as it might be due to quinine resistance in this area of Sudan. Previously, we have observed quinine resistance by *in vivo* testing and it has been confirmed by *in vitro* testing in a nearby area [*8,19*]. We have previously shown 6% quinine resistance or re-infection during pregnancy in central Sudan [*4*].

In conclusion, quinine in a low-dose regimen of 2 times/day causes fewer subjective side-effects and therefore is likely to improve patient compliance than the standard 3 times/day regimen. It also has a lower risk of hypoglycaemia (which is important in the outpatient setting) and of preterm labour. Its disadvantage is the higher probability of recrudescence, which is important in the light of emerging resistance in Africa, where the drug is still the first line for the treatment of severe falciparum malaria. However, there is an urgent need to test and apply other alternative drugs, especially sulfadoxine–pyrimethamine combination, which is free of side-effects such as hypoglycaemia and preterm labour.

References

1. Ahmed SM et al. Malaria parasitemia during delivery. ***Saudi medical journal***, 2001, 23:684–8.

2. Taha TE et al. Levels and determinants of perinatal mortality in Central Sudan. ***In-***

ternational journal of gynaecology and obstetrics, 1994, 45:109–15*.*

3. Taha TE et al. Malaria and low birth weight in central Sudan. ***American journal of epidemiology***, 1993, 138:318–25.

4. Adam et al. Quinine therapy in severe ***Plasmodium falciparum*** malaria during pregnancy in Sudan. ***Eastern Mediterranean health journal***, 2004, 10(1/2): 159–66.

5. ***Maternal mortality in Sudan. Inter-regional meeting on the prevention of maternal mortality, Geneva 11–15 November, 1985***. Geneva, World Health Organization, 1985 (Unpublished document FHE/PMM/85.95).

6. Dafallah SE, El-Agib FH, Bushra GO. Maternal mortality in a teaching hospital in Sudan. ***Saudi medical journal***, 2003, 24:369–73.

7. Dolan G et al. Bed nets for the prevention of malaria and anaemia in pregnancy. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1993; 87:620–6.

8. Adam I et al. In the Sudan: chloroquine resistance is worsening and quinine resistance is emerging. ***Sudan medical journal***, 2001, 39:1–5.

9. Elkheir HK et al. Efficacy of sulphadoxine and pyrimethamine, doxycycline and their combination in the treatment of chloroquine resistant falciparum malaria. ***Saudi medical journal***, 2001, 228: 690–3*.*

10. Adam I et al. Efficacy of sulfadoxine-pyrimethamine in the treatment of uncomplicated ***Plasmodium falciparum*** malaria in a small sample of Sudanese children. ***Eastern Mediterranean health journal***, 2004, 10(3):309–14.

11. Yousif MA, Adeel AA. Antimalarial prescribing pattern in Gezira State: precepts and practice. ***Eastern Mediterranean health journal***, 2000, 6:939–47.

12. World Health Organization, Division of Control of Tropical Diseases. Severe and complicated malaria. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1990, 84(suppl.2):1–65.

13. Kofoed PE et al. Treatment of ***Plasmodium falciparum*** malaria with quinine in Guinea-Bissau: one daily dose is sufficient. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 2002, 96:185–8.

14. World Health Organization, Communicable Diseases Cluster. Severe falciparum malaria. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 2000, 94(suppl.1):S1–90.

15. Brockman A et al. Application of genetics marker to the identification of recrudescent ***P. falciparum*** infection on the North-Western border of Thailand. ***American journal of tropical medicine and hygiene***, 1999, 60:14–21.

16. Looareesuwan S et al. Quinine and severe falciparum malaria in late pregnancy. ***Lancet***, 1985, 2:4–8.

17. McGready R et al. Quinine and mefloquine in the treatment of multidrug-resistant ***Plasmodium falciparum*** malaria in pregnancy. ***Annals of tropical medicine and parasitology***, 1998, 92:643–53*.*

18. Mukherjee S, Bhose LN. Induction of labour and abortion with quinine infusion in intrauterine fetal deaths. ***American journal of obstetrics and gynecology***, 1968, 101:853–4*.*

19. Khalil IF. ***Sensitivity of chloroquine resistant*** Plasmodium falciparum ***to fansimef, mefloquine and halofantrine in Gadaref, eastern Sudan*** [MSc thesis]. Khartoum, Sudan, University of Khartoum, 1995.

Quinine for chloroquine-resistant falciparum malaria in pregnant Sudanese women in the first trimester

I. Adam[1], H.M. Idris[1] and M.I. Elbashir[2]

الكينين لمعالجة الملاريا المنجلية المقاوِمة للكلوروكين في الحوامل السودانيات في الأثلوث الأول من الحمل

إسحق آدم، حيدر محمد الإدريس، مصطفى إدريس البشير

الخلاصة: أُجريت دراسة استباقية سريرية في شرق السودان لوصف فعالية وسُمِّية تناوُل الكينين في بداية الحمل لدى الحوامل المصابات بالملاريا المنجلية المقاوِمة للكلوروكين. فقد أُعطيت 26 من الحوامل السودانيات في الأثلوث الأول من حملهن (العمر الحملي الوسطي 8.5 أسبوعاً) 10 ميلي غرام/كيلو غرام من الكينين ثلاث مرات يومياً لمدة سبعة أيام، وتلا ذلك تكرار المعالجة كل أسبوعين حتى الولادة. وقد أجهضت إحدى المريضات (3.8٪) وعانت مريضتان (7.7٪) من التهديد بالإجهاض، إلا إنهما أتمتا حملهما وولدتا طفلَيْن في الأوان. وقد لوحظ النكس أو عودة العدوى في اليوم الحادي والعشرين لدى إحدى المريضات. ومات أحد الولدان في عمر 6 أشهر، ولم يكن هناك أي تشوُّه ولادي يمكن كشفه ولا عيوب سمعية أو بصرية أو عصبية لدى الأطفال الآخرين عند ولادتهم، وحتى بعد مرور سنة على ذلك. ويستنتج من ذلك أن الكينين قد يكون مأموناً في الأثلوث الأول من الحمل.

ABSTRACT A prospective clinical study in eastern Sudan described the efficacy and toxicity of quinine in early pregnancy in mothers with chloroquine-resistant falciparum malaria. Twenty-six pregnant Sudanese women in their first trimester (mean gestational age 8.5 weeks) were given quinine 10 mg/kg 3 times per day for 7 days and followed up every 2 weeks until delivery. One patient aborted (3.8%) and 2 patients (7.7%) experienced threatened abortion but delivered term babies. Recrudescence or re-infection was observed on day 21 in 1 patient. One baby died aged 6 months. There were no detectable congenital malformations, no auditory or visual defects or any other neurological deficits in the remaining infants at birth or 1 year later. Quinine may be safe in the first trimester of pregnancy.

La quinine pour le paludisme à falciparum chloroquino-résistant chez des femmes enceintes soudanaises durant le premier trimestre de la grossesse

RÉSUMÉ Une étude clinique prospective au Soudan oriental a décrit l'efficacité et la toxicité de la quinine au début de la grossesse chez des mères atteintes de paludisme à falciparum résistant à la chloroquine. On a administré de la quinine à raison de 10 mg/kg trois fois par jour pendant 7 jours à vingt-six femmes enceintes soudanaises durant le premier trimestre de la grossesse (âge gestationnel moyen de 8,5 semaines) et celles-ci ont été suivies toutes les 2 semaines jusqu'à l'accouchement. Une patiente a avorté (3,8 %) et 2 patientes (7,7 %) ont débuté une menace d'avortement mais ont mis au monde leur bébé à terme. Une recrudescence ou une réinfection a été observée au 21e jour chez une patiente. Un bébé est décédé à l'âge de six mois. Il n'y avait aucune malformation congénitale décelable, aucun handicap visuel ou auditif ou autre déficit neurologique chez les autres enfants à la naissance ou un an plus tard. La quinine peut être considérée comme sans danger durant le premier trimestre de la grossesse.

[1]New Halfa Hospital, New Halfa, Sudan.
[2]Faculty of Medicine, University of Khartoum, Khartoum, Sudan.
Received: 14/07/03; accepted: 28/10/03

Introduction

Malaria is a major health problem in tropical countries especially sub-Saharan Africa, where about 90% of clinical cases occur. There are nearly 500 million clinical cases of malaria worldwide each year and 1.1 to 2.7 million people die annually [*1*]. In areas where malaria transmission is seasonal, as in eastern Sudan, there is low transmission and hence low immunity. In Sudan, pregnant women are particularly vulnerable to falciparum malaria; the disease has adverse effects on pregnancy, affecting all parities [*2,3*], and all manifestations are seen including cerebral malaria and haemoglobinuria [*4*]. In central Sudan, falciparum malaria was found to be the leading cause of low birth weight, maternal anaemia and maternal and perinatal mortality [*5–7*].

Plasmodium falciparum isolates from eastern Sudan show the highest levels of antimalarial drug resistance in the country with a rate of chloroquine resistance among isolates of 76% [*8,9*]. This situation necessitates the use of alternative antimalarial drugs for the treatment of falciparum malaria. Quinine the drug of choice for severe falciparum malaria in Sudan.

Worldwide, very few studies have been made on the safety of quinine therapy during early pregnancy [*10,11*]. Quinine has long been believed to induce abortion and labour [*12*]; however, malaria itself can also lead to abortion, while quinine, by lowering fever, may in fact be helpful [*13*]. This is important as the treatment of chloroquine-resistant falciparum malaria in pregnancy is complicated by the poor safety of other drugs, as both artemether and sulphadoxine-pyrimethamine are reported to cause fetal resorption when given in early pregnancy [*14,15*].

In the light of the emerging multi-drug resistance in malaria-endemic areas, we describe here the efficacy and toxic effects of quinine on a small group of women with chloroquine-resistant malaria in early pregnancy and its outcome on the infants at 1-year follow-up.

Methods

Patients

The study was carried in New Halfa Hospital, eastern Sudan, between October 2000 and November 2002. The study group were all pregnant women in their first trimester of pregnancy with symptoms of falciparum malaria and failure to respond to chloroquine. Patients presenting with vaginal bleeding were excluded. The women were asked specifically about symptoms suggestive of malaria (fever, headache, sweating, joint pain and vomiting). Physical examination was performed and all information was kept in case report format.

Investigations

Peripheral capillary blood smears were prepared, stained with Giemsa and examined under oil immersion for parasites. Parasites and leukocytes were counted in the same fields until 200 leukocytes were counted; parasites densities were estimated using an assumed leukocyte count of 6000 leukocytes/µL blood. Baseline investigations (haemoglobin, urea, creatinine, albumin and bilirubin levels) were also performed.

Ultrasound was performed initially to confirm the pregnancy, gestational age and viability of the fetus, and repeated every 4–6 weeks for placental localization and to exclude congenital malformations.

Treatment and follow-up

The women were treated with quinine (Laboratoires Renaudin, France) at a dose of 30 mg salt/kg/day for 7 days. It was given at first by intravenous infusion in 5% dextrose solution over 2–4 hours, and

when the patient could tolerate it, therapy was continued orally in the form of tablets.

The patients were discharged after completing the full dose of quinine on day 8, then seen on days 14, 21, 28, and every 2 weeks in the antenatal clinic until delivery. In the clinic they were examined by the obstetrician for weight, pallor, temperature, pulse, blood pressure, fundal level, fetal heart sounds and oedema. At every visit the patient's haemoglobin was estimated and blood films for malaria were taken. The obstetrician supervised all hospital deliveries and kept close links with those who decided to deliver at home.

A paediatrician examined all the infants at birth for congenital malformations and made all necessary anthropometric measurements. Infants, both hospital- and home-delivered, were followed up to 1 year of age by the same paediatrician.

Definitions

Chloroquine-resistance was defined as the detection of *P. falciparum* malaria parasites in peripheral blood after a complete course of chloroquine. Abortion was defined as expulsion of a dead fetus before 28 weeks of gestation. Premature labour was delivery after 28 weeks and before 37 weeks of gestation. Perinatal death was death of the baby from 28 weeks *in utero* until the age of 1 week post-delivery.

Analysis

Data were analysed using *SPSS/PC*. Simple frequency distributions, percentages, means and standard deviations were calculated.

Ethics

The study received ethical clearance from the Faculty Research Board at the Faculty of Medicine, University of Khartoum and the Federal Ministry of Health. Written consent for participation in the study was obtained from the patients and their husbands.

Results

Out of 28 patients, 26 pregnant Sudanese women in their first trimester were given quinine to treat falciparum malaria after failure of chloroquine treatment. Two patients were excluded because they presented with vaginal bleeding. Fever, nausea, vomiting, headache, giddiness and insomnia were the major presenting symptoms. Table 1 shows the main clinical and biochemical data at the time of presentation.

During quinine treatment, 1 patient (2.8%) developed vaginal bleeding and abdominal pain. After the third dose of quinine, the cervix was found to be open, implying inevitable abortion, and evacuation was carried out. Two more patients (7.7%) developed slight vaginal bleeding, i.e. threatened abortion, during quinine

Table 1 **Major clinical and laboratory findings on admission in 26 pregnant women with chloroquine-resistant malaria**

Parameter	Mean	SD
Age (years)	26.2	3.5
Parity (No.)	2.8	2.6
Gestational age (weeks)	8.5	0.9
Weight (kg)	65.8	4.6
Temperature (°C)	38.2	0.6
Haemoglobin (g/dL)	9.2	1.3
Parasite count (rings/µL)[a]	5856	1652
Blood glucose (mg/dL)	123.6	12.9
Blood urea (mg/dL)	27.3	3.6
Serum bilirubin (mg/dL)	1.09	0.12

[a]Geometric mean.
SD = standard deviation.

therapy on day 2 and 3 respectively, but their pregnancies continued until the delivery of term babies.

All patients had negative blood films on day 7. However, 1 patient presented on day 21 with recurrence of malaria symptoms and the blood film was positive for falciparum malaria parasites. She was readmitted at the 10th week of gestation and given artemether intramuscularly, 80 mg initially followed by 80 mg after 12 hours and then daily for 4 days. She was discharged after completing the treatment with full recovery and was followed up closely until delivery.

Just under half the patients (12/26, 46.2%) delivered in the hospital, the rest (14/26, 53.8%) delivered at home. The mean (SD) birth weight of babies whose mothers delivered at hospital was 2.9 (0.4) kg.

One of the babies died at home at the age of 6 months due to unexplained febrile illness. There were no detectable congenital malformations and no auditory, visual or other neurological deficits in the remaining infants at birth or 1 year later.

Discussion

Pregnant women are more susceptible to malaria infection which can lead to many adverse effects on the pregnancy such as abortion, premature labour and maternal anaemia [*3*]. The World Health Organization recommends that pregnant women with demonstrable malaria illness should receive prompt treatment with effective and safe antimalarial drugs [*16*]. This situation is limited by the safety profile of antimalarial drugs themselves [*14,15*] and the spread of chloroquine-resistant strains of *P. falciparum*.

In this study, 1 patient showed reappearance of the parasite on day 21, which might due to re-infection or parasite resistance to quinine therapy. In Sudan, resistance to chloroquine has been recorded in almost every region of the country and even quinine resistance has been shown by *in vivo* and *in vitro* tests in the area of the study and in a nearby area [*8,17*]. We have previously observed that quinine failed to treat 2/33 (6%) of pregnant women in central Sudan [*4*]. This phenomenon warrants more investigations since quinine is still the first line of treatment for severe falciparum malaria in Africa.

One patient aborted and 2 patients threatened to abort but their pregnancies continued until term. This agrees with McGready and colleagues' report of quinine in early pregnancy [*11*], where the rate of abortion was not different from the population in our community. In a recent community-based study of risk factors for anaemia in our area, around 50% of women gave a history of previous abortion [*18*]. We have previously observed that no patient aborted among 33 patients treated with quinine for severe falciparum malaria in central Sudan [*4*]. However, in that study 3 patients delivered prematurely, 1 of them during the quinine therapy. In another 2 studies there was no effect of quinine on the rate of abortion or preterm labour [*19,20*]. In the latter studies the patients presented later in pregnancy (the gestational age was > 20 weeks) and this might explain the rate of abortion (1/26, 3.8%) in the present study where quinine was used in early pregnancy. There are difficulties in interpreting the findings of abortion, because malaria itself is a known cause of abortion especially during epidemics [*21*]. Certainly in our study, 2 out of 28 malaria patients presented with vaginal bleeding and their pregnancies aborted before quinine was started (these women were excluded from the study). Quinine has long ago been reported to induce abortion and

labour [*12*] and we believe that this has been influential in limiting the use of quinine during pregnancy. The situation remained so until in 1985 it was declared that malaria and its fever were responsible for abortion, while quinine, by lowering temperature, may in fact decrease the amplitude of uterine contractions as confirmed by fetal monitoring [*13*].

In our study, we found no hearing or visual defects and no congenital or developmental abnormalities in the infants after 1 year. This confirms another recent study [*11*]. However, deafness and hypoplasia of the optic nerve have been described in children born after unsuccessful attempts to induce abortion in women taking quinine overdoses [*22*]. These were retrospective reports and the exact numbers of patients were not known.

In conclusion, our study and that of McGready and colleagues [*11*] suggests that quinine could be used safely as a cost-effective therapy during the first trimester of pregnancy.

Acknowledgements

The authors thank the women who participated in the study, Mrs Asma Abd Elwakeil, Mr Abdalla Ahmed Hafazalla for technical assistance, and the staff of New Halfa Hospital for support and cooperation.

References

1. ***WHO expert committee on malaria: twentieth report.*** Geneva, World Health Organization, 2000 (WHO Technical Report Series No. 892).

2. Brabin BJ et al. A study of the consequences of malaria infection in pregnant women and their infants ***Parassitologia***, 1993, 35(suppl.):9–11.

3. Nosten F et al. Malaria during pregnancy in an area of unstable endemicity. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1991, 85:424–9.

4. Adam I al. Quinine therapy in severe ***Plasmodium falciparum*** malaria during pregnancy in Sudan. ***Eastern Mediterranean health journal,*** 2004, 10(1/2):159–66.

5. Taha Tel T, Gray RH, Mohamedani AA. Malaria and low birth weight in central Sudan. ***American journal of epidemiology***, 1993, 138:318–25.

6. Ahmed SM et al. Malaria parasitemia during delivery. ***Saudi medical journal.*** 2001, 23:684–8.

7. Taha TE et al. Levels and determinants of perinatal mortality in central Sudan. ***International journal of gyneacology and obstetrics***, 1994, 45:109–15***.***

8. Adam I et al. In the Sudan: chloroquine resistance is worsening and quinine resistance is emerging. ***Sudan medical journal***, 2001, 39:5–11***.***

9. Babiker HA et al. Genetic diversity of ***Plasmodium falciparum*** in a village in Eastern Sudan. 2. Drug resistance, molecular karyotypes and the mdr1 genotype of recent isolates. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1991, 85:578–83***.***

10. Heinonen OP, Slone D, Shapiro S. ***Birth defects and drugs in pregnancy.*** Littleton, Massachusetts, Publishing Sciences Group, 1977.

11. McGready R et al. The effects of quinine and chloroquine antimalarial treatment in the first trimester of pregnancy. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 2002, 96:180–4.

12. Mukherjee S, Bhose LN. Induction of labour and abortion with quinine infusion in intrauterine fetal deaths. ***American journal of obstetrics and gynecology***, 1968, 101:853–4.

13. Looareesuwan S et al. Quinine and severe falciparum malaria in late pregnancy. ***Lancet***, 1985, 2:4–8.

14. Briggs GC, Freeman RK, Yaffe SJ, eds. ***Drugs in pregnancy and lactation***, 2nd ed. Baltimore, William and Wilkins, 1986: 537–53.

15. Uche-Nwachi EO, Caxton-Martins AE. Sulfadoxine–pyrimethamine embryopathy in Wistar rats. ***Kaibogaku zasshi***, 1998, 73:135–9.

16. ***WHO expert committee on malaria: eighteenth report***. Geneva, World Health Organization, 1986:57–78 (WHO Technical Report Series, No. 735).

17. Khalil IF. ***Sensitivity of chloroquine resistant*** Plasmodium falciparum ***to fansimef***, ***mefloquine and halofantrine in Gadaref***, ***eastern Sudan*** [MSc thesis]. Khartoum, Sudan, University of Khartoum, 1995.

18. Adam I et al. Anemia in pregnant Sudanese women: community based study. ***Saudi medical journal***, 2004, 25:447–8.

19. McGready R et al. Quinine and mefloquine in the treatment of multidrug-resistant ***Plasmodium falciparum*** malaria in pregnancy. ***Annals of tropical medicine and parasitology***, 1998, 92:643–53.

20. McGready R et al. Randomized comparison of mefloquine–artesunate versus quinine in the treatment of multidrug-resistant falciparum malaria in pregnancy. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 2000, 94:689–93.

21. Menon R. Pregnancy and malaria. ***Medical journal of Malaysia***, 1972, 27:115–9.

22. Studies on the toxicity of qinghaosu and its derivatives. China Cooperative Research Group on qinghaosu and its derivatives as antimalarials. ***Journal of traditional Chinese medicine***, 1982, 2: 31–8.

Impact of the national protocol for malaria treatment on prescribing patterns in Gezira state, Sudan

M.E. Ahmed[1] and M.A. Yousif[2]

أثر البروتوكول الوطني لمعالجة الملاريا في نماذج وصف الأدوية في ولاية الجزيرة – السودان

ماجدة الهادي أحمد، ميرغني عبد الرحمن يوسف

الخلاصة: أُجريت دراسة مستعرضة لتقييم أثر البروتوكول الوطني لمعالجة الملاريا على طرق معالجة الملاريا، وذلك في ولاية الجزيرة في وسط السودان، عام 2001. وتبيَّن أن معظم الأطباء المئة والخمسة والستّين ومساعديهم، الذين أُجريت المقابلات معهم (وهم يشكّلون 80٪ من العدد الكلّي) لم يتلقّوا تدريباً على استعمال البروتوكول، وكثير منهم (57.5٪) لايزال كلٌّ منهم متمسكاً ببروتوكول خاص به. وقد أوضح التحليل لـ 410 من الوصفات أن الكلوروكين هو أكثر الأدوية المضادة للملاريا شيوعاً (69.5٪ من الوصفات). وعندما قُورنَتْ هذه الدراسة مع دراسة سبق أن أُجريت قبل استخدام البروتوكول، تبيَّن أن كثيراً من الوصفات تحقّق معايير البروتوكول من حيث الاستخدام الصحيح للكلوروكين، في حين أن النظام العلاجي لإعطاء الكينين حقناً وريدياً لايزال غير كاف. وقد أوضحت الدراسة فقد الإشراف المستمر والتدريب والمتابعة حول تطبيق الدلائل الإرشادية للبروتوكول فضلاً عن بعض المواقف السلبية من بعض الاختصاصيِّين العاملين في المستشفيات إزاء هذا البروتوكول.

ABSTRACT A cross-sectional study to assess the impact of the national protocol for malaria treatment was conducted in a town in Gezira state, central Sudan, in 2001. Most of the 165 doctors and medical assistants interviewed (80.0%) had not been trained in the protocol and many (57.5%) were still using their own protocols. Analysis of 410 prescriptions showed chloroquine was the most common antimalarial drug used (69.5% of prescriptions). Compared with a study before implementation of the protocol, more prescriptions met the protocol standards for correct chloroquine dose, whereas regimens for administration of intravenous quinine were still inadequate. The study showed a lack of continuous supervision, training and follow-up in the protocol guidelines and negative attitudes of hospital specialists towards the protocol.

Impact du protocole national de traitement du paludisme sur les modes de prescription dans l'État de Gezira (Soudan)

RÉSUMÉ Une étude transversale a été réalisée dans une ville de l'État de Gezira (Soudan central) en 2001 afin d'évaluer l'impact du protocole national pour le traitement du paludisme. La plupart des 165 médecins et auxiliaires médicaux interrogés (80,0 %) n'avaient pas été formés à l'utilisation du protocole et beaucoup (57,5 %) utilisaient toujours leur propre protocole. L'analyse de 410 ordonnances a montré que la chloroquine était l'antipaludique le plus couramment utilisé (69,5 % des ordonnances). Par rapport à une étude effectuée avant l'application du protocole, un plus grand nombre d'ordonnances se conformaient aux normes du protocole concernant la dose correcte de chloroquine, alors que les schémas d'administration de quinine par voie intraveineuse demeuraient inappropriés. L'étude a montré un manque de supervision continue, de formation et de suivi pour les directives du protocole et des attitudes négatives des spécialistes hospitaliers vis-à-vis du protocole.

[1]Department of Community Medicine, Faculty of Medicine; [2]Faculty of Pharmacy, University of Gezira, Gezira, Sudan.

Received: 08/08/02; accepted: 18/08/03

Introduction

Sudan has contributed to and endorsed the World Health Organization (WHO) global strategy for malaria control and 'Roll back malaria'. It has been observed that, unless diagnosed and treated promptly, patients with malaria deteriorate rapidly and the outcome is grave; hence plans to formulate a national protocol for the treatment of malaria were a priority in Sudan [*1*]. The national protocol is a set of recommendations and regulations concerning antimalarial drugs and their utilization in a country. It defines the national malaria control policy and forms part of the national drug policy, which expresses and prioritizes the medium- to long-term goals set by the government for the pharmaceutical sector. The national drug policy is both a commitment to a goal and a guide for action, identifying the main strategies for attaining them, and providing a framework within which the activities of the pharmaceutical sector can be coordinated [*2*].

The idea of formulating an antimalarial drug policy was encouraged in Sudan through a coordinated effort between the Directorate of Malaria, the Federal Ministry of Health and WHO. A preliminary workshop of consultants was held in the Faculty of Medicine, University of Gezira, in April 1998, followed by a national committee in June 1998, which finalized the policy under evaluation [*1*].

A study of antimalarial drug prescribing patterns was carried out in Wad Medani town in Gezira state before the implementation of the protocol in 1999 [*3*]. The study showed poor standards of prescribing of antimalarial drugs, in terms of overprescribing of chloroquine tablets and incorrect regimens for intravenous administration of quinine. The same study revealed that most of the medical practitioners tended to follow their own regimens to treat malaria infection.

The present study is the first attempt to measure the influence of the national protocol on prescribing patterns in the same area. It is important to make an evaluation of knowledge, attitudes and practices of health providers towards the national protocol, so that unintended consequences or constraints can be identified and successful interventions and strategies reinforced.

Methods

This cross-sectional study was carried out in Wad Medani, a town situated in Gezira state in central Sudan. The study was conducted in October, the month in which a normal rise of malaria infection is annually observed.

The research process consisted of 3 steps. The first step was an interview with the state director of the malaria control programme. In the second step, we contacted all 181 doctors and medical assistants (from both public and private sectors) who were providing medical services in the town; 165 were available for interview. Questions were asked to assess their knowledge, attitudes and practices relating to the national protocol. In the third step, a sample of 6 pharmacies was selected using stratified random sampling from 3 strata. Over 3 consecutive days, 410 prescriptions from both general practitioners and hospital outpatients departments were collected and a pre-tested checklist was filled in to assess their conformity to the protocol standards of drug dosage, frequency of administration, etc.

Standard treatment regimens at that time according to the Malaria Administration Department of the Federal Ministry of Health were as follows.

- First line treament for simple malaria: chloroquine oral 25 mg/kg over 3 days. For chloroquine injection of adults: 1 ampoule (200 mg base) followed by 1 ampoule after 6 hours then 2 times per day (12 hours apart) for a total of 7 injections. For chloroquine injection of children: 2.5–3.5 mg/kg.
- Second line treatment: pyrimethamine-sulfadoxine, 25/500 mg. For adults: 3 tablets at once. For children: according to weight.
- Third line treatment: mefloquine or quinine.

The data were tabulated and analysed using *SPSS*.

Results

Interview with state director

The interview with the state director of the malaria control programme revealed that 6 training courses had been conducted for 145 doctors and medical assistants over a 2-year period. The 3-day training sessions, which were run at 2 different centres, covered the epidemiology, clinical picture and treatment of malaria according to the national protocol guidelines. The protocol guidelines had been distributed to all health workers after training, but neither continuous supervision nor surveys to assess the implementation of the protocol had been carried out by the malaria control programme.

Interviews with health workers

Overall, the majority of the 165 health workers interviewed (132, 80.0%) reported that they had not received training about the national protocol guidelines. None of the 58 house officers or 25 consultants had been trained. No training had been received by 88.8% of hospital registrars, 64.0% of medical assistants or 52.0% of general practitioners. A significant difference was observed in the training status among different categories of health worker (Table 1).

With regard to the level of awareness of the protocol, around two-thirds of the health workers (107, 64.8%) were aware of the guidelines. Hospital house officers had the lowest level of awareness (37.9%). The difference was significant across different categories of health worker (Table 1). Regarding the availability of the guidelines, only 5 health workers (3.0%) reported having it in their clinic at the time of the study.

Adherence to the protocol was checked by asking the health workers what regimens they used for the treatment of simple malaria and complicated malaria compared to the standard regimens recommended by the Malaria Administration at the Ministry of Health. Despite the relatively high rate of awareness, just over half of the interviewed health workers (95, 57.5%) showed no adherence to the protocol, with a significant difference between the different categories (Table 1). When asked about reasons for not adhering to the protocol guidelines, one-third of health workers mentioned lack of awareness of them (Table 2). Among the senior hospital staff, however, it was due to negative attitudes towards the protocol, since 72.0% of consultants and 100% of registrars claimed that the protocol was ineffective. Some health workers (11.5%) said that they did not adhere to the guidelines in order to satisfy patients.

When evaluating the impact of the training on the adherence to the protocol guidelines a significant difference was observed. The 33 trained staff were more likely to adhere to the protocol (60.6% adhering) than the 132 untrained staff (only 37.9% adhering) ($\chi^2 = 4.691$, $P < 0.05$).

Table 1 **Training in, awareness of and adherence to the guidelines of the Sudan national protocol of malaria treatment according to type of health worker**

Variable	Medical assistants (*n* = 25)		GPs (*n* = 48)		House officers (*n* = 58)		Registrars (*n* = 9)		Consultants (*n* = 25)		Total (*n* = 165)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Trained about guidelines	9	36.0	23	48.0	0	0	1	11.2	0	0	33	20.0
Not trained about guidelines	16	64.0	25	52.0	58	100.0	8	88.8	25	100.0	132	80.0
					$\chi^2 = 48.58$, $P < 0.01$							
Aware of protocol	18	72.0	36	75.0	22	37.9	9	100.0	22	88.0	107	64.8
Not aware of protocol	7	28.0	12	25.0	36	62.1	0	0	3	12.0	58	35.2
					$\chi^2 = 31.92$, $P < 0.01$							
Adhering to protocol	10	40.0	30	62.5	19	32.8	4	44.4	7	28.0	70	42.4
Not adhering to protocol	15	60.0	18	37.5	39	67.2	5	55.6	18	72.0	95	57.5
					$\chi^2 = 12.34$, $P = 0.015$							

n = ***total number of respondents.***
GPs = general practitioners.

Table 2 **Reasons given by the health workers for not adhering to the guidelines of the national protocol of malaria treatment (those adhering gave hypothetical answers)**

Variable	Medical assistants (*n* = 25)		GPs (*n* = 48)		House officers (*n* = 58)		Registrars (*n* = 9)		Consultants (*n* = 25)		Total (*n* = 165)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Lack of awareness of protocol	10	40.0	16	33.3	30	51.7	0	0	0	0	56	33.9
Believe protocol ineffective	5	20.0	24	50.0	19	32.8	9	100.0	18	72.0	75	45.5
Better patient satisfaction	4	16.0	8	16.7	7	12.1	0	0	0	0	19	11.5
Others	6	24.0	0	0	2	3.4	0	0	7	28.0	15	9.1

n = ***total number of respondents.***
GPs = general practitioners.

Prescription analysis

Out of 410 prescriptions, 128 were for antimalarial drugs (31.2%). Most (91) were written by general practitioners, 11 by medical assistants, and 26 by consultants. Overall, 102 (79.7%) of antimalarial drug prescriptions were judged to be adequate in terms of correct dosage according to the protocol. No significant difference was observed between different specialties regarding correct dosage; 80.2% of prescriptions from GPs followed the protocol, 72.2% from medical assistants and 80.8% from consultants.

Chloroquine was the most commonly prescribed antimalarial drug (89 prescriptions, 69.5%), followed by quinine (22, 17.2%), pyrimethamine-sulfadoxine (13, 10.2%), artemether (2, 1.6%), halofantrine (1, 0.8%) and primaquine (1, 0.8%).

The proportion of antimalarial drug prescriptions that correctly complied with the protocol recommendations showed that intramuscular quinine was the formulation most often prescribed incorrectly (4 out of 9 prescriptions, 30.8%). One-fifth of prescriptions (5 out of 25, 19.2%) for chloroquine oral tablets were incorrect, generally for more than the recommended 10 tablets. Conversely, many prescriptions for intravenous chloroquine prescribed too few ampoules (15 out of 56 prescriptions, 26.8%), as many doctors were still following the former recommendations for 5 ampoules instead of 7 ampoules in the 1999 protocol guidelines. The poor compliance with protocol guidelines for quinine oral tablets (2 out 8 prescriptions incorrect, 25.0%) was mostly due to dispensing too few tablets.

Discussion

The implementation of a national drug policy faces several constraints, such as the logistics of distribution, the large number and variety of people and institutions involved and the rising cost of treatment [*4*]. Appropriate planning is therefore essential for successful implementation. In this study, some constraints and problems were highlighted which reflect on the implementation of the protocol for national malaria control in Sudan.

The study has revealed the impact of training on adherence to the protocol guidelines, which highlights the importance of continuous in-service training. Although the house officers constituted the majority of health providers, they were not targeted in the training process. This was obvious from the level of non-adherence to the protocol. It might be necessary to introduce the protocol in the pre-service training.

The great majority of health workers did not have the protocol guidelines in their clinic at the time of the study, reflecting a lack of continuous supervision and follow-up of the protocol.

Lack of awareness was an important reason for the non-adherence in the majority of the health workers and this can be mostly attributed to the rapid turnover of health workers. Patient satisfaction was another reason for non-adherence to the protocol by some categories of health worker, suggesting that education of the community about the malaria treatment protocol would also be of value.

Although awareness of the protocol was high among consultants, they were not adhering well to the protocol. Poor attitudes of senior staff are a concern as they may be an influence on junior staff, especially house officers being trained. The consultants justified their non-compliance in the belief that the protocol was not effective due to the appearance of chloroquine-resistant malaria in the area. The resistance to chloroquine has been studied

in Sudan by Abdel-Hamid et al., who concluded that chloroquine-resistant malaria was more than 25% in 4 sentinel posts [*5*]. Another recent study in the same area in the year 2000 revealed that 38% of *Plasmodium falciparum* were resistant to chloroquine [S.A. Faragalla, unpublished report, 2002]. Thus, monitoring and updating of the protocol is highly necessary.

The study revealed that the majority of prescriptions (70.0%) were written by general practitioners, thus highlighting the importance of targeting them in future interventions. This is the routine practice in the Sudan malaria control programme, according to the director of the programme; however the continuous turnover of general practitioners has had a negative impact on the effectiveness of training.

The rate of prescriptions for antimalarial drugs as a proportion of all prescriptions in this study (31.2%) was similar to the national figure (30.0%) [*6*]. Chloroquine was the most commonly prescribed antimalarial drug (69.5%), as in the previous study (52.2%) [*3*]. Warrel observed that despite the extensive spread of *P. falciparum* resistant strains, chloroquine is still the most widely used antimalarial drug in the world [*7*] as it is readily available and comparatively cheap [*8*]. Two antimalarial drugs recently launched in Sudan, artemether and halofantrine, appeared on prescriptions in this study although they should be reserved for complicated malaria cases (which are treated as hospital inpatients) as recommended by the protocol.

The proportion of antimalarial drug prescriptions that were compliant with the protocol (79.7%) reflects a marked improvement compared with the study before the implementation of the protocol (33.3%) [*3*]. However, regimens for administration of intravenous quinine were still inadequate in 30% of cases and this should be stressed in future interventions.

We recommend the following: monitoring and updating of the protocol; introducing the protocol guidelines in pre-service training; and thorough distribution of the protocol guidelines to health workers, with close follow-up and supervision.

Acknowledgements

Thanks are due to Professor Ali Ahmed Idris, Department of Community, Faculty of Medicine, University of Gezira for his invaluable assistance. We also thank the Batch 18 pharmacy students at the University of Gezira who contributed to data collection.

References

1. Department of Quality Assurance of Diagnosis and Treatment. ***National protocol for the treatment of malaria.*** Khartoum, Sudan, National Malaria Administration, 2001.

2. ***WHO policy perspectives on medicines. How to develop and implement a national drug policy***. Geneva, World Health Organization, 2003 (WHO/EDM/2002.5).

3. Yousif MA, Adeel AA. Antimalarial prescribing patterns in Gezira State: precepts and practices. ***Eastern Mediterranean health journal***, 2000, 6(5): 939–47.

4. ***Antimalarial drug polices: data requirements, treatment of uncomplicated malaria and management of malaria in pregnancy. Report of an informal consultation. Geneva, 14–18 March 1994***. Geneva, World Health Organization, 1994 (WHO/MAL/94.1070).

5. Abdel-Hameed AA, El-Jak IE, Faragalla IA. Sentinel posts for monitoring therapeutic efficacy of antimalarial drugs against ***Plasmodium falciparum*** infections in the Sudan. ***African journal of medical sciences***, 2001, 30(suppl.):1–5.

6. Malaria Administration Unit. ***Report on malaria therapy***. Khartoum, Sudan, Federal Ministry of Health, 1998.

7. Warrel DA. Treatment and prevention of malaria. In: Gilles HM, Warrel DA, eds. ***Bruce-Chwatt's essential malariology***, 3rd ed. London, Arnold, 1993:164–95.

8. Adome RO, Whyte SR. Hardon A. ***Popular pills: community drug use in Uganda.*** Amsterdam, Het Spinhuis, 1996.

Funds and technical support are available: however, malaria is still a serious challenge in the Region

Dr Hussein Gezairy, WHO Regional Director for the Eastern Mediterranean, called upon governments and the private sector in the most countries affected by malaria to ensure that safe and effective drugs are made affordable and accessible to patients, and that the implementation of available vector control tools is through intersectoral action for health – including community-based initiatives and outreach health services.

The Regional Director pointed out that malaria is still a serious problem in the Eastern Mediterranean Region, with more than 15 million estimated cases every year and five of the worst-affected countries in the world, namely Afghanistan, Djibouti, Somalia, Sudan and Yemen. The Region still faces a serious malaria challenge to which the Regional Office is responding in many ways.

Source: WHO/EMRO Press release No. 7
22 May 2004

Larvicidal activity of a neem tree extract (Neemarin) against mosquito larvae in the Islamic Republic of Iran

H. Vatandoost[1] and V.M. Vaziri[1]

الفعالية المضادة لليرقات في خلاصة شجر النيم على يرقات البعوض في جمهورية إيران الإسلامية

حسن وطن دوست، وحيدة معين وزيري

الخلاصة: تناول هذا البحث دراسة تأثير دواء مضاد لليرقات يتضمَّن الأزاديراختين، المستخلص من شجرة النيم (الأزادرخت الهندي)، على يرقات البعوض في جمهورية إيران الإسلامية، في شروط المختبر وفي الظروف الميدانية. وقد كانت الجرعة المميتة للنصف بالنسبة للأنوفيلة الاصطفانية وهي أكثر العوامل نقلاً للملاريا على الصعيد المحلي، 0.35 ميلي غرام/لتر، والجرعة المميتة لتسعين بالمئة منه 1.81 مغ/ل، في حين كانت الجرعة المميتة للنصف للباعضات الخماسية الخطوط، 0.69 مغ/ل، والجرعة المميتة لتسعين بالمئة منه 3.18 مغ/ل. وكان التأثير القاتل في طور الخادرة أعلى بشكل ملحوظ منه في الأطوار الأخرى. أما في التجارب الميدانية فإن استعمال الجرعات الموصى بها وهي لتر أو لترَان لكل هكتار، قد قَتَلَ من يرقات الأنافيل أكثر ممَّا قَتَلَ من يرقات البعوض. وقد أصبح من الضروري الاهتمام أكثر بالوقاية من البالغات، إذ يبدو أن فعالية هذا المركب قد اقتصرت أو كادت على قتل الخادرات. وكان الوقت الأقصى للفعالية سبعة أيام باستعمال التركيز الأقصى (لترَان لكل هكتار).

ABSTRACT An insecticide containing azadirachtin, a neem tree (***Azadirachta indica***) extract, was tested against mosquito larvae in the Islamic Republic of Iran under laboratory and field conditions. LC_{50} and LC_{90} values for Neemarin were 0.35 and 1.81 mg/L for ***Anopheles stephensi,*** the main local malaria vector, and 0.69 and 3.18 mg/L for ***Culex quinquefasciatus.*** The mortality in the pupal stage was significantly higher than the other stages. In field trials, using recommended dosages of 1 and 2 L/hectare, mortality of ***Anopheles*** spp. larvae was also higher than ***Culex*** spp. Prevention of adult emerged and pupal mortality was the main activity of this compound. The maximum time of efficacy was 7 days at the highest concentration (2 L/hectare).

Activité larvicide d'un extrait du margousier (Neemarin) contre les larves de moustiques en République islamique d'Iran

RÉSUMÉ Un insecticide contenant de l'azadirachtine, un extrait du margousier (***Azadirachta indica***), a été testé en laboratoire et sur le terrain pour la lutte contre les larves de moustiques en République islamique d'Iran. Les valeurs CL_{50} et CL_{90} pour le Neemarin étaient de 0,35 et 1,81 mg/L pour ***Anopheles stephensi,*** le principal vecteur local du paludisme, et 0,69 et 3,18 mg/L pour ***Culex quinquefasciatus.*** La mortalité au stade nymphe était significativement plus élevée qu'aux autres stades. Dans les essais sur le terrain, en utilisant les dosages recommandés de 1 et 2 L/hectare, la mortalité des larves d'***Anopheles*** spp. était également plus élevée que pour ***Culex*** spp. La prévention de l'éclosion imaginale et la mortalité des nymphes constituaient la principale activité de ce composé. Le temps d'efficacité maximum était de sept jours à la concentration la plus élevée (2 L/hectare).

[1]School of Public Health and Institute of Health Research, Tehran University of Medical Science, Tehran, Islamic Republic of Iran.
Received: 22/10/02; accepted: 18/08/03

Introduction

Malaria is the most important problem of developing countries. According to the latest report, it kills between 1.5–2.7 million people every year [*1*]. Malaria has always been considered as the most important vector-borne disease in the Islamic Republic of Iran due to its socioeconomic effects on the population [*2*].

Since the discovery of the insecticide dichloro-diphenyl-trichloroethane (DDT) before the Second World War, the widespread use of synthetic insecticides for the control of pests as well as human disease vectors has led to concerns about their toxicity and environmental impact [*3*]. Because of this, the search for new environmentally safe, target-specific insecticides is active throughout the world. To find new modes of action and to develop active agents based on natural plant products, efforts are being made to isolate, screen and develop phytochemicals possessing pesticidal activity. These categories of pesticides are known as biopesticides [*3*].

The neem tree *(Azadirachta indica*) is a member of the mahogany family (Meliacea) that is native to India and Burma, but it was introduced to other countries in the late 19th century [*4*]. Six species in the family Meliacea have been studied for pesticidal properties in different parts of the world. They are *Azadirachta indica* Juss, *A. excelsa* Jack, *A. siamens* Valeton, *Melia azadirachta* L., *M. toosendan* Sieb. and Zucc. and *M. volkensii* Gurke [*3*]. However, the most promising phytochemical pesticides studied in recent years are those based on extracts of *Az. indica* [*3*].

Various neem products have been researched extensively for their phytochemistry and exploitation in pest control programmes [*3*]. A number of bioactive components have been isolated from various parts of the neem tree. These chemical compounds have different designations, among which azadirachtin A is the major component. In addition to azadirachtin, a number of other active ingredients have also been isolated and identified from different parts of the neem tree, such as salannin, meliantriol and nimbin [*3,4*]. Two new triterpenoids (22,23-dihydronimocinol and des-furano-6-alpha-hydroxyazadiradione) were isolated from a methanolic extract of the fresh leaves of *Az. indica* along with a known meliacin, 7-alpha-senecioyl-(7-deacetyl)-23-O-methylnimocinolide [*5*].

Neem components show multiple effects against different insects such as mosquitoes, flies, triatomine bugs, cockroaches, fleas, lice and ticks [*3,4*]. The effect of neem on the activity of insects has been neglected up to now, possibly because it does not rapidly lead to mortality. However, affected insects cannot survive adverse environmental conditions in the same way as normal, healthy individuals; for example insects with reduced activity (reduced sight, jumping, crawling and flying ability) may be caught more easily by natural predators. Because of the variety of components and different mechanisms of action, insect resistance to neem compounds seems likely to be low [*8–10*].

The repellent activity of neem oil solutions in coconut oil against populations of mosquitoes consisting mainly of *Mansonia* spp. in Gambella, western Ethiopia, was demonstrated by Hadis et al. [*6*]. The aim of the present study was to evaluate the efficacy and durability of a neem extract against the main mosquito species in the southern part of the Islamic Republic of Iran.

Methods

Laboratory and field trials were carried out using an azadirachtin-rich product, Neemarin 0.15% (Biotech International Limited, New Delhi, India). The formulation consists of active ingredient (0.15% w/w), inert material (1.35% w/w) and propylene glycol (98.5% w/w).

Laboratory tests

Larvae of laboratory-reared strains of *Anopheles stephensi* and *Culex quinquefasciatus* (originally from the Bandar-e-Abass city area) were tested with different concentrations of Neemarin at the late 3rd instar and early 4th instar stages in a room at 25 °C ± 1 °C in autumn and winter 1999, according to WHO methods [*11*]. The strains are susceptible to different insecticides such as DDT, organophosphates, carbamates and pyrethroids. Preliminary testing was carried out to establish suitable concentrations. Selected stock solutions of Neemarin after preliminary tests were as follows: 0.0586, 0.117, 0.234, 0.469, 0.938, 1.875, and 3.750 mg/L. Lower logarithmic concentrations of Neemarin were diluted by adding the required volume of alcohol solvent to the main stock of Neemarin.

At each concentration, 200 mosquitoes representing individuals of 25 larvae were tested on 4 occasions. Each test run consisted of 74 mL water, 1 mL of Neemarin stock solution (by use of sampler) and then 25 larvae in 25 mL water were added, so that the final volume was 100 mL. In control runs, 1 mL alcohol was added instead of Neemarin.

Mortality counts were made every 24 hours after exposure until the test was terminated (when all the adults had emerged). In the analysis, both dead and moribund larvae were considered as dead, and the numbers alive at different stages (larvae, pupae, adults) were scored separately. The percentage mortality in the treated larvae was corrected relative to the controls using Abbotts formula [*11*]. The data were subjected to probit regression analysis according to Finney [*12*]. Goodness of fit of the points to a straight line was tested by chi-squared analysis.

Field trials

Field trials were carried out in artificial ponds (100 × 30 × 50 cm) in Jadas, Kazeroun, in the south-eastern part of the Islamic Republic of Iran in summer 2000, according to the method of Mulla and WHO recommendations [*11,13*]. The ponds were constructed separately, without vegetation and were exposed to sunlight.

Replicate ponds were created for each treatment: 2 control ponds and 4 treatment ponds. In the treatment ponds, Neemarin was sprayed on the water surface using a manual sprayer at 2 different concentrations (1 L/hectare and 2 L/hectare), as recommended by other researchers [*9,14*].

The number of larvae in the artificial ponds before and after the application of Neemarin (up to 10 days) were counted using a standard dipper. The frequency of *Anopheles* and *Culex* spp. larvae were counted using the method of Mulla with a cubic metal frame incorporated into the net for keeping and counting larvae in artificial ponds [*13*].

The larvae were identified according to the national identification key described by Shahgudian [*15*].

Results

Laboratory tests

Using probit regression analysis software, regression lines were plotted for the dose–

response to Neemarin treatment of laboratory strains of *An. stephensi* and *Cx. quinquefasciatus* larvae (Figures 1 and 2). For *An. stephensi* the LC_{50} (lethal concentration to cause 50% mortality in the population) was measured as 0.35 mg/L and the LC_{90} (lethal concentration to cause 90% mortality in the population) was 1.81 mg/L. For *Cx. quinquefasciatus* the LC_{50} was 0.69 mg/L and LC_{90} was 3.18 mg/L respectively (Table 1). Thus, *An. stephensi* larvae needed a significantly lower concentration of Neemarin than *Cx. quinquefasciatus* to cause the same mortality ($P < 0.05$).

The mortality among the pupal stages was greater than other stages ($P < 0.05$). For example, among 400 larvae of *Anopheles* species tested at the highest concentration, the mortality rate of larvae, pupae and adults were 15.8%, 79.8% and 40.3% respectively. Similar data were obtained for other concentrations and for *Culex* species. Inhibition of adult emerged larvae through mortality of pupae was the main action of Neemarin.

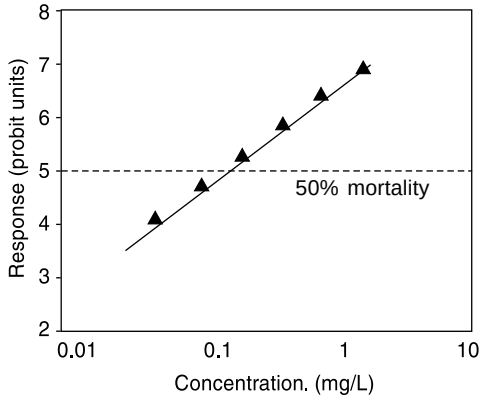


Figure 1 **Probit regression line for response of *Anopheles stephensi* larvae to Neemarin treatment in laboratory tests**

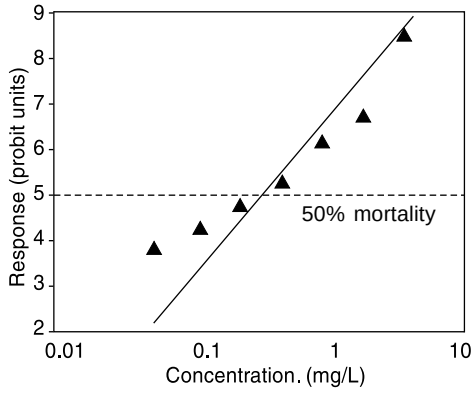


Figure 2 **Probit regression line for response of *Culex quinquefasciatus* larvae to Neemarin treatment in laboratory tests**

Field trials

In the field trials in artificial ponds, the distribution of species identified during the first run of the test were *An. stephensi* (29%), *An. fluviatilis* (27%), *An. dthali* (13%), *An. superpictus* (6%) and *Culex* spp. (25%) for 500 mosquito larvae. During the second run of the test the species were as follows: *An. stephensi* (26%), *An. dthali* (22%), *An. superpictus* (13%) and *Culex* spp. (38%) for 450 mosquito larvae.

Tables 2 and 3 show the mortality rates of *Anopheles* and *Culex* spp. at different stages (larvae, pupae, adult), comparing controls with 2 different concentrations of Neemarin treatment (combining the 2 replicate runs). The main indicator of treatment response was the percentage inhibition of emerged adults. The inhibitory effect of Neemarin declined over the 3 days of treatment. For *Anopheles* species, inhibition of emerged adults fell from 33% and 56% at 1 L/hectare and 2 L/hectare after 1 day to 5% and 20% respectively after 3 days. For *Culex* species, inhibition of emerged adults fell from 30% and 46% at 1 L/hectare and 2

Table 1 **Probit regression line parameters of response of *Anopheles stephensi* and *Culex quinquefasciatus* to Neemarin treatment in laboratory tests**

Mosquito species	Intercept	Slope (SE)	LC_{50} (mg/L)	95% CI	LC_{90} (mg/L)	95% CI	χ^2 (df)	*P*-value
An. stephensi	1.31	1.78 (0.07)	0.35	0.18–0.37	1.81	0.96–2.05	26.70 (4)	< 0.0001
Cx. quinquefasciatus	0.85	1.91 (0.06)	0.69	0.36–0.74	3.18	1.68–3.38	29.08 (5)	< 0.0001

SE = standard error.
LC_{50} = lethal concentration to cause 50% mortality in population.
LC_{90} = lethal concentration to cause 90% mortality in population.
CI = confidence interval.
χ^2 (df) = heterogeneity about the regression line (degrees of freedom).

L/hectare after 1 day to 1% and 21% respectively after 3 days. The frequency of larvae in the artificial ponds were different before and after application and increased after 7 days in all replicates, that shows maximum time of efficacy and inhibition of emerged adults at 7 days after application did not show a significant difference ($P < 0.05$).The maximum time of efficacy was 7 days at the 2 L/hectare concentration ($P < 0.05$). The durability of the product depended on the dosage applied ($P < 0.05$).

As in the laboratory tests, pupal mortality was higher than the other stages for *Anopheles* (Table 2) and *Culex* spp. (Table 3). A lower concentration of Neemarin was needed for *Anopheles* spp. larvae than for *Culex* spp. to cause the same mortality ($P < 0.05$).

Table 2 **Mortality of *Anopheles* spp. at different stages in artificial ponds, comparing controls with 2 different concentrations of Neemarin**

Time after treatment	Larvae tested No.	Mortality rate Larvae %	Pupae %	Adults %	Total %	Survival rate %	Inhibition[a] (SE) %
1 day							
Controls	93	7	8	3	18	82	
1 L/hectare	130	18	22	5	45	55	33 (4.1)
2 L/hectare	272	24	29	11	64	36	56 (2.9)
2 days							
Controls	90	9	6	3	18	82	
1 L/hectare	160	10	18	3	31	69	16 (3.6)
2 L/hectare	337	14	27	10	51	49	40 (2.7)
3 days							
Controls	105	12	14	5	18	82	
1 L/hectare	200	6	9	2	17	78	5 (2.6)
2 L/hectare	310	11	18	5	34	66	20 (2.6)

[a]Percentage inhibition of adult emerged larvae comparing treatment with controls.
SE = standard error.

Table 3 **Mortality of *Culex* spp. at different stages in artificial ponds, comparing controls with 2 different concentrations of Neemarin**

Time after treatment	Larvae tested No.	Mortality rate Larvae %	Pupae %	Adults %	Total %	Survival rate %	Inhibition[a] (SE) %
1 day							
Controls	61	7	4	2	13	87	
1 L/hectare	50	14	22	3	39	61	30 (4.2)
2 L/hectare	75	16	26	11	53	47	46 (5.3)
2 days							
Controls	45	5	5	7	17	83	
1 L/hectare	60	5	15	1	21	79	5 (4.3)
2 L/hectare	90	8	20	6	34	66	20 (4.2)
3 days							
Controls	54	6	7	0.4	13	87	
1 L/hectare	51	5	8	1	14	86	1 (3.6)
2 L/hectare	110	8	18	5	31	69	21 (3.8)

[a]***Percentage inhibition of adult emerged larvae comparing treatment with controls. SE = standard error.***

The findings of the present study were compared with other researchers' results using different neem extract formulations (Neemazal, ANSKE, AZT-VR-K-E and MTB) on *Aedes aegypti* mosquitoes. The EC_{50} for above formulations (molar concentration of product which produces 50% of the maximum possible response) were 8.4, 78.2, 18.1 and 5.9 ppm respectively (Table 4).

Discussion

Neem products are capable of producing multiple effects on a number of insect species, such as anti-feeding effects, growth regulation, fecundity suppression and sterilization, oviposition repellency or attractancy and changes in biological fitness [*3*].

In some cases, neem has repellent effects. For example, the percentage protection against sand fly bites provided by neem oil was significantly higher than N,N-diethyphenylacetamide (DEPA) when applied at 1% and 2% concentrations [*16,17*]. Neem extracts have been shown to have repellent activity against *Mansonia* spp. mosquitoes in Gambella, western Ethiopia [*5*].

Studies on the anti-feeding activity of the neem extracts showed that crops treated with an aqueous suspension of neem seeds were protected from attack by locusts. Host plant selection is mainly governed by the responses of the insect's gustatory and olfactory sensilla. Since azadirachtin is non-volatile, the specificity and responsiveness of receptors on the insect's taste neurons are likely to be critically important in this process.

The effects of neem products on the reproduction of insects have been known since 1975 and reproduction reduction effects have been found in Caelifera,

Table 4 **Comparison of effectiveness of different neem formulations in laboratory tests on mosquito species**

Mosquito species	Neem formulation	EC_{50} (ppm)	Reference
Aedes aegypti	Neemazal	8.4	[***11***]
Ae. aegypti	ANSKE	78.2	[***11***]
Ae. aegypti	AZT-VR-K-E	18.1	[***11***]
Ae. aegypti	MTB	5.9	[***11***]
Anopheles stephensi	Neemark	0.05	[***6***]
Culex quinquefasciatus	Neemark	0.22	[***6***]
An. stephensi	Neemarin	0.18	Present study
Cx. quinquefasciatus	Neemarin	0.36	Present study

Neemazal (Trifolio-M GmbH, Lahnau, Germany) 10 g/L azadirachtin.
ANSKE = aqueous neem seed kernel extract.
AZT-VR-K-E = enriched and formulated neem seed kernel extract.
MTB = neem seed extract.
Neemarin (Biotech International Limited, New Delhi, India) 0.15% azadirachtin.
EC_{50} = molar concentration of product which produces 50% of the maximum possible response.

Heteroptera, Homoptera, Hymenoptera, Lepidoptera and Diptera [*3,9*]. A large number of abortions (dead-born larvae) in the tsetse flies *Glossina morsitans morsitans* and *Glossina pallidipes* after treatment of pregnant females with neem oil and the azadirachtin-enriched neem seed kernel extract AZT-VR-K were found.

In mosquitoes, compounds extracted from *Az. indica* showed mortality for fourth instar larvae of *An. stephensi*, with LC_{50} values of 60 and 43 ppm, respectively [*4*]. This compares with the LC_{50} and LC_{90} in our study of 0.36 and 1.81 ppm for *An. stephensi* and 0.69 and 3.18 ppm for *Cx. quinquefasciatus* respectively using a commercial preparation of neem extract, Neemarin. Our results were comparable with findings from other researchers as shown in Table 4. The variation in LC_{50} is due to mosquito species, formulation, climate and method of application.

In order to compare the larvicidal effect of Neemarin with WHO-recommended larvicides (malathion, fenitrothion, temephos, chlorpyrifos), the regression lines were compared. This showed that the toxicity of Neemarin is less than other chemicals and the LC_{50} and LC_{90} of Neemarin on laboratory strains of *An. stephensi* were to some extent similar to temephos [*1*].

Neem extracts act like insect growth regulators, so the mortality at different stages were considered. Mortality of the pupae stage was significantly higher than the larvae and adult stages. In addition, the mortality of *Cx. quinquefasciatus* was significantly lower than *An. stephensi*.

We conclude that Neemarin, at the recommended concentrations in field studies of 1 and 2 L/hectare, significantly reduces the frequency of larvae and the estimated residual effect is 7 days.

Acknowledgements

We would like to thank all of the staff members of the Medical Entomology Department and Giahpezeshk Limited for their kind collaboration.

References

1. ***Report of the fourth meeting of the global collaboration for development of pesticides for public health. Geneva 24–25 June, 2004***. Geneva, World Health Organization, 2004 (WHO/CDS/WHOPES / GCDPP/2004.8).

2. Zaim M. Malaria control in Iran, present and future. ***Journal of the American Mosquito Control Association***, 1987, 3:392–6.

3. Mulla MS, Su T. Activity and biological effects of Neem products against arthropods of medical and veterinary importance. ***Journal of the American Mosquito Control Association***, 1999, 15(2): 133–52.

4. Ruskin FR. ***Neem: a tree for solving global problems***. Washington DC, National Academy Press, 1992.

5. Siddiqui BS et al. Two new triterpenoids from ***Azadirachta indica*** and their insecticidal activity***. Journal of natural products***, 2002, 65(8):1216–8.

6. Hadis M et al. Field trials on the repellent activity of four plant product against mainly ***Mansonia*** population in western Ethiopia. ***Phytotherapy research***, 2003, 17(3):202–5.

7. Sharma SK, Sharma VP. Field studies on the mosquito repellent action of neem oil. ***Southeast Asian journal of tropical medicine and public health***, 1995, 26(1): 180–2.

8. Sharma VP, Dhiman RC. Neem oil as a sandfly (Diptera: Psycodidae) repellent. ***Journal of the American Mosquito Control Association***, 1993, 9:364–6.

9. Dhar R et al. Effect of volatiles from neem and other natural products on gonotrophic cycle and oviposition of ***Anopheles stephensi*** and ***An. culicifacies*** (Diptera:Culicidae). ***Journal of medical entomology***, 1996, 33:195–201.

10. Rao DR, Reuben R. Evaluation of neem cake power and neem cake coated urea as mosquito larvicides in rice fields. In: Uren MF, Block J, Manderson LH, eds. ***Arbovirus research in Australia. Proceedings of the Fifth Symposium 28 August to 1 September 1989***. Brisbane, Australia, CSIRO Tropical Animal Science, 1989:138–42.

11. ***Instructions for determining the susceptibility or resistance of mosquito larvae to insect development inhibitors.*** Geneva, World Health Organization, 1981 (WHO/ VBC/81.812).

12. Finney DJ. ***Probit analysis***, 3rd ed. New York, Cambridge University Press, 1971.

13. Mulla M.S. Insect growth regulators for the control of mosquito pests and disease vectors. ***Chinese journal of entomology***, 1991, 6:81–91.

14. Boschitz C, Grunewald J. The effect of NeemAzal on ***Aedes aegypti*** (Diptera: Culicidae). ***Applied parasitology***, 1994, 35(4):251–6.

15. Shahgudian ER. A key to the Anophelines of Iran. ***Acta medica Iranica***, 1960, 3(3):38–48.

16. Srinivasan R, Kalyanasundaram M. Relative efficacy of DEPA and neem oil for repellent activity against ***Phlebotomus papatasi***, the vector of leishmaniasis.

Journal of communicable diseases, 2001, 33(3):180–4.

17. Parida MM et al. Inhibitory potential of neem (***Azadirachta indica*** Juss) leaves on dengue virus type-2 replication. ***Journal of ethnopharmacology***, 2002, 79(2): 273–8.

Malaria control in the Eastern Mediterranean Region

Significant progress was made in 2003 with the development of appropriate technical guidelines for the improvement of key strategies for the control of malaria and other vector-borne diseases. These included the regional strategic framework for integrated vector management, guidelines on monitoring insecticide resistance, regional guidelines on the management of public health pesticides, including country profiles, and guidelines on malaria microscopy and quality assurance. The WHO publications *Instructions for treatment and use of insecticide-treated mosquito nets* and *Basic malaria microscopy* were translated into Arabic. National strategic plans on use of insecticide-treated nets were finalized for Afghanistan, Djibouti, Saudi Arabia, Sudan and Yemen. A regional network for monitoring vector resistance was initiated and country-level partnership was fostered at the annual meeting of national malaria programme managers held in Lahore, Pakistan in June 2003.

Source: The Work of WHO in the Eastern Mediterranean Region. Annual Report of the Regional Director 1 January–31 December 2003
Available at: http://www.emro.who.int/rd/AnnualReports/2003/index.htm

Characteristics of districts in Pakistan with persistent transmission of wild poliovirus, 2000–2001

S.A. Lowther,[1] T. Mir,[2] M.K. Bile,[2] R. Abdul Hafiz[3] and A.W. Mounts[2]

خصائص المناطق التي تستمر فيها سراية الفيروس البري لشلل الأطفال في باكستان 2000-2001

سارة آن لوثر، طاهر مير، خليف بله محمد، ريحان عبد الحافظ، أنتوني واين ماونتس

الخلاصة: كان هدف الدراسة التعرُّف على العوامل المرافقة للمناطق التي تؤلف مستودع الفيروس البري لشلل الأطفال في باكستان. وقد مُيِّزَتْ المناطق التي تؤلف مستودع الفيروس البري لشلل الأطفال عن غيرها، وفقاً لمعطيات ترصُّد الشلل الحاد الرخو، وإحصائيات تعداد السكان، والمعطيات المجموعة من مسح للموظفين الصحيين في المقاطعات. وقد تم استعراف 11 مقاطعة على أنها مستودع للفيروس البري لشلل الأطفال، ووجد أن الكثافة السكانية فيها أعلى بشكل ملحوظ (550 شخصاً وسطياً في كل كيلومتر مربع) مما هي عليه في المقاطعات التي لا تؤلف مستودعاً للفيروس البري لشلل الأطفال (والتي تبلغ الكثافة السكانية الوسطى فيها 175 شخصاً لكل كيلومتر مربع)، وبمعامل دقة مقدارُه P = 0.001. وقد أبلغ الموظفون الصحيون في المقاطعات التي تؤلف مستودعاً للفيروس البري عن أن التخطيط قد تأثر بالمهجَّرين وعن أن الموظفين يتنقَّلون أكثر من نظرائهم في المقاطعات التي لا تؤلف مستودعاً للفيروس البري (وسطي تنقلات العاملين الصحيين في المقاطعات التي تؤلف مستودع 5 مقابل 3 في المقاطعات التي لا تؤلف مستودعاً) وبمعامل دقة P = 0.005. وقد أكَّد التحليل المتعدِّد المتغيِّرات، أن المقاطعات التي تؤلف مستودعاً، فيها كثافة سكانية مرتفعة في غالب الأحيان، ويتكرَّر فيها كثيراً تنقُّل متكرِّر للموظفين الصحيِّين. ويرى الباحثون أن تقييم الخصائص الإدارية على مستوى المنطقة، يمكن أن يعزز طرق الترصُّد التقليدية للوصول إلى المزيد من التحسين للبرامج الصحية.

ABSTRACT We sought to identify factors associated with being a reservoir district for wild poliovirus in Pakistan. Differences between reservoir and non-reservoir districts were identified using acute flaccid paralysis surveillance data, population census statistics and data from a survey of district health officials (DHOs). Of the 11 poliovirus reservoir districts identified, population density was significantly higher (median 550 persons/km^2) than the non-reservoirs (median 175 persons/km^2). DHOs from reservoir districts more often reported that planning was affected by refugees and they had more frequent DHO transfers compared with non-reservoir districts. Multivariate analysis confirmed that reservoirs more often had high population density and frequent DHO transfers. Assessment of district-level and management characteristics can supplement surveillance methods to further improve health programmes.

Caractéristiques des districts où la transmission du poliovirus sauvage continue au Pakistan, 2000-2001

RÉSUMÉ Nous avons cherché à identifier les facteurs qui font qu'un district est une zone de réservoir du poliovirus sauvage au Pakistan. Les différences entre les districts qui sont ou non une zone de réservoir ont été identifiées en utilisant les données de la surveillance de la paralysie flasque aiguë, les statistiques du recensement de la population et des données tirées d'une enquête des responsables sanitaires de district. Dans les 11 districts identifiés comme étant une zone de réservoir du poliovirus, la densité de population était significativement plus élevée (médiane de 550 personnes/km^2) que dans les districts qui ne sont pas des zones de réservoir (médiane de 175 personnes/km^2). Les responsables sanitaires des districts qui sont des zones de réservoir signalaient plus souvent que la planification était affectée par les réfugiés et étaient plus fréquemment transférés par rapport aux districts qui ne sont pas une zone de réservoir. L'analyse multivariée a confirmé que les zones de réservoir avaient plus souvent une forte densité de population et dans ces zones, les transferts de responsables sanitaires de district étaient plus fréquents. L'évaluation des caractéristiques de la gestion et au niveau du district peut compléter les méthodes de surveillance traditionnelles pour améliorer davantage les programmes de santé.

[1]World Health Organization, Polio Eradication Initiative, Islamabad, Pakistan (Consultant, 2001).
[2]World Health Organization, Islamabad, Pakistan.
[3]National Institutes of Health, Expanded Programme on Immunization, Islamabad, Pakistan,
Received: 31/03/03; accepted: 14/01/04

Introduction

Global poliomyelitis incidence has decreased 99% since the World Health Assembly agreed to instigate the Poliomyelitis Eradication Initiative in 1988 [*1*]. Pakistan began poliomyelitis eradication activities in 1994 and has had considerable success [*2*]. These activities are conducted with the ongoing World Health Organization (WHO) Expanded Programme on Immunization (EPI), which seeks to vaccinate children against poliomyelitis, measles, diphtheria, pertussis, tuberculosis, tetanus, and hepatitis B.

Numerous national immunization days (NIDs) have resulted in a considerable decline and localization of cases in Pakistan [*2*]. However, despite these efforts, several areas in Pakistan appear to be reservoirs where wild poliovirus circulation persists throughout the year, repeatedly reintroducing infection to nearby susceptible populations during the higher transmission season. Presumably a certain threshold of susceptible population would be required to sustain virus circulation in these districts; however, other factors such as effective management of health resources may also be important.

In Pakistan, the administrative tiers of the health system include the federal, provincial and district levels. The federal office is responsible for national health policy decisions, vaccine procurement and distribution of resources to provinces. Provincial health offices are responsible for the administration of health programmes throughout the province, distribution of vaccines and supplies to districts, and supervision and monitoring of district-level activities. Programme implementation, daily management and control of resources are performed at the district level by district health officers (DHOs) (or by agency surgeons in the case of federally administered tribal agencies). In 2000 there were 122 districts-level administrative areas (including 7 tribal agencies).

Areas with continued transmission of wild poliovirus have been examined and identified through ongoing active surveillance [*1*]. However, no published studies have taken an ecologic approach to examining district-level management characteristics that may affect the success of the administrative area in poliomyelitis eradication. Using acute flaccid paralysis (AFP) surveillance data, we sought to describe the characteristics of districts where there appeared to be persistent wild poliovirus transmission in Pakistan. This study examines the relationship between several characteristics of districts, district health management and the presence of a poliovirus reservoir to identify specific factors that might be modified to improve the effectiveness of poliomyelitis eradication in Pakistan.

Methods

On February 28, 2001 a national conference on poliomyelitis eradication was held in Islamabad, Pakistan. All 122 DHOs and agency surgeons were asked to attend. (For this study, the designation "DHO" will include both district health officers and agency surgeons.) DHOs were asked to complete a self-administered survey to collect demographic information such as age, sex, educational achievements, training and years of experience. Information on their district health system that might affect health programme planning, such as data on population migration (e.g. refugees or drought-related movement) was collected. The survey was also used as a forum to express opinions (e.g. describe specific

weaknesses or gaps in their district in personnel or supplies). Surveys were later mailed to those DHOs that either did not attend the conference or did not complete the survey at the time of the conference. Because of its nature as a feedback mechanism, the survey was neither anonymous nor confidential, and respondents were informed that the information they provided would be examined to give feedback and assess programme planning with specific regard to their district.

AFP surveillance data reported from 2000 through 2001 were analysed to identify districts with persistent and low transmission season wild poliovirus circulation. Adequacy of surveillance data was assessed using standard surveillance indicators, i.e. rates of non-poliomyelitis AFP (1 case per 100 000 population expected), 60-day case follow-up (expected to be done on all cases), and adequate stool collection (greater than 80% of all stool specimens collected met the requirements of 2 stool specimens per case collected at least 24 hours apart, within 14 days of the onset of paralysis, and arriving in the laboratory with intact reverse cold chain and sufficient quantity for analysis). Data on population size, area size and population density were obtained from the Population Census Bureau [*3*].

Analysis

Reservoir districts were defined as those districts with wild poliovirus isolated during 5 out of 8 quarters of the years 2000 and 2001 and with virus isolated during low transmission season (December through March) at least one of the years 2000 and 2001.

Several continuous variables were recoded for assessment. For example, because of its broad range among districts, population density was transformed to a logarithmic scale [i.e. ln (population density)] and was categorized into 2 levels: high density, defined as ln (population density) > 7.0 and low density, defined as ln (population density) ≤ 7.0. The number of DHOs transferred in the past 5 years was also categorized into 2 levels: frequent transfers (more than 4 per 5 years) and less frequent transfers (4 or fewer per 5 years). Univariate analysis was performed using *Epi-Info* software where differences were examined between poliovirus reservoir districts and non-reservoir districts. The Kruskal–Wallis test was used to compare district-level characteristics whose values were coded as continuous with exact *P*-values reported. Odds ratios (OR) and exact 95% confidence intervals (95% CI) were used to compare characteristics coded as categorical. Any factors found to be significantly associated with being a reservoir district from univariate analysis were included in multivariate analysis using SAS (Cary, North Carolina, United States of America) statistical software. For all statistical tests a *P*-level of 0.05 was used as significant.

Results

Reservoirs for wild poliovirus

Fifty-nine districts had poliovirus isolated in 2000 and 34 in 2001; 11 administrative districts met our definition of reservoir district. These included Quetta district in Balochistan province; Bannu and Peshawar districts in North-west Frontier Province, Faisalabad district in Punjab province; and Hyderabad, Jacobabad, and Karachi districts in Sindh province (Figure 1). Karachi included 5 administrative districts of Karachi Central, Karachi South, Karachi East, Karachi West and Karachi Malir. As can be

Figure 1 **Districts identified from acute flaccid paralysis surveillance to have persistent wild poliovirus transmission in Pakistan during 2000–2001 (defined as districts with wild poliovirus isolated during 5 out of 8 quarters of the years 2000 and 2001 and with the virus isolated during low transmission season (December–March) in at least 1 of the years)**

seen from Figure 1, the districts were not clustered together geographically which argues against a single large poliovirus reservoir. Surveillance indicators for 2000 from reservoir districts (rates of non-polio AFP, 60-day follow-up and adequate stool collection) were not significantly different from non-reservoir districts, and met the worldwide standards for such indicators of adequate surveillance (Table 1). Population density was higher among reservoir districts compared with non-reservoir districts (median = 550.7 versus 175.9 persons per square km, $P = 0.001$).

Characteristics of DHOs

In all, 101 DHOs responded to the survey (21 never responded) from all provinces of Pakistan. There were no differences in the DHO response rate by reservoir district status, AFP surveillance characteristics, geographic location/province, or population density. The median age of respondents was 50 years (range 40–60 years) and all DHOs were male. All DHOs were physicians (MBBS) and 46% had a public health degree or diploma; 10% reported receiving management training in the past 3 years. In addition, 97% reported having assigned a specific person to be responsible for EPI. As regards the complications of health programme planning, 90% of DHOs reported seasonal migration as a complication, 51% cited refugees 36% cited drought-related migration, 11% cited nomads or gypsies, 4% cited other complications including tribal clashes, border or line-of-control conflict, or smuggling routes. About 16% reported having a private practice. Prior experience as a DHO was reported by 49% of respondents with a median of 6 years of experience (range 0–27 years). In the past 5 years, 59% of

Table 1 **Characteristics among districts and district health officials comparing wild poliovirus reservoir districts to non-reservoir districts, Pakistan, 2000–2001**

Characteristics	Reservoir district		Non-reservoir district		Statistical analysis	
Continuous variables	**Median**		**Median**		**Kruskal–Wallis**	**P-value[a]**
Surveillance indicators						
No. poliomyelitis cases 2001	3.5		0.0		32.70	0.000
Non-poliomyelitis AFP rate (1.00 expected)	1.95		1.42		2.75	0.097
Non-poliomyelitis enterovirus rate (0.10 expected)	0.15		0.17		0.16	0.690
Percentage with 60-day follow-up	100		100		0.25	0.617
Percentage with adequate stool collection	74		71		0.02	0.892
District-level characteristics						
Population density (persons per km^2)	550.7		175.9		13.1	0.001
Area size (km^2)	2268		5286		6.80	0.009
Population size	1 724 915		805 235		6.99	0.008
Total district health officers in last 5 years	5		3		7.73	0.005
Categorical variables	**No.**	**%**	**No.**	**%**	**Odds ratio**	**95% CI[a]**
District-level characteristics						
Log (population density) > 7.0	3	33	1	1	45.5	4.1–506.2
Log (population density) ≤ 7.0	6	67	91	99	1	–
5 to 8 district health officers per 5 years	6	67	20	22	7.2	1.7–31.4
≤ 5 district health officers per 5 years	3	33	72	88	1	–
District health officer characteristics						
Respondents	9/11	82	101/111	91	0.98	0.2–9.5
Previous experience as district health officer	6/9	67	42/93	45	2.38	0.6–10.1
Has private practice	0/9	0	16/96	17	Undef	–
Has public health degree	2/9	22	44/94	47	0.3	0.1–1.6
Specific person assigned to manage EPI	9/9	100	89/92	97	Undef	–
Had management training in last 5 years	0/9	0	10/91	11	Undef	–
Reports drought affects district	3/9	33	31/89	35	0.92	0.2–3.9
Reports refugees affect district	8/9	89	43/91	47	8.74	1.1–72.8
Reports seasonal migration affects district	8/9	89	89/92	97	0.88	0.10–7.8

[a]***Exact P-value and 95% confidence intervals (CI) are given. A P-level of 0.05 and 95% CI excluding 1.0 was considered statistically significant.***

AFP = acute flaccid paralysis. EPI = Expanded Programme on Immunization.

DHOs reported 2 or 3 transfers, with 20% reporting zero or 1 transfer and 21% reporting 4 to 7 transfers.

In univariate analysis, several differences were identified between reservoir and non-reservoir districts (Table 1) among characteristics of DHOs and districts. There was no difference in DHO response rate between reservoir and non-reservoir districts (82% versus 92% respectively, $P = 0.97$). DHOs from reservoir districts were more likely to report that problems in health programme planning were affected by refugees (OR = 8.74, $P = 0.02$) but were equally likely as non-reservoir DHOs to report that problems in planning were affected by factors such as drought or seasonal movement. DHOs from reservoir and non-reservoir districts did not differ by educational status, additional public health training, or years of experience. DHOs reported that reservoir districts had significantly more DHOs in the last 5 years compared with non-reservoir districts (median = 5 versus 3 DHOs, $P = 0.005$).

Multivariate analysis included 2 district-level characteristics (population density and frequency of DHO transfers) and 1 DHO characteristic (reporting that refugees affected health programme planning). This analysis indicated that reservoir districts were more likely to be those among districts of high population density [ln(population density) > 7.0] (adjusted aOR = 28.1, 95% CI: 2.2–361.0) and districts with frequent DHO transfers (> 4 DHO transfers in the last 5 years) (aOR = 5.1, 95% CI: 1.03–25.5). However, after controlling for population density and frequency of DHO transfers, DHOs reporting that refugees affected programme planning was no longer significantly associated with reservoir district status.

Discussion

This analysis describes characteristics of districts and their DHOs in Pakistan with persistent transmission of wild poliovirus, and considers the effect of management and administration on the outcomes of a disease eradication programme. Our data showed that districts with less frequent change of managers were less likely to be poliovirus reservoirs than those with frequent turnover, indicating that consistency of management may improve the outcome of poliomyelitis eradication activities in a given district. Other characteristics of the DHO, such as previous experience as a DHO, management training or total years of experience, were not associated with poliovirus reservoir status. DHOs in the Pakistan health care system are the primary managers of all national public health programmes and are key individuals responsible for a programme's success. Some examples of the responsibilities of DHOs in regard to poliomyelitis eradication planning include: supervising and monitoring of district logistical and personnel planning, disbursement of financial resources and communication with local authorities for involvement.

Our analysis also demonstrated that reservoir districts were more likely to be among districts with the highest population density. This finding is consistent with evidence that urban areas with increased population density are high-risk poliovirus reservoirs [*4*]. In addition, our analysis illustrates the process of identifying reservoir districts based on natural seasonality of the virus in Pakistan. We believe this method helped improve the effectiveness of immunization campaigns by allowing the concentration of resources in areas needing

additional support; it continues to be an important step in the final stages of poliomyelitis eradication.

Our data also suggest that the presence of a substantial refugee population may affect the success of poliomyelitis eradication at the district level. This is consistent with supplementary individual-level epidemiological data collected during 2001 which indicated that Afghan refugees were at higher risk of poliomyelitis in Pakistan [*2*]. The additional population may burden a health programmes' allocation of resources as well as increase virus transmission because of a raised population density. Continued attention to identifying high-risk groups will be invaluable as has been illustrated in outbreak situations [*5,6*].

Previous studies have shown why individual children were under-vaccinated thereby creating reservoirs for wild poliovirus [*7,8*]. However our study is the first to examine risk factors for district and management characteristics of these reservoirs. In Pakistan during 1994, children missed during NIDs were also those more likely to have been unvaccinated or partially-immunized through routine immunization services [*9*]. Elsewhere, risk factors for children missed during NIDs included failure to be reached by methods of social mobilization, increased distance to NID site [*10*], lower parental literacy or educational status [*2*], and age 0–6 months [*11*]. All polio vaccination campaigns in Pakistan have been house-to-house since 1998 [*12*] because they have been found to be more complete in coverage and cost-effective. While the house-to-house strategy is shown consistently to improve coverage, published studies to describe reasons why children are missed during house-to-house coverage are lacking. House-to-house immunization campaigns are a massive undertaking which involve considerable planning and more complex logistics on multiple administrative levels. It is therefore conceivable that quality and consistency of programme administration and management may play a greater role in the successful outcomes of eradication activities.

Our assessment makes no attempt to explain all the reasons for the continued transmission of poliovirus in Pakistan. In the recent past, poliomyelitis cases in Pakistan have been un- or under-vaccinated through routine immunization [*8*]. Routine immunization coverage data could not be validated for the time period of study for every district, and complete, validated countrywide district-specific NID coverage estimations were not available.

The relationship between population density, management turnover rate and poliovirus reservoir may be complex. While a certain population density is necessary to sustain poliovirus circulation, it may also be that densely populated areas, particularly urban areas, may be more desirable posts resulting in more frequent transfer of staff. Alternatively, DHOs in densely populated urban areas may have more difficulties in meeting expected performance standards. Other factors, such as a district literacy rates, socioeconomic status, or per capita health programme funding, may help to describe areas having barriers to successful health programme outcomes. Because of its exploratory nature, our questionnaire did not capture specific reasons for DHO transfer. However, our analysis did identify DHO transfer to be associated with district reservoir status with no association found among factors such as total years of experience, previous experience as a DHO, and training or certification in management. Further assessment of district management may be warranted, both in performance expectations and achievements.

This analysis identifies a management factor that may have an impact on the success of a high-priority disease eradication programme. Our data suggest that decreasing the frequency of transfers in district management may improve the quality of programme implementation. As a result of this study, the United Nations Children's Fund (UNICEF) and WHO have now placed district support teams, comprised of individuals with varying skills, to work directly under the district managers and support all poliomyelitis- and EPI-related activities. These teams receive technical supervision from international and national consultants from the 2 United Nations agencies who are assigned to high-risk districts for periods of up to 1 year and provide additional programme support and continuity.

During both 2002 and 2003 Pakistan conducted 4 rounds of NIDs and 4 rounds of sub-NIDs, which are targeted at areas with factors (such as those described in our analysis) that indicate a high risk for continuing virus transmission [*13*]. In addition, Pakistan introduced wide- scale independent monitoring of coverage through third-party survey companies to improve the quality of supplementary immunization activities by immediately identifying and vaccinating children initially missed during NIDs.

In conclusion, our analysis has identified DHO transfer rate and population density as important determinants of poliomyelitis eradication success. These aspects are now being addressed along with other critical factors to improve efforts to stop transmission of wild poliovirus. We beleive that the findings described in our paper have implications beyond poliomyelitis eradication and should be considered in other disease control programmes.

Acknowledgements

We would like to thank Mr Abid Sheik for his administrative assistance in survey collection, and Alex and Samantha Rowe for their critical review of the manuscript.

References

1. Progress toward global eradication of poliomyelitis, 2001. ***Morbidity and mortality weekly report***, 2002, 51:253–6.
2. Progress toward poliomyelitis eradication—Pakistan and Afghanistan, January 2000–April 2002. ***Morbidity and mortality weekly report***, 51(24):523–4.
3. ***1998 census report of Pakistan***. Islamabad, Population Census Organization, Statistics Division, Government of Pakistan, 1999.
4. Hull HF et al. Paralytic poliomyelitis: seasoned strategies, disappearing disease. ***Lancet***, 1994, 343:1331–7.
5. Aylward RB et al. Unimmunized gypsy populations and implications for eradication of poliomyelitis in Europe. ***Journal of infectious diseases***, 1997, 175 (suppl. 1):S86–8.
6. Reichler MR et al. Outbreak of paralytic poliomyelitis in a highly immunized population in Jordan. ***Journal of infectious diseases***, 1997, 175(suppl. 1): S62–70.
7. Hennessey KA et al. Widespread paralytic poliomyelitis in Pakistan: a case-control study to determine risk factors and implications for poliomyelitis eradi-

cation. ***Journal of infectious diseases***, 2000, 182(1):6–11.

8. Hennessey KA et al. Widespread paralytic poliomyelitis in Pakistan: a case–control study to determine risk factors and implications for poliomyelitis eradication. ***Journal of infectious diseases***, 2000, 182(1):6–11.

9. Reichler MR et al. Evaluation of oral poliovirus vaccine delivery during the 1994 national immunization days in Pakistan. ***Journal of infectious diseases***, 1997, 175(suppl. 1):S205–9.

10. Reichler MR et al. Cluster survey evaluation of coverage and risk factors for failure to be immunized during the 1995 national immunization days in Egypt. ***International journal of epidemiology***, 1998, 27(6):1083–9.

11. Singh B et al. Pulse polio immunization in Delhi—1995–96: a survey. ***Indian journal of pediatrics***, 1997, 64(1):57–64.

12. Linkins RW et al. Evaluation of house-to-house versus fixed-site oral poliovirus vaccine delivery strategies in a mass immunization campaign in Egypt. ***Bulletin of the World Health Organization***, 1995, 73(5):589–95.

13. Progress toward poliomyelitis eradication—Afghanistan and Pakistan, January 2002–May 2003. ***Morbidity and mortality weekly report***, 2003, 52(29): 683–5.

Poliomyelitis eradication in the Eastern Mediterranean Region

Rapid and significant progress towards the eradication of poliomyelitis is continuing in all countries of the Eastern Mediterranean Region. Poliovirus transmission has been interrupted in 17 countries of the Region for more than 3 years. Comprehensive information about the poliomyelitis eradication programme in the Eastern Mediterranean Region can be found at: http://www.emro.who.int/polio/

Characterization of *Leishmania* infection in rodents from endemic areas of the Islamic Republic of Iran

M. Mohebali,[1] E. Javadian,[1] M.R. Yaghoobi-Ershadi,[1] A.A. Akhavan,[1] H. Hajjaran[1] and M.R. Abaei[1]

خصائص عدوى القوارض بالليشمانيات في المناطق الموطونة بها في جمهورية إيران الإسلامية

مهدي محبّ علي، عزة الدين جواديان، محمد رضا يعقوبي إرشادي، أمير أحمد أخوان، محمد رضا عبائي، حمه حجاران

الخلاصة: تمَّ استفراد أنواع الليشمانيات والتعرُّف على خصائصها وعلى النظائر الإنزيمية فيها، كما تم تحليل الجزيئات المأخوذة من القوارض التي أمسك بها في أجزاء مختلفة من جمهورية إيران الإسلامية في ما بين عامَيْ 1991 و2000. أما في المناطق الموطونة بداء الليشمانيات الجلدي فقد وُجدت الطفيليات الآتية التي كشفت بالفحص المجهري المباشر من 18.6٪ من اللطاخات التي أُخذت من 566 نموذج: الليشمانيات الكبيرة وقد تم استفرادُها من 4 نماذج. المعيَّنات الأوبيمية والمريونيسة الليبية والتاتيريَّة الهندية والمريونية الهريانية. وقد استُفردت الليشمانية الطورانية لأول مرة في هذا البلد من المعيَّنات الأوبيمية. وفي المناطق الموطونة بداء الليشمانيات الحشوية لوحظت الطفيليات في كبد وطحال 13.7٪ من أصل 504 من القوارض. وقد كانت نتيجة الزرع إيجابية في حالتَيْن، واستُفردت المُشَيْقات من المريونية الفارسية، وأمكن من دراسة خصائصها التعرُّف على أنها من نوع الليشمانية الدونوفانية ذات الإنزيم LPN50 ومن المتوسطة الذهبية، وقد أمكن من دراسة خصائصها التعرُّف على أنها من الليشمانية الطِّفلية ذات الإنزيم LON49.

ABSTRACT Between 1991–2000, ***Leishmania*** species were isolated and characterized by isoenzyme and molecular analysis from rodents caught in various parts of the Islamic Republic of Iran. In areas endemic for cutaneous leishmaniasis, parasites were observed by direct microscopy in smears from 18.6% of 566 specimens. ***L. major*** was isolated from 4 species: ***Rhombomys opimus, Meriones libycus, Tatera indica*** and ***Mer. hurrianae***. ***L. turanica*** was isolated from ***R. opimus*** for the first time in this country. In endemic areas of visceral leishmaniasis, parasites were observed in liver and spleen from 13.7% of 504 rodents. Two species were positive on culture; promastigotes isolated from ***Mer. persicus*** were characterized as ***L. donovani*** zymodeme LON50 and from ***Mesocricetus auratus*** as ***L. infantum*** LON49.

Caractérisation de l'infection à *Leishmania* chez des rongeurs des zones endémiques de la République islamique d'Iran.

RÉSUMÉ Entre 1991 et 2000, des espèces de ***Leishmania*** ont été isolées et caractérisées par isoenzymes et analyse moléculaire chez des rongeurs capturés dans diverses parties de la République islamique d'Iran. Dans les zones d'endémie de la leishmaniose cutanée, des parasites ont été observés par microscopie directe dans des frottis provenant de 18,6 % des 566 échantillons. ***L. major*** a été isolé chez quatre espèces : ***Rhombomys opimus, Meriones libycus, Tatera indica*** et ***Mer. hurrianae. L. turanica*** a été isolé chez ***R. opimus*** pour la première fois dans ce pays. Dans les zones d'endémie de la leishmaniose viscérale, des parasites ont été observés dans le foie et la rate de 13,7 % des 504 rongeurs. Deux espèces ont donné des cultures positives ; les promastigotes isolés chez ***Mer. persicus*** ont été caractérisés comme zymodème LON50 de ***L. donovani*** et ceux isolés chez ***Mesocricetus auratus*** comme LON49 de ***L. infantum.***

[1]School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran.

Received: 14/04/03; accepted: 26/10/03

Introduction

Leishmaniasis is an important health problem in the Islamic Republic of Iran. There are several foci of zoonotic cutaneous leishmaniasis (CL) in the north, east and south of the country [*1–6*]. Zoonotic CL is essentially a disease of gerbils, transmitted by *Phlebotomus papatasi* and *P. cocausicus* and other species of sand fly that breed in gerbil burrows [*7*]. The human disease is secondary to the infection of gerbils and is seen only in places where the infected gerbils live [*8*]. Three different epidemiological types of zoonotic CL have been observed in this country and 4 species of rodents (Gerbillidae) are the principal animal reservoir hosts in all foci [*9*].

Visceral leishmaniasis (VL), or kala-azar, is also seen sporadically all over the Islamic Republic of Iran and is of the Mediterranean type. Wild and domestic carnivores are the main animal reservoirs [*10–12*], but rodents have been reported as reservoirs in the Meshkin-Shar district [*13*]. Sand flies of the genus *Phlebotomus* are the most likely vector of VL in the endemic areas [*10*].

The study of *Leishmania* infection in rodents in the Islamic Republic of Iran started in 1953 in the north-east of the country [*8*] but, while it was extended to other parts of the country, the isolation and characterization of the parasites has not been investigated in these areas. In this study, we report the isolation and characterization of *Leishmania* species infection from a number of species of rodents that were trapped alive in different parts of the Islamic Republic of Iran in the last decade.

Methods

Study area

The investigation was conducted over a period of 10 years from 1991 to 2000 in endemic foci of zoonotic CL and VL in the Islamic Republic of Iran (Figure 1).

Collection and examination of rodents

The study sites were determined by reports from local health authorities of outbreaks of human CL and VL infection. The active colonies of rodents were identified and the rodents were trapped alive in various parts of these areas. Specimens were collected from the colonies of gerbils located about 1–1.5 km around villages where CL or VL were endemic. Around 20–30 live traps were used each week and rodents were caught in all seasons. The genus and species of the rodents were determined by external characteristics: colour, body measurements, ears, tail, feet, teeth and cranium [*14,15*].

Isolation of parasites from the caught rodents

For detecting CL infection, 2 impression smears were taken from the ears of each rodent [*13,16*]. For detecting VL parasites, 2 impression smears from the spleen and liver of each rodent were prepared. The smears were fixed in methanol, stained by standard Giemsa methods and examined for parasites by light microscope at high magnification (× 1000).

The samples from infected rodents were cultured in Novy–MacNeal–Nicolle (NNN) culture and liver infusion broth tryptose (LIT) and RPMI 1640 medium (Gibco Life Technologies, New York, USA) containing 10% heat-inactivated fetal calf serum. The cultures were checked for promastigotes twice a week for a period of 6 weeks.

Leishmania species were characterized by random amplified polymorphic DNA–polymerase chain reaction (RAPD–PCR)

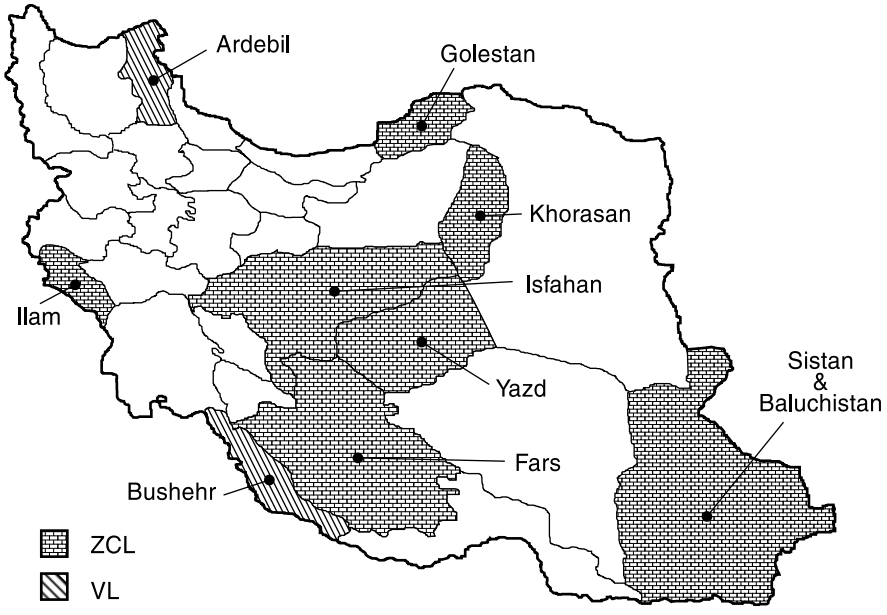


Figure 1 **Areas endemic for zoonotic cutaneous leishmaniasis (ZCL) and visceral leishmaniasis (VL) where rodents were collected for the study**

analysis [*17*,*18*] at the Medical Faculty, Shiraz University of Medical Sciences and the School of Pubic Health, Tehran University of Medical Sciences and by isoenzyme analysis at the London School of Hygiene and Tropical Medicine, United Kingdom, and the Faculty of Medicine, University of Montpellier, France.

Characterization of isolated parasites

For the RAPD–PCR analysis, DNA was extracted from the promastigotes, cultured at 20 °C in RPMI1640 medium (10 000 parasites per 10 mL) and washed with Locke's solution. The pellet was resuspended in 100 µL lysis buffer. The lysate was extracted once with equal volumes of 1:1 (v/v) phenol:chloroform and once with 24:1 (v/v) chloroform isoamylalcohol and precipitated by ethanol. The DNA was resuspended in the specified materials and amplification were done in a mixture containing 20 mmol/L $(NH_4)_2(SO_4)$, 75 mmol/L Tris-HCl, pH.9, 0.01% (w/v) Tween 20, 2 mmol/L $MgCl_2$, 200 µmol/L deoxynulcleotide triposphate, 1 mmol/L primer and 1 unit of Taq polymerase. Then 1 µL of DNA (20 ng/µL) was added by centrifugation through the mineral oil overlay and the reaction was carried out in a thermocycler (Genius, Techne Ltd, United Kingdom) programmed for 1 cycle of 2 min at 94 °C, followed by 30 cycles of 30 s at temperatures of 94 °C, 1 min at 36 °C and 2 min at 72 °C. Aliquots from each reaction (12 µL) were run on 1.5% agarose gel and visualized under ultraviolet light with ethidium

bromide. The primers used in this study were as follows:

- AB1-07 GGT GAC GCA G
- 327. ATA CGG CGT C
- 329. GCG AAC CTC C
- 333. GAA TGC GAC G
- 335. TGG ACC ACC C

For the isoenzyme characterization, after mass production of promastigotes, samples were cultured in monophasic media with 10% to 20% fetal calf serum, washed with phosphate-buffered saline at 4 °C with centrifugation at 2500–3000 × g for 20 min 3 times and freeze-thawed in liquid nitrogen several times, followed by electrophoresis on polyacrylamide gel. In this technique 12 enzymes were used: pyruvate kinase (PK), superoxide dismutase (SOD), phosphoglucomutase (PGM), peptidase D (PEPD), alanine aminotransferase (ALT), aspartate aminotransferase (AST), nucleoside hydrolase (NH), glucose-6-phosphate dehydrogenase (G6PD), glucose-6-phosphate isomerase (GPI), esterase (ES), methanol dehydrogenase (MDH) and mannose-6-phosphate isomerase (MPI) [*19*].

Results

Areas endemic for cutaneous leishmaniasis

Altogether, 566 rodents (Gerbillidae) were trapped alive in several CL-endemic areas throughout the Islamic Republic of Iran from 1991 to 2000. *Leishmania* parasites were observed in cutaneous smears from 105 (18.6%) of the rodents by direct high magnification microscopy examination (Table 1).

L. major was isolated from *Rhombomys opimus*, *Meriones libycus*, *Tatera indica* and *Mer. hurrianae* and characterized by isoenzyme analysis and molecular procedures (RAPD–PCR). All of the *Leishmania* species and strains were similar to *Leishmania* species that had been isolated from human infection in the same areas. *L. turanica* was isolated from an infected *R. opimus* for the first time in this country.

R. opimus was the principal reservoir host of zoonotic CL in the north-eastern (Minoo Dasht) district where 85.2% of isolates tested positive (Table 1). It was also prominent in the central parts of the country (Badrood, Ardakan and Sabzevar districts). *Mer. libycus* was found in 35.1% of isolates in the south-west (Fars province) and 25.0% in the central area. *T. indica* was the main reservoir host in foci of the south-west (14.3%) and south (Dashti and Dashtestan districts) of the country (4.5% of isolates tested positive). In the south-east of the country (including southern parts of Baluchistan, Dashtyari, Konarak and Chabahar areas) the main animal reservoir was *Mer. hurrianae* (17.9% of isolates).

Areas endemic for visceral leishmaniasis

A further 504 rodents (Gerbillidae, Cricetidae) were caught during 1994 to 2000 in 2 areas endemic for VL: Meshkin-Shahr district (north-west) and Dashti and Dashtestan districts (south). *Leishmania* parasites were seen in livers and spleens of 69 (13.7%) of these rodents by microscopy (Table 2).

Leishmania spp. were isolated from 2 specimens of *Mer. persicus* and 1 specimen of *Mesocricetus auratus* in culture media (Table 2). Although parasites were observed in a few specimens of *Cricetulus migratorius*, none were positive on culture. Using isoenzyme techniques the promastigotes isolated from *Mer. persicus* were characterized as *L. donovani* zymodeme

Table 1 ***Leishmania*** **species isolates from rodents caught in areas of the Islamic Republic of Iran endemic for cutaneuos leishmaniasis (1991–2000)**

Location of capture/ rodent species	No. tested	Positive on microscopy No.	%	*Leishmania* species identified
North-east (Minoo Dasht district)				
Rhombomys opimus	27	23	85.2	***L. major***
Meriones libycus	1	0	0	–
South (Dashti and Dashtestan district)				
Tatera indica	133	6	4.5	***L. major***
Meriones crassus	48	0	0	–
Rattus rattus	3	0	0	–
Nesokia indica	3	0	0	–
Mus musculus	5	0	0	–
South-east (Baluchestan)				
Meriones hurrianae	28	5	17.9	***L. major***
Tatera indica	27	1	3.7	–
Rattus rattus	3	0	0	–
Rattus norvegicus	4	0	0	–
Mus musculus	5	0	0	–
Nesokia indica	2	0	0	–
Funambulus pennanti	1	0	0	–
West (Mehran district)				
Tatera indica	22	2	9.1	***L. major***
Nesokia indica	8	0	0	_
Central (Badrood district)				
Meriones libycus	36	9	25.0	***L. major***
Rhombomys opimus	25	8	32.0	***L. major***
South-west (Fars province)				
Meriones libycus	97	34	35.1	***L. major***
Tatera indica	21	3	14.3	–
Central (Ardakan district)				
Rhombomys opimus	26	3	11.5	***L. major***
Meriones libycus	19	3	15.8	–
Central (Sabzevar district)				
Rhombomys opimus	22	8	36.4	***L. major*** and ***L. turanica***
Total	566	105	18.6	

LON50 and those from *Mes. auratus* were identified as *L. infantum* LON49.

Discussion

Both CL and VL are endemic in the Islamic Republic of Iran. Mucosal leishmaniasis is usually an extension of the cutaneous form, except for 3 cases of lesions of the palate for which the causative organisms are unknown [*20*].

The cutaneous form of leishmaniasis is seen in 2 forms: anthroponotic and zoonotic. Anthroponotic CL is endemic in many large- and medium-size cities, as well as villages in the suburbs of these foci. The main reservoir host of CL is man, although the lesions have been observed on dogs in Tehran, Mashad, Shiraz and Kerman [*9*]. Zoonotic CL is endemic in many foci in the north, east and south of the country [*9*]. This is essentially a disease of gerbils, transmitted by sand flies that live and breed in the gerbil burrows. The human disease is secondary to the infection of gerbils and is seen only in places where the infected gerbils live.

Our results show that *R. opimus* (great gerbil) is the principal reservoir host of zoonotic CL in the central and north-east parts of the country. *Mer. libycus* (Libyan jird) was also found to be infected and can act as a secondary reservoir host in the absence of *R. opimus*. Of course, in some areas from the centre and south of the country, gerbils have become the primary reservoir of zoonotic CL due to ecological changes [*21*]. Other foci are in Turkemen-Sahara, Lotfabad and Sarakhs, that is the border with Turkemenistan Republic, Esfarayen in Khorasan, Bakran in Semnan, Abarkuh in Yazd, Neiriz and Estahban in Fars provinces. Natural *Leishmania* spp. infection of *R. opimus* is found in Abardej of Varamin near Tehran but far from human residences and *Leishmania* species have not yet been determined [*9,22*].

T. indica (Indian jird) is the main reservoir host of zoonotic CL in foci of the south-west and south of the country.

Table 2 ***Leishmania*** **species isolates from rodents caught in areas of the Islamic Republic of Iran endemic for visceral leishmaniasis (1994–2000)**

Location of capture/ rodent species	No. tested	Positive on microscopy		Positive on culture media		*Leishmania* species and zymodemes identified
		No.	%	No.	%	
Meshkin-Shahr						
Cricetulus migratorius	15	2	13.3	0	0	–
Mesocricetus auratus	2	1	50.0	1	50.0	***L. infantum*** LON49
Meriones persicus	394	66	16.8	2	0.5	***L. donovani*** LON50
Mus musculus	7	0	0	0	0	–
Allactaga spp.	1	0	0	0	0	–
Dashti and Dashtestan district						
Tatera indica	85	0	0	0	0	–
Total	504	69	13.7	3	0.6	

These areas include the Iran–Iraq borders from Sumar to the Gulf, all the provinces of Khuzestan and some parts of Ilam, Bushehr and Hormozegan [*1*,*11*,*23*].

In foci of the south-east of the country, the main animal reservoir is *Mer. hurrianae* (Indian desert jird). These areas include the southern parts of Baluchistan, Dashtyari, Konarak and Chabahar areas. This type of zoonotic CL is similar to the foci of the disease reported from Rajasthan in India [*4*,*7*,*9*].

The visceral form of leishmaniasis is seen in sporadic form all over the Islamic Republic of Iran and is endemic in Ardebil and east Azerbaijan provinces in the north-west, and in Fars and Bushehr in the south. Wild and domestic dogs are the main reservoir hosts of VL [*12*]. In this study, amastigotes were observed in 13.7% of the rodents on microscopic examination of the smears prepared from internal organs.

L. donovani LON-50 was isolated from 2 specimens of *Mer. persicus* (Persian jird). It seems to transmit from infected rodents to humans in these endemic areas. *L. infantum* LON-49 was isolated from 1 specimen of *Mes. auratus* (golden hamster). This species of *Leishmania* is zoonotic and had been previously isolated from humans [*10*] and dogs in the Meshkin-Shahr area [*12*], and also from dogs and foxes in the Dashti district of Bushehr province [*11*]. *L. infantum* had been isolated from *Rattus rattus* (black rat) in Italy and Iraq [*24*]. In one study, *Mer. persicus* was reported to be naturally infected with *Leishmania* spp. in east Azerbaijan, in the north-west of the Islamic Republic of Iran. In the smears prepared from the cutaneous lesion of this gerbil, considerable numbers of amastigotes were seen. However, microscopic examination of the smears prepared from the internal organs and blood of this rodent did not show any amastigotes [*25*]. In the other study that was carried out in the Semeskandeh area of Mazanderan province in the north of the Islamic Republic of Iran, *Leishmania* spp. infection was reported in internal organs of *R. rattus* but *Leishmania* parasites were not isolated from them (Gholami, personal communication).

In conclusion, this study has shown that rodents harbour *Leishmania* spp. infection and may therefore have a role in transmission of leishmaniasis to humans, particularly to children. Further ecological and biological studies of rodents and sand flies are necessary in endemic foci of zoonotic VL from the Islamic Republic of Iran until the exact role of the rodents as animal reservoirs is clarified completely.

Acknowledgements

We are very grateful to the field staff of the provincial health department of Isfahan, Golestan, Bushehr, Baluchistan, Ilam, Fars and Yazd provinces. The authors would like to thank Dr D. Evans and Dr S. Mazlumi from the London School of Hygiene and Tropical Medicine; Dr J.P. Dedet from Montpellier, France, for isoenzyme characterization of the *Leishmania* isolates; and Dr K.P. Chang from Chicago University, USA, and student Kayako for performing PCR-RFLP. Thanks are also due to Dr Y. Hamzavi and Dr H. Kathiri for field activities. This investigation was supported by the School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences.

References

1. Javadian E et al. Reservoir host of cutaneous leishmaniasis in Iran [Abstract]. ***Proceedings of the XIIth International Congress of Tropical Medicine and Malaria.*** Amsterdam, The Netherlands, 18–23 September, 1988.

2. Nadim A, Seyedi-Rashti MA, Mesghali A. Epidemiology of cutaneous leishmaniasis in Turkemen Sahara, Iran. ***Journal of tropical medicine and hygiene***, 1968, 71:238–9.

3. Nadim A, Seyedi-Rashti MA. A brief review of the epidemiology of various types of leishmaniasis in Iran. ***Acta medica iranica***, 1971, XIV:99–106.

4. Seyedi-Rashti MA et al. Cutaneous leishmaniasis in Baluchistan, Iran [Abstract and Poster]. ***Proceedings of the XI International Congress of Tropical Medicine and Malaria***. Calgary, Canada, 16–22 September, 1984.

5. Yaghoobi-Ershadi MR et al. Epidemiology study in a new focus of cutaneous leishmaniasis due to ***Leishmania major*** in Ardestan town, Central Iran. ***Acta tropica***, 2002, 79:115–21.

6. Hamzavi Y et al. Epidemiological studies of cutaneous leishmaniasis (human infection, animal reservoirs) in Dashti and Dashtestan districts, Bushehr province. ***Iranian public health***, 2000, 29(1–4): 177–91.

7. ***Control of the leishmaniases. Report of a WHO Expert Committee.*** Geneva, World Health Organization, 1990:1–158 (WHO Technical Report Series, No. 793).

8. Nadim A, Faghih M. The epidemiology of cutaneous leishmaniasis in the Isfahan province of Iran. I. The reservoir. II. The human disease. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1968, 62:534–42.

9. Nadim A. Leishmaniases. In: Azizi F et al., eds. ***Epidemiology and control of prevalent diseases in Iran***, 2nd ed. Isfahan, Iran, Endocrine and Metabolism Research Centre, 2000:524–34 [in Farsi].

10. Edrissian GhH et al. Visceral leishmaniasis: the Iranian experience***. Archives of Iranian medicine***, 1998, 1(1):22–6.

11. Mohebali M et al. Seroepidemiological study of visceral leishmaniasis among humans and animal reservoirs in Bushehr province, Islamic Republic of Iran. ***Eastern Mediterranean health journal***, 2001, 7:912–7.

12. Mohebali M et al. Study on canine visceral leishmaniasis in the various parts of Iran. ***Veterinary journal of Tehran University***, 2001, 56(3):55–9.

13. Mohebali M et al. Rodents: another group of animal reservoir hosts of visceral leishmaniasis in Meshkin-Shahr district, the Islamic Republic of Iran. ***Eastern Mediterranean health journal***, 1998, 4(2):376–8.

14. Ziaei H. ***A field guide for identifying of Iranian desert mammalians***, 1st ed. Tehran, Iran, Iranian Environment Organization, 1996:129–87.

15. Boitani L, Bartoli S. ***Macdonald encyclopedia of mammals***. London, Macdonald & Co., 1980.

16. Edrissian GH, Zovein Z, Nadim A. A simple technique for preparation of smears from the ear of ***Rhombomys opimus*** for the detection of leishmanial infection. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1982, 76:706–7.

17. Noyes HA, Belli AA, Maingon R. Appraisal of various RAPD–PCR primers

for ***Leishmania*** identification. ***American journal of tropical medicine and hygiene***, 1996, 55(1):98–105.

18. Motazedian H, Noyes H, Maingon R. ***Leishmania*** and ***sauroleishmania***: the use of random amplified polymorphic DNA for identification of parasites from vertebrates and invertebrates. ***Experimental parasitology***, 1996, 83:150–4.

19. Evans DB. ***Handbook on isolation, characterization and cryopreservation of*** Leishmania***. UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.*** Geneva, World Health Organization, 1989:14–32.

20. Yaghoobi MR et al. Mucosal leishmaniasis: report of three cases. ***Archives of Iranian medicine***, 2001, 4(3):138–40.

21. Yaghoobi-Ershadi MR, Akhavan AA, Mohebali M. ***Meriones libycus*** and ***Rhombomys opimus*** (Rodentia: Gerbillidae) are the main reservoir hosts in a new focus of zoontic cutaneous leishmaniasis in Iran. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1996, 90(5):503–4.

22. Seyedi-Rashti MA et al. A new focus of zoonotic cutaneous leishmaniasis near Tehran, Iran***. Proceedings of the VIIth International Congress of Parasitology, Paris, France, 20–24 August. Bulletin de la Societe Francaise de Parasitology***, 1990, (suppl.)2:1145.

23. Javadian E et al. Confirmation of ***Tatera indica*** (Rodentia:Gerbillidae) as the main reservoir host of zoonotic cutaneous leishmaniasis in the west of Iran. ***Iranian journal of public health***, 1998, 27(1–2):55–60.

24. Desjeux P. ***Information of epidemiology and control of the leishmaniases by country or territory***. Geneva, World Health Organization, 1991 (WHO/LEISH/91.30).

25. Edrissian GH, Ghorbani M, Tahvildar-Bidruni G. ***Meriones persicus***, another probable reservoir of zoonotic cutaneous leishmaniasis in Iran. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1975, 69(5–6):517–9.

Smoking in Oman: prevalence and characteristics of smokers

A.A. Al Riyami[1] and M. Afifi[1]

التدخين في عُمان: معدل الانتشار وخصائص المدخنين

آسيا الريامي، مصطفى عفيفي

الخلاصة: أجرى الباحثان دراسة مسحية مستعرضة لمعدل انتشار التدخين، وخصائص المدخنين الحاليِّين والسابقين، من البالغين العُمانيِّين. واتضح أن المعدل الخام لانتشار التدخين حالياً 7٪ (13.4٪ ذكور و0.5٪ إناث)، في حين كان 2.3٪ لدى المدخنين السابقين، وقد لوحظ أعلى معدل انتشار إجمالي للتدخين الحالي (11.1٪) فيمن هم في عمر يتراوح بين 40 و49 عاماً (18.7٪ من الذكور و0.9٪ من الإناث). أما في الأعمار الأكثر تقدُّماً (أكبر من 40 عاماً) فإن لكل من المستوى التعليمي والحجم العائلي الكبير دوراً في الوقاية من التدخين. وقد كان العمر الوسطي لبدء التدخين 18.7 عاماً للذكور و24.3 عاماً للإناث. ورغم انخفاض معدل انتشار التدخين في عُمان، فإن الوقاية يجب أن توجَّه عَبْر برامج التثقيف الصحي، مع التركيز على إذكاء الوعي لدى المراهقين. كما يُوصَى باتخاذ إجراءات حكومية مثل زيادة الضرائب على التبغ، وفرض قوانين تضمن نظافة الهواء، وحظر الإعلان عن الدخان.

ABSTRACT We carried out a cross-sectional survey to study the prevalence and the characteristics of current and former smoking among Omani adults. Crude prevalence of current smoking was 7.0% (males 13.4%, females 0.5%); 2.3% were former smokers. The overall highest prevalence of current smoking (11.1%) was observed in those 40–49 years (18.7% of males, 0.9% of females). Older age (≥ 40 years), higher educational level and larger family size were protective against smoking. Mean age for starting smoking was 18.7 years for males and 24.3 years for females. Although smoking prevalence is low in Oman, prevention should be addressed in health education programmes, with the emphasis on heightening awareness in adolescents. Government action, e.g. tobacco taxation, clean air laws and bans on advertising, is also recommended.

Le tabagisme à Oman : prévalence et caractéristiques des fumeurs

RÉSUMÉ Nous avons réalisé une enquête transversale pour étudier la prévalence et les caractéristiques des fumeurs actuels et des anciens fumeurs parmi les Omanais adultes. La prévalence brute du tabagisme actuel était de 7,0 % (hommes : 13,4 %, femmes : 0,5 %) ; 2,3 % étaient des anciens fumeurs. La prévalence globale du tabagisme actuel la plus élevée (11,1 %) était observée chez les personnes de 40 à 49 ans (18,7 % d'hommes, 0,9 % de femmes). Un âge plus avancé (≥ 40 ans), un niveau d'études plus élevé et une famille de plus grande taille représentaient une protection contre le tabagisme. L'entrée dans le tabagisme avait lieu à un âge moyen de 18,7 ans chez les hommes et 24,3 ans chez les femmes. Bien que la prévalence du tabagisme soit faible à Oman, la prévention devrait être envisagée dans le cadre des programmes d'éducation sanitaire, en mettant l'accent sur la sensibilisation chez les adolescents. Une action des pouvoirs publics, par exemple par les taxes sur le tabac, les lois sur la pureté de l'air et l'interdiction de la publicité, est également recommandée.

[1]Department of Research and Studies, Ministry of Health, Muscat, Oman.
Received: 07/01/03; accepted: 20/10/03

Introduction

Worldwide, it is estimated that tobacco causes about 8.8% of deaths (4.9 million) and 4.1% of disability adjusted life years (59.1 million). Attributable mortality is greater in males (13.3%) than in females (3.8%) [*1*]. Tobacco use is a growing health concern in the developing world, particularly in places where disposable income is increasing [*2*]. Smoking prevalence has increased in adolescents since 1991 even though there has been a decline in the overall prevalence of smoking in many industrialized countries [*3*].

According to the most recent estimate by the World Health Organization, 4.9 million people worldwide died in 2000 as a result of their addiction to nicotine, about half of them prematurely [*1*]. Developing countries already account for half of all deaths attributable to tobacco. The proportion will rise to 7 out of 10 by 2025 because smoking prevalence has been increasing in many low-income and middle-income countries while it is falling in richer countries, especially among men [*4*]. Lam et al. concluded that among middle aged men the proportion of deaths caused by smoking was more than twice as great in Hong Kong in 1998 as in mainland China 10 years earlier [*5*]. Another study on smoking and mortality from tuberculosis and other diseases in India showed that the death rates from medical causes of ever-smokers were double those of never smokers [*6*]. In Saudi Arabia, Al Khadra found that smoking was the main risk factor for having acute myocardial infarction at a young age (< 45 years), followed by low high-density lipoprotein cholesterol, high low-density lipoprotein cholesterol and diabetes [*7*].

Oman and other oil-producing countries in the Middle East have experienced rapid economic, sociodemographic and epidemiological transitions over the past 3 decades. The sociocultural and economic patterns of the Omani population do not typically correspond to either the Western community or to the developing countries in Asia. This is why data on smoking in Oman would be valuable and therefore why we conducted our study.

The aim of the study was to estimate prevalence of smoking among adults of both sexes aged 20 years and above, to study the characteristics of current smokers, to identify the age of starting smoking, reasons for smoking and factors related to smoking cessation in a community-based survey as a part of the Omani National Health Survey, 2000.

Methods

Sample

The sample for the survey was selected to be representative of the nation as a whole. The survey adopted a multi-stage, stratified probability-sampling design. In the first stage, all 10 regions of Oman were selected and the sample was distributed according to proportional allocation of the population in each. In each region, 1 or more *wilayat* (districts) were randomly chosen according to the size of the population. The number of *wilayat* selected was 16 out of a total of 59 (27%). Then, each *wilayat* was stratified into 2 strata; the first stratum was the *wilayat* centre, covering the urban area and the second stratum was the villages or remote areas, the rural areas. The urban:rural ratio was 2:1, which is similar to the ratio in the 1993 national census [*8*].

The second stage was the random selection of the population sampling units in each stratum. These population sampling units were the census units which were used during the 1993 population census.

The third stage was the selection of households from these population sampling units. Maps of the selected population sampling units were updated and a complete listing of all Omani households in each unit was made to obtain the sampling frame, then households were systematically randomly selected. All individuals aged 20 years and above in the selected household were invited to participate in the survey. The total number of households selected was 1968 with a total of 7011 people fulfilling the selection criteria. The prevalence of the least expected disorder of the lifestyle risk factors studied (smoking rate among female adults, 0.2%) was used to calculate the sample size of the survey. The response rate varied, according to the type of measurement or completed laboratory investigation, from 83% (for fasting blood sugar) to 91.5% (for blood pressure measurement).

Questionnaire and measurements

The questionnaire covered demographic and socioeconomic data (age, sex, marital status, educational status, work status, family size and place of residence) and included questions related to current smoking, age of starting smoking, number of cigarettes smoked per day, type of tobacco product smoked, reasons for smoking, history of temporarily quitting smoking for a year or more, being a former smoker and the number of years of smoking cessation and reasons for smoking cessation. Measurements of blood pressure, weight, height, waist circumference and hip circumference were registered in the questionnaire. World Health Organization procedures were used for taking the measurements [*9*]. The questionnaire also included items for the laboratory investigations for fasting blood sugar and serum cholesterol.

Specimen collection and analysis

The survey was carried out by 25 teams. Each consisted of a nurse to take the measurements, a laboratory technician to draw the blood samples, a health educator to interview the subjects, a health inspector to transport the samples to the laboratory and a field supervisor (statistician) to supervise and review the questionnaires during field operations. They were all trained on the methodology of the survey for 2 weeks.

The eligible members of the selected households were asked to start fasting 1–2 hours before midnight the night before they were due a visit by the survey team. The following morning at 07.00 the participants were interviewed, measurements were taken, and venous fasting blood samples were collected. Fasting blood samples for glucose were collected in sodium fluoride potassium oxalate tubes, labelled and transferred immediately with laboratory forms to the laboratory in the *wilayat* hospital in coldboxes. Samples were then immediately centrifuged, the plasma was separated and fasting plasma glucose was determined by a glucose oxidase method on the same day using the Hitachi 911 automated clinical chemistry analyser (Boehringer Mannheim, Germany) [*10*]. The same manufacturer supplied the reagents. The samples for estimation of cholesterol were collected in tubes containing lithium heparin anticoagulants and transferred to the laboratory in the same way. Estimation of serum cholesterol was done by enzymatic colorimetric method using the Hitachi 911 automated clinical chemistry analyser [*11*].

Diagnostic criteria

The World Health Organization criteria (1999) for diagnosis of hypertension, hypercholesterolaemia, anthropometric mea-

surement and glucose intolerance were used [*12*].

Prevalence of hypertension was estimated by adding the number of people self-reporting systolic or diastolic hypertension (whether their blood pressure was normal or not at the screening time) and the number of people with mean of 2 readings ≥ 140 mmHg systolic blood pressure or ≥ 90 mmHg diastolic phase 5 blood pressure i.e. either isolated systolic or diastolic hypertension. Blood pressure was taken in a sitting position at 5-minute intervals; the average of these readings was calculated to the nearest 5 mmHg.

High total cholesterol was defined as ≥ 5.2 mmol/L or ≥ 200 mg/dL.

Participants were considered underweight if their body mass index (BMI) was < 18.5 kg/m^2, normal if their BMI was 18.5–24.9 kg/m^2, overweight if their BMI was 25.0–29.9 kg/m^2, obese if their BMI was 30.0–39.9 kg/m^2, morbid obese if their BMI was ≥ 40.0 kg/m^2.

Abnormal waist:hip ratio [waist circumference (m)/hip circumference (m)] (central obesity) was defined as ≥ 0.85 for females and ≥ 0.95 for males.

Impaired fasting glucose (IFG) was defined as fasting blood glucose 6.1–6.9 mmol/L. Diabetes prevalence was estimated by adding the number of people selfreporting diabetes and the number of people with fasting blood glucose ≥ 7.0 mmol/L. The total number of participants with IFG was the sum of those with IFG and those with diabetes.

Pilot study

A pretest was carried out to test the households and the individual questionnaires and forms to obtain information about operational and organizational procedures and to get an indication of the general response to physical examination and specimen collection. A total of 120 households were selected from different areas in Muscat governorate. All the survey questionnaires and forms were interpolated and were revised by experts. Measurements and specimens were also taken. The questionnaires and forms and some organizational procedures were adjusted after the debriefing session for interviewers and supervisors. The problems, performance rates and general receptivity to the survey were analysed and discussed.

Data processing and analysis

Data entry was done using *Epi-Info*, version 6. The preparation of the data file was completed by July 2000. Respondents were defined as current smokers if they were smoking at the time of the survey and had smoked more than 100 cigarettes in their lifetime; they were defined as former smokers if they had smoked more than 100 cigarettes in their lifetime but no longer smoked; and they were defined as never smokers if they had never smoked or had smoked less than 100 cigarettes in their lifetime.

Analysis of the data was done using *SPSS*, version 5.0. Data were given as counts, means and percentages. Likelihood chi-squared test examined the distribution of data while group means were compared using analysis of variance. Logistic regression was conducted to test the most important independent associated factors (age, level of education, marital status, family size, residence, work status, hypertension, total IFG, hypercholesterolaemia, obesity or central obesity) with the dependent or the outcome variable (current smoking) with and the adjusted odds ratio (OR) was calculated for these factors. Logistic regression determines the independence of the associations observed in bivariate analysis by controlling for potential confound-

ing variables. The OR shows the change in the odds of the dependent variable when the independent changes from 0 to 1. $P < 0.05$ was considered statistically significant.

Results

A total of 7011 respondents aged 20 years and over [mean age 38 years, standard deviation (SD) 15.2] participated in the study, 3506 of them males (50% of the sample, mean age 38.4 years, SD = 16.7) and 3505 females (mean age 37.6 years, SD = 15.6). Overall, 7.0% of the respondents were classified as current smokers, 2.3% as former smokers and 90.7% as never smokers.

The majority of current smokers smoked cigarettes (82.9%), 6.4% smoked *shisha* (water pipe), 7.9% smoked *gadou* (gouza, a differently shaped pipe that uses different tobacco and a more direct burning method), 7.7% smoked a pipe, and 4.5% used other tobacco products e.g. chewing tobacco.

Current smokers constituted 13.4% of males; 4.6% were former smokers and 82.1% were never smokers. Only 0.5% of females were current smokers, 0.1% were former smokers and 90.4% were never smokers. Of current smokers, 16.7% had a history of smoking cessation for 1 year or more then returned to smoking; 41.8% of them stopped smoking for only 1 year.

Table 1 shows the number of current smokers according to age group, marital status, education level, etc. In males and in the overall sample, smoking prevalence was highest in the age group 40–49 years, with 18.7% of males, 1.0% of females, and 11.1% overall in this age group (χ^2 test significant at $P < 0.05$).

For the whole sample, the prevalence of smoking was also significantly associated with marital status, education level, work status and family size. For males, the same pattern was shown except for work status (χ^2 test significant at $P < 0.05$). For females, smoking was only associated with age and education level (Fisher exact test significant at $P < 0.05$). Smoking was not significantly associated with total IFG for the overall sample, males or females, whereas it was significantly associated with hypertension for all 3 groups. We found no association between smoking and hypercholesterolaemia, obesity or central obesity in the overall sample or the male sub-sample.

Using multiple logistic regression, age, level of education, marital status and family size were the strongest determinants of current smoking for males (Table 2). The test was not done for the female group due to the very low prevalence.

The majority of male smokers (58.7%) started smoking before the age of 20 years, while among females the highest percentage (31.6%) started smoking at a later age (20–29 years) (Table 3). The mean age of starting smoking was 18.7 years for males and 24.3 years for females and the difference was significant at $P < 0.05$ by analysis of variance test (data not shown).

Of the current male smokers, 49.7% smoked 10 cigarettes or fewer per day, 38.0% smoked 11–20 cigarettes per day (Table 4), while former smokers smoked fewer cigarettes: 62.3% smoked 1–10 cigarettes per day. The same pattern was noticed for the overall sample.

Of the current smokers, 46.0% said that the reason for smoking was out of habit, while 21.5% of them said smoking helped them to relax. In addition, 13.4% of the sample smoked because their friends smoked and 11.5% looked on smoking as leisure (data not shown in tables).

Table 1 **Prevalence of smoking in males and females for some demographic and health characteristics**

Characteristic	Males (*n* = 3506)			Females (*n* = 3505)			Total (*n* = 7011)		
	n	No.	%	*n*	No.	%	*n*	No.	%
Age group (years)									
20–29	1454	167	11.5	1431	2	0.1	2885	169	5.9
30–39	674	118	17.5	789	5	0.6	1463	123	8.4
40–49	465	87	18.7	344	3	0.9	809	90	11.1
50–59	391	57	14.6	552	4	0.7	943	61	6.5
60–64	189	14	7.4	136	3	2.2	325	17	5.2
≥ 65	329	26	7.9	249	2	0.8	578	28	4.8
Marital status									
Married	2327	337	14.5	2336	14	0.6	4663	351	7.5
Single, divorced, widowed	1168	131	11.2	1156	5	0.4	2324	136	5.9
Education level									
Illiterate/preparatory school	2492	413	16.6	2658	19	0.7	5150	432	8.4
Secondary and above	964	52	5.4	789	0	0.0	1753	52	3.0
Work status									
Working	2348	327	13.9	429	0	0.0	2777	327	11.8
Not working	1141	140	12.3	3044	18	0.6	4185	158	3.8
Residence									
Urban	2592	343	13.2	2548	17	0.7	5140	360	7.0
Rural	910	126	13.8	953	2	0.2	1863	128	6.9
Family size									
≤ 10 members	1818	286	15.7	1870	12	0.6	3688	298	8.1
> 10 members	1684	183	10.9	1631	7	0.4	3315	190	5.7
Total IFG									
Normal	2340	317	13.5	2441	13	0.5	4781	330	6.9
TIFG	531	76	14.3	471	6	1.3	1002	82	8.2
Blood pressure									
Normal	1975	252	12.8	2312	7	0.3	4287	259	6.0
Hypertension	1079	168	15.6	1042	12	1.2	2121	180	8.5
Cholesterol									
Normal	1747	240	13.7	1726	10	0.6	3473	250	7.2
Hypercholesterolaemia	1171	157	13.4	1201	9	0.8	2372	166	7.0
Obesity									
No	1654	253	15.3	1694	10	0.6	3348	263	7.9
Yes	1417	171	12.1	1659	9	0.5	3076	180	5.9
Central obesity									
No	1947	258	13.3	1179	8	0.7	3126	266	8.5
Yes	896	122	13.6	2145	11	0.5	3041	133	4.4

Some categories do not sum to the total sample due to missing data.
TIFG = total impaired fasting glucose.

Table 2 **Multiple logistic regression for variables significantly associated with current smoking among males**

Variable	OR	95% CI	*P*
Age group (years)			
20–39[a]			
≥ 40	0.61	0.47–0.79	< 0.01
Education level			
Illiterate/preparatory school[a]			
Secondary and above	0.26	0.18–0.38	< 0.01
Family size			
< 10 members[a]			
≥ 10 members	0.6	0.48–0.77	< 0.01
Marital status			
Married[a]			
Single, divorced, widowed	0.73	0.55–0.97	0.03

OR = odds ratio.
CI = confidence interval.
[a]Reference category.

Of the current smokers, 17.12% had a history of temporarily stopping smoking for 1 year or more. Of these, 40.7% had stopped for 1 year, 45.1% for 2–5 years and 14.2% for more than 5 years then returned to smoking. As regards former smokers, 21.1% stopped smoking for curative reasons, 33.6% because in the negative effects of smoking and 27.5% realized that there was no benefit in smoking. About 7% of the former smokers had ceased smoking for 1 year, 31.5% for 2–5 years, 24.2% for 6–10 years and the rest for more than 10 years. There was no significant association between the reason for smoking cessation and the number of years of smoking cessation. (χ^2 = 0.01, P = 0.9) (data not shown in tables).

Table 3 **Age when started smoking for current and former smokers among males, females and overall sample**

Age at starting smoking (years)	Males		Females		Total	
	No.	%	No.	%	No.	%
≤ 10	32	5.6	1	5.3	33	5.6
11–14	81	14.3	3	15.8	84	14.3
15–19	221	38.8	4	21.1	225	38.3
20–29	195	34.3	6	31.6	201	34.2
30–39	31	5.4	3	15.8	34	5.8
≥ 40	9	1.6	2	10.5	11	1.9

Discussion

There are few published data on the epidemiology of smoking in Gulf countries, including Oman. Comparable data on the prevalence of smoking are not widely available and are often inaccurate, especially when age-specific data are required. More importantly, current prevalence of smoking is a poor proxy for the cumulative hazards of smoking, which depend on several factors, including the age at which smoking began, duration of smoking, number of cigarettes smoked per day, degree of inhalation, and cigarette characteristics such as tar and nicotine content or type of filter [*1*]. Smoking is related to substantially increased risk of mortality from lung cancer, upper aerodigestive cancer, several other cancers, heart disease, stroke, chronic respiratory disease and a range of other medical conditions. As a result, in populations where smoking has been common for many decades, tobacco use accounts for a considerable proportion of mortality, as illustrated by estimates of smoking-attributable deaths in industrialized countries [*5,13*].

In 1995, the Oman Family Health Survey revealed that an estimated 6.7% of those aged 15 years or over were current

Table 4 **Number of cigarettes smoked per day for former and current smokers**

No. cigarettes per day	Males				Females				Total			
	Current smokers		Former smokers		Current smokers		Former smokers		Current smokers		Former smokers	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
≤ 10	217	49.7	94	62.3	10	62.5	2	66.7	227	50.1	96	62.3
11–20	166	38.0	44	29.1	5	31.3	1	33.3	171	37.8	45	29.2
21–30	33	7.6	6	4.0	1	6.3	0	0.0	34	7.5	6	3.9
31–40	21	4.8	4	2.6	0	0.0	0	0.0	21	4.6	4	2.6
> 40	0	0.0	3	2.0	0	0.0	0	0.0	0	0.0	3	1.9
Mean (SD)	13.8 (9.3)		11.8 (10.3)		10.2 (8.5)		9.7 (9.1)		13.7 (9.3)		11.8 (10.3)	

SD = standard deviation.

smokers, 13.2% for males and 0.2% for the female respondents (A.J.M. Sulaiman, A. Al Riyami, S. Farid, unpublished data, 1995). The results of the 1995 survey were only descriptive in nature and there was, therefore, a need to study the epidemiology and correlates of smoking. The smoking rate in our study did not show any significant rise compared to 1995. The prevalence of smoking in Oman is lower than that in other Gulf or Asian countries. In Kuwait, smoking rate was 38.1% among physicians [*14*], 30% among male students [*15*], 37% among married men and 0.5% among married women [*16*]. In Saudi Arabia, the 1994 smoking rate was 40.0% for males and 8.2% for females [*17*]. In Bahrain, in a study conducted in the year 2000, the prevalence of smoking was high for both sexes: 32.1% among men and 20.7% among women aged 30–79 years [*18*]. In China, the rate was much higher for males, 66.6%, whereas it was low, 1.7%, among females [*19*].

Women in Oman as well as other developing countries tend to have lower rates of smoking than men [*20*, A.J.M. Sulaiman, A. Al Riyami, S. Farid, unpublished data, 1995]. They also start smoking later than men and smoke fewer cigarettes. This is mainly the result of sociocultural, religious or economic factors. In some societies, it may be considered improper or indecent for females to be seen smoking in public; in addition there may be religious or economic arguments against it.

Smoking rates were significantly lower in people having a higher educational level (secondary and above) using bivariate and multivariate analysis. The same results were found by Memon et al. in Kuwait [*20*]. In contrast, Saeed, Khoja and Khan in Saudi Arabia found that smoking rates were significantly higher among literate than illiterate people, which could be explained by smoking being popular in higher social classes as it could denote prestige [*17*]. Older age was a protective factor against smoking; the majority of the current and former smokers in our study, almost 55%, began smoking in adolescence. For this reason, a major effort should be directed towards implementing health education for children and adolescents. Anti-tobacco education should be included as an integral part of the curriculum in schools.

Conclusion and recommendations

Although the study revealed lower rates of smoking in Oman in comparison with other Gulf countries, anti-tobacco programmes should be vigorously implemented to prevent the health consequences of smoking. Tobacco is not cultivated or produced in Oman. A pack of 20 imported cigarettes costs around US$ 1, and the war against tobacco is not easy. Children and adolescents should be targeted, and reasons for smoking cessation and the diseases associated with smoking should be taken into consideration in planning a health education programme.

Because some of the issues concerning tobacco control may be beyond the domain of national policies and legislation, tobacco control policies are not being implemented worldwide at a rate that current scientific knowledge about the dangers of tobacco warrants. International collaboration should be aimed for in order to share policy and programme information and implement tobacco control strategies. Government action in the form of tobacco taxation; clean indoor air laws in public places through legislation and enforcement; comprehensive bans on advertising of tobacco through legislation; dissemination of information through health warning labels, counter-advertising and various consumer information packages; and nicotine replacement therapy targeting current smokers aged 20–60 years are recommended. The benefits of reduction in tobacco use now, although taking longer to materialize than those resulting from reduction of some other risks, are great and long lasting. This is seen in the estimated tens of millions of healthy life years to be saved by 2010 and 2020 as a result of preventing and reducing tobacco use [*1*].

References

1. ***The world health report 2002: reducing risks, promoting healthy life***. Geneva, World Health Organization, 2002.
2. World Bank. ***World development report 1993: investing in health***. New York, Oxford University Press, 1993.
3. Wechsler H et al. Increased levels of cigarette use among college students: a cause for national concern. ***Journal of the American Medical Association***, 1998, 280(19):1673–8.
4. de Beyer J, Brigden LW, eds. ***Tobacco control policy: strategies, success, and setbacks***. Washington, World Bank and Research for International Tobacco Control, 2003:1.
5. Lam TH et al. Mortality and smoking in Hong Kong: a case–control study of all adult deaths in 1998. ***British medical journal***, 2001, 323(7309):361–7.
6. Gajalakshmi V et al. Smoking and mortality from tuberculosis and other diseases in India: retrospective study of 43 000 adult male deaths and 35 000 controls. ***Lancet***, 2003, 362(9383):507–15.
7. Al Khadra AH. Clinical profile of young patients with acute myocardial infarction in Saudi Arabia. ***International journal of cardiology***, 2003, 91(1):9–13.
8. ***Facts and figures: Special issue on development efforts 1970–2000.*** Muscat, Oman, Ministry of National Economy, Information and Publication Centre, 2000: 4.
9. King H, Minjoot-Pereira G. ***Diabetes and noncommunicable disease risk factor***

surveys: a field guide. Geneva, World Health Organization, 1999.

10. Kadish AH, Hall DA. A new method for the continuous monitoring of blood glucose by measurement of dissolved oxygen. ***Clinical chemistry***, 1965, 11(9): 869–75.

11. Allain CC et al. Enzymatic determination of total serum cholesterol. ***Clinical chemistry***, 1974, 20(4):470–5.

12. ***Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consultation. Part 1: Diagnosis and classification of diabetes mellitus.*** Geneva, World Health Organization, 1999 (WHO/NCD/NCS/99.2).

13. Boyle P. Cancer, cigarette smoking and premature death in Europe: a review including the Recommendations of European Cancer Experts Consensus Meeting, Helsinki, October 1996. ***Lung cancer***, 1997, 17(1):1–60.

14. Bener A, Gomes J, Anderson JA. Smoking habits among physicians in two Gulf countries. ***Journal of the Royal Society of Health***, 1993, 113(6):298–301.

15. Moody PM, Al Bustan A, Al Shatti A. Cigarette smoking habits among Kuwait University male students pre- and post-invasion periods. ***Journal of the Kuwait Medical Association***, 1996, 28(3): 274–8.

16. Radovanovic Z, Shah N, Behbehani J. Prevalence of smoking among currently married Kuwaiti males and females. ***European journal of epidemiology***, 1999, 15(4):349–54.

17. Saeed AA, Khoja TA, Khan SB. Smoking behaviour and attitude among adult Saudi nationals in Riyadh City, Saudi Arabia. ***Tobacco control***, 1996, 5(3):215–9.

18. Hamadeh RR, Musaiger AO. Life style patterns in smokers and non-smokers in the state of Bahrain. ***Nicotine and tobacco research***, 2000, 2(1):65–9.

19. Gong YL et al. Cigarette smoking in China. Prevalence, characteristics and attitudes in Minhang district. ***Journal of the American Medical Association***, 1995, 274(15):1232–4.

20. Memon A et al. Epidemiology of smoking among Kuwaiti adults: prevalence, characteristics, and attitudes. ***Bulletin of the World Health Organization***, 2000, 78(11):1306–15.

Some risk factors for hypertension in the United Arab Emirates

S. Sabri,[1] A. Bener,[2] V. Eapen,[1] M.S.O. Abu Zeid,[3] A.M. Al-Mazrouei[4] and J. Singh[5]

بعض عوامل اختطار فرط ضغط الدم في الإمارات العربية المتحدة

سفيان صبري، عبد الباري بنير، فيلسما إيبين، محمد أبو زيد، أحمد المزروعي، جيبول سنغ

الخلاصة: استهدفت هذه الدراسة للحالات والشواهد، تقييم العلاقة بين فرط ضغط الدم وبين عدد من عوامل الاختطار الاقتصادية الاجتماعية المتعلقة بنمط الحياة، في مدينة العين. وقد شملت الدراسة مسح 426 من البالغين الذين تتراوح أعمارهم بين 20-65 عاماً من المصابين بفرط ضغط الدم، من الذين يراجعون عيادات حضرية وشبه حضرية، إلى جانب 436 من الشواهد ذوي ضغط الدم الطبيعي ممن تم اختيارهم عشوائياً. وقد لوحظ أن فرط ضغط الدم كان أكثر شيوعاً بين الرجال ممن تتراوح أعمارهم بين 40 و49 عاماً، وبَيْن غير المواطنين، وبَيْن من يعيشون في المناطق الحضرية، وبين المتزوجين حديثاً، وبَيْن من لديهم أطفال، وبَيْن الأميِّين، وبَيْن من يعملون في وظائف إدارية أو مهنية، وبَيْن من يعيشون في منزل تقليدي، وبَيْن من دخلهم منخفض. كما اتضح أن هناك فروقاً هامة بين الحالات المدروسة، وبين الشواهد في ما يتعلق بالبدانة، وارتفاع مستوى الكولسترول، ونقص النشاط البدني، ووجود سوابق عائلية لأمراض القلب أو أمراض الكلية أو السكَّري. وقد أظهر التَحَوُّف اللوجستي المتعدِّد المتغيِّرات، أن البدانة والدخل المتوسط أو المرتفع، وسوابق الإصابة بالسكَّري، ونقص النشاط البدني، وتربية أكثر من ثلاثة أطفال، يترافق بفرط ضغط الدم بشكل واضح.

ABSTRACT A case–control study evaluated the relationship between hypertension and socioeconomic and lifestyle factors in Al-Ain city. The survey included 426 hypertensive adults aged 20–65 years attending urban and semi-urban clinics and a randomly selected sample of 436 normotensive controls. Hypertension among cases was higher for men, age 40–49 years, non-UAE nationals, urban living, currently married, having children, illiterate, administrative/professional job, living in traditional house and low income. There were significant differences between cases and controls with regard to obesity, raised cholesterol level, low physical activity and family history of heart disease, kidney disease or diabetes. Multivariate logistic regression analysis revealed that obesity, medium/high income, history of diabetes, low physical activity and having 3+ children were significantly associated with hypertension.

Certains facteurs de risque d'hypertension aux Émirats arabes unis

RÉSUMÉ Une étude cas-témoins a évalué la relation entre l'hypertension et des facteurs socio-économiques et liés au mode de vie dans la ville d'Al-Ain. L'étude comprenait 426 adultes hypertendus âgés de 20 à 65 ans qui consultaient dans des dispensaires urbains et semi-urbains et un échantillon, sélectionné de manière aléatoire, de 436 témoins normotendus. L'hypertension parmi les cas était plus élevée chez les hommes, âgés de 40 à 49 ans, non ressortissants des Émirats arabes unis, vivant en milieu urbain, mariés au moment de l'étude, ayant des enfants, analphabètes, occupant un emploi administratif/professionnel, vivant en maison traditionnelle et ayant un faible revenu. Il y avait des différences significatives entre les cas et les témoins concernant l'obésité, un taux de cholestérol élevé, une activité physique faible et des antécédents familiaux de maladie cardiaque, de maladie rénale ou de diabète. L'analyse de régression logistique multivariée a révélé que l'obésité, un revenu moyen/élevé, des antécédents de diabète, une activité physique faible et le fait d'avoir plus de trois enfants étaient significativement associés à l'hypertension.

[1]Department of Psychiatry, Faculty of Medicine and Health Science, UAE University, United Arab Emirates.
[2]Department of Medical Statistics and Epidemiology, Hamad Medical Corporation and School of Epidemiology and Health Sciences, University of Manchester, United Kingdom.
[3]Primary Health Care Clinic, Oud Al Thoba, Ministry of Health, Al-Ain, United Arab Emirates.
[4]Khalifa Hospital, Abu Dhabi Health Authority, Abu Dhabi, United Arab Emirates.
[5]Department of Biological Sciences, University of Central Lancashire, United Kingdom.
Received: 22/06/03; accepted: 23/12/03

Introduction

The United Arab Emirates (UAE), like other developing countries, has undergone rapid changes during the past 2 decades [*1*]. The discovery of oil in the middle of the last century has contributed to significant social change, and UAE, along with other Gulf Arab states, have experienced a rapid transition in its socioeconomic status. People in UAE now enjoy a high standard of living and substantial improvements in their living conditions. There has been a dramatic rise in the national economy, expressed in terms of per capita income. In 2001, the gross domestic product (GDP) per capita were estimated as US$ 22 800. The infant mortality rate has decreased from 10.5 per 1000 live births in 1981 to 6.6 in 2000 and life expectancy has increased from 68 years in 1977 to 75 years in 2000 (Ministry of Health, Annual Report, 1980–2000) [*2*].

Rapid economic growth in UAE has, however, brought about marked changes both in lifestyle and in patterns of health and disease. With the greater availability of housekeepers, cars, televisions and sophisticated household appliances, the lifestyle of the people of UAE has become more sedentary, and watching television and eating snack foods are the main leisure-time activities. Hypertension has become one of the leading public health problems.

Hypertension is a major contributor to atherosclerosis-induced cardiovascular disease [*3,4*]. The prevalence is higher in men than in women below the age of 35 years but by the age of 65 years the prevalence is higher in women [*5*]. In elderly women, it is the single most important risk factor for cardiovascular disease [*6*].

Data available from several Eastern Mediterranean countries indicate that hypertension is emerging as an important cause of morbidity and mortality. Epidemiological surveys on hypertension report a prevalence of 20% to 26% in the adult population [*7*]. In some urban areas high blood pressure may affect up to 30% of the adult population [*8*]. The prevalence of hypertension appears to be lower in rural than in urban areas [*9–11*]. Other risk factors, such as obesity, dyslipidaemia, diabetes and smoking, are also higher among hypertensive than normotensive people [*12*]. There is also a significant association between hypertension and diabetes mellitus in the UAE [*3,4,13*].

There have been no systematic studies in the UAE population of the relationship between health and socioeconomic factors such as income or demographic factors including education and occupation. Since each community has its own common and unique socioeconomic determinants for cardiovascular diseases, particularly hypertension, it is important to study these variables in different populations. In the UAE it is believed that the effect of education and occupation on health are much weaker than in the Western European countries due to differences in the educational system and the influence of the industrial economy in Europe.

The present study in the city of Al-Ain, UAE, compared hypertensive patients attending primary health care clinics with non-hypertensive controls. The aim was to investigate the importance of socioeconomic status and lifestyle habits in relation to hypertension.

Methods

This was a matched case–control study to determine the relationship between hypertension and demographic, socioeconomic and lifestyle factors. The survey was conducted from October 2001 to July 2002.

Sampling procedure

A multi-stage stratified cluster sampling design was developed using the administrative divisions of the Al-Ain city medical health district which have approximately equal numbers of inhabitants. In order to secure a representative sample of the study population, sampling was stratified with proportional allocation according to stratum size from urban and semi-urban areas. The sample size was determined on the *a priori* assumption that the prevalence of hypertension in the UAE would be more or less similar to the 20% rate observed in the pilot study. Assuming the prevalence of hypertension to be 20% and allowing for an error of 5% at the 1% level of significance (Type 1 error) a sample size of 500 cases and 500 matched controls would be required. Of the total 22 primary health care clinics in Al-Ain medical health district, 8 clinics were selected randomly (7 from urban and 1 from semi-urban areas).

Selection of participants

The study population was identified by recruiting consecutive hypertensive patients aged 20–65 years attending any of the clinics for follow-up examination or any other cause during a specified period of time. The researcher visited each clinic in a rotation of 2–3 weeks and reviewed the medical records of the first 20 hypertensive patients attending any of the specified primary health centres until the target sample was reached. The exclusion criteria were non-Arab national, any severe chronic disease, age less than 20 and more than 65 years.

To select the control group, for every hypertensive case a matching pair who was non-hypertensive and met the same inclusion criteria were recruited from the same clinic. The control group subjects were identified from the visitors escorting the patients to the health care centre or those attending for any other reason. Cases and controls were matched for age, sex and nationality. Before conducting the interview, the investigator reviewed the medical file of the controls (history and examination) to ensure they were suitable for the inclusion criteria of the research, in particular to check that they were free of any severe chronic diseases.

Data collection

Patients were checked by the general practitioner to see whether they met the inclusion criteria of the study and whether they had any family history of severe chronic diseases. The recruited patients were given a brief explanation about the study and were instructed to give their consent to participate in the study. They were asked by either the principal investigator or the nurse to fill out the questionnaire. Qualified nurses measured the blood pressure, height, and weight of the participants.

The survey was based on standardized interviews performed by trained health professionals and nurses. Informed consent was obtained from each person who agreed to enter the study. The participants were interviewed about their age, sex, nationality, educational level, occupation, place of living (urban or semi-urban), lifestyle habits, previous family history of hypertension, diabetes or kidney problems and current use of medication for hypertension and diabetes. Blood pressure was measured and height and weight were measured using standardized methods with participants wearing light clothes without shoes. Information on cholesterol level was collected from the patient's medical record.

Blood pressure measurement was carried out by practising nurses who were trained for 1 week on the use of the sphygmomanometer and how to measure blood

pressure with patients in the sitting position. It was measured from the right upper arm, with a random zero sphygmomanometer with a 14 cm cuff, after the participants had rested for 10 minutes and was recorded to the nearest mmHg. Systolic pressure was recorded at the appearance of sounds (first Korotkoff sounds) and diastolic pressure was recorded at the disappearance of sounds (fifth Korotkoff sounds). The mean value obtained from 3 readings was used in the analysis.

Questionnaire

The questionnaire and criteria for hypertension were designed to meet the objectives of this study. A translated Arabic version of the questionnaire was revised by the bilingual physician (M.S.O.A-Z) and translated back by a bilingual co-investigator, unacquainted with the original English version. Both translators met and made the necessary corrections, modifications and rewording after considering the minor differences and discrepancies that had occurred.

In a pilot study as a part of the process of validation, the first 20 patients were asked about the clarity and appropriateness of items on the questionnaire. Minor changes were made in the questionnaire taking into account their feedback.

In addition to the questionnaire, a review was made of the medical files of all participants recruited.

Definitions

Hypertension was defined according to World Health Organization (WHO) standardized criteria [*14*] as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/or the use of antihypertensive medication [*14*]. Control participants were those with systolic blood pressure < 140 mmHg or diastolic < 90 mmHg and not currently taking antihypertensive medication.

BMI was calculated as the weight in kilograms (1 kg subtracted to allow for clothing) divided by height squared in meters. Subjects were classified into 3 categories: acceptable weight (BMI < 25 kg/m^2); overweight (BMI 25–29.9 kg/m^2); and obese (BMI 30+ kg/m^2) [*15*].

Smoking behaviour was classified as: current smoker (regularly smoked at least 1 cigarette per day), ex-smoker (given up smoking for at least 6 months) and non-smoker (never smoked regularly).

High cholesterol was a total cholesterol level > 230 mg/dL, low-density lipoprotein (LDL) cholesterol level > 130 mg/dL or triglyceride level 200–400 mg/dL.

Alcohol consumption was defined as: never drank, current drinker or ex-drinker. No data were obtained on alcohol consumption among women because it is uncommon among females and due to the difficulty in gathering information on this subject in this conservative Muslim community.

Physical activity was classified as follows: sedentary and relatively inactive (not practising sports or practising < 1 hour/week); relatively active (practising sports for 1–3 hours a week); or highly active (practising sports for > 3 hours a week).

Healthy eating was assessed by recording the number of times per week that fruit and vegetables were consumed.

Analysis

The data were analysed using *SPSS*, version 11. Student *t*-test was used to find the difference between means of systolic and diastolic blood pressure among hypertensive and non-hypertensive patients. Mann–Whitney test was used for non-parametric distribution. The chi-squared test was used

for comparison of frequencies between hypertensive and non-hypertensive people and the frequency of other associated socioeconomic and lifestyle factors. Logistic regression analysis was used to adjust for potential confounders and to order the importance of risk factors (determinants) for hypertension. Logistic regression results were expressed as odds ratios (OR) and 95% confidence interval (CI) along with *P* values (derived from likelihood ratios statistics which have a chi-squared distribution). The level $P < 0.05$ was the cut-off value for significance.

Results

Of the 500 patients with hypertension recruited, 64 did not participate in the study and thus 436 cases and 436 matched non-hypertensive controls were included in the final analysis (87.2% response rate for completion of the study).

Among hypertensive patients, the mean and standard deviation (SD) of blood pressure [systolic 141.9 (17.1) mmHg/diastolic 92.7 (9.8) mmHg] was significantly higher than for controls [systolic 116.8 (8.7) mmHg/ diastolic 75.7 (6.2) mmHg] ($P < 0.0001$).

Among the hypertensive patients, the categories with the highest rates of hypertension were: men (55.3%), age group 40–49 years (39.7%), non-UAE nationals (52%), urban living (93.3%), currently married (86.7%), having children (93.6%), illiterate (33.7%), administrative/professional job (40.7%), living in mud-brick or traditional house (56.9%) and low income (< 5000 dirhams per month) (34.1%) (Table 1).

Table 1 compares the sociodemographic characteristics of hypertensive patients and normotensive controls. There were statistically significant differences between cases and controls in the percentage of participants having 3 or more children ($P = 0.034$), administrative/professional occupation ($P < 0.037$), (low/medium income (5000–9999 dh) ($P < 0.001$) and obesity (BMI > 30 kg/m^2) ($P < 0.001$).

Table 2 compares the lifestyle habits of cases and controls. Significantly more patients with hypertension than controls were current smokers ($P = 0.047$), consumed alcohol ($P < 0.03$) and had a low level of physical activity ($P = 0.007$).

Table 3 shows a comparison of the medical conditions of hypertensive patients and non-hypertensive control participants. Significantly more patients with hypertension than controls had raised cholesterol levels ($P < 0.001$) or a family history of heart disease ($P < 0.001$), kidney disease ($P < 0.033$) or diabetes ($P < 0.001$).

A stepwise logistic regression analysis was used to adjust for potential confounders and order the importance of risk factors (determinants) for hypertension status (0 for non-hypertensive and 1 hypertensive) (Table 4). The logistic regression model was adjusted for age, sex, nationality and marital status. As can be seen from this table, factors associated with hypertension were: obesity (BMI > 30 kg/m^2) ($P < 0.0001$), medium/high income (5000+ dh) ($P < 0.001$), family history of diabetes ($P < 0.001$), no physical activity ($P = 0.003$) and a high number of children (3+) ($P = 0.026$).

Discussion

Hypertension is the most common of the cardiovascular diseases and is one of the most powerful contributors to cardiovascular morbidity and mortality especially from strokes and congestive heart failure [*16–18*]. In the present study, hypertension was found to be associated with poor

Table 1 **Socioeconomic characteristics of clinic attenders with hypertension and non-hypertensive controls in Al-Ain city, United Arab Emirates (UAE)**

Variable	Cases (*n* = 436) No.	%	Controls (*n* = 436) No.	%	Odds ratio	95% CI	*P*-value
Sex							
Female	195	44.7	217	50.2	1.00		
Male	241	55.3	219	49.8	0.903	0.79–1.03	0.154
Age (years)							
< 40	98	22.4	134	31.1	1.00		
40–49	173	39.7	172	39.9	0.73	0.51–1.03	0.062
50–59	93	21.3	74	17.2	0.80	0.54–1.18	0.239
60+	72	16.5	51	11.8	0.89	0.54–1.47	0.628
Nationality							
UAE	209	48.0	207	47.7	1.00		
Other Arab	226	52.0	227	52.3	1.014	0.77–1.32	0.946
Area							
Urban	402	93.3	375	86.4	1.00		
Semi-urban	29	6.7	59	13.6	1.30	0.87–1.87	0.242
Marital status (current)							
Married	372	86.7	359	83.9	1.00		
Single	57	13.3	69	16.1	1.25	0.84–1.87	0.242
No. of children							
< 3	101	23.3	123	29.1	1.00		
3+	304	70.2	265	62.8	0.72	0.52–0.99	0.034
Not married	28	6.5	34	8.1	1.39	0.80–2.44	0.216
Educational level							
Illiterate	145	33.7	126	29.2	1.00		
Elementary/preparatory	103	24.0	86	20.0	0.96	0.65–1.42	0.833
Secondary	44	10.2	40	9.3	1.09	0.63–1.88	0.746
College/university	138	32.1	179	41.5	1.43	0.86–2.38	0.148
Occupation type							
Not working	50	11.6	45	10.3	1.00		
Unskilled/semi-skilled labourer	62	14.3	46	10.6	0.82	0.46–1.49	0.495
Administrative/ professional	176	40.7	206	47.5	1.58	1.00–2.48	0.037
Housewife	144	33.3	137	31.6	0.81	0.59–1.12	0.188
Type of residence							
Villa	92	21.3	94	21.8	1.00		
Traditional mud-brick/ prefabricated	245	56.9	244	56.3	0.97	0.69–1.39	0.882
Apartment	94	21.8	95	21.9	1.01	0.72–1.44	0.931

Table 1 **Socioeconomic characteristics of clinic attenders with hypertension and non-hypertensive controls in Al-Ain city, United Arab Emirates (UAE) *(concluded)***

Variable	Cases (*n* = 436) No.	%	Controls (*n* = 436) No.	%	Odds ratio	95% CI	*P*-value
Monthly income (dh)[a]							
< 5000	138	34.1	98	25.1	1.00		
5000–9999	140	34.6	176	45.1	1.77	1.24–2.53	< 0.001
10 000–14 999	57	14.1	60	15.4	0.84	0.54–1.31	0.413
15 000+	80	17.3	56	14.4	0.66	0.39–1.13	0.108
BMI (kg/m²)							
Acceptable (< 25)	99	25.1	163	40.9	1.00		
Overweight (25–29.9)	132	33.5	150	37.6	0.69	0.48–0.99	0.035
Obese (30+)	163	41.4	86	21.6	0.46	0.32–0.67	< 0.001

[a]***US$ 1 = 3.68 dirhams.***
n ***= total number of participants (data were missing in some categories).***
CI = confidence interval.
BMI = body mass index.

Table 2 **Comparison lifestyle habits of clinic attenders with hypertension and non-hypertensive controls in Al-Ain city, United Arab Emirates**

Variable	Cases (*n* = 436) No.	%	Controls (*n* = 436) No.	%	Odds ratio	95% CI	*P*-value
Tobacco smoking							
Never	292	68.4	344	79.8	1.00		
Current smoker	55	12.9	42	9.7	0.65	0.41–1.02	0.047
Ex-smoker	80	18.7	45	10.4	0.74	0.41–1.31	0.270
Alcohol consumption							
Never	402	94.1	413	97.2	1.00		
Current/ex-drinker	25	5.9	12	2.8	0.47	0.22–0.99	0.030
Physical activity							
Yes[a]	188	43.1	229	52.5	1.00		
No	248	56.9	207	47.5	0.72	0.52–0.89	0.007
Vegetable consumption							
3+ times /week	366	87.4	359	85.4	1.00		
< 3 times /week	53	12.6	61	14.6	1.17	0.78–1.78	0.428
Fruit consumption							
3+ times /week	341	81.6	342	81.8	1.00		
< 3 times /week	77	18.4	76	18.2	0.98	0.68–1.42	0.928

n ***= total number of participants (data were missing in some categories).***
CI = confidence interval.
[a]***If subject practised sport more than 1 hour per week.***

Table 3 **Comparison of medical condition of clinic attenders with hypertension and non-hypertensive controls in Al-Ain city, United Arab Emirates**

Variable	Cases (*n* = 436) No.	%	Controls (*n* = 436) No.	%	Odds ratio	95% CI	*P*-value
Cholesterol level							
Normal	149	34.6	128	29.5	1.00		
Higher than normal	140	32.5	12	2.8	0.10	0.05–0.19	< 0.001
Not measured	142	32.9	294	67.7	–	–	
Family history of diabetes							
No	345	80.4	399	93.7	1.00		
Yes	84	19.6	27	6.3	0.28	0.17–0.45	< 0.001
Family history of heart disease							
No	352	82.1	415	98.1	1.00		
Yes	77	17.9	8	1.9	0.09	0.04–0.19	< 0.001
Family history of kidney problems							
No	404	94.8	411	97.6	1.00		
Yes	22	5.2	10	2.4	0.45	0.19–1.00	0.033

n ***= total number of participants (data were missing in some categories).***
CI = confidence interval.

Table 4 **Stepwise logistic regression analysis for hypertension and associated socioeconomic and family history characteristics of clinic attenders with hypertension and non-hypertensive controls in Al-Ain city, United Arab Emirates**

Independent variable	Odds ratio	95% CI	*P*-value
BMI			
(< 30 kg/m^2 = 0, 30+ kg/m^2 = 1)	4.29	2.76–6.66	0.0001
Income[a]			
(< 5000 dh = 0, 5000+ dh = 1)	2.69	1.76–4.10	0.001
Family history of diabetes			
(no = 0, yes = 1)	2.58	1.69–3.74	0.001
Physical activity			
(yes = 0, no = 1)	1.80	1.20–3.69	0.003
No. of children			
(< 3 = 0, 3+ = 1)	1.67	1.23–2.11	0.026

[a]***US$ 1 = 3.68 dirhams.***
CI = confidence interval.
BMI = body mass index.

health status as indicated by raised cholesterol levels and a family history of heart disease, renal disease or diabetes.

The present study confirms the hypothesis of an association between hypertension and poorer socioeconomic factors and more sedentary lifestyle. We found a positive association between hypertension and physical inactivity, smoking and obesity. These finding are similar to those of Johansson and colleagues in a study carried out in Sweden [*19*]. This has implications for preventive strategies, because smoking behaviour, body fatness and physical activity have been shown to be major candidates for possible early interventions [*20*].

Perhaps the common link to hypertension for all these sociodemographic factors is physical inactivity. If this were the case, it would suggest a number of potentially modifiable factors that could be targeted for intervention. A study in Finland has shown that the mean intensity of leisure time physical activity had a positive dose–response relationship with level of education and income [*21*]. It was also shown that married or engaged men, those less educated, on lower incomes and unemployed or retired had a shorter duration of conditioning physical activity especially in urban areas than others [*21*]. The authors of the study concluded that physical activity protects against poor health irrespective of high BMI and smoking.

Our finding that more expatriates than UAE nationals had hypertension is in keeping with previous findings of a Swedish study [*22*], which found that foreign-born individuals had a higher risk for poor health than Swedes after adjustment for sociodemographic and lifestyle factors.

In conclusion, the present study supports the importance of socioeconomic factors, lifestyle habits and family history in shaping risk for hypertension in UAE and indicates a need for more effective prevention programmes for control of hypertension in this fast developing Arab country.

References

1. Bener A, Gomes J, Hamouda MFB. Hypertension among workers occupationally exposed to hydrocarbons and organic solvents. ***Journal of environmental science and health***, ***Part-A***, 1996, 31:291–303.
2. ***Annual report. Preventive medicine in 20 years***. Abu Dhabi, United Arab Emirates, Ministry of Health, 2000:1–270.
3. Bener A et al. ***Acanthosis nigricans***, hyperinsulinaemia and risk factors for cardiovascular disease. ***Eastern Mediterranean health journal***, 2000, 6:416–24.
4. Corrao JM et al. Coronary heart disease risk factors in women. ***Cardiology***, 1990, 77(suppl. 2):8–24.
5. Rowland M, Roberts J. ***Blood pressure levels and hypertension in persons aged 6–74 years: United States, 1976–1980. National Health and Nutrition Examination Survey 1***. Hyattsville, Maryland, US Department of Health and Human Services, 1982.
6. Sarraf-Zadegan N et al. Prevalence of hypertension and associated risk factors in Isfahan, Islamic Republic of Iran. ***Eastern Mediterranean health journal***, 1999, 5:992–1001.
7. Alwan A. ***Prevention and management of hypertension.*** Alexandria, World Health Organization, Regional Office for the Eastern Mediterranean, 1996 (WHO EMRO Technical Publication, No. 23).

8. Alwan A. ***Prevention and control of cardiovascular diseases.*** Alexandria, World Health Organization, Regional Office for the Eastern Mediterranean, 1995 (WHO EMRO Technical Publication, No. 22).

9. Sarraf-Zadegan N, Amini-Nik S. Blood pressure pattern in urban and rural areas in Isfahan, Iran. ***Journal of human hypertension***, 1997,11:425–8.

10. Sayeed MA et al. Prevalence of hypertension in Bangladesh: effect of socioeconomic risk factor on difference between rural and urban community. ***Bangladesh Medical Research Council bulletin***, 2002, 28:7–18.

11. Faruqui A. Heart disease in South Asia: experiences in Pakistan. In: Hurst JW, ed. ***Clinical essays on the heart.*** Volume 2. New York, McGraw–Hill, 1983.

12. Laurenzi M et al. Multiple risk factors in hypertension: results from the Gubbio study. ***Journal of hypertension***, ***supplement***, 1990, 8:S7–12.

13. Bener A et al. Association between blood levels of lead blood pressure and risk of diabetes and heart disease in workers. ***International archives of occupational and environmental health***, 2001, 74(5):375–8.

14. World Health Organization/International Society of Hypertension. Guidelines for the management of hypertension. ***Journal of hypertension***, 1999, 17:151–82.

15. Bray GA. Definition, measurement and classification of the syndrome of obesity. ***International journal of obesity***, 1978, 2:99–112.

16. Kannel WB, Thom TJ. Declining cardiovascular mortality. ***Circulation***, 1984, 70:331–6.

17. MacMahon S et al. Blood pressure, stroke and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. ***Lancet***, 1990, 335:765–74.

18. National Center for Health Statistics. Annual summary of births, marriages, divorces and deaths, United States, 1989. ***Monthly vital statistics report***, 1990:38(13).

19. Johansson SE, Sundquist J. Change in lifestyle factors and their influence on health status and all-cause mortality. ***International journal of epidemiology***, 1999, 28(6):1073–80.

20. Twisk JW, Kemper HC, van Mechelen W. Tracking of activity and fitness and the relationship with cardiovascular disease risk factors. ***Medicine and science in sports and exercise***, 2000, 32(8):1455–61.

21. Lakka TA, Kauhanen J, Salonen JT. Conditioning leisure time physical activity and cardiorespiratory fitness in sociodemographic groups of middle-ages men in eastern Finland. ***International journal of epidemiology***, 1996, 25(1): 86–93.

22. Sundquist J. Living conditions and health. A population-based study of labour migrants and Latin American refugees in Sweden and those who were repatriated. ***Scandinavian journal of primary health care***, ***supplement***, 1995, 13(2):128–34.

Diabetic nephropathy as a cause of end-stage renal disease in Egypt: a six-year study

A. Afifi,[1] M. El Setouhy,[2] M. El Sharkawy,[1] M. Ali,[1] H. Ahmed,[1] O. El-Menshawy[3] and W. Masoud[4]

اعتلال الكلية السكّري كأحد أسباب المراحل المتأخرة من المرض الكلوي في مصر: دراسة لمدة ست سنوات

عادل عفيفي، ماجد السطوحي، مجدي الشرقاوي، مدحت علي، هيام أحمد، أسامة المنشاوي، وليد مسعود

الخلاصة: درس الباحثون معدلات انتشار اعتلال الكلية السكّري كأحد أسباب المراحل المتأخرة من المرض الكلوي في مصر، في دراسات مستعرضة صغيرة، وكانت النتائج متعارضة، مما استدعى دراسة واسعة المجال. وقد أجرى الباحثون هذه الدراسة المتعدِّدة المستعرضة على مدى ست سنوات. واختيرَتْ عينة من المرضى في المراحل المتأخرة من المرض الكلوي، المسجَّلين في نظام البيانات الكلوية المصري، وتم تقييمهم خلال المدّة 1996-2001 من حيث معدل انتشار اعتلال الكلية السكّري. وقد ازداد معدل الانتشار تدريجياً من 8.9٪ عام 1996 حتى 14.5٪ عام 2001. وكان العمر الوسطي للمرضى المصابين باعتلال الكلية السكّري أعلى بكثير منه في المصابين بالمراحل المتأخرة من المرض الكلوي بسبب آخر. أما معدل الوفيات فقد كان أعلى بشكل واضح لدى السكّريِّين المصابين بالمراحل المتأخرة من المرض الكلوي.

ABSTRACT The prevalence of diabetic nephropathy as a cause of end-stage renal disease (ESRD) in Egypt has been examined in small cross-sectional studies, with conflicting results. The need for a large-scale study prompted us to perform this 6-year multiple cross-sectional study. A sample of ESRD patients enrolled in the Egyptian renal data system was evaluated during the period 1996–2001 for the prevalence of diabetic nephropathy. Prevalence gradually increased from 8.9% in 1996, to 14.5% in 2001. The mean age of patients with diabetic nephropathy was significantly higher than that of patients with ESRD from other causes. Mortality was also significantly higher in diabetic patients with ESRD.

La néphropathie diabétique comme cause de l'insuffisance rénale terminale en Égypte : étude sur six ans

RÉSUMÉ La prévalence de la néphropathie diabétique comme cause de l'insuffisance rénale terminale en Égypte a été examinée dans de petites études transversales, donnant des résultats contradictoires. Le besoin d'une étude à grande échelle nous a incités à réaliser une étude transversale multiple sur six ans. Un échantillon de patients souffrant d'insuffisance rénale terminale enregistrés dans le système égyptien de données rénales a fait l'objet d'une évaluation pendant la période 1996-2001 pour la prévalence des néphropathies diabétiques. La prévalence a augmenté progressivement, passant de 8,9 % en 1996 à 14,5 % en 2001. L'âge moyen des patients souffrant de néphropathie diabétique était significativement plus élevé que celui des patients souffrant d'insuffisance rénale terminale due à d'autres causes. La mortalité était aussi significativement plus élevée chez les diabétiques ayant une insuffisance rénale terminale.

[1]Department of Internal Medicine and Nephrology; [2]Department of Public Health and Occupational Medicine, Ain Shams University, Cairo, Egypt.
[3]Department of Internal Medicine and Nephrology, Al Minya University, Egypt.
[4]Department of Nephrology, Ahmed Maher Teaching Hospital, Cairo, Egypt.
Received: 09/06/03; accepted: 26/10/03

Introduction

Egypt, a developing country in North Africa, had a population of approximately 68 million in 2001. The estimated number of dialysis patients in Egypt in that year was 25 518 [*1*]

Diabetic nephropathy is rapidly becoming the leading cause of end-stage renal disease (ESRD), particularly in the industrialized countries of the world [*2*]. Ethnic and racial origin play an important role, resulting in increased prevalence rates of diabetic nephropathy in certain regions [*3*].

In many studies from Western European countries as well as many other regions of the world, diabetic nephropathy has been reported as the main cause of ESRD. Variable incidence and prevalence rates have been reported in Eastern Europe. Table 1 gives a summary of reported prevalence of this condition in a number of countries. Data from 12 countries in the Asian Pacific region, including Australia and New Zealand, showed an increase in both incidence and prevalence between 1998 and 2000 [*4*].

The prevalence of diabetic nephropathy as a cause of ESRD in Egypt has previously been examined in 2 small cross-sectional studies with conflicting results [*22,23*]. Other reports on prevalence of diabetic nephropathy also produced the following widely divergent figures: 8.4% [*11*], 13.7% [*24*], 20.1% [*12*] and 8.9% [*25*]. These marked differences in the reported prevalence rates may reflect the effect of urbanization.

The need for a large-scale study has prompted us to carry out this 6-year, multiple, cross-sectional study. The aim of our study was to critically evaluate the prevalence of diabetic nephropathy as a cause of ESRD in Egypt.

Table 1 **Reported prevalence of diabetic nephropathy as a cause of renal disease for various parts of the world**

Location	End-stage renal disease Prevalence of diabetic nephropathy (%)	Reference No.
United States of America	~ 50	5
Western Europe	Leading cause	6
Japan	Leading cause	7
France	Leading cause	8
Germany	21	9
Norway	10% of the incident RRT population	10
Egypt	8.4	11
Egypt	20.1	12
	Primary renal disease	
Yugoslavia	7	13
Czech Republic	25.0	14
Slovakia	17.9	14
Poland	10.3	15
South America	16.0	16
Puerto Rico	51.2	16
Asian Pacific region including Australia and New Zealand	17.3	4
China	4.7	17
Taiwan	24.8	18
Saudi Arabia	27.9	19
Tunisia	11.4	20
Kuwait	21.2	21

RRT = renal replacement therapy.

Methods

A sample of patients with ESRD enrolled in the Egyptian renal data system was evaluated during the period 1996–2001 for the

prevalence of diabetic nephropathy. Centre and patient questionnaires were sent to all identified dialysis centres (370 centres). All responding centres and all patients reported from these centres were included in the study. The number of patients evaluated was 4905 in 1996, 3013 in 1997, 1754 in 1998, 1616 in 1999, 2150 in 2000 and 3172 in 2001. Requested data included number of patients, age, sex, renal biopsy results, cause of ESRD, and cause of death.

Criteria used for diagnosing diabetic nephropathy included:

- long duration of diabetes before onset of chronic renal failure (usually more than 10 years)
- normal sized kidneys by ultrasound
- presence of diabetic retinopathy by fundus examination
- absence of haematuria or red blood cell casts in urine
- proteinuria still present when the patient has already started dialysis.

The data collected were processed using an IBM-compatible PC and *SPSS*, version 6.1 for statistical analysis.

Results

The prevalence of diabetic nephropathy among ESRD patients in Egypt increased from 8.9% in 1996 to 14.5% in 2001 (Figure 1).

The main causes of ESRD in Egypt other than diabetic nephropathy included hypertensive kidney disease, chronic glomerulonephritis, undetermined etiology, reflux and chronic pyelonephritis, schistosomal obstructive uropathy and schistosomal nephritis (Table 2).

The mean age of patients with diabetic nephropathy was higher than that of patients having other causes of ESRD in the years we studied (Table 3). Mortality among diabetic patients with ESRD was higher than in patients with ESRD from other causes (Figure 2).

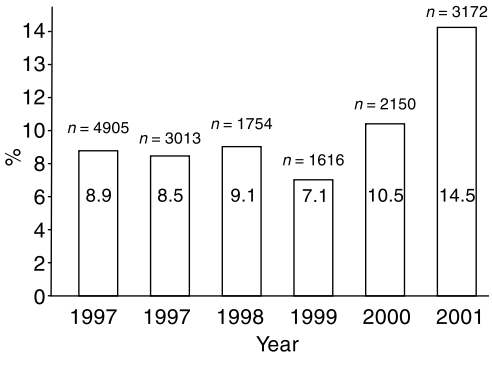


Figure 1 **Prevalence of diabetic nephropathy among Egyptian patients with end-stage renal disease, 1996–2001**

Discussion

The prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and is predicted to rise to 5.4% by the year 2025. It is higher in industrialized than in developing countries. The number of adults with diabetes in the world is forecast to rise from 135 million in 1995 to 300 million in the year 2025. Most of this increase will occur in developing countries [*26*].

A series of surveys of diabetes mellitus have been performed in Egypt using World Health Organization criteria for diagnosis and classification. Average prevalence for people above the age of 10 years was 4.3%, with distinct geographical differences: 5.7% in urban areas, 4.1% in rural agricultural areas, and 1.5% in rural desert areas. In some remote villages, diabetes was almost completely absent [*22*]. A more recent study in Egypt revealed that the prevalence of diabetes in rural areas was

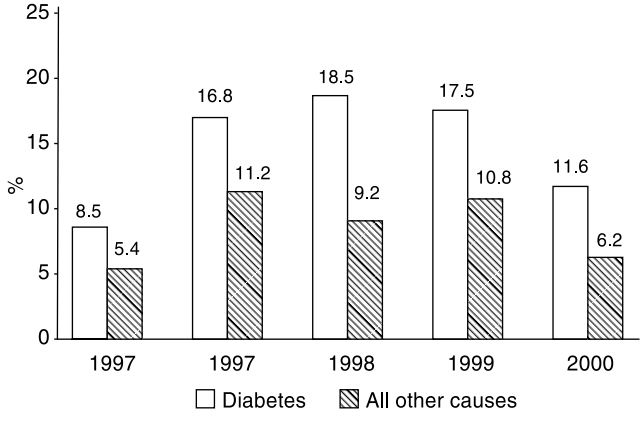


Figure 2 **Cause of mortality among diabetic and non-diabetic Egyptian patients with end-stage renal disease**

4.9%, increasing to 13.5% in lower socioeconomic urban areas and 20% in higher socioeconomic urban areas [*23*].

Diabetic nephropathy is the commonest cause of ESRD in industrialized countries [*26*]. All countries with registries have reported a massive increase in the incidence and prevalence in their dialysis population. This increase is caused by an actual increase in prevalence of diabetes, increasing age of the dialysis population and better survival rates for patients with diabetes, thus allowing more time for diabetic nephropathy to develop [*2*].

In Egypt, the estimated prevalence of ESRD increased from 225 per million pop-

Table 3 **Mean age of diabetic nephropathy patients and patients with end-stage renal disease (ESRD) from other causes**

Year	Diabetic nephropathy		Other causes of ESRD		*P*-value
	Mean age (years)	SD	Mean age (years)	SD	
1996	55.7	9.9	44.6	14.1	> 0.001
1997	54.9	11.4	44.9	16.8	> 0.001
1998	54.2	15.1	45.2	15.3	> 0.001
1999	56.6	11.6	45.4	15.3	> 0.001
2000	56.1	10.9	45.2	15.5	> 0.001
2001	56.5	29.2	46.1	16.1	> 0.001

SD = ***standard deviation.***

Table 3 **Main causes of end-stage renal disease in Egypt other than diabetic nephropathy**

Year	Main causes of end-stage renal disease						
1996	Hypertension: 28.0%	Chronic glomerulonephritis: 16.6%	Undetermined 16.2%	Chronic pyelonephritis: 14.6%	Obstructive uropathy: 9.3%	Diabetic nephropathy: 8.9%	Schistosomal obstructive uropathy: 6.0%
1997	Hypertension: 19.6%	Chronic glomerulonephritis: 13.2%	Undetermined: 12.5%	Chronic pyelonephritis: 10.4%	Diabetic nephropathy: 8.5%	Schistosomal obstructive uropathy: 7.6%	Obstructive uropathy: 7.5%
1998	Undetermined: 22.1%	Hypertension: 21.0%	Chronic glomerulonephritis: 11.0%	Obstructive uropathy: 9.5%	Diabetic nephropathy: 9.1%	Schistosomal obstructive uropathy: 6.7%	Chronic pyelonephritis: 5.5%
1999	Hypertension: 23.6%	Undetermined: 18.4%	Chronic glomerulonephritis: 13.9%	Obstructive uropathy: 9.2%	Chronic pyelonephritis: 7.8%	Diabetic nephropathy: 7.1%	Adult polycystic: 4.3%
2000	Hypertension: 23.5%	Undetermined: 21.8%	Chronic glomerulonephritis: 12.4%	Diabetic nephropathy: 10.5%	Chronic pyelonephritis: 7.4%	Obstructive uropathy: 6.0%	Schistosomal obstructive uropathy: 4.0%
2001	Hypertension: 22.1%	Diabetic nephropathy: 14.5%	Chronic glomerulonephritis: 12.4%	Undetermined: 12.1%	Chronic pyelonephritis: 5.6%	Obstructive uropathy: 5.1%	Schistosomal obstructive uropathy: 4.4%

ulation in 1996 [*25*] to 375 per million in 2001 [*1*]. We found that the prevalence of diabetic nephropathy as a cause of ESRD increased from 8.9% of patients in 1996 to 14.5% in 2001. The mean age of diabetic nephropathy patients was higher than that of patients with ESRD due to other causes for the years studied.

Mortality among diabetic patients with ESRD in Egypt is higher than mortality for all other causes of ESRD which is probably related to the well known cardiovascular complications of diabetes (Figure 2).

Conclusions

Diabetic nephropathy is the commonest cause of ESRD in the industrialized countries. In Egypt, there is a slower increase in the prevalence of ESRD due to diabetic nephropathy, probably because of the higher incidence of infections causing glomerulonephritis, delayed referral to nephrologists and increased mortality among diabetic patients due to cardiovascular disease and strokes before ESRD can develop.

References

1. Afifi A. ***Sixth annual report of the Egyptian Society of Nephrology***. Paper presented at the 22nd Congress of the Egyptian Society of Nephrology, 4–8 February 2003, Sharm El Sheikh, Egypt.
2. Ritz E et al. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. ***American journal of kidney disease***, 1999, 34(5): 795–808.
3. Earle KK et al. Variation in the progression of diabetic nephropathy according to racial origin. ***Nephrology, dialysis, transplantation***, 2001, 16(2):286–290.
4. Lee G. End-stage renal disease in the Asian-Pacific region. ***Seminars in nephrology***, 2003, 23(1):107–14
5. US Renal Data System. ***USRDS 2002 annual data report***. Bethesda, Maryland, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2002.
6. Jager K, Van Dijk P. ***2002 ERA-EDTA registry annual report, XXXIX ERA-EDTA congress***. Copenhagen, Denmark, European Renal Association, 2002.
7. Hollenberg NK. Higher incidence of diabetic nephropathy in type 2 than in type 1 diabetes in early-onset diabetes in Japan. ***Current hypertension reports***, 2001, 3(3):177.
8. Halimi S et al. Huge progression of diabetes prevalence and incidence among dialysed patients in mainland France and overseas French territories. A second national survey six years apart. (UREMIDIAB 2 study). ***Diabetes and metabolism***, 1999, 25(6):507–12.
9. Frei U, Schober-Halstenberg HJ. Annual report of the German renal registry 1998. QuaSi-Niere task group for quality assurance in renal replacement therapy. ***Nephrology, dialysis, transplantation***, 1999, 14(5):1085–90.
10. Bergrem H, Leivestad T. Diabetic nephropathy and end-stage renal failure: the Norwegian story. ***Advances in renal replacement therapy***, 2001, 8(1):4–12.
11. El-Sharkawi M. ***Changing pattern of etiology of chronic renal failure among dialysis patients*** [thesis]. Cairo, Ain Shams University, 1996.
12. Ahmed T. ***Clinical and laboratory features of patients with chronic renal failure at the start of dialysis*** [thesis]. Cairo, Ain Shams University, 1991.
13. Djukanovic L et al. Epidemiology of end-stage renal disease and current status of

hemodialysis in Yugoslavia. ***International journal of artificial organs***, 2002, 25(9):852–9.

14. Rutkowski B et al. Evolution of renal replacement therapy in Central and Eastern Europe 7 years after political and economical liberation. ***Nephrology, dialysis, transplantation***, 1998, 13(4):860–4.

15. Rutkowski B et al. Renal replacement therapy in an era of socioeconomic changes–report from the Polish Registry. ***Nephrology, dialysis, transplantation***, 1997, 12(6):1105–8.

16. Mazzuchi N et al. Latin American registry of dialysis and renal transplantation: 1993 Annual dialysis data report. ***Nephrology, dialysis, transplantation***, 1997, 12(12):2521–7.

17. Li L. End-stage renal disease in China. ***Kidney international***, 1996, 49(1):287–301.

18. Yang WC et al. The impact of diabetes on economic costs in dialysis patients: experiences in Taiwan. ***Diabetes research and clinical practice***, 2001, 54(suppl. 1):S47–54.

19. Al-Khader AA. Impact of diabetes in renal diseases in Saudi Arabia. ***Nephrology, dialysis, transplantation***, 2001, 16(11):2132–5.

20. Ben Abdallah. ***Report of dialysis registry in Tunisia***. Paper presented at the 21st Congress of the Egyptian Society of Nephrology, 15–20 February 2002, Cairo, Egypt.

21. El-Reshaid K et al. End-stage renal disease and renal replacement therapy in Kuwait–epidemiological profile over the past 4½ years. ***Nephrology, dialysis, transplantation***, 1994, 9(5):532–8.

22. Arab M. Diabetes mellitus in Egypt. ***World health statistics quarterly***, 1992, 45(4): 334–7.

23. Harman WH et al. Diabetes mellitus in Egypt: risk factors and prevalence. ***Diabetic medicine***, 1995, 12(12):1126–31.

24. Ibrahim T. ***Etiology of chronic renal failure among a sample of Egyptian population*** [thesis]. Cairo, Ain Shams University, 1998.

25. Afifi A, Karim MA. Renal replacement therapy in Egypt: first annual report of the Egyptian Society of Nephrology, 1996. ***Eastern Mediterranean health journal***, 1999, 5(5):1023–9.

26. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. ***Diabetes care***, 1998, 21(9): 1414–31.

Antiphospholipid syndrome and retinal vein occlusion in adults

R.M. Maaroufi,[1,3] R. Hamdi,[2] N. Jmili,[3] M. Ghorbal,[2] F. Bel Hadj Hamida[2] and T. Mahjoub[3]

متلازمة مضادات الفوسفوليبيد وانسداد الوريد الشبكي بين البالغين

راوي منير معروفي، رشيد حمدي، ناجية جميلي، محمد غربال، فافاني بالحاج حميدة، تهامي محجوب

الخلاصة: قد يكون لأضداد الفوسفوليبيدات دور هام في إحداث انسداد الأوعية الشبكية، وقد قام الباحثون باستقصاء معدل انتشار هذه الأضداد في 33 مريضاً بانسداد الشرايين والأوردة الشبكية و80 من الشواهد. وقد بلغ معدل الانتشار بين المرضى 33٪ وبين الشواهد 5٪. وأظهر الفحص العيني وتصوير الأوعية بالفلوريسين أن الانسداد كان ناجماً عن أحداث نقص التَّروية. وقد شخصت متلازمة مضادات الفوسفوليبيد لدى 11 مريضاً، تمت معالجة 9 مرضى منهم بنجاح بالتخثير بالليزر وبالأدوية المضادة للتخثر والمضادة لتكدُّس الصفيحات، في حين كانت معالجة مريضين بهذه المتلازمة المصحوبة بالمقاومة للبروتين سي المفعَّل دون نتائج مشجعة. وتشير النتائج التي توصَّل إليها الباحثون إلى وجود ترابط بين متلازمة مضادات الفوسفوليبيد وانسداد الأوردة الشبكية، ولذلك فإنهم يوصون بإجراء بحوث منهجية حول دور أضداد الفوسفوليبيدات في الانسداد غير المفسَّر المنشأ وحول المعالجة بالتخثير بالليزر وبالأدوية المضادة للتخثر والمضادة للتكدُّس على المدى الطويل.

ABSTRACT Antiphospholipid antibodies may play an important role in the pathogenesis of retinal vascular occlusions; therefore, we investigated the prevalence among 33 patients with retinal vein and artery occlusions and 80 controls. Prevalence was 33% and 5% respectively. Ophthalmic examination and fluorescein angiography showed that occlusions were due to ischaemic events. The 11 patients were diagnosed with antiphospholipid syndrome: 9 patients were treated successfully with laser photocoagulation and anticoagulant and anti-aggregant therapy. Two patients with antiphospholipid antibodies associated with resistance to activated protein C had unfavourable outcomes. Our results suggest a correlation between antiphospholipid syndrome and retinal vein occlusions; we recommend a systematic search for antiphospholipid antibodies in occlusions of unexplained origin and laser photocoagulation treatment and long-term oral anticoagulant and anti-aggregant therapy.

Le syndrome des antiphospholipides et l'occlusion veineuse rétinienne chez l'adulte

RÉSUMÉ Les antiphospholipides peuvent jouer un rôle important dans la pathogenèse des occlusions vasculaires rétiniennes ; nous avons donc étudié la prévalence chez 33 patients atteints d'occlusions veineuses et artérielles rétiniennes et 80 témoins. La prévalence s'élevait à 33 % et 5 % respectivement. L'examen ophtalmologique et l'angiographie fluorescéinique ont montré que les occlusions étaient dues à des événements ischémiques. Le syndrome des antiphospholipides a été diagnostiqué chez 11 patients : neuf patients ont été traités avec succès par photocoagulation au laser associant un traitement anticoagulant et antiagrégant. Deux patients présentant des anticorps antiphospholipides associés à une résistance à la protéine C activée ont eu une issue défavorable. Nos résultats semblent indiquer une corrélation entre le syndrome des antiphospholipides et les occlusions veineuses rétiniennes ; nous recommandons une recherche systématique des anticorps antiphospholipides dans les occlusions d'origine inexpliquée et un traitement par photocoagulation au laser et un traitement anticoagulant et antiagrégant de longue durée.

[1]Higher Institute of Biotechnology, Monastir, Tunisia.
[2]Department of Ophthalmology, Farhat Hached University Hospital, Sousse, Tunisia.
[3]Haematology and Autoimmune Diseases Unit, Faculty of Pharmacy, University of Monastir, Tunisia.
Received: 29/04/03; accepted: 23/12/03

Introduction

Antiphospholipid antibodies are a heterogeneous family of antibodies directed to plasma protein co-factors bound to anionic phospholipids. The clinical relevance of antiphospholipid antibodies derives from the association with venous and arterial thrombosis, recurrent abortions and thrombocytopenia [*1*]. Antiphospholipid antibodies include lupus anticoagulant and anticardiolipin antibodies [*2,3*]. This association has been termed the antiphospholipid syndrome (APS), which may occur alone (primary APS) or in the setting of an underlying disease, mainly systemic lupus erythematosus (SLE) [*4–7*].

Hypercoagulable states, including a variety of disorders such as reduced levels of antithrombin, protein C, protein S or presence of antiphospholipid antibodies, are common in patients with retinal vein occlusions and may contribute to the etiology of the disease [*8*].

In particular, retinal vascular occlusions in patients with primary APS, i.e. with antiphospholipid antibodies but with no other conventional risk factors, result from thrombus formation in either the retinal vein, artery or both [*9–12*].

We investigated the prevalence of antiphospholipid antibodies in a group of 33 patients with retinal vein occlusion and in 80 normal controls. Whether antiphospholipid antibodies included lupus anticoagulant, anticardiolipin antibodies or both was also investigated. This study aimed to assess the relationship between the occurrence of antiphospholipid antibodies in primary APS and occlusive retinal vascular events.

Methods

From January–December 2002, 33 patients (14 men and 19 women, mean age 37 years and age range 22–63 years) with retinal vein (29) or artery (4) occlusions were selected from the Department of Ophthalmology of the Farhat Hached Hospital, Sousse, Tunisia. Exclusion criteria were diabetes, hypertension, hypercholesterolaemia and hypertriglyceridaemia. We used 80 normal controls from among healthy blood donors at the Centre Régional de Transfusion Sanguine of Farhat Hached Hospital. Informed consent was obtained from patients and controls prior to their participation in our study.

Patients were examined clinically. A questionnaire was administered before patients underwent ophthalmologic examination and retinal flourescein angiography.

Biological assays for cholesterol and triglycerides were performed. Antinuclear antibodies were investigated with standardized enzyme-linked immunosorbent assay (ELISA).

Screening studies for APS included assays for anticardiolipin antibodies and lupus anticoagulant. Anticardiolipin antibodies (IgG and IgM isotypes) were also determined by ELISA assay (Diagnostica Stago, Asnières, France). Lupus anticoagulant was assayed with clotting techniques. Anticardiolipin antibodies and lupus anticoagulant were measured 8 weeks later.

We also screened for abnormalities in the coagulation process. Activated partial thromboplastin time and kaolin clotting time tests were performed. The levels of protein C and protein S were determined by ELISA assay (Diagnostica Stago, Asnières, France). Antithrombin III level was evaluated by colorimetric assay (Asserachrom, Diagnostica Stago, Asnières, France) and levels of factors VIIIc and XI were determined with clotting assays (Diagnostica Stago, Asnières, France). Factor V Leiden was investigated through the evaluation of the activated protein C–sensitivity ratio

(Accelerimat, bioMérieux, Marcy l'Etoile, France). Genetic analysis of factor V Leiden mutation was performed as previously described [*13*].

Chi-squared test was used to compare the patient and control groups.

Results

All patients underwent fundus fluorescein angiography and ophthalmologic examination. Almost all suffered from retinal vein occlusions (29 of 33 patients); the occlusive events primarily involved the central (9 patients) and the temporal (8 patients) veins. Only 4 patients had artery occlusions (Table 1). The prevalence of antiphospholipid antibodies in the study group was 33% (11 of 33 patients) while in the control group it was 5% (4 of 80). This difference was statistically significant ($\chi^2 = 16.29$, $P < 0.001$).

All patients with antiphospholipid antibodies had retinal vein occlusions, particularly temporal vein occlusions (5 of 11 patients). Only 1 patient with antiphospholipid antibodies had a central vein occlusion. None of the patients with artery occlusions tested positive for any of the assays.

In the study group 2 patients were positive for IgG-anticardiolipin antibodies, 3 patients for IgM-anticardiolipin antibodies and 1 patient for both isotypes IgG and IgM-anticardiolipin antibodies. The 5 remaining patients were negative for anticardiolipin antibodies but showed positivity for lupus anticoagulant (Table 1). Two patients had associated protein C resistance. All patients were negative for antinuclear antibodies. No deficiency in antithrombin III, protein C or protein S was found. Factors VIII and XI levels were within normal.

Table 1 **Presence of anticardiolipin antibodies, lupus anticoagulant and factor V Leiden among the 11 retinal vein occlusion patients testing positive for antiphospholipid antibodies**

Measurand	No.
Anticardiolipin antibodies	6[a]
IgG	2
IgM	3
IgG and IgM	1
Lupus anticoagulant	5
Associated factor V Leiden	2
Antinuclear antibodies	0

Discussion

The etiology of retinal vein occlusion is still not well understood although thrombosis does occur histologically. Hypercoagulable states seem to be common in patients with retinal vein occlusions [*8*]. The presence of antiphospholipid antibodies in APS is likely to generate a hypercoagulable state such as to cause thrombosis to occur [*1*]. It is known that antiphospholipid antibodies impair the metabolism of arachidonic acid in endothelial cells and platelets causing the inhibition of prostaglandin I2 (PGI2) production by endothelial cells and activation of platelets through stimulating thromboxane A2 generation [*14*,*15*]. Furthermore, antiphospholipid antibodies inhibit protein C and protein S, preventing coagulation factors Va and VIIa from inactivation [*16*,*17*]. Among other implications of the antiphospholipid antibodies syndrome is an increase in tissular factor release and in plasminogen activator inhibitor level. These implications could make it possible for thrombosis to occur even in veins or arteries, although

most vascular occlusions (81%) were found to affect venous vessels in a recent study [*11*].

Elevated levels of anticardiolipin antibodies have recently been associated with acute vascular occlusions of the eye although their role remains unclear [*12,18–21*]. Of 33 patients with retinal vascular occlusions, 11 (33%) were diagnosed with APS. They possibly had primary APS without any underlying immune disorder like lupus erythematosus because each was negative for antinuclear antibodies. None of our patients, however, was investigated for other possible immune disorders. It is noteworthy that 9 of the 11 patients had no other conventional risk for thrombosis, whereas the presence of antiphospholipid antibodies was associated with resistance to activated protein C for the 2 others.

The high prevalence of antiphospholipid antibodies in our study indicates that antiphospholipid antibodies may play an important role in the pathogenesis of retinal vein occlusions and thus may represent a risk factor of importance in the etiology of the disease. This may also suggest the necessity of screening for antiphospholipid antibodies in such patients. Furthermore, in our study group, the prevalence of antiphospholipid antibodies seemed to be related to retinal vein occlusions mainly involving the temporal vein and not to artery vein occlusions. This warrants further investigation. It should be noted that the role of antiphospholipid antibodies in retinal vein occlusion is still controversial. Our results provide more support for such a role of antiphospholipid antibodies in the pathogenesis of this disease.

Our results (33% prevalence of antiphospholipid antibodies in patients with retinal vascular occlusions) were dissimilar from studies that identified lower prevalences of 5%, 7.5% and 9% respectively among patients with primary APS [*18,9,12*]; however, in the two latter studies, these levels could have been 22.5% and 22% if antiphospholipid antibodies were associated with lupus erythematosus, the elevation of circulating immune complexes or complement deficiencies respectively [*9,12*]. Our results nevertheless indicate higher prevalence of antiphospholipid antibodies in retinal vein occlusions than the results of these authors. It should be noted that our study is the first of its kind in Tunisia and that a cohort study among the Tunisian population is needed.

In our study, all patients with antiphospholipid antibodies except 2 were treated successfully with laser photocoagulation and anticoagulant and anti-aggregant therapy (acenocoumarol, to get the patient's international normalized ratio to 2–4, and lysine acetylsalicylate, 250 mg per day) [*22*]. The 2 exceptions had associated resistance to activated protein C with the presence of antiphospholipid antibodies and experienced unfavourable developments. One had an occlusive event in the second eye and the other became blind even though therapy was provided.

In retinal vascular occlusions of unexplained origin, antiphospholipid antibodies may play an important role in pathogenesis. Detecting these antibodies in the serum of patients with retinal vascular occlusions may help to determine the appropriate treatment. The high prevalence of anticardiolipin antibodies in these patients who are free of conventional risk factors leads us to recommend a systematic search for specific antiphospholipid antibodies for them. This should be part of a treatment combining laser photocoagulation, and long-term anti-aggregant and oral anticoagulant therapy [*19*].

References

1. De Groot PG, Oosting JD, Derksen RH. Antiphospholipid antibodies: specificity and pathophysiology. ***Balliere's clinical haematology***, 1993, 6:691–709.

2. Exner T, Triplett DA. Lupus anticoagulants: characteristics, methods of laboratory detection and some clinical associations. In: Harris EN et al., eds. ***Phospholipid binding antibodies***. Boca Raton, Florida, CRC Press, 1991:141–58.

3. Loizou S et al. Measurement of anticardiolipin antibodies by an enzyme-linked immunosorbent assay (ELISA): standardization and quantitation of results. ***Clinical and experimental immunology***, 1985, 62:738–45.

4. Harris EN et al. Clinical and serological features of the antiphospholipid syndrome (APS). ***British journal of rheumatology***, 1987, 26:19.

5. Alarcon-Segovia D, Sanchez-Guerrero J. Primary antiphospholipid syndrome. ***Journal of rheumatology***, 1989, 16:482–8.

6. Italian registry of antiphospholipid antibodies (IR–APA). Thrombosis and thrombocytopenia in antiphospholipid syndrome (idiopathic and secondary to SLE): first report from the Italian registry. ***Haematologica***, 1993, 78:313–8.

7. Khamashta MA. Management of thrombosis in the antiphospholipid syndrome. ***Lupus***, 1996, 5(5):463–6.

8. Abu El-Asrar AM et al. Hypercoagulable states in patients with retinal vein occlusion. ***Documenta ophthalmologica***, 1998, 95(2):133–43.

9. Cobo-Soriano R et al. Antiphospholipid antibodies and retinal thrombosis in patients without risk factors: a prospective case–control study. ***American journal of ophthalmology***, 1999, 128(6):725–32.

10. Coniglio M et al. Antiphospholipid antibodies are not an uncommon feature in retinal venous occlusions. ***Thrombosis research***, 1996, 83(2):183–8.

11. Demirci FY et al. Ocular involvement in primary antiphospholipid syndrome. Ocular involvement in primary APS. ***International ophthalmology***, 1998, 22(6):323–9.

12. Cobo Soriano R et al. Trombosis retiniana en pacientes jóvenes. Aspectos inmunológicos y clínicos. [Retinal thrombosis in young patients. Immunological and clinical aspects.] ***Archivos de la Sociedad Española de Oftalmología***, 2001, 76(11):641.

13. Ridker PM et al. Mutation in the gene coding for coagulation factor V and the risk of myocardial infarction, stroke and venous thrombosis in apparently healthy men. ***New England journal of medicine***, 1995, 332:912–7.

14. Lellouche F et al. Influence of thromboxane/prostacyclin biosynthesis in patients with lupus anticoagulant. ***Blood***, 1991, 78:2894–9.

15. Karmochkine M et al. The effect of sera with antiphospholipid antibodies on endothelial cell procoagulant activity is dependent upon the charge of the phospholipids against which they are directed. ***Thrombosis research***, 1994, 74:435–40.

16. Cariou R et al. Effect of lupus anticoagulant on antithrombogenic properties of endothelial cells. Inhibition of thrombomodulin-dependent protein C activation. ***Thrombosis and haemostasis***, 1988, 60:54–8.

17. Smirnov MD et al. On the role of phosphatidylethanolamine in the inhibition of protein C activity by antiphospholipid antibodies. ***Journal of clinical investigation***, 1995, 95:309–18.

18. Glacet–Bernard A et al. Antiphospholipid antibodies in retinal vascular occlusions. A prospective study of 75 patients. ***Archives of ophthalmology***, 1994, 112(6):790–5.

19. Wiechens B et al. Primary antiphospholipid antibody syndrome and retinal occlusive vasculopathy. ***American journal of ophthalmology***, 1997, 123(6): 848–50.

20. Ermakova NA et al. Rol' antifosfolipidnykh antitel v okkliuzii sosudov setchatki pri razlichnykh sosudistykh zabolevaniiakh glaza. [Role of antiphospholipid antibodies in occlusion of retinal vessels in various vascular eye diseases.] ***Vestnik oftalmologii***, 2002, 118(2):29–32.

21. Carbone J et al. Antiphospholipid antibodies: a risk factor for occlusive retinal vascular disorders. Comparison with ocular inflammatory diseases. ***Journal of rheumatology***, 2001, 28(11):2437–41.

22. Dunn JP et al. Antiphospholipid antibodies and retinal vascular disease. ***Lupus***, 1996, 5(4):313–22.

Correction

Screening for congenital hypothyroidism in the Islamic Republic of Iran: strategies, obstacles and future perspectives A. Ordookhani, P. Mirmiran, R. Hajipour, M. Hedayati and F. Azizi. *Eastern Mediterranean Health Journal*, 2002, Vol. 8 Nos 4/5, pages 480–9.

The title of the French abstract should read:

Dépistage de l'hypothyroïdie congénitale en République islamique d'Iran : stratégies, obstacles et perspectives futures and hypothyroïdie should replace hyperthyroïdie throughout the text of the abstract.

Hyperhomocysteinaemia: risk of retinal vascular occlusion

G.H. Yaghoubi,[1] F. Madarshahian[2] and M. Mosavi[3]

فرط الهوموسيستين في الدم: خطر انسداد الأوعية الشبكية

غلام حسين يعقوبي، فرح مدارشاهيان، ميرناغي موسوي

الخلاصة: لدراسة العلاقة المحتملة بين فرط الهوموسيستين في الدم وبين انسداد الأوعية الشبكية، قمنا بقياس مستوى الهوموسيستين في 25 مريضاً في سوابقهم قصة انسداد الأوعية الشبكية خلال العامَيْن المنصرمَيْن، إلى جانب مجموعة من الشواهد عدد أفرادها 24 شخصاً. و لم يكن الفرق بين المستويات الوسطية للهوموسيستين في البلاسما ملحوظاً. وقد كان الجميع باستثناء 5 منهم مصابين بفرط ضغط الدم والسكَّري وفرط شحميات الدم. وكان لدى معظم المرضى انسداد في فرع الوريد الشبكي مترافق مع بدءٍ حديث للانسداد. ويرى الباحثون أنه ربما يكون لبعض العوامل الأخرى مثل الوضع العاطفي والمرض الجهازي المرافق، دور في التأهب لانسداد الأوعية الشبكية، وأن الحاجة تَمَسُّ لدراسات أكثر دقة لتحديد دور عوامل الاختطار المحتملة لفرط الهوموسيستين في الدم في انسداد الأوعية الشبكية.

ABSTRACT To investigate the possible relationship between hyperhomocysteinaemia and retinal vascular occlusion, we measured plasma homocysteine levels in 25 patients with a history of retinal vascular occlusion in the previous 2 years and in a control group of 24. The difference in mean plasma homocysteine levels was not statistically significant. All except 5 of the cases had hypertension, diabetes mellitus or hyperlipidaemia. Most of the patients had branch retinal vein occlusion associated with recent onset of occlusion. Factors such as emotional status and associated systemic disease may play a role in predisposition of retinal vascular occlusion, so more-precise studies are needed to determine the possible risk factors of hyperhomocysteinaemia in retinal vascular occlusion.

Hyperhomocystéinémie : risque d'occlusion vasculaire rétinienne

RÉSUMÉ Afin d'examiner le lien possible entre l'hyperhomocystéinémie et l'occlusion vasculaire rétinienne, nous avons mesuré les taux d'homocystéine plasmatique chez 25 patients ayant fait une occlusion vasculaire rétinienne dans les deux années précédentes et dans un groupe témoin de 24 sujets. La différence des taux moyens d'homocystéine plasmatique n'était pas statistiquement significative. Tous les cas sauf cinq avaient une hypertension, un diabète sucré ou une hyperlipidémie. La plupart des patients avaient une occlusion de branche veineuse rétinienne associée à la survenue récente de l'occlusion. Des facteurs tels que l'état émotionnel et une maladie systémique associée peuvent jouer un rôle dans la prédisposition à l'occlusion vasculaire rétinienne. Des études plus précises sont donc nécessaires pour déterminer les facteurs de risque possibles de l'hyperhomocystéinémie dans l'occlusion vasculaire rétinienne.

[1]Department of Ophthalmology, Valiaser Hospital; [2]Nursing College, Birjand Medical University, Birjand, Islamic Republic of Iran.
[3]Department of Ophthalmology, Mashhad University of Medical Science, Mashhad, Islamic Republic of Iran.
Received: 09/05/03; accepted: 20/10/03

Introduction

Thrombophilia is an increased tendency to thrombosis which is sustained by an ongoing stimulus to thrombogenesis or by a defect in the normal anticoagulant or fibrinolytic mechanism. Genetic factors are important in thrombophilia since thrombosis can be familial and may be associated with congenital deficiencies of the protein C anticoagulant pathway, antithrombin III, heparin cofactor II or plasminogen. Although the relationship between hyperhomocysteinaemia and vascular occlusion is still uncertain, it is of increasing interest that less severe abnormalities of methionine metabolism may predispose to the development of premature vascular disease. Endothelial dysfunction is also a factor in the complex changes that occur in vessel walls in hyperhomocysteinaemia [*1,2*]. Retinal vein occlusion is a major cause of retinal vascular disease, second only to diabetic retinopathy [*3*]. Branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) are the 2 major categories, both having a similar potential for loss of vision owing to complications causing macular oedema and neovascularization [*4*].

Considering the various uncertainties regarding the many possible risk factors for retinal vascular occlusion, this study was carried out to measure plasma homocysteine levels in patients diagnosed with retinal vascular occlusion and to compare the results with those of a control group to determine whether elevated homocysteine level is a risk factor in retinal vascular occlusion.

Methods

We carried out a retrospective study of 25 out of 31 patients with retinal vein occlusion who consecutively attended the eye clinic of Valiasr Hospital, a teaching hospital of Birjand Medical University, from May 2002 to December 2002. Diagnosis of retinal vascular occlusion was based on clinical findings of ophthalmoscopic examination (well-demarcated haemorrhage and oedema along obstructed retinal vein). In uncertain cases fluorescein angiography was also done. A matched control group of 24 individuals was selected from people attending the clinic but who had no signs of retinal vascular occlusion, glaucoma, uveitis or intraocular surgery/trauma.

All participants completed a checklist consisting of questions covering demographic data, current disease, disease history, eye trauma and consumption of drugs. Then the fasting plasma homocysteine levels of the patients who had agreed to participate and had given informed consent was measured. Patients were classified into 3 major categories of retinal vascular occlusion based on their first episode: CRVO, BRVO (macular or main branch) or central retinal artery occlusion. The cases and controls were matched for age and sex.

Fasting blood samples were collected in heparinized tubes from all participants. After immediate centrifugation, the resultant plasma samples were packed in an icebox and sent to the Pars Laboratory, Tehran to measure plasma homocysteine levels.

Analysis of data was done with respect to presence/absence of a systemic condition, sex, age group and mean plasma homocysteine as independent variables and retinal vein occlusion as the dependent variable.

Results

Of the 25 patients with retinal vascular occlusion, 14 had BRVO and 10 had CRVO. Central retinal artery occlusion was diagnosed in a single case.

The onset of occlusion in 6 patients occurred within the previous 6 months (1–6 months); in the rest, occlusion had occurred more than 6 months previously (7–30 months).

The characteristics of all participants, both cases and controls, are shown in Tables 1 and 2. A more detailed comparison of related disease in both cases and controls is shown in Table 3. The mean total plasma homocysteine level was 15.0 (SD, 5.7) μmol/L for patients with retinal vascular occlusion and 13.4 (SD 4.1) μmol/L for the control group (Table 4). The mean level was 13.8 μmol/L in patients with BRVO and 16.5 μmol/L in patients with CRVO. Of the 25 patients, 20 had at least 1 associated disease (diabetes mellitus, hypertension, hyperlipidaemia, asthma) for which they were under treatment by their primary care doctor and were taking medication. In the control group, these conditions were present in only 4 of the 24. The independent *t*-test showed no significant difference between plasma homocysteine levels for cases and controls ($P = 0.24$).

The Mann–Whitney test showed no significant difference between homocysteine levels in patients with BRVO and those with CRVO ($P = 0.33$). The Fisher test showed that there was also no significant difference in homocysteine level between hypertensive patients with BRVO and those with CRVO ($P = 0.67$).

Visual acuity in all BRVO cases was 1.1 or better in comparison to hand motion perception, and 0.1 in CRVO patients.

Discussion

In this study, we found no significant clinical association between hyperhomocysteinaemia and retinal vascular occlusion, although mean plasma homocysteine levels were higher in patients than in the control group. Most of these patients had at least 1 associated systemic disease.

The sample size in our study was small and both the patients and those in the control group were hospital-based subjects. This was a single blind study, in which the results may have been affected by the type of retinal vascular occlusion (most of the cases had BRVO). Our findings are similar to those of Larsson et al., who also reported that hyperhomocysteinaemia was not an important factor in the etiology of CRVO [*5*].

There may be different pathogeneses for the different kinds of retinal vascular occlusion. If there is an association with the location of the vascular obstruction, this finding may be related to increasing plasma homocysteine levels, or more probably to homodynamic change or local vascular insult. This was discussed by Cahill et al., who considered CRVO to be associated with similar risk factors to retinal arterial occlusive disease. Local factors such as atherosclerotic retinal arteries compressing the retinal vein at arteriovenous crossings may be more important in the etiology of BRVO [*6*].

Hyreh et al. recommended that, apart from routine medical evaluation, an extensive and expensive workup for systemic disease is unwarranted in the vast majority of patients with retinal vein occlusion [*7*]. This raises 2 points. First, is vascular occlusion pathophysiologically different in different organs? If so, we can consider that the attributing factors must be produced in greater amounts or elevated in larger vessels of the affected organ. Second, how much time has passed between the occurrence of vascular occlusion and the measurement of the plasma homocysteine level, because homocysteine levels are affected by many factors (diet, emotional state, etc.).

Table 1 **Characteristics of patients with retinal vascular occlusion**

Patient	Age (years)	Sex	Eye	Type of occlusion	Associated disease	Addiction	Plasma homocysteine (µmol/L)
1	42	Female	L	BRVO	HY	None	6.6
2	76	Male	R	CRVO	HY	None	25.0
3	68	Male	R	CRVO	HY	None	11.9
4	60	Male	L	CRVO	HY	None	16.8
5	71	Female	L	BRVO^{MB}	None	None	17.9
6	48	Female	R	CRAO	None	None	17.4
7	60	Female	R	BRVO	HY, DI	None	25.0
8	66	Female	L	BRVO	HY	None	18.0
9	56	Female	L	BRVO	HY	None	12.4
10	68	Female	R	CRVO	DI	None	12.5
11	45	Male	L	BRVO	None	None	14.2
12	48	Male	L	CRVO	DI, HCH	None	13.0
13	40	Male	L	BRVO^{MB}	HY, HCH	None	12.7
14	38	Female	R	BRVO	HY, DI	None	14.6
15	56	Female	R	BRVO	HCH	None	11.0
16	60	Female	R	BRVO	HY	None	15.5
17	60	Female	L	BRVO	HY	None	11.5
18	63	Female	R	BRVO	HY, HCH	None	12.6
19	63	Male	L	CRVO	AS	None	18.0
20	61	Female	R	BRVO	HCH	None	10.3
21	65	Female	L	CRVO	None	None	9.2
22	70	Male	R	BRVO	HY	None	10.5
23	70	Male	R	CRVO	HCH	None	27.0
24	80	Male	L	CRVO	None	None	10.5
25	80	Male	L	CRVO	HY	None	21.0

CRVO = central retinal vein occlusion.
BRVO = branch retinal vein occlusion.
CRAO = central retinal artery occlusion.
MB = macular branch.
HY = hypertension.
HCH = hypercholesterolaemia.
DI = diabetes.
AS = asthma.

Although our study did not find a significant difference in hyperhomocysteinaemia levels between the case and the control groups, Lahey et al. have reported that hypercoagulability plays a role in thrombus formation in patients with CRVO who are

Table2 **Characteristics of participants in the control group**

Participant	Age (years)	Sex	Associated disease	Addiction	Plasma homocysteine (µmol/L)
1	79	Male	None	None	7.0
2	77	Female	None	None	16.9
3	75	Female	None	None	11.7
4	25	Female	None	None	7.1
5	53	Female	HY	None	13.0
6	61	Female	DI	None	15.4
7	52	Male	None	None	21.0
8	57	Male	HY	None	19.4
9	47	Male	None	None	9.0
10	65	Female	None	Smoking	10.2
11	67	Female	None	None	11.8
12	47	Male	None	None	17.6
13	47	Female	None	None	7.3
14	47	Male	None	None	14.0
15	50	Female	None	None	11.8
16	51	Female	HY	None	13.8
17	60	Male	None	None	17.3
18	65	Female	None	None	9.9
19	70	Male	None	None	11.5
20	70	Male	None	None	12.5
21	74	Male	None	None	11.5
22	76	Male	None	None	22.0
23	80	Female	None	None	16.2
24	85	Male	None	None	13.8

HY = hypertension.
DI = diabetes.

under 56 years old [*8*]. They concluded that hypercoagulability may play a part in the pathogenesis of CRVO, but the cause remains multifactorial, and laboratory tests alone cannot determine the cause in most patients. They recommended examining blood pressure, intraocular pressure, complete blood count, glucose level and a lipid panel in all patients with CRVO. When tests for these common risk factors for CRVO are negative, they would consider ordering selected tests in young patients with CRVO to rule out thrombophilia. Furthermore, in 2 other studies the authors describe sclerotic thickening of the central retinal artery that could easily compress the adjacent central

Table 3 **Characteristic of cases with retinal vascular occlusion and participants in the control group**

Variable	Cases (*n* = 25)		Controls (*n* = 24)	
	%	Mean homocysteine (µmol/L)	%	Mean homocysteine (µmol/L)
Male sex	44.0	–	50.0	–
Hypertension	56.0	15.3	12.5	15.4
Hyperlipidaemia	24.0	14.4	0.0	–
Diabetes mellitus	16.0	16.2	4.2	15.4
Without disease	16.0	13.8	83.3	12.4

Mean age of cases and controls was 60.5 and 61.7 years respectively (P = 0.77).
Mean homocysteine level in cases and controls was 15.0 and 13.4 µmol/L respectively (P = 0.24).

retinal vein and begin the sequence that leads to thrombus formation. Therefore, hyperhomocysteinaemia may represent a "double hit" in the multifactorial pathogenesis of CRVO [*9,10*].

Although many reports suggest hyperhomocysteinaemia is a risk factor for vascular occlusion, our study shows that it plays a less important role than systemic risk factors for retinal vascular occlusion. Systemic hypertension was more common in cases than in control subjects. Also, most of the cases had at least 1 systemic disease (e.g. hypertension, diabetes, hyperlipidaemia). Therefore, hyperhomocysteinaemia may represent a coincidental association in the pathogenesis of retinal vascular occlusion. These paradoxical results not only demand repeating cohort studies with a larger sample size, they also

Table 4 **Distribution of cases according to type of retinal vascular occlusion**

Type of occlusion	No.	Diabetes mellitus No.	Hypertension No.	Hyperlipidaemia No.	Mean homocysteine (µmol/L)
CRAO	1	0	0	0	17.4
CRVO	10	2	4	2	16.5
BRVO	14	2	10	4	13.8
Total	25	4	14	6	15.5

CRAO = central retinal artery occlusion.
CRVO = central retinal vein occlusion.
BRVO = branch retinal vein occlusion.

highlight the need to assess the preventive effects of lowering homocysteine levels on the recurrence of retinal vascular occlusion in cases compared to future attacks in control subjects.

Acknowledgement

We wish to thank our colleague Hydari Behroze for his valuable assistance.

References

1. Fermo I et al. Prevalence of moderate hyperhomocysteinaemia in a patients with early-onset venous and arterial occlusive disease. ***Annals of internal medicine***, 1995, 123(10):747–53.
2. Faraci FM. Hyperhomocysteinemia: a million ways to lose control. ***Arteriosclerosis, thrombosis, and vascular biology***, 2003, 23(3):371–3.
3. Blice JP, Brown GC. Retinal vascular occlusive disease. In: Spaide RF ed. ***Diseases of the retina and vitreous.*** Philadelphia, W.B. Saunders Company, 1999:116.
4. Clarkson JG. Central retinal vein occlusion. In: Ryan SJ. ***Retina***. Singapore, CV Mosby, 2001:1368.
5. Larsson J, Hultberg B, Hillarp A. Hyperhomocysteinemia and the MTHFR C677T mutation in central retinal vein occlusion. ***Acta ophthalmologica scandinavica***, 2000, 78(3):340–3.
6. Cahill M et al. Raised plasma homocysteine as a risk factor for retinal vascular disease. ***British journal of ophthalmology***, 2000, 84(2):154–7.
7. Hayreh SS et al. Systemic diseases associated with various types of retinal vein occlusion. ***American journal of ophthalmology***, 2001, 131(1):61–77.
8. Lahey JM et al. Laboratory evaluation of hypercoagulable states in patients with central retinal vein occlusion who are less than 56 years of age. ***Ophthalmology***, 2002, 109(1):126–31.
9. Vine AK. Hyperhomocysteinemia: a new risk factor for central retinal vein occlusion. ***American journal of ophthalmology***, 2000, 129(5):640–4.
10. Brown BA et al. Homocysteine: a risk factor for retinal venous occlusive disease. ***Ophthalmology***, 2002, 109(2):287–90.

Aspects cytologiques des leucémies aiguës : à propos de 193 cas colligés dans la région centrale de la Tunisie

N. Braham Jmili,[1] A. Ben Abdelaziz,[2] M. Nagara,[1] T. Mahjoub,[1] H. Ghannem[2] et M. Kortas[1]

الملامح السيتولوجية لابيضاض الدم الحاد في المنطقة الوسطى من تونس

براهم جميلي ناجية، بن عبد العزيز أحمد، نقارة محمد، محجوب توهامي، غنام حسن، قرطاس منذر

الخلاصة: نظراً لعدم توافُر سجل سكاني في تونس، فإن المعلومات حول ابيضاض الدم الحاد نادرة. وقد درس الباحثون الملامح السيتولوجية والوبائية (الإبيديميولوجية) في 193 من المرضى المصابين بابيضاض الدم الحاد. وأجرى الباحثون دراسة للصيغة الدموية ولطاخات من الدم المحيطي ومن النقي لكل مريض. وقد تراوحت أعمار المرضى بين 10 شهور و83 سنة، مع رجحان لدى الذكور (بنسبة 1.27). أما بالنسبة لنمط ابيضاض الدم فإن 40.4٪ كانوا من المصابين بابيضاض دم حاد بالأرومات اللمفاوية و51.8٪ كانوا من المصابين بابيضاض دم حاد بالأرومات النقوية، و7.8٪ كانوا من المصابين بابيضاض الدم غير المصنَّف. وكان التشخيص قد وضع قبل أقل من عشر سنوات لدى 31.6٪ من الحالات، وكان نمط الابيضاض لدى 72٪ منهم من الأرومات اللمفاوية. ولوحظ وجود فقر الدم (هيموغلوبين أقل من 11 غرام/ديسي لتر) في 85٪ من الحالات، ووجود نقص في الصفيحات (أقل من مئة ألف صفيحة في كل ميلي متر مكعب) لدى 80.5٪ من الحالات. كما لوحظ فرط الكريات البيض (تعداد الكريات البيض يزيد عن مئة ألف كرية بيضاء في كل ميلي متر مكعب) في 14.5٪ من الحالات مع وجود الأرومات في الدم المحيطي في 92٪ من الحالات.

RÉSUMÉ En Tunisie, peu de données concernant les leucémies aiguës sont disponibles en l'absence d'un registre de population. Nous avons étudié les caractéristiques épidémiologiques et cytologiques de 193 patients atteints de leucémie aiguë. Des hémogrammes ont été réalisés et des frottis de sang et de moelle ont été examinés pour chaque patient. L'âge des patients variait de 10 mois à 83 ans avec une prédominance masculine (rapport : 1,27). Concernant le type de leucémie aiguë, 40,4 % avaient une leucémie aiguë lymphoblastique, 51,8 % une leucémie aiguë myéloblastique et 7,8 % étaient des cas difficiles à classer. Dans notre série, 31,6 % des cas de leucémie aiguë s'observaient à un âge de moins de 10 ans et 72 % de ces cas étaient de type lymphoblastique. Une anémie (hémoglobine <11 g/dL) a été observée dans 88,5 % des cas, une thrombopénie (plaquettes <100 000/mm^3) dans 80,5 %, une hyperleucocytose > 100 000/mm^3 dans 14,5 % avec une blastose sanguine dans 92 % des cas.

Cytological features of acute leukaemia in the central region of Tunisia

ABSTRACT In Tunisia, because of an absence of population registry, data on acute leukaemia are scarce. We studied the epidemiological and cytological characteristic of 193 patients with acute leukaemia. Haemograms were carried out and slides for peripheral blood and bone marrow were prepared for each patient. The age range of the patients was 10 months to 83 years with a predominance of males (ratio: 1.27). As regards type of leukaemia, 40.4% had acute lymphoblastic leukaemia, 51.8% had acute myeloblastic leukemia and 7.8% were unclassified. Diagnosis was made at less than 10 years in 31.6% of cases and 72% of these were the lymphoblastic type. Anaemia (Hb < 11 g/dL was found in 85% of cases, thrombocytopenia (platelets < 100 000/mm^3) in 80.5% and hyperleukocytosis (WBC > 100 000/mm^3) in 14.5% of cases with blasts in peripheral blood in 92% of cases.

[1]Laboratoire d'Hématologie; [2]Service d'Epidémiologie, C.H.U. Farhat Hached, Sousse (Tunisie).
Reçu : 13/08/03 ; accepté : 22/01/04

Introduction

Les leucémies aiguës (LA) constituent un groupe hétérogène d'affections hématologiques clonales caractérisées par une prolifération maligne dans la moelle osseuse d'un clone cellulaire anormal du tissu hématopoïétique et bloqué à un stade précis de différenciation avec expansion de cellules immatures (blastes) qui peuvent être présentes dans le sang périphérique [*1,2*].

En Europe et aux États-Unis, les LA représentent 80 % des leucémies et environ 35 % des cancers de l'enfant [*2,3*]. En Tunisie, les leucémies représentent la première hémopathie maligne diagnostiquée et traitée [*4*].

Dès les premières descriptions, la sous-classification des LA en une série de variétés distinctes s'est imposée du simple fait de leur diversité morphologique. Ces subdivisions ont montré par la suite un intérêt pronostique du fait de leur sensibilité différente aux chimiothérapies [*1,5*]. Malgré le développement de nouvelles technologies pour la caractérisation des différentes entités de leucémies aiguës dans les applications cliniques [*6-8*], on continue à utiliser dans beaucoup de pays en développement les recommandations anciennes de la classification FAB (*French-American-British*), mise au point en 1976 et basée sur des caractéristiques morphologiques et cytochimiques [*9*].

En Tunisie, en l'absence d'un registre de population, les laboratoires d'anatomopathologie et les dossiers hospitaliers constituent les principales sources d'information sur l'épidémiologie des cancers [*10*]. Toutefois, peu de données nationales concernant le profil épidémiologique et cytologique des leucémies aiguës sont disponibles.

L'objectif de ce travail est de décrire, à travers une série de 193 cas, les caractéristiques épidémiologiques et cytologiques du sang périphérique et de la moelle chez les patients atteints de leucémie aiguë dans la région du centre de la Tunisie.

Méthodes

Il s'agit d'une étude descriptive réalisée au Laboratoire d'Hématologie de l'Hôpital Farhat Hached de Sousse. Cette étude a concerné tous les patients chez lesquels une leucémie aiguë a été diagnostiquée entre le 1er janvier 1998 et le 30 juin 2002.

Les échantillons de sang ont été prélevés par ponction veineuse sur des tubes avec EDTA K3 (acide éthylène diamine tétracétique tripotassique). La ponction de la moelle osseuse a été pratiquée chez l'adulte au sternum et en épine iliaque postérieure chez l'enfant.

L'hémogramme a été déterminé sur « Coulter MAXM ». Les frottis de sang et de moelle ont été colorés au *MGG* (*May-Grünwald-Giemsa*) par la méthode automatique (HEMATEK-AMES). Pour chaque patient, trois lectures indépendantes des frottis de sang et de moelle ont été assurées et validées par des cytologistes.

Le diagnostic de LA a été porté dès qu'il y avait plus de 30 % de blastes dans la moelle osseuse. L'examen de sang a permis d'établir la formule leucocytaire sanguine et a contribué à la classification des LA selon le groupe FAB. La séparation entre les sous-groupes des LA a été basée sur l'appréciation du pourcentage des blastes dans la moelle, le type de blastes et le compte absolu des monocytes sanguins [*11*].

La sous-classification morphologique des leucémies aiguës lymphoblastiques

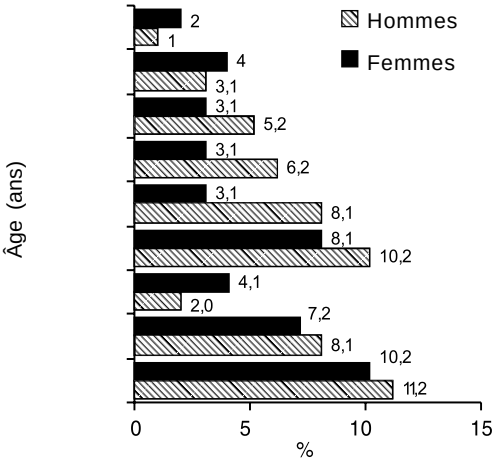
a été basée sur un système de score utilisant les caractères cellulaires suivants : le rapport nucléocytoplasmique, la présence de nucléoles, l'irrégularité du profil nucléaire et la présence de grandes cellules [*12*]. La recherche de l'activité myéloperoxydasique par la technique à la pyronine a été la réaction cytochimique appliquée sur un frottis de moelle dans le cas où l'aspect myéloïde n'était pas évident et elle a été considérée négative si on notait une proportion de moins de 3 % de blastes peroxydase positive.

Les données répertoriées ont été ensuite informatisées sur le logiciel de traitement statistique (SPSS.10) au Service d'Epidémiologie du C.H.U. Farhat Hached de Sousse. Les statistiques descriptives (moyennes, fréquences) ont été utilisées pour résumer les données.

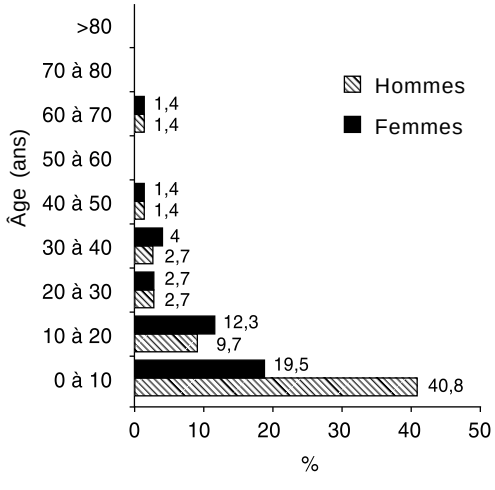
Résultats

La répartition de 193 cas de LA selon les mois a montré une variation saisonnière avec deux pics : printemps et automne. L'âge des patients variait de 10 mois à 83 ans. Le rapport était de 1,27 en faveur du sexe masculin. Les leucémies aiguës touchaient tous les âges avec une fréquence plus élevée chez l'enfant (Figure 1).

L'examen cytologique des frottis de sang et de moelle ont permis d'affirmer le diagnostic des 193 cas de LA et d'en préciser le type cellulaire (Tableau 1) : 40,4 % des cas étudiés étaient de type lymphoblastique dont 56,4 % étaient de type L1 et 32,1 % étaient de type L2. La réaction de myéloperoxydase était indispensable dans 36 % des cas, vu l'absence de signe de différenciation cytologique, et il était impossible de classer 7,8 % des frottis examinés. Les leucémies aiguës de type myéloïde



A : LAL (Leucémie aiguë lymphoblastique)



B : LAM (Leucémie aiguë myéloïde)

Figure 1 **Répartition par âge et par sexe de 193 cas de leucémie aiguë colligés dans la région centrale de la Tunisie**

Tableau 1 **Classification cytologique des 193 cas de leucémie aiguë colligés dans la région centrale de la Tunisie**

Cas	Nbre	%
LAM [1]	100	51, 8
LAM1	12	12,0
LAM2	17	17,0
LAM3	15	15,0
LAM4	16	16,0
LAM5	15	15,0
LAM6	7	7,0
LAM7	1	1,0
LAMDAC[2]	17	17
LAL[3]	78	40,4
LAL1	44	56,4
LAL2	25	32,1
LAL3	4	5,1
LALDAC[4]	5	6,4
LADAC[5]	15	7,8
Total	193	100

[1]LAM : leucémie aiguë myéloïde.
[2]LAMDAC : leucémie aiguë myéloïde difficile à classer.
[3]LAL : leucémie aiguë lymphoïde.
[4]LALDAC : leucémie aiguë lymphoïde difficile à classer.
[5]LADAC : leucémie aiguë difficile à classer.

représentaient 51,8 % des cas avec une distribution homogène des différents sous-types 1, 2, 3, 4 et 5. Les LAM 6 et 7 étaient plus rares. Le sous-typage était impossible dans 17 % des LAM et 6,6 % des LAL.

L'étude de la numération et formule sanguine de ces 193 patients atteints de LA a conclu aux différentes anomalies illustrées par la figure 2. Elle a montré une blastose sanguine dans 92 % des cas. L'anémie a été observée dans 88,5 % des cas avec une thrombopénie dans 80,5 % des cas.

Discussion

Depuis une vingtaine d'années, la classification des LA fait appel aux recommandations du groupe FAB. L'intérêt longtemps porté à cette classification tient à sa relative simplicité basée sur une description morphologique simplifiée, après coloration des frottis de sang et de moelle par la méthode de *May-Grünwald-Giemsa* complétée par des examens cytochimiques [*11*], accessible à tous les laboratoires et tenant compte des anomalies cytologiques du sang et de la moelle. Cette approche reste toujours la base du diagnostic des LA en application clinique malgré ses limites.

En effet, dans notre étude, le plus souvent le diagnostic des LA est évident. Cependant, des difficultés de classement se sont posées en cas de frottis pauvres ou mal étalés. La ponction est difficile à réaliser en cas de myélofibrose pouvant gêner l'aspiration de moelle. D'où la nécessité de caractériser la population blastique par d'autres marqueurs immunologiques et cytogénétiques pour affirmer ou même modifier le diagnostic et aussi mieux cibler les indications thérapeutiques initiées [*2*]. C'est la confrontation de l'examen des frottis sanguins et l'étude des molécules membranaires de surface qui permettra un diagnostic dans les cas difficiles [*13*,*14*]. En effet, l'immunophénotypage est indispensable pour confirmer le diagnostic des LAL, rechercher une LA biphénotypique et éliminer une LAM indifférenciée (LAM0) [*15*]. L'intérêt du caryotype dans les leucémies aiguës est bien établi. Les anomalies décelées représentent l'un des critères de classement d'une LA [*6*,*16*]. De même, la biologie moléculaire a fait aujourd'hui son entrée dans l'évaluation des LA, notamment pour la mise en évidence des translocations cryptiques et l'analyse des échecs du caryotype et surtout son intérêt majeur

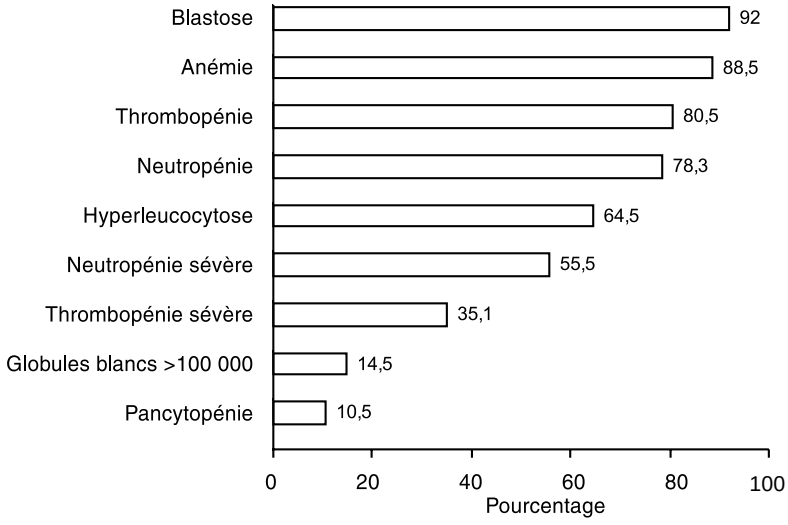


Figure 2 **Anomalies de l'hémogramme chez 193 cas de leucémie aiguë colligés dans la région centrale de la Tunisie.**
Anémie (hémoglobine < 11 g/dL), thrombopénie (plaquettes < 100 000/mm3), neutropénie (polynucléaires neutrophiles < 1500/mm³) hyperleucocytose (globules blancs > 10 000/mm³), neutropénie sévère (polynucléaires neutrophiles < 1000/mm³), thrombopénie sévère (plaquettes < 20 000/mm³), pancytopénie (anémie, thrombopénie et leucopénie : globules blancs < 4000/mm³)

pour l'évaluation de la maladie résiduelle [*7*]. Ainsi, la classification des LA proposée par l'OMS intègre les données morphologiques, immunophénotypiques, génétiques et cliniques dans le but de définir des entités biologiquement homogènes et cliniquement pertinentes [*17*]. Le classement des leucémies aiguës est basé sur l'appartenance des blastes à une lignée lymphoïde ou myéloïde.

Les leucémies aiguës lymphoïdes (LAL) sont divisées en LAL à précurseurs B et LAL à précurseurs T.

Les leucémies aiguës myéloïdes (LAM) comprennent 4 grandes catégories [*8,17*] :

- LAM avec anomalies génétiques récurrentes ;
- LAM avec signes de dysplasie touchant plusieurs lignées ;
- LAM secondaires à des thérapeutiques ;
- LAM autres, n'entrant pas dans les catégories précédentes.

Toutefois, il faut noter que ces nouvelles techniques sont longues à mettre en œuvre et nécessitent une certaine pratique, ce qui les réserve à des laboratoires spécialisés, et devant l'extrême urgence de la maladie, l'examen cytologique du sang et de la moelle reste un moyen rapide qui permet, dans l'heure qui suit le prélèvement, le diagnostic de la majorité des LA.

Les deux variétés L1 et L2 des LAL ne sont pas réellement distinctes par une catégorie particulière de cellules blastiques mais plutôt par des proportions différentes d'éléments cellulaires qu'elles peuvent

avoir en commun [*4*]. La valeur pronostique des formes L2 par rapport aux formes L1 n'a jamais pu être mise en évidence [*11*].

Cinq pour cent (5 %) des LAL étaient de type L3. Cette forme, distinguée par un critère cytoplasmique très particulier des cellules de Burkitt, doit être considérée à part des LAL classiques. Le type L3 est peu fréquent en France, tant chez l'adulte (9,7 %) que chez l'enfant (4,6 %) [*18*]. Les LAL de type Burkitt étaient classiquement de pronostic très péjoratif mais l'instauration de protocoles de chimiothérapie intensive et brève a entraîné un changement de pronostic et une amélioration des chances de guérison.

La présence de granulations dans les blastes fait suspecter une origine myéloblastique. Le diagnostic peut être porté avec certitude sur un très faible pourcentage de blastes s'ils renferment un ou des corps d'Auer, témoignant de leur caractère malin [*15*]. Les caractères cytologiques des LAM ont une valeur pronostique discutée ; des études ont montré que le taux de rémission complète a été plus élevé dans les catégories M1, M2 et M3 que dans les formes M4, M5 et M6, mais ces constatations n'ont pas été partagées par d'autres auteurs [*19*].

La littérature médicale rapporte que les LA de l'enfant, bien que rares en soi, représentent la première cause de cancer pédiatrique (30 %) et surviennent surtout avant 9 ans. En Europe et aux États-Unis, les LAL représentent 75 % à 80 % des leucémies et environ 20 % des cancers de l'enfant de moins de 15 ans [*3*]. En effet, les LAL touchent de préférence les âges extrêmes avec une distribution bimodale de l'incidence et de la mortalité (<15 ans et > 80 ans). Chez l'adulte, elles sont au contraire quatre fois plus rares que les LAM (environ 5 % des leucémies) [*18*].

Dans notre série, 31,6 % des cas de LA s'observent à un âge de moins de 10 ans, et 72 % des cas sont de type lymphoblastique. Cependant, notre série comportait seulement 2 cas de LAL chez les patients âgés de plus de 50 ans et nous pensons que cette fréquence pourrait être sous-estimée et que la pathologie serait sous-diagnostiquée dans cette tranche d'âge. En revanche, nos résultats corroborent ce qui est rapporté dans les différentes séries concernant la fréquence des LAM chez l'adulte. Les LAM étaient quatre fois plus importantes que les LAL dans la tranche 20 à 60 ans, puis la fréquence restait stable jusqu'à un âge supérieur à 80 ans.

L'âge est le facteur de pronostic le plus important pour la réussite du traitement d'induction des LAM [*20*]. Concernant les LAL, chez l'adulte, le risque de rechute ou d'échec primaire s'accroît au-dessus de 35 ans ; la maladie est souvent hyperleucocytaire avec une atteinte méningée initiale, et le traitement est plus toxique à cet âge. Chez l'enfant plus grand, le pronostic se dégrade à partir de 10-11 ans pour rejoindre celui de l'adulte à partir de 15 ans. Le pronostic est très défavorable si l'âge est inférieur à 12 mois, et surtout inférieur à 6 mois [*2*].

Le genre humain a une moindre valeur pronostique. Dans notre série, le rapport a été de 1,27 en faveur du sexe masculin avec une nette prédominance du sexe masculin à l'âge adulte. La prédominance masculine a été manifeste pour les leucémies aiguës de type lymphoblastique (Figure 1). Le pronostic est plus défavorable pour le sexe masculin dans ce cas (rechute testiculaire dans 5 % des cas). Contrairement aux LAL, le sexe ne semble pas être un facteur de pronostic dans les LAM.

Les leucémies aiguës associent à des degrés variables des signes de prolifération et d'insuffisance médullaire. L'étude de

l'hémogramme a montré des cellules blastiques dans 92 % des cas mais cela n'a pas été suffisant pour poser le diagnostic [*2*]. La détermination de la numération et formule sanguine a permis par ailleurs d'apprécier :

- le degré de l'anémie : un chiffre normal d'hémoglobine (11,5 % des cas) traduit souvent une forme rapidement évolutive et de plus mauvais pronostic ;
- l'intensité de la thrombopénie et le risque hémorragique : on notait une thrombopénie sévère avec un risque d'hémorragie cérébrale dans 35,1 % des cas ;
- la leucocytose qui constitue un facteur pronostique majeur. Le pronostic est plus favorable quand la leucocytose est inférieure à 100 000/mm^3 [2]. Dans notre série, les LA se présentaient fréquemment sous une forme hyperleucocytaire (64,5 % des cas). Le chiffre de globules blancs a été supérieur à 100 000/mm^3 dans 14,5 % des cas avec une pancytopénie uniquement dans 10,5 % des 193 cas.
- Le degré de la neutropénie absolue prédit le risque infectieux. Nos résultats ont montré une neutropénie dans 78,3 % des cas ; elle a été sévère dans 55,5 % des cas. Des résultats similaires ont été déjà décrits et ont trouvé notamment une leucocytose supérieure à 100 000/mm^3 dans 5 à 10 % [2].

Conclusion

Un hémogramme complet avec une lecture minutieuse des frottis de sang et de moelle complétée par des réactions cytochimiques permettent encore le classement de la plupart des LA. Cependant l'étude d'autres marqueurs cytogénétiques, immunologiques et moléculaires est devenue nécessaire pour confirmer le diagnostic des LAL et pour identifier des LA d'aspect atypique. La classification OMS nouvellement proposée utilise une combinaison de l'ensemble de ces approches, prenant en considération leur capacité à définir des entités biologiques qui, avec l'âge et les anomalies de l'hémogramme, permettent de définir le schéma thérapeutique et représentent les éléments utiles au pronostic [*9,17*].

Références

1. Hollard D. Les leucémies aiguës. EMC (Paris-France). Sang, 1983, 13015 A^{20} : 5-1983, 5–13.
2. Hunault-Berger M, Pellier I, Norbert I. Leucémie aiguë lymphoblastique (adulte et enfant). ***La Revue du Praticien***, 1999, 49:441–5.
3. Chan KW. Acute myeloid leukaemia. Acute lymphoblastic leukaemia. ***Current problems in pediatric and adolescent health care***, 2002, 32(2):40–9.
4. Laatiri M, Ennabli S. Lymphomes non hodgkiniens. In : Maalej M, ed. ***Cancérologie pratique***. Tunis, Centre de Publication universitaire, 1999: 447–55
5. Flandrin G et al. Classification des leucémies aiguës. EMC (Paris-France), Sang, 13015 A^{10}, 7-1988, 5–10.
6. Charrin C, Mugneret F. Cytogénétique des leucémies aiguës de novo. ***La Revue du Praticien***, 1996, 46:37–41.
7. Gabert J. Utilité de la biologie moléculaire dans le diagnostic des leucémies aiguës et l'évaluation de la maladie résiduelle. ***La Revue du Praticien***, 1996, 46:42–7.

8. Paredes-Aguilera R et al. Flowcyto-metric analysis of cell-surface and intra cellular antigens in the diagnosis of acute leukaemia. ***American journal of hematology***, 2001, 68(2):69–74.

9. Flandrin G. La nouvelle classification OMS des hémopathies malignes. Hémopathies myéloïdes. ***Hématologie***, 2001, 7(2):136–41.

10. Ben abdallah M. Epidémiologie des cancers en Tunisie. In : Maalej M, ed. ***Cancérologie pratique***. Tunis, Centre de Publication universitaire, 1999:33–7.

11. Imbert M, Jouault H, Tulliez M. Cytologie des leucémies aiguës. ***La Revue du Praticien***, 1996, 46:23–9.

12. Bennet JM et al. The morphological classification of acute lymphoblastic leukaemia: concordance among observers and clinical correlation. ***British journal of haematology***, 1981, 47(4):553–61.

13. Feki S et al. Contribution of flow cytometry to acute leukaemia classification in Tunisia. ***Disease markers***, 2000, 16: 131–3.

14. Cabrera E et al. Acute myeloid leukaemia: clinical and laboratory characteristics. ***Revista modica de Chile***, 1999, 125(4):433–7.

15. Imbert M. Place du biologiste dans le diagnostic et le suivi des leucémies aiguës. ***Revue Française des Laboratoires***, 2002, 344:67–70.

16. Bennett JM et al. Hypergranular promyelocytic leukaemia: correlation between morphology and chromosomal translocations including t(15;17) and t(11;17). ***Leukaemia***, 2000, 14(7):1197–200.

17. Valensi F. Classification des leucémies aiguës : nouvelles propositions de l'OMS. ***Revue Française des Laboratoires***, 2002, 344:19–24.

18. Roy P, Coleman MP. Epidémiologie des leucémies aiguës lymphoïdes. ***Revue d'épidémiologie et de santé publique***, 1992, 40:323–34.

19. Reiffers J, Perel Y, David B. Traitement des leucémies aiguës. In : Breton-Gorius J et al., eds. ***L'hématologie de Bernard Dreyfus***. Paris, Flammarion, 1992 :805–25.

20. Xavier T, Belharbi A. Leucémies aiguës myéloïdes du sujet âgé : Mise au point. ***Bulletin du cancer***, 2002, 2(2):143–54.

Physicians' knowledge, attitude and practice towards erectile dysfunction in Saudi Arabia

M.F. Abdulmohsen,[1] I.S. Abdulrahman,[1] A.H. Al-Khadra,[1] A.A. Bahnassy,[2] S.A. Taha,[3] B.A. Kamal[3], A.M. Al-Rubaish[1] and A.H. Al-Elq[1]

معارف ومواقف وممارسات الأطباء في المملكة العربية السعودية تجاه خلل وظيفة النعوظ

محمد فخري عبد المحسن، إبراهيم سعيد عبد الرحمن، أكرم الخضرا، أحمد عبد اللطيف بهنسي، سعود أسعد طه، باهر علي كامل، عبد الله محمد الربيش، عبد المحسن حبيب العِلق

الخلاصة: تهدف هذه الدراسة لمعرفة معارف ومواقف وممارسات الأطباء تجاه خلل وظيفة نعوظ القضيب (الانتصاب) في المحافظات الشرقية من المملكة العربية السعودية. فقد استكمل 159 طبيباً ممن حضروا مؤتمراً علمياً حول خلل وظيفة النعوظ، وهم ينتمون إلى القطاعَيْن العام والخاص، استبياناً يتضمَّن 34 مدخلاً، وبشكل شخصي. وقد كان الـحَرَز الوسطي الإجمالي للمعارف والمواقف والممارسات للمجموعة أقل من المعيار المتوقع وهو 60٪. وكانت أَحْراز الأطباء أعلى من أَحْراز الطبيبات. وقد أحرز الاختصاصيون في الأمراض البولية أعلى الدرجات، تلاهم الاختصاصيون بأمراض الذكورة والأطباء النفسانيون. ومما يستدعي الاستغراب أن الأطباء ذوي المؤهلات العالية كانوا أقل أَحْرازاً من الأطباء ذوي المؤهلات المتوسطة بل وأقل من الأطباء الممارسين. وكانت أَحْراز من زادت مدَّة ممارسته على 10 سنوات أفضل ممن قلَّت مدَّة ممارسته عن 10 سنوات. وقد نوقش الدور المحوري لأطباء القلب في تشخيص ومعالجة المرضى بخلل وظيفة النعوظ.

ABSTRACT We aimed to test the knowledge, attitude and practice (KAP) of physicians towards erectile dysfunction in the Eastern province of Saudi Arabia. At a scientific meeting about erectile dysfunction, 159 physicians from both government and private sectors answered a 34-item questionnaire in private. The mean total KAP score for the group was below the expected standard of 60%. Male physicians scored significantly higher than females. Urologists scored the highest, followed by andrologists. Surprisingly, physicians with higher qualifications scored lower than those with intermediate qualifications and even less than general practitioners. Those who had practised for ≥ 10 years scored better than those with < 10 years practice. The role of cardiologists in the diagnosis and management of erectile dysfunction is discussed.

Connaissances, attitudes et pratiques des médecins concernant le dysfonctionnement érectile en Arabie saoudite

RÉSUMÉ Cette étude visait à tester les connaissances, attitudes et pratiques (CAP) des médecins concernant le dysfonctionnement érectile dans la province orientale d'Arabie saoudite. Lors d'une réunion scientifique sur le dysfonctionnement érectile, 159 médecins du secteur gouvernemental et du secteur privé ont répondu en privé à un questionnaire de 34 items. Le score CAP total moyen pour le groupe était en deçà du niveau escompté de 60 %. Les médecins hommes ont obtenu un score significativement plus élevé que les médecins femmes. Les urologues ont eu les scores les plus élevés, suivis par les andrologues. De manière surprenante, les médecins ayant les qualifications les plus élevées ont eu des scores inférieurs à ceux qui avaient des qualifications intermédiaires et même à ceux des généralistes. Les médecins qui pratiquaient depuis 10 ans ou plus ont eu de meilleurs scores que ceux qui pratiquaient depuis moins de 10 ans. Le rôle joué par les cardiologues dans le diagnostic et la prise en charge du dysfonctionnement érectile est examiné.

[1]Department of Internal Medicine; [2]Department of Family and Community Medicine; [3]Department of Urology, College of Medicine, King Faisal University, Dammam, Saudi Arabia.
Received: 06/05/03; accepted: 19/11/03

Introduction

Erectile dysfunction is one of the more commonly under-diagnosed medical disorders in the world [*1*]. It is defined as the persistent inability to maintain or to achieve an erection of sufficient rigidity to have satisfying sexual activity [*2*]. Recent estimates from the National Institutes of Health (NIH) in the United States suggest that about 30 million Americans have partial or complete erectile dysfunction [*1*].

The problem of erectile dysfunction is mainly linked to age, as shown in the Massachusetts Male Aging Study, where 52% of the male study population aged 40–70 years had some degree of erectile dysfunction [*3*]. Surprisingly, only about 1 in 10 men with erectile dysfunction between 18 and 59 years of age seek medical advice about their problem [*4*]. In another study, 44% of 500 patients who were consulting their urologists for reasons other than erectile dysfunction were found to have a history of erectile dysfunction but failed to inform their physicians about their problem. The reason given by 74% of them was embarrassment [*5*].

It is believed that there are 2 major reasons for overlooking erectile dysfunction as a major health disorder. First, the majority of men with erectile dysfunction do not seek medical advice despite the growing awareness of the available treatment options. The main causes for that are: social as well as religious; concerns about embarrassment and shame; indifference; and fears about side-effects of treatment. Secondly, the majority of physicians do not ask enough questions to identify men with erectile dysfunction or encourage them to seek treatment [*6*].

The prevalence of erectile dysfunction in non-insulin dependent Saudi diabetic men from the Mecca region was 81.1% [*7*]. The risk factors for erectile dysfunction were: age, history of long standing diabetes for more than 10 years, and poor metabolic control. In another study including 388 patients with different degrees of erectile dysfunction from Jeddah, Saudi Arabia, the severity of erectile dysfunction was mainly age-related, and physical inactivity, alcohol consumption and drug addiction were the only independent risk factors after adjusting for age. It has also been found that severe erectile dysfunction was a strong predictor of poor quality of life [*8*]. Therefore, physicians in general, and cardiologists in particular, should take the initiative to open the discussion about sexual activity with their male patients for several important reasons. First, erectile dysfunction and coronary artery disease share many risk factors such as diabetes mellitus, hypertension, smoking, dyslipidaemia and ageing. Secondly, it is possible that the same vascular and endothelial changes that take place in the coronary arteries are likely to occur in the cavernosal arteries that supply the penile erectile tissue [*2,3,9*]. The evaluation of erectile function of a male patient may thus open a clinical window to a silent, yet growing coronary, peripheral or cerebrovascular disease and to other undiagnosed medical problems such as hypertension, diabetes mellitus and dyslipidaemia [*10–16*]. One more aspect of the problem of overlooking erectile dysfunction in our opinion is the inappropriate knowledge, attitude and practice (KAP) of physicians towards erectile dysfunction, which may alter their ability to provide their patients with proper advice about the treatment options.

The objective of this study was to assess the KAP of practising physicians towards erectile dysfunction in one region of Saudi Arabia.

Methods

Sample

This was a cross-sectional study carried out in the Eastern province of Saudi Arabia. The estimated sample size was 200 physicians, selected from both the government and private medical sectors in Dammam region (Dammam, Al-Qatif and Al-Khobar). A multistage random sample was used, where physicians were classified into 2 main strata: government and private. Using proportional allocation, a systematic random sample was used to select the required number of physicians from each stratum.

Questionnaire

A questionnaire with 36 questions was designed to collect information on: demographic and professional data of the recruited physicians (8 items), current knowledge (13 items), attitudes towards erectile dysfunction (8 items) and practices when dealing with a patient suffering from erectile dysfunction (7 items).

The questionnaire was designed by the authors and validated by a panel of experts in the field. A pilot study was undertaken on 20 physicians from the university hospital who were excluded from the study population before choosing the sample. Based on the results of the pilot study, the questionnaire was modified. The weighting of each question relating to knowledge, attitude and practice was determined by the research team and experts in epidemiological studies. The total score was 100 marks and the maximum scores for knowledge, attitude and practice questions were 42, 28 and 30 marks respectively.

Data collection and analysis

The targeted physicians were invited to attend a scientific meeting on erectile dysfunction at 2 different locations, one for the private and the other for the government hospital doctors.

The questionnaires were distributed and answered in a 45-minute private session at the beginning of the scientific meeting. The second part of that scientific meeting was a comprehensive lecture about erectile dysfunction including anatomy and pathophysiology, delivered by the principal investigator.

The data were entered into the personal computer using *SPSS*, version 10. Descriptive statistics for all variables were performed after scrutinizing the data. Statistical analysis was made using *t*-test, Mann–Whitney test, analysis of variance and Kruskal–Wallis as appropriate.

Results

Two hundred (200) physicians were invited to attend the 2 scientific meetings. A total of 192 physicians were able to attend (96%) and out of that number, 159 answered the questionnaire, giving a response rate of 82.8%. The number of male physicians was much higher than female physicians: 151 (95.6%) and 7 (4.4%) respectively. One physician failed to mention his/her sex.

The mean and standard deviation (SD) overall KAP score for all the respondents was 55.6 (14.9) (maximum 100), the knowledge score was 19.0 (8.2) (maximum 42), the attitude score was 19.0 (4.5) (maximum 28) and the practice score was 17.3 (5.3) (maximum 30).

Table 1 shows the mean total KAP score by sex. The mean overall KAP score for females was significantly lower than that of male physicians ($P < 0.001$). This was reflected in significantly lower mean knowledge and practice scores for females ($P = 0.021$ and $P = 0.011$ respectively). The

Table 1 **Knowledge, attitude and practice scores for physicians by sex, specialty, qualifications and years of practice**

Variable	No.	Mean (SD)			
		Knowledge (max. 42)	Attitude (max. 28)	Practice (max.30)	Total (max. 100)
Sex					
Male	151	19.4 (8.1)	19.0 (4.5)	17.6 (5.2)	58.2 (14.9)
Female	7	11.4 (5.6)	17.4 (3.4)	12.5 (3.9)	42.9 (9.6)
		P = 0.011	***P*** = 0.353	***P*** = 0.013	***P*** = 0.021
Specialty					
Urologist	14	29.0 (6.2)	19.7 (4.5)	23.6 (2.9)	73.0 (8.9)
Andrologist	11	24.3 (10.6)	21.1 (4.0)	21.6 (3.8)	67.0 (14.9)
Psychiatrist	7	20.0 (7.3)	20.9 (6.6)	19.3 (3.5)	60.1 (14.1)
General surgeon	16	20.7 (8.2)	20.8 (3.4)	16.9 (5.6)	58.9 (15.9)
Cardiologist	10	20.4 (8.9)	18.6 (4.9)	18.3 (6.1)	57.3 (18.1)
Gynaecologist	6	19.7 (9.9)	21.5 (3.6)	13.2 (6.7)	54.4 (19.2)
Other specialty	84	16.9 (6.5)	18.3 (4.2)	16.3 (4.6)	51.8 (11.8)
		P < 0.001	***P*** = 0.087	***P*** < 0.001	***P*** < 0.001
Qualifications					
MD or equivalent	31	14.5 (6.3)	17.1 (4.6)	15.0 (4.3)	47.4 (11.7)
MSc or equivalent	55	21.0 (8.9)	20.1 (3.9)	18.3 (5.2)	59.5 (15.3)
GP with MB BS	66	19.9 (7.7)	19.4 (4.4)	18.1 (5.3)	57.5 (14.2)
		P < 0.001	***P*** = 0.007	***P*** = 0.008	***P*** < 0.001
Years of practice					
< 10	52	17.3 (6.8)	18.3 (4.0)	15.9 (4.6)	51.6 (13.0)
≥ 10	97	20.5 (8.6)	19.5 (4.7)	18.4 (5.3)	58.7 (15.1)
		P = 0.021	***P*** = 0.112	***P*** = 0.005	***P*** = 0.005

GP = general practitioner.
SD = standard deviation.
[a]Number of respondents; responses missing for some categories.

mean attitude score was also lower for females than males but this difference was not statistically significant.

The mean overall KAP score of physicians was significantly different by speciality (Table 1). Urologists scored the highest marks followed by androlgists, psychiatrists, general surgeons, cardiologists, gynaecologists and other specialties including general practitioners ($P < 0.001$). The knowledge score of the urologists was the highest, followed by androlgists, then general surgeons, cardiologists, psychiatrists, gynaecologists, and other specialities ($P < 0.001$). The highest score for attitude was obtained by gynaecologists and the lowest by other specialities, but the difference was not significant ($P = 0.087$). The score for practice was significantly different among different specialities ($P < 0.001$). Urologists scored the highest marks, followed by androlgists, psychia-

trists, cardiologists, general surgeons, other specialities, and the lowest score by gynaecologists.

Table 1 also shows physicians' KAP towards erectile dysfunction in relation to their qualifications. Surprisingly, the physicians with highest qualifications, e.g. medical doctorate or equivalent, scored the lowest marks [mean knowledge score 14.5 (SD 6.3)] compared with physicians with intermediate qualifications, e.g. master's degree or equivalent, (21.0, SD = 8.9) or general practitioners (19.9, SD = 7.7) ($P < 0.001$). There was a similar trend on the attitude and practice sections, with significant differences among the physicians according to level of qualifications ($P = 0.007$ and $P = 0.008$ respectively).

The mean overall KAP score was significantly higher for physicians with 10 or more years practice than those with less than 10 years practice ($P = 0.005$) (Table 1). The difference between the 2 groups was significant for knowledge and practice ($P = 0.021$ and $P = 0.005$ respectively) but not for attitude ($P = 0.112$).

Some examples of responses to individual questions are as follows. Question no. 10 (knowledge question) asked for the proper definition of erectile dysfunction; this was correctly answered by 66.5% of physicians. Question no.12 (attitude question) inquired about the most common etiology of erectile dysfunction; surprisingly, 52.5% of the physicians believe that it is mainly a psychogenic problem. Question no. 23 (practice question) inquired about the actions to be considered in dealing with a patient reporting a new onset of erectile dysfunction; 46.2% believed that such patients should be referred to the urologist, whereas 14.0% did not know the correct answer to this question. Question no. 26 (practice question) dealt with the therapeutic modality of choice for treating the majority of cases of erectile dysfunction, and 83.9% of the physicians were able to give the correct answer.

Discussion

Erectile dysfunction is a major public health problem worldwide, but is commonly under-diagnosed [*1,2,7,13*]. In this study, we aimed to answer the main question: "Do physicians know enough about erectile dysfunction and do they have the right attitude and practice towards it?"

The study results revealed a high response rate, with 159 out of 192 meeting attendees (83%) answering the questionnaire. The mean overall KAP score for all physicians was below 60% of the total, the known accepted standard for the evaluation of both undergraduate and postgraduate medical students. The performance of female physicians was significantly lower than the performance of male physicians, despite the assurance of the highest degree of confidentiality. Social and cultural factors may account for the significant gap in both knowledge and interest of the female physicians in this part of the world.

Approximately 80% of cases of erectile dysfunction are due to an organic cause, especially atherosclerosis of the cavernosal arteries of the penile tissue, and only 20% of the cases are due to psychiatric and psychogenic disorders [*1–3*]. Therefore, the clinical evaluation and treatment of erectile dysfunction should have a multidisciplinary approach. Fifty per cent (50%) of the members of NIH Consensus Development Panel on Impotence held in 1992 were urologists, 14% were psychiatrists and 35% were representatives of other medical specialities [*1*]. This misconception that erectile dysfunction is under the domain of urologists agrees with our results. Urolo-

gists had the highest marks in the total KAP score (73%), followed by andrologists and psychiatrists, as compared with the rest of the specialities who scored lower. Despite the fact that 66.5% of the studied physicians were able to define erectile dysfunction correctly, 52.5% still believed that the etiology of this problem is mainly psychogenic. Furthermore, 46% of the studied physicians preferred to refer patients presenting with new onset erectile dysfunction directly to the urologist, and 60% of them ignored the importance of obtaining a detailed medical history, performing a proper physical examination or requesting the necessary investigations (such as fasting blood sugar, lipid profile, testosterone, prolactin, luteinizing hormone and follicle-stimulating hormone) [*2,9*].

The total KAP score of the study population was strongly affected by the level of qualifications. Unexpectedly, physicians with higher qualifications scored much lower than physicians with intermediate qualifications, and even less than general practitioners. The poor performance of highly qualified physicians may be related to an inappropriate attitude towards erectile dysfunction, whose diagnosis and management was thought to be mainly under the domain of urologists and/or psychiatrists. Physicians with higher qualifications and who are highly specialized may have little interest in updating their general medical knowledge. However, the duration of physicians' practice in years was a positive predictor of better performance. Physicians who had more than 10 years practice scored significantly higher than those with less than 10 years practice.

The increased understanding of the pathogenesis, proper evaluation and accurate diagnosis, and the available treatment options of erectile dysfunction, should stimulate health care planners to find ways of improving public awareness and physicians' up-to-date knowledge about this major medical problem.

Conclusion and recommendations

The role of physicians, especially cardiologists, is pivotal in the process of evaluation and management of erectile dysfunction. In this study of physicians who have a scientific and clinical interest in erectile dysfunction, the overall KAP scores for all physicians were below the expected standard. We recommend that:

- Undergraduate curricula and postgraduate training programmes should be modified to accommodate and emphasize up-to-date knowledge about early detection, evaluation and management of erectile dysfunction.
- The Ministry of Health, through health policy planners, universities and other medical sectors should find the proper approach and plans to improve the general public awareness regarding the importance of early diagnosis and treatment of erectile dysfunction.

Acknowledgements

We are grateful to Dr Emmanuel Larbi, Consultant Internist/Clinical Pharmacology and Professor of the Department of Internal Medicine, King Faisal University, and King Fahd Hospital of the University for his invaluable effort in reviewing this manuscript, and Mr Ramesh Kumar for his secretarial support.

References

1. NIH Consensus Development Panel on Impotence. ***Journal of the American Medical Association***, 1993, 270:83–90.
2. Miller TA. Diagnostic evaluation of erectile dysfunction. ***American family physician***, 2000, 61(1):95–104, 109–10.
3. Feldman HA et al. Impotence and its medical and psychological correlates, results of the Massachusetts Male Aging Study. ***Journal of urology***, 1994, 151:54–61.
4. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. ***Journal of the American Medical Association***, 1999, 281:537–44.
5. Baldwin KC, Ginsberg PC, Harkaway RC. ***Underreporting of erectile dysfunction among men with unrelated urologic conditions.*** Abstract presented at the Annual Meeting of the American Urological Association, April 29–May 4, 2000, Atlanta, Georgia.
6. Levine LA, Kloner RA. Importance of asking questions about erectile dysfunction. ***American journal of cardiology***, 2000, 86:1210–3.
7. El-Sakka AI, Tayeb KA. Erectile dysfunction risk factors in noninsulin dependent diabetic Saudi patients. ***Journal of urology***, 2003, 169(3):1043–7.
8. Abolfotouh MA, Al-Helali NS. Effect of erectile dysfunction on quality of life. ***Eastern Mediterranean health journal***, 2001, 7(3):510–8.
9. DeWire DM. Evaluation and treatment of erectile dysfunction. ***American family physician***, 1996, 53:2101–8.
10. Pritzker MR. ***The penile stress test: a window to the hearts of man.*** Abstract presented at the 72nd Scientific Session of the American Heart Association, November 7–10, 1999, Atlanta, Georgia.
11. Billups K, Friedrich S. ***Assessment of fasting lipid panels and Doppler ultrasound testing in men presenting with erectile dysfunction and no other medical problems.*** Abstract presented at the American Urological Association, April 29–May 4, 2000, Atlanta, Georgia.
12. Cheitlin MD et al. ACC/AHA expert consensus document. Use of sildenafil citrate (Viagra) in patients with cardiovascular disease. ***Journal of the American College of Cardiology***, 1999, 33: 273–82.
13. Jackson G. Erectile dysfunction and cardiovascular disease. ***International journal of clinical practice***, 1999, 53:363–8.
14. Jackson G et al. A systematic approach to erectile dysfunction in the cardiovascular patient: a consensus statement. ***International journal of clinical practice***, 1999, 53:445–51.
15. Jackson G. Sexual intercourse and angina pectoris. ***International rehabilitation medicine***, 1979, 3:35–7.
16. O'Kane PD, Jackson G. Erectile dysfunction: is there silent obstructive coronary artery disease? ***International journal of clinical practice***, 2001, 55:219–20.

Report

SARS: the new challenge to international health and travel medicine

S. Venkatesh[1] and Z.A. Memish[2]

SUMMARY Severe acute respiratory syndrome (SARS), the first severe new infectious disease of this millennium, caused widespread public disruption. By July 2003, 8427 probable SARS cases had been reported from 29 countries with a case fatality rate of 9.6%. The new febrile respiratory illness spread around the world along the routes of international air travel, with outbreaks concentrated in transportation hubs or densely populated areas. The etiologic agent was identified as a novel coronavirus, SARS-CoV. The disease is transmissible person-to-person through direct contact, large droplet contact and indirect contact from fomites and unwashed hands. Saudi Arabia successfully prevented the entry of the disease by imposing travel restrictions, special entry requirements, screening procedures at airports, including temperature checks, and quarantine. Ongoing efforts are aimed at developing case investigation, case management and surveillance protocols for SARS.

Introduction

In the first half of 2003, the global community saw the emergence and impact of severe acute respiratory syndrome (SARS), the first severe and easily transmissible new infectious disease of the new millennium. From Guangdong province of China, the SARS virus spread along international travel routes to 30 countries and became deeply embedded in 6 of them. By 11 July 2003, 8427 probable SARS cases had been reported from 29 countries with 813 deaths [*1*]. There was widespread public panic, and social stability was jeopardized in some of the hardest hit areas. Economists estimated the costs in the Far East alone at US$ 30 billion. The containment of SARS, however, was achieved through the diligent application of centuries' old control measures. The most pressing questions now are whether SARS is seasonal and could return in winter, and whether the SARS virus could hide in some animal or environmental reservoir and resurface when conditions again become favourable for spread to humans.

Development of the SARS pandemic

The first cases of a life-threatening respiratory disease of unknown cause are now known to have appeared in Guangdong province in China in mid-November 2002 [*2*]. But it was only on 11 February 2003, that the World Health Organization (WHO) received the first official report of an outbreak of atypical pneumonia in the prov-

[1]Medical Affairs Division; [2]Infection Prevention and Control Program and Infectious Diseases Division, Department of Medicine, King Abdulaziz Medical City, Riyadh, Saudi Arabia.
Received: 24/08/03; accepted: 25/01/04

ince, said to have affected 305 persons and caused 5 deaths. An infected medical doctor, who had treated patients in his hometown in Guangdong province, carried the SARS infection out of China on 21 February 2003 to Hong Kong. Guests and visitors to the hotel's ninth floor where he stayed seeded outbreaks in the hospital systems of Hong Kong, Viet Nam and Singapore days later [*2*].

Dr Carlo Urbani, a WHO epidemiologist who investigated the Hanoi outbreak, was the first to recognize the condition as a distinct entity. The WHO designated the illness as severe acute respiratory syndrome (SARS) in late February 2003. Considerable progress was achieved in the following months in understanding its epidemiology and clinical features. A collaborative network of scientists from 11 laboratories around the world worked hard and successfully identified the etiologic agent as a new species of coronavirus, now called SARS-CoV [*3–5*]. WHO confirmed the Guangdong cases to be consistent with the definition of SARS after its team was permitted on 2 April 2003 to visit the province.

SARS began spreading along air travel routes, as persons who came in contact with the earliest cases travelled internationally. Hanoi, Hong Kong, Singapore and Toronto were the initial "hot zones" for SARS, with rapid increases in the number of cases, especially in health care workers (who exposed themselves without barrier protection) and their close contacts. Subsequent chains of secondary transmission occurred outside the health care environment.

The new disease showed a clear capacity to spread around the world along the routes of international air travel. The maximum incubation period, estimated at 10 days, allows spread via air travel between any 2 cities in the world. Mounting evidence now points to certain source cases making a special contribution to the rapid spread of SARS infection. An imported hospitalized SARS case infected health care workers and other patients; they infected their close contacts and then the disease moved into the larger community. Epidemiological analyses revealed that the outbreaks of greatest concern were concentrated in transportation hubs or densely populated areas.

Clinical features and management

The Centers for Disease Control and Prevention (CDC) defines a "suspected case" of SARS as a person with onset of fever and lower respiratory tract symptoms (temperature > 38 ºC or 100.4 ºF) within 10 days of either travel to an area with documented transmission of SARS or close contact with a person believed to have SARS [*6,7*]. If a suspected case develops chest radiographic findings of pneumonia, acute respiratory distress syndrome (ARDS) or an unexplained respiratory illness resulting in death, with autopsy findings of ARDS without identifiable cause then he/she is reclassified as a "probable case" of SARS. Laboratory findings further reclassify suspected and probable cases into "laboratory positive", "laboratory negative" or "indeterminate". Household members or persons caring for or sharing personal items with a SARS patient are considered a "close contact" [*6*].

The incubation period for the disease varied from 2 to 10 days with a mean and median of 5 and 6 days respectively [*8–12*]. The classical presentation was of a febrile illness followed in 48–72 hours by dry cough, which progressed rapidly to cause respiratory compromise and hypoxaemia. This necessitated ventilator support in one-

quarter of the patients and led to mortality in 20%–45% of cases. The mortality was highest among elderly patients who had other co-morbid conditions [*9*]. Exposure to a high viral load was another factor suggested to explain the mortality from SARS among previously healthy young health care workers. Interestingly, SARS affected relatively few children and appeared milder in this age group [*13*]. Serological studies have shown that a symptomatic or subclinical infection is uncommon.

None of the therapeutic modalities tried in different parts of the world (broad-spectrum antibiotics, steroids, ribavirin, interferon, and retinovir/lopinavir) have shown conclusive evidence of curative effect on the disease and no standard regimen has been developed [*14*]. Current management of the disease therefore is purely supportive and efforts should be focused on appropriate infection control measures to prevent its spread.

Infection control

The epidemiological features of the disease suggest that it is transmissible from person-to-person through direct contact, large droplet contact, and through indirect contact from fomites and unwashed hands [*8*]. The virus is present in the respiratory secretions of infected patients and has also been found in the urine and faeces, raising the possibility of faecal–oral spread in some situations.

It is critical that patients with suspected SARS be identified promptly to institute the isolation precautions needed to prevent the spread of the disease. Triage screening has been recommended, with a questionnaire to identify SARS symptoms and history of possible exposure. Patients suspected of having SARS need to be immediately separated from other patients, given a mask and evaluated carefully by a health care worker wearing a gown, gloves, and N-95 respirator, ideally in a negative pressure room. One way of avoiding the spread of disease in hospitals is to set up a fever triage clinic outside the hospital emergency room, equipped with all necessary contact precaution supplies. These clinics were developed in Taiwan and Toronto during the peak of the SARS epidemic.

Patients who need to be admitted should be isolated in a negative pressure room in a special isolation ward, with restrictions on visitors and the number of health care workers involved in the patient care. Medical procedures such as bronchoscopy or respiratory nebulization of medications should be avoided. If the number of patients exceeds the hospital's capacity for negative pressure rooms, then the priority should be to keep patients with SARS pneumonia in isolation negative pressure rooms while maintaining other SARS patients in private rooms.

Restricting employees' access to hospitals with SARS patients and identifying the employees who are taking care of SARS patients are critical steps to ensuring that health care workers do not suffer unprotected exposure to SARS patients. Staff should be actively monitored for any signs and symptoms of SARS, i.e. new onset upper respiratory tract illness and high temperature, for early detection of cases. Health care workers with symptoms should be immediately confined to their homes with daily reporting of symptoms to the employee health department or infection control personnel at the hospital. All personnel involved in aerosol-generating procedures on patients with confirmed SARS should be quarantined for 10 days if

adequate precautionary measures were not taken during the procedure.

Intensive education of health care workers and family is mandatory. This includes proper infection control precautions, which should stress the 2 most likely modes of transmission of SARS: contact and respiratory droplets. Health care workers need personal protective equipment appropriate for standard, contact and airborne precautions (i.e. hand hygiene, gown, gloves and N-95 respirator) in addition to eye protection, and use of these should be enforced. Household members should be educated about the mode of spread of the disease and proper precautions when in contact with the infected person by wearing gloves and mask and washing and disinfecting the hands frequently. If they develop symptoms, they should call the public health department and arrange to be examined by a qualified person. This coordination is crucial to preventing the spread of the disease from infected family members to health care workers who may be unaware of the risk of SARS contact.

Suspect or possible cases that do not require admission to hospital should be managed as outpatients. These patients should be given clear instructions about hand hygiene practices with frequent hand washing and wearing a surgical mask to cover the mouth for coughing and sneezing. In addition, they should not share eating utensils, towels and bedding with family members until washed. These patients should remain at home until 10 days after the resolution of fever, if cough and other respiratory symptoms have resolved or improved. When no respiratory symptoms or fever are present, family members need not be restricted from going out and carrying out their usual activities including work or school.

Global action

WHO issued a global alert on 12 March 2003 about cases of severe atypical pneumonia with unknown etiology that appeared to place health workers at high risk. On 15 March 2003, WHO increased the level of the global alert to a rare emergency travel advisory for international travellers, health care professionals, and health authorities to the perceived worldwide threat to health from SARS. The Global Outbreak Alert and Response Network (GOARN) teams from WHO provided support at all the main outbreak sites.

WHO regarded every country with an international airport, or bordering an area having recent local transmission, as being at potential risk of an outbreak. The lack of vaccine and effective treatment forced health authorities to resort to control tools dating back to the earliest days of empirical microbiology: isolation and quarantine. Countries around the world, guided by WHO, adopted aggressive and unprecedented measures including travel restrictions, special entry requirements, screening procedures at airports including temperature checks and quarantine. Other control measures included public information and education to encourage prompt reporting of symptoms, early identification and isolation of patients, vigorous contact tracing, and management of close contacts. These succeeded to a large extent in containing the disease.

Hospitals, schools, and borders were closed, and several governments advised their citizens not to travel to hard-hit areas. Some airlines decided not to carry passenger with a fever of 37.5 °C or above on any of their flights regardless of local government regulations. Hong Kong adapted an electronic tracking system used in criminal investigations for contact tracing and mon-

itoring of compliance with quarantine. Singapore deployed its military forces to assist in contact tracing and to enforce quarantines that halted the normal lives of thousands of people [*7*]. The country also banned visitors at public hospitals.

On being notified by Singapore, through WHO, Germany removed a physician from Singapore (returning from New York after attending a medical conference who had symptoms suggestive of SARS) along with his 2 accompanying family members from their flight at a stopover in Frankfurt, immediately isolated them and placed them under hospital care. This prompt action saved Germany from any further spread.

The WHO announced in late June that Hong Kong and Beijing, the 2 most severely affected areas, had interrupted transmission. Toronto and Taiwan followed shortly afterwards. On 5 July 2003, the WHO decided [*15*], on the basis of country surveillance reports, that all known person-to-person transmission of SARS-CoV had ceased and the global SARS outbreak was contained as it removed Taiwan from its list of areas with recent local transmission of the disease. The human chains of SARS virus transmission appeared to have been broken everywhere. While the containment was a milestone, nations were cautioned against becoming complacent, and to maintain vigilance against the re-emergence of the illness that resulted in over 800 deaths worldwide, mostly in China and Hong Kong, and for which there is no simple treatment. Some experts say it could be seasonal.

Saudi Arabia

Saudi Arabia had a special reason for concern. It has a large expatriate working population of 5.3 million persons coming from various regions of the world. Around 2 million international pilgrims from over 140 countries visit Mecca, the focal point of Islam, for the annual *hajj* pilgrimage; a smaller number visit the country throughout the year for the individual and shorter *umra* pilgrimage. The country also receives a large number of business travellers the year round. Were measures not taken immediately to prevent the entry of SARS, it would spread quickly and wreak havoc.

Acting promptly, the Saudi Ministry of Health, on 10 April 2003, banned the entry of people who had visited any of the 5 SARS-stricken South East Asian countries—China, Hong Kong, Taiwan, Singapore and Viet Nam. The ban was enforced to protect both citizens and expatriates in the country. Saudi Arabian citizens were advised against travelling to SARS affected countries. The Saudi missions in China, Singapore, Hong Kong and the Philippines were instructed to stop issuing *umra* visas indefinitely. Isolation wards were designated in major hospitals in all regions to quarantine all suspected cases of SARS and admit confirmed SARS cases. The Sahari hospital, a new tuberculosis hospital in Riyadh, was the designated hospital for the Central region. Mass media was used extensively to increase awareness of SARS among the population.

Customs, passport and health employees at international airports were ordered to put on masks while dealing with flights arriving from countries with cases of SARS. All arriving passengers were required to fill in a mandatory health declaration form for immigration clearance. At the same time, the health officers at the airport distributed a health alert card with information about SARS. The card advised persons to contact doctors or designated hospitals if they later developed symptoms suggestive of

SARS, such as high fever (> 38 °C, > 100.4 °F), dry cough, shortness of breath or breathing difficulties.

Health personnel checked all incoming passengers for fever. Within weeks, thermal scanners were installed before immigration clearance at the 3 international airports at Riyadh, Jeddah and Dammam in Saudi Arabia to identify persons with raised body temperature. This non-intrusive check did not affect passengers, as it did not delay them. Passengers with temperature below 38 °C were allowed to proceed for immigration clearance as normal. Those with body temperature above 38 °C were taken for a secondary temperature check. Where fever was confirmed, the staff asked the passenger a series of health-related questions recommended by the WHO: if they have other symptoms of SARS, such as cough, breathing difficulty or shortness of breath; if they or their family members have had close contact with any person/s who have been diagnosed with SARS; and if, in the last 10 days, they had travelled to any SARS-affected areas. When SARS was suspected, the passenger was to be referred to the airport health department for follow-up to be kept under observation for 10 days. Saudi Arabian citizens and expatriate workers returning from or transiting through SARS-affected countries within the incubation period of SARS, when cleared by checking for fever and symptoms in the airport, were quarantined in their homes; staff from the Ministry of Health visited them daily to check their temperature until the 10th day.

The measures were further stepped up on 28 April 2003. The Saudi Ministry of Health set up a special committee in Riyadh with branches throughout the country to coordinate efforts to fight the disease. The Ministry barred entry to nationals of SARS-affected countries as a precautionary measure. All international airlines were notified not to transport any passenger coming to the Kingdom from the SARS-hit countries via a third country unless that passenger had stayed at least 10 days in that third country after departing from the last SARS-stricken station.

The Saudi Arabia and 6 other Gulf countries met in Qatar in the first week of May to coordinate their efforts against SARS. The countries agreed to inform each other about SARS cases registered among their citizens or expatriates.

The ban on passengers coming to Saudi Arabia from countries affected by SARS was lifted on 8 July 2003 following positive reports from WHO that no new cases had been reported for the past 20 days, including Canada and China. The Saudi Arabian health authorities, however, continued to monitor the country's entry points in order to prevent the incursion of any potential SARS-carrier. For the subsequent *hajj* (at the end of January/beginning of February 2004), plans were made that all pilgrims coming from the earlier SARS endemic countries would not be allowed to enter the country unless there was evidence on his/her passport that he/she had been outside of the country for a minimum of 10 days immediately prior to arrival in Saudi Arabia.

Perspective

SARS is a particularly serious threat for public health internationally. It also had far-reaching economic and social consequences. Alerted by WHO, all countries with imported cases, with the exception of provinces in China, were able through rapid case detection, immediate isolation, strict infection control, and vigorous contact tracing to successfully prevent further transmission.

The high level of mass media attention focused on SARS and the concerted work of medical professionals, together with WHO's pragmatic leadership role, helped create widespread awareness of the severity of the infectious disease threat, and united the global community. Scientists and clinicians in various countries collaborated and pooled expertise and resources to combat the shared threat. This helped health authorities to identify imported SARS cases quickly, prevent a SARS outbreak, and thus avoid the devastating consequences seen elsewhere. The SARS experience in countries like Viet Nam and Singapore showed that immediate political commitment at the highest level can prove decisive in combating the spread of the disease.

SARS has posed important challenges for medical professionals. There are concerns over the future evolution of outbreaks as the virus belongs to a family notorious for its frequent mutations. Genomic studies have shown a remarkable genetic conservation of the virus; there appears little likelihood of mutation to a benign infection with attenuated symptoms. With neither herd immunity nor attenuation of the virus, the next epidemic when it occurs will have large-scale outbreaks with severe symptoms. Efforts are on to develop case investigation, case management and surveillance protocols for SARS in the post-outbreak environment.

The major challenges of the disease are its poorly understood epidemiology and pathogenesis, its non-specific and common initial symptoms, the limitations in the available diagnostic tests and the vulnerability of hospital staff, the human resource vital for SARS control [*8*]. The requirement for intensive care for SARS cases is a strain on hospital resources. A rapid diagnostic test needs to be developed urgently for diagnosing SARS within days of onset for differentiating it from other atypical pneumonias. Research should be intensified to identify the possible animal reservoir. A global database on SARS has to be developed and an evidence-based approach used for therapeutic approaches for SARS treatment [*2*].

The efforts at combating the threat of SARS have revealed the strengths and weaknesses of national, regional and global capacities to respond to infectious disease threats. Areas for urgent improvement have now been highlighted in the health surveillance systems of various countries. These need to be addressed so that countries are adequately prepared when the world is next confronted with SARS or another infectious disease pandemic.

References

1. ***Cumulative number of reported cases of severe acute respiratory syndrome (SARS).*** Geneva, World Health Organization, 2003 (http://www.who.int/csr/sars/country/2003_07_11/en, accessed 12 January 2005).
2. ***Severe acute respiratory syndrome (SARS): status of the outbreak and lessons for the immediate future***. Geneva, World Health Organization, 2003.
3. Peiris JSM et al. Coronavirus as a possible cause of severe acute respiratory syndrome. ***Lancet***, 2003, 361:1319–25.
4. Ksiazek TG et al. A novel coronavirus associated with severe acute respiratory syndrome. ***New England journal of medicine***, 2003, 348:1953–66.
5. Drosten C et al. Identification of a novel coronavirus in patients with severe

acute respiratory syndrome. ***New England journal of medicine***, 2003, 348: 1967–76.

6. Centers for Disease Control and Prevention. Updated interim surveillance case definition for severe acute respiratory syndrome (SARS)—United States, April 29, 2003. ***Morbidity and mortality weekly report***, 2003, 52(17):391–3.

7. Centers for Disease Control and Prevention. Severe acute respiratory syndrome—Singapore, 2003. ***Morbidity and mortality weekly report***, 2003, 52:405–11.

8. Conly JM, Johnston BL. SARS: a tale of two epidemics. ***Adult infectious disease notes***, 2003, 14(3) (http://www.pulsus.com/Infdis/14_03/conl_ed.htm, accessed 12 January 2005).

9. Peiris JS et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. ***Lancet***, 2003, 361:1767–72.

10. Poutanen SM et al. Identification of severe acute respiratory syndrome in Canada. ***New England journal of medicine***, 2003, 348:1995–2005.

11. Hsu LY et al. Severe acute respiratory syndrome (SARS) in Singapore: clinical features of index patient and initial contacts. ***Emerging infectious diseases***, 2003, 9(6):713–7.

12. Booth CM et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. ***Journal of the American Medical Association***, 2003, 289:2801–9.

13. Hon KLE et al. Clinical presentations and outcome of severe acute respiratory syndrome in children. ***Lancet***, 2003, 361:1701–13.

14. So LK et al. Development of a standard treatment protocol for severe acute respiratory syndrome. ***Lancet***, 2003, 361: 1615–7.

15. ***SARS outbreak contained worldwide. Press release.*** Geneva, World Health Organization, 2003 (http://www.who.int/mediacentre/releases/2003/pr56/en accessed 12 January 2005).

Review

Prevalence of physical inactivity in Saudi Arabia: a brief review

***H.M. Al-Hazzaa*[1]**

SUMMARY Major lifestyle changes in recent years in Saudi Arabia may be leading to physical inactivity and a low level of physical fitness. This paper reviews the current literature about physical inactivity in the Saudi Arabian population and discusses its implications for health. Available data from a small number of studies suggests a high prevalence (43.3%–99.5%) of physical inactivity among Saudi children and adults alike. Furthermore, the proportion of Saudi children and adults who are at risk due to inactivity is much higher than for any other coronary heart disease risk factor. It is recommended that a national policy encouraging activity in daily life be established and more studies are carried out to address physical activity patterns with representative samples of the Saudi Arabian population.

Introduction

Until recent times, the physical demands of daily life and work in Saudi Arabia were sufficient to maintain a lean body mass and an appropriate level of physical fitness among the population. However, during the past 25 years, rapid developments in standards of living in the Kingdom of Saudi Arabia and increased mechanization have touched all aspects of people's lives. As a result, great changes in physical activity and eating habits have occurred in our society and low levels of physical activity and sedentary living are becoming increasingly prevalent among the Saudi population [*1–9*]. Moreover, with massive urbanization and increased reliance on computer and telecommunication technology, further reductions in physical activity are projected for the coming years.

These lifestyle changes that are rapidly occurring in Saudi Arabia (as well as in the rest of the Gulf Cooperation Council countries) have a considerable impact on the health of society. In fact, such lifestyle transformation is thought to be responsible for the epidemic of non-communicable diseases, and their complications, in this part of the world [*1,10–16*]. In addition, the World Health Organization (WHO) has recognized physical inactivity as a major threat to worldwide population health [*17*]. WHO recommended some possible goals and priority actions aimed at promoting active living. Included in these actions is the need to assess the level of physical activity among various segments of the population.

This paper aims to provide a brief overview of the published data about the level of physical activity in the Saudi Arabian population and discuss the implications of physical inactivity on the health of Saudi society.

[1]Exercise Physiology Laboratory, King Saud University, Riyadh, Saudi Arabia.
Received: 06/06/03; accepted: 23/12/03

Prevalence of physical inactivity among the Saudi Arabian population

A MEDLINE search was made for studies published from 1990 onwards, using the words "physical activity and Saudi Arabia" and "physical inactivity and Saudi Arabia". Seven papers were found, 3 of which were relevant and were included in the review. A manual search of the local medical journals was conducted, which revealed 5 additional papers related to physical inactivity in Saudi Arabia.

That little research has been published on this important public health issue shows that research into the epidemiology of physical activity in Saudi Arabia and neighbouring countries is still in its infancy. No nationally representative population study has been made to describe the patterns of physical activity and energy expenditure of the Saudi people. The available published data on the physical activity profile of Saudi people come from studies largely conducted in urbanized areas and few of these have used large and randomized samples [*2–9*]. In addition, in some cases, assessment of physical activity was not the primary focus of the study [*6,8*].

Table 1 presents a summary of physical inactivity prevalence among various segments of the Saudi population [*1–9*]. Seven out of the 8 reported studies used questionnaires [*3–9*], while 1 study involving preadolescent boys utilized continuous heart rate monitoring [*2*]. Across all of the studies shown in Table 1, the total rate of inactivity ranged from 43.3% to 99.5%. Only 2 studies included data for both males and females and their findings indicated that females were much less active than males [*6,9*].

Based on the results of 1 recent study involving adult men living in Riyadh city and using a fairly large and random sample, there appears to be a curvilinear relationship between inactivity prevalence and age [*5*]. As shown in Figure 1, the proportion of inactive men was highest during the middle-age years (30–49 years). In the same study, physical inactivity was shown to be higher among the less educated Saudi males [*5*]. Furthermore, the most important reasons for being physically inactive among Saudi males were time constraints and lack of facilities, as reported by more than 70% of the respondents [*5*]. In another study [*9*], the prevalence of physical inactivity in males increased from early adulthood (16–30 years) to reach its peak at a later age (46–60 years).

Overall, what is striking from the findings of these studies is that the prevalence of inactivity among the Saudi population seems to be higher than rates reported in many industrialized countries of Europe and America [*18–22*]. However, according to the WHO report, 60% of the world population is sedentary or not active enough to gain health benefits [*17*].

As shown also in Table 1, the percentage of Saudi boys who do not take moderate daily physical activity, i.e activity that raises the heart rate to above 139 beats per minute (bpm), for 30 minutes or more was reported to be 57.1% [*1,2*]. Such a level of moderate intensity physical activity has been recommended as a minimum level of physical activity for children and adolescents [*18,23–26*]. In addition, Saudi boys spend, on average, limited time on activities that raise the heart rate above 159 bpm. This level of vigorous activity is considered necessary for optimal cardiovascular health and fitness in children and adolescents [*24–26*]. In addition, according to a recent survey conducted on a sample of adolescent boys in Riyadh city, the rate of inactive adolescents (exercising for 1 day or less per

Table 1 **Physical activity rates in the Saudi Arabian population**

Population	Region [reference]	Assessment method	No. of subjects	Age (years) Mean (SD)	Age (years) Range	Level of physical activity Never active %	Level of physical activity Irregular activity %	Level of physical activity Total inactive[a] %
Children								
Pre-adolescent boys	Riyadh city [***1,2***]	Continuous heart rate monitoring	92	9.6 (1.5)	7–12	–	–	57.1[b]
Adolescents								
Adolescent boys	Riyadh city [***3***]	Questionnaire[c]	894	15.7 (1.8)	12–20	–	–	48.4
Adults								
College men	Riyadh city [***4***]	Questionnaire	362	21.9 (2.1)	17–30	45.8	32.4	78.2
Adult men	Riyadh city [***5***]	Questionnaire	1333	41.1 (9.7)	19–68	53.4	27.5	80.9
Primary care patients	Eastern province [***6***]	Questionnaire	227					
Male				41.5 (11.2)		43.3	–	–
Female				32.5 (11.4)		84.7	–	–
Primary care physicians	Riyadh city [***7***]		98	42.0 (6.5)	26–60	21.5	55.0	76.5
Andrology and urology patients	Jeddah city [***8***]	Questionnaire	388	43.2 (12.5)	20–86	82.0	–	–
Lowlanders and highlanders	Asir province [***9***]	Questionnaire[d]	905					
Male					16–60	27.5	31.9	59.4
Female					16–60	88.6	11.3	99.5

[a]Total represents both never exercise and irregular physical activity.
[b]Percentage of boys not taking exercise sufficient to raise heart rate > 139 bpm for at least 30 minutes per day.
[c]Frequency of physical activity ≤ 1 time/week.
[d]Using Lipid Research Clinic Questionnaire (inactive means those reporting no strenuous exercise for ≥ 3 times per week).
SD = standard deviation.

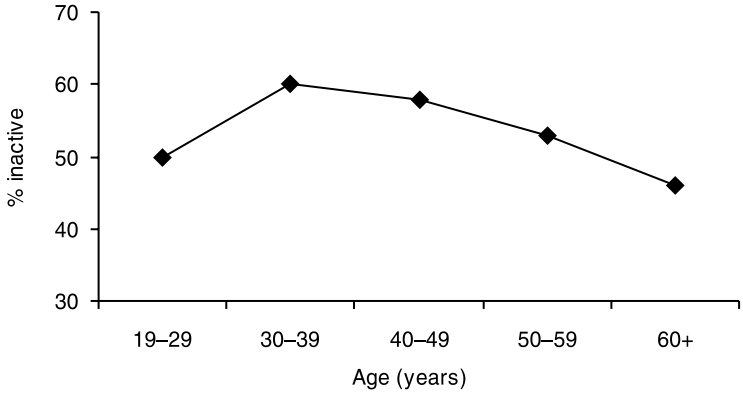


Figure 1 **Prevalence of physical inactivity among Saudi Arabian males by age [*5*]**

week) was approximate 50% [*3*]. The major determinants of physical activity in Saudi children and adolescents appear to be cardiorespiratory fitness, obesity, the quality of the physical education programmes, TV viewing and parental influence [*27*]. From a comparative point of view, it seems that both levels of moderate (heart rate > 139 bpm) and vigorous (> 159 bpm) physical activity of Saudi boys are considerably lower than those levels reported for children from other countries [*19,28,29*].

Health implications of physical inactivity in Saudi Arabian society

It is now well recognized that physical inactivity and increased sedentary habits represent a risk factor for a number of chronic diseases including coronary heart disease (CHD) and obesity [*30,31*]. On the other hand, regular physical activity has been shown to reduce the risk of both cardiovascular disease and all-cause mortality [*18,23,30,32*]. Furthermore, research on physical activity epidemiology indicates that inactivity appears to be far more important risk factor than was previously estimated [*33,34*]. The reason is that there are higher proportions of the population who are inactive and at risk for CHD than those who are at risk for any of the other CHD risk factors [*33,34*]. Figure 2 illustrates this point using data from a recent physical activity study conducted on Saudi males [*5*]. The proportion of Saudi adults who are at risk due to inactivity is much higher than those at risk due to any of the other CHD risk factors, including hypertension [*13*], hypercholesterolaemia [*14*], obesity [*15*] and cigarette smoking [*35*]. Therefore, health promotion strategies aiming at decreasing the proportion of inactive Saudi adults should be a priority public health concern.

The proportion of Saudi boys who are at risk of CHD due to inactivity relative to other risk factors is similar to that of Saudi adults. Figure 3 clearly shows that the percentage of Saudi boys who are physically inactive is twice the rate of those with hyperlipidaemia. Diseases such as CHD and obesity, for which inactivity is a likely risk factor, have their origin in childhood [*36,37*]. Moreover, CHD risk factors were shown to track from childhood to adult-

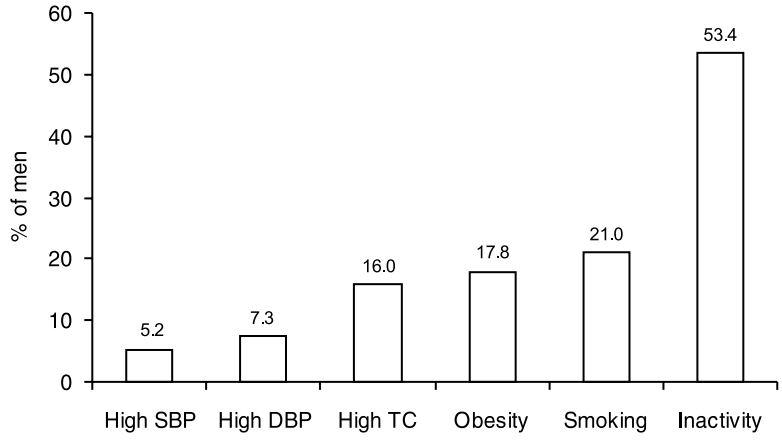


Figure 2 **Risk factors for coronary heart disease among Saudi Arabian males: proportions with physical inactivity [*5*], high systolic (SBP) and high diastolic (DBP) blood pressure [*13*], high total cholesterol level (TC) [*14*], obesity [*15*] and cigarette smoking [*35*]**

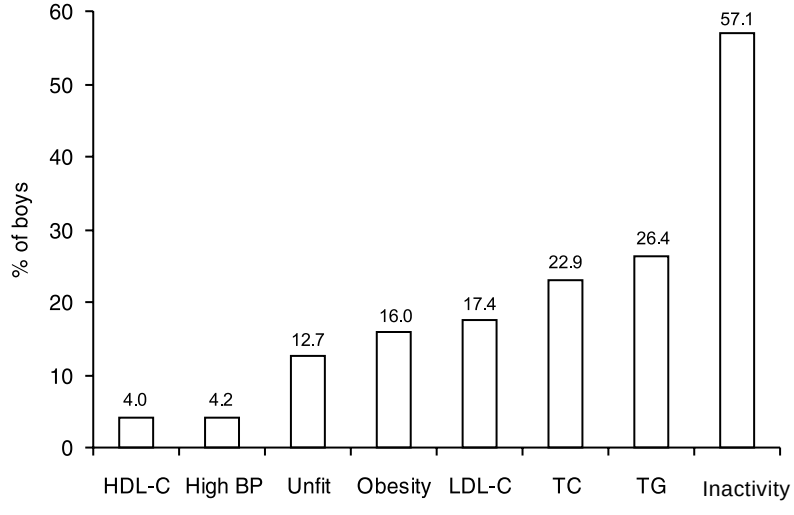


Figure 3 **Risk factors for coronary heart disease among Saudi Arabian boys: proportions with physical inactivity [*1,2*], low high-density lipoprotein cholesterol level (HDL-C), high blood pressure (BP), low cardiorespiratory fitness (unfit), obesity (fat > 25% body mass), high low-density lipoprotein cholesterol level (LDL-C), high total cholesterol level (TC) and high triglycerides level (TG) [*10*]**

hood [*38*]. Thus, prevention of lifestyle-related disease at an early age is an important public health priority, especially considering the fact that children and adolescents account for more than 50% of the Saudi population. Indeed, a recent statement from the American Heart Association's Council on Cardiovascular Disease in the Young has recommended that physicians should incorporate physical activity counselling into medical practice as a way of promoting physical activity among children and adolescents [*39*].

Conclusion and Recommendations

From this brief review of the current level of physical activity in Saudi Arabia, it can be concluded that the prevalence of physical inactivity among Saudi children, adolescents and adults is high. This may be largely the result of the recent dramatic changes in the people's lifestyle. Moreover, the proportion of Saudi children and adults who are at-risk due to inactivity is much higher than for any of the other CHD risk factors. It is recommended, therefore, that a national policy encouraging active living and discouraging inactivity be established. Such an approach has been recommended previously [*12,27*]. Health care providers have an important role in promoting physical activity and fitness among all Saudi people. Finally, national studies addressing physical activity patterns with representative samples of the Saudi population are urgently needed. Such surveillance will provide invaluable information for public health authorities and policy-makers.

References

1. Al-Hazzaa HM. Physical activity, fitness and fatness among Saudi children and adolescents: implications for cardiovascular health. ***Saudi medical journal***, 2002, 23:144–50.
2. Al-Hazzaa HM, Sulaiman MA. Maximal oxygen uptake and daily physical activity in 7-to-12 year-old boys. ***Pediatric exercise science***, 1993, 5:357–66.
3. Al-Rukban MO. Obesity among Saudi male adolescents in Riyadh, Saudi Arabia. ***Saudi medical journal***, 2003, 24:27–33.
4. Al-Hazzaa HM. Physical activity profile of college male subjects. ***King Saud University journal***, 1990, 2:383–96 [in Arabic].
5. Al-Refaee S, Al-Hazzaa HM. Physical activity profile of Saudi males: implications for health. ***Saudi medical journal***, 2001, 22:784–9.
6. Taha AZ, Bella H. Heart disease risk factors: prevalence and knowledge in a primary care setting, Saudi Arabia. ***East Mediterranean health journal***, 1998, 4:293–300.
7. Al-Shahri M, Al-Almaei S. Promotion of physical exercise by primary health care physicians in Riyadh city. ***Saudi medical journal***, 1998, 19:67–9.
8. Al-Helali NS, Abolfotouh MA, Ghanem HM. Pattern of erectile dysfunction in Jeddah city. ***Saudi medical journal***, 2001, 22:34–8.
9. Khalid M. The association between strenuous physical activity and obesity in high and low altitude populations in southern Saudi Arabia. ***International journal of obesity and related metabolic disorders***, 1995, 19:776–80.
10. Al-Hazzaa H et al. Prevalence of coronary artery disease risk factors in Saudi

children. ***Journal of the Saudi Heart Association***, 1993, 5:126–33.

11. Al-Hazzaa H et al. Cardiorespiratory fitness, physical activity patterns, and selected coronary artery disease risk factors in preadolescent boys. ***International journal of sports medicine***, 1994, 15:267–72.

12. Alwan A. Noncommunicable diseases: a major challenge to public health in the Region. ***Eastern Mediterranean health journal***, 1997, 3:6–16.

13. Al-Nozha M, Ali M, Osman A. Arterial hypertension in Saudi Arabia. ***Annals of Saudi medicine***, 1997, 17:170–4.

14. Al-Nuaim A et al. Prevalence of hypercholesterolemia in Saudi Arabia, epidemiological study. ***International journal of cardiology***, 1996, 19:41–9.

15. Al-Nuaim AR et al. High prevalence of overweight and obesity in Saudi Arabia. ***International journal of obesity and related metabolic disorders***, 1996, 20: 547–52.

16. El-Hazmi M et al. Diabetes mellitus and impaired glucose tolerance in Saudi Arabia. ***Annals of Saudi medicine***, 1996, 4:381–5.

17. ***Annual global Move for Health initiative: a concept paper***. Geneva, World Health Organization, 2003 (WHO/NMH/PAH/ 03.1)

18. US Department of Health and Human Services. ***Physical activity and health: a report of the Surgeon General***. Atlanta, Georgia, Centers for Disease Control and Prevention (CDC), National Centers for Chronic Disease Prevention and Health Promotion, 1996 (http:// www.cdc.gov/nccdphp/sgr/sgr.htm, accessed 26 December 2004).

19. US Department of Health and Human Services. ***Healthy people 2010: understanding and improving health***, 2nd ed. Washington, DC, US Government Printing Office, 2000 (http://www. healthypeople.gov/Document/ tableofcontents.htm, accessed 26 December 2004).

20. Crespo CJ et al. Prevalence of physical inactivity and its relation to social class in US adults: results from the Third National Health and Nutrition Examination Survey, 1988–1994. ***Medicine and science in sports and exercise***, 1999, 31:1821–7.

21. Caspersen CJ, Merritt RK. Physical activity trends among 26 states, 1986–1990. ***Medicine and science in sports and exercise***, 1995, 27:713–20.

22. Caspersen C, Merritt R, Stephens T. International physical activity patterns: a methodological perspective. In: Dishman R, ed. ***Advances in exercise adherence***. Champaign, Illinois, Human Kinetics, 1994:73–110.

23. National Institutes of Health. NIH consensus development panel on physical activity and cardiovascular health. ***Journal of the American Medical Association***, 1996, 276:241–6.

24. American College of Sports Medicine. ***ACSM's guidelines for exercise testing and prescription***. Baltimore, Williams and Wilkins, 2000.

25. Cavill N, Biddle S, Sallis J. Health enhancing physical activity for young people: statement of the United Kingdom expert consensus conference. ***Pediatric exercise science***, 2001, 13:12–25.

26. Sallis J, Patrick K. Physical activity guidelines for adolescents: consensus statement. ***Pediatric exercise science***, 1994, 6:302–14.

27. Al-Hazzaa H. Patterns of physical activity among Saudi children, adolescents and adults with special reference to health. In: Musaiger A, Miladi S, eds. ***Nutrition***

and physical activity in the Arab countries of the Near East. Manama, Bahrain Centre for Studies and Research, 2000: 109–27.

28. Armstrong N, Bray S. Physical activity patterns defined by continuous heart rate monitoring. ***Archives of disease in childhood***, 1991, 66:245–7.

29. Sallo M, Silla R. Physical activity with moderate to vigorous intensity in preschool and first grade schoolchildren. ***Pediatric exercise science***, 1997, 9:44–54.

30. Leon A, ed. ***Physical activity and cardiovascular health. A national consensus***. Champaign, Illinois, Human Kinetics, 1997.

31. Bijnen FC, Caspersen CJ, Mostard WL. Physical inactivity as a risk factor for coronary heart disease: a WHO and International Society and Federation of Cardiology position statement. ***Bulletin of the World Health Organization***, 1994, 72(1):1–4.

32. Blair SN et al. Physical fitness and all-cause mortality: a prospective study of healthy men and women. ***Journal of the American Medical Association***, 1989, 262:2395–401.

33. Caspersen CJ. Physical activity epidemiology: concepts, methods and applications to exercise science. ***Exercise and sport sciences reviews***, 1989, 17: 423–73.

34. Powell K. Population attributable risk of physical inactivity. In: Leon A, ed. ***Physical activity and cardiovascular health. A national consensus***. Champaign, Illinois: Human Kinetics, 1997:40–7.

35. Jarallah JS et al. Prevalence and determinants of smoking in three regions of Saudi Arabia. ***Tobacco control***, 1999, 8:53–6.

36. Berenson G et al. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. ***New England journal of medicine***, 1998, 338(23):1650–6.

37. McGill HC Jr et al. Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth. ***Circulation***, 2000, 102:374–9.

38. Webber LS et al. Tracking of serum lipids and lipoproteins from childhood to adulthood. The Bogalusa Heart Study. ***American journal of epidemiology***, 1991, 133: 884–99.

39. Williams C et al. Cardiovascular health in childhood. A statement for health professionals from the committee on atherosclerosis, hypertension, and obesity in the young (AHOY) of the council on cardiovascular disease in the young, American Heart Association. ***Circulation***, 2002, 106:143–60.

Report

Frequency of the *CCR5*-delta 32 chemokine receptor gene mutation in the Lebanese population

W. Karam,[1] R. Jurjus,[2] N. Khoury,[3] H. Khansa,[3] C. Assad,[4] P. Zalloua[5] and A. Jurjus[2]

SUMMARY A direct correlation between HIV infection and mutation in the chemokine receptor (***CCR5***) gene has been established. However, such correlation has never been investigated in Lebanon. We report the frequency of the ***CCR5***-delta 32 mutation in a random sample of 209 healthy, HIV-1 seronegative Lebanese aged 19–68. Overall, 4.8% were heterozygous for the mutation. Homozygosity was absent from our sample. The frequency for the ***CCR5***-delta 32 allele was 2.5%. Distribution of the mutation was unaffected by sex, age, religion or educational level. The frequency in the Lebanese population is consistent with that in the origin of the mutation in northern Europe. This could be attributed to a gene flow into the Middle East from northern Europe.

Introduction

According to a World Health Organization report, 42 million people were living with HIV/AIDS worldwide in 2002; 92% were adults, 46% women, and 8% children under the age of 15. This resulted in 3.1 million deaths in 2002. In North Africa and the Middle East alone, 550 000 people are currently living with HIV/AIDS [*1*]. In Lebanon, the cumulative number of reported HIV/AIDS cases reached 987 by the end of 2002, while the estimated number could be as much as 3000 [*2*].

It has been established that infection by HIV-1 is influenced by a mutation in the chemokine receptor (*CCR5*) gene [*3,4*]. The product of the *CCR5* gene encodes a CC-type seven-transmembrane G-protein-coupled chemokine receptor that binds RANTES, MIP-1alpha and MIP-1beta, and has been shown to mediate entry of M-tropic HIV-1 strains into target cells [*5–7*]. CCR5 also serves as an entry co-receptor for primary human immunodeficiency virus strains that infect monocytes and macrophages [*7–9*]. The *CCR5* gene is located on chromosome 3p21.3. Individuals resistant to repeated exposure to the virus have been shown to be homozygous for a 32 bp deletion in the *CCR5* gene [*5,6*]. Heterozygosity for the mutation is associated with a slower progression to AIDS following HIV-1 infection with a typical delay of 2–4 years [*4,6,10*]. The 32 bp deletion in the gene causes a frame shift at amino acid 185,

[1]Faculty of Public Health, Balamand University, Beirut, Lebanon.
[2]Faculty of Medicine, American University of Beirut, Beirut, Lebanon.
[3]Faculty of Public Health, Lebanese University, Beirut, Lebanon.
[4]Division of Medical Sciences and Public Health, Lebanese Council for Scientific Research, Beirut, Lebanon.
[5]Chronic Care Centre, Hazmieh, Lebanon.
Received: 14/05/03; accepted: 14/09/03

which results in a stop codon and premature truncation within the third extracellular domain. Analysis of the infectability of cells of 3 different genotypes by Liu et al. demonstrated that HIV-1 replicated in wild-type homozygous cells but failed to replicate in homozygous delta-32 cells, whereas replication of the virus in cells heterozygous for the mutation proceeded at an intermediate rate [*5*].

In this study we report the frequency of the *CCR5*-delta 32 mutation in the Lebanese population.

Methods

The participants were selected from Lebanese adults attending the blood bank of a major teaching hospital in Beirut, Lebanon over a 6-month period between July and December 2001. Sample size was 220. Participants were healthy, HIV-1 seronegative, of both sexes, and ages ranged from 19 to 68 years. Palestinian, Syrian, and Armenian donors were not included in the study. None of the blood samples collected tested positive for HIV. In addition, the donated blood was further screened for antibody titres and potential pathogens before being considered suitable for donation. Every third qualified donor was included in the study; people who donated blood at night or on Sundays, however, were excluded. The donors were not inconvenienced in any way. An anonymous questionnaire was completed for each participant. The questionnaire included questions relating to marital status, number of sex partners, practice of safe sex, drug use, history of blood or blood products transfusion, and whether the participant had previously been tested for HIV. Institutional ethical clearance and informed consent of the blood donors were obtained. We followed the Helsinki Declaration (1964, amended in 1975 and 1983) of the World Medical Association.

About 2 mL of donated peripheral venous blood was collected from each participant. The GFX genomic blood DNA purification kit (Amersham Pharmacia Biotech Europe GmbH, Freiburg, Germany) was used to extract genomic DNA from white blood cells following the lysis of red blood cells. DNA was eluted in 100 µL molecular biology grade water and stored at –20 °C. DNA concentrations were determined spectrophotometrically.

Polymerase chain reaction was performed following the methods of Martinson et al. [*11*]. Briefly, 100 ng of genomic DNA was denatured at 94 °C for 10 minutes, following which it was subjected to 30 cycles of denaturation, annealing and extension. The last cycle was followed by an incubation at 72 °C for 10 minutes. The reaction mixture of 50 µL contained, 50 mmol KCl, 10 mmol Tris-HCl, pH 8.3, 800 µmol dNTPs, 100 µg/mL gelatin, 10 pmoles of each of the *CCR5*-specific forward and reverse primers, and 1.5 units of Taq polymerase enzyme (GibcoBRL Life Technologies GmbH, Karlsruhe, Germany). Electrophoresis was performed in Tris-Borate EDTA running buffer and polymerase chain reaction products were detected in 2% agarose containing 1 µg/mL ethidium bromide, and visualized by transillumination with ultraviolet light [*11*].

Cross contamination was avoided by using pipette-tips fitted with aerosol barrier filters, and frequent decontamination of work surfaces with short ultra-violet light irradiation and diluted bleach. Carry-over contamination was prevented by physically separating the extraction, amplification and detection areas.

Both deleted and normal PCR products were extracted from agarose gels using the PCR product clean-up kit from (Roche

Molecular Biochemicals GmbH, Mannheim, Germany) and dideoxytermination cycle sequencing (Applied Biosystems, Foster City, California,) of normal and deleted polymerase chain reaction products was performed to confirm the identities of amplicons and to determine the exact nature and location of the deletion along the *CCR5* gene.

Eleven samples did not yield amplifiable DNA, consequently, the effective number of donors included in the study was 209.

Statistical analysis was performed and individual parameters were tested for significance by analysis of variance.

Results

Overall, 4.8% of the people we studied were heterozygous for the mutation; homozygosity was not found. The frequency for the *CCR5*-delta 32 allele was 2.5%. Distribution of the mutation was unaffected by sex ($P = 0.21$), age ($P = 0.41$), or education level ($P = 0.62$), and was similar among the religious groups that we examined ($P = 0.43$) (Table 1). The sequencing of the polymerase chain reaction products purified from agarose gels confirmed their identity with that of the *CCR5* gene (GenBank X91492). Also, the nature and location of the deletion identified by sequencing of the deleted polymerase chain reaction products were identical to that reported by Liu et al. [*5*].

Table 1 **Distribution of *CCR5* genotype in healthy HIV-1 seronegative Lebanese adults (*n* = 209)**

Variable	No. with *CCR5*/*CCR5*	No. with *CCR5*/*CCR5*-delta 32	*P*-value[a]
Total	199 (95.2%)	10 (4.8%)	
Sex			
M	112	6	0.21
F	87	4	
Age (years)			
Range	19–68	20–60	0.41
≤ 40	125	5	
> 40	32	3	
Unknown	42	2	
Ethnicity			
Christian	119	8	0.43
Muslim	40	2	
Unknown	40	0	
Education			
University	84	5	0.62
High school	63	3	
Technical	31	2	
Other	21	0	

[a] ***All P-values were > 0.05, indicating no significant effect of age, sex, education or ethinicity in this case on the mutation frequency.***

Discussion

A north to south gradient in the delta 32 allele frequency has been reported across Europe, with the highest allele frequencies in the Finnish and other populations living around the Baltic Sea (10%–20% heterozygous; 1% homozygous), and the lowest in Sardinia and Greece, where the frequency drops to almost zero [*11–13*]. The mutation is also seen at very low frequencies in populations from Saudi Arabia, Syrian Arab Republic, Islamic Republic of Iran, Tunisia, Morocco, Cyprus (Greek), India, Pakistan and Asia. It is virtually absent in native populations from sub-Saharan Africa and Oceania [*11–15*]. Based on the demographic distribution, it is believed that the mutation arose in northern Europe in response to selective pressures such an infection epidemic. Our results are consistent with reports in the medical literature: we detected the mutated allele in our study population at

a frequency of 2.5%, which is close to what is being reported in the Syrian Arab Republic (1.4%), Islamic Republic of Iran (2.4%), Tunisia (1%), Morocco (1.5%) and Cyprus (2.8%) [*15*].

The frequency in the Lebanese population is consistent with the location of the origin of the mutation in northern Europe. This could be attributed to a gene flow into the Middle East from northern Europe. In addition, frequencies of the deletion gradually decrease as the distance from Europe becomes greater and it is virtually absent in Asia, the Far East, Oceania and South Africa. We therefore propose that, in addition to the gradient seen in Europe, a gradient outside Europe also exists for the mutation across the Middle East region and into Asia, the Far East and Oceania and across Europe into Africa. This is in accord with a single point of origin for the mutation located in northern Europe, where the highest frequencies for the deletion have been reported.

Acknowledgement

The authors would like to acknowledge the support of the Lebanese Scientific Research Council for funding the study.

References

1. ***AIDS epidemic update***. Geneva, World Health Organization, 2002.
2. ***National AIDS program annual report 2002***. Beirut, Lebanon, Ministry of Public Health, 2002.
3. Huang Y et al. The role of a mutant ***CCR5*** allele in HIV-1 transmission and disease progression. ***Nature medicine***, 1996, 2(11):1240–3.
4. Fowke KR et al. Resistance to HIV-1 infection among persistently seronegative prostitutes in Nairobi, Kenya. ***Lancet***, 1996, 348(9038):1347–51.
5. Liu R et al. Homozygous defect in HIV-1 coreceptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. ***Cell***, 1996, 86(3):367–77.
6. Dean M et al. Genetic restriction of HIV-1 infection and progression to AIDS by a deletion allele of the CKR5 structural gene. Hemophilia growth and development study, Multicenter AIDS cohort study, Multicenter hemophilia cohort study, San Francisco City cohort, ALIVE study. ***Science***, 1996, 274(5290): 1856–62.
7. Dragic T et al. HIV-1 entry into CD4+ cells is mediated by the chemokine receptor CC-CKR-5. ***Nature***, 1996, 381(6584): 667–73.
8. Alkhatib G et al. CC CKR5: a RANTES, MIP-1alpha, MIP-1beta receptor as a fusion cofactor for macrophage-tropic HIV-1. ***Science***, 1996, 272(5270):1955–8.
9. Zhao SF et al. Chemokine receptors and the molecular basis for human immunodeficiency virus type 1 entry into peripheral hematopoietic stem cells and their progeny. ***Journal of infectious diseases***, 1998, 178(6):1623–34.
10. Michael NL et al. The role of viral phenotype and ***CCR-5*** gene defects in HIV-1 transmission and disease progression. ***Nature medicine***, 1997, 3(3):338–40.
11. Martinson JJ et al. Global distribution of the ***CCR5*** gene 32-basepair deletion. ***Nature genetics***, 1997, 16(1):100–3.
12. Libert F et al. The deltaccr5 mutation conferring protection against HIV-1 in Caucasian populations has a single and recent origin in Northeastern Europe. ***Human molecular genetics***, 1998, 7(3): 399–406.

13. Magierowska M et al. Distribution of the ***CCR5*** gene 32 base pair deletion and SDF1-3′ A variant in healthy individuals from different populations. ***Immunogenetics***, 1998, 48(6):417–9.

14. Szalai C et al. High frequency of the ***CCR5*** deletion allele in Gypsies living in Hungary. ***Immunology letters***, 1998, 63(1):57–8.

15. Lu Y et al. Genotype and allele frequency of a 32-base pair deletion mutation in the ***CCR5*** gene in various ethnic groups: absence of mutation among Asians and Pacific Islanders. ***International journal of infectious diseases***, 1999, 3(4):186–91.

Genetics in developing countries

Low- to middle-income countries vary in their capacities in medical genetics. Some may not have the resources to set up appropriate genetic services. Others provide genetic services but need assistance to improve equity of access to these services. The World Health Organization is supporting country capacity building by constructing educational modules and pilot studies to develop national community genetics, including the ethical, legal and societal implications (ELSI).

Source: WHO Fact sheet: genetics and health
Available at: http://www.who.int/genomics/en/E_hgn-_final.pdf

Report

Evaluation of cervical smears at King Hussein Medical Centre, Jordan, over three and a half years

S.R. Malkawi,[1] R.M. Abu Hazeem,[1] B.M. Hajjat[1] and F.K. Hajjiri[1]

SUMMARY Cervical smears taken from women referred for a check-up or with vaginal itching/discharge over a period of 3.5 years were reviewed at the King Hussein Medical Centre, Jordan. All smears were fixed with 96% alcohol, stained with Papanicolaou stain and screened microscopically. Of the smears from 1176 women aged 18–70 years, 4.5% were classified as inadequate, 7.7% were normal and 79.9% showed non-specific inflammation. Abnormal vaginal flora was found in 4.8% of cases, ***Candida albicans*** in 1.2%, ***Trichomonas vaginalis*** in 0.9% and actinomycosis in 1 case. Dysphasic changes were rare: 9 cases (0.8%) were classified as atypical squamous cells of undetermined significance (ASCUS) and 2 cases (0.2%) were low-grade squamous intraepithelial lesion (LSIL). No cases of human papillomavirus infection (HPV) or cervical carcinoma were found.

Introduction

The cervical smear (Papanicolaou, Pap smear) is a routine screening test used for the detection of early cervical abnormalities, namely precancerous dysplastic changes of the uterine cervix [*1*], together with viral, bacterial, and fungal infections of the cervix and vagina. Cervical screening is a relatively simple, low cost and non-invasive method. Regular screening for cervical cancer reduces both the mortality and incidence of cervical carcinoma. Cervical neoplasia typically develops into invasive cancer over a 10-year period [*3–6*] and apparent cases of rapidly progressive cervical cancer are likely to be among women who have escaped screening and proper follow-up. Annual screening reduces the probability of developing invasive carcinoma by over 95% [*2*].

There is also epidemiological and experimental evidence that Pap smears are beneficial in detecting infections that are risk factors associated with cervical cancer, such as human papillomavirus (HPV) [*7*,*8*]. Societies where sexual activity starts at a young age and where multiple partners are common are at a higher risk of exposure to HPV than in conservative societies such as Jordan. HPV is a virus that infects reproducing cells, thus enhancing proliferation of the cell population; this increases the risk of transformation to high-grade lesions or carcinomas [*9–11*]. A cervical smear also detects vaginal infections such as *Candida albicans*, where patients present with physical discomfort, excess vaginal discharge, itching and other complaints.

In the absence of a national cervical screening programme in Jordan, the aim of

[1]Princess Iman Research and Laboratory Sciences Centre, King Hussein Medical Centre, Amman, Jordan.

Received: 21/05/03; accepted: 03/08/03

this study was to evaluate the prevalence of cervical lesions in cervical smears analysed at the Princess Iman Research and Laboratory Sciences Centre, Jordan.

Methods

Over a period of 3.5 years from August 1999 to February 2003, a retrospective review was made of records of 1176 cervical smears analysed at the Princess Iman Research and Laboratory Sciences Centre at King Hussein Medical Centre in Jordan. Patients were those who had been referred from all military hospitals in Jordan to the gynaecology clinic at the Centre with complaints of vaginal itching or discharge, and those who came for a first-time or follow-up cervical smear.

Cervical smears were taken by gynaecologists at the clinics using a speculum and brush; endocervical cells were smeared onto slides with direct fixation by 96% ethanol.

Smears were sent to the laboratory fixed in 96% ethyl alcohol. All smears were stained with Papanicolaou stain and stained slides were screened microscopically by trained staff comprising 2 cytotechnologists and 1 pathologist. The adequacy of smears was determined by the presence of a good number of ecto- and endocervical components, no air dryness and no artefacts. All smears were routinely stained by Papanicolaou stain using a Leica Autostainer programmed for the purpose.

Slides were classified into 5 main categories: specific cervicitis, non-specific cervicitis, normal, cervical dysplasia, cervical carcinoma and inadequate.

Results

Of the cervical smears from 1176 women aged from 18–70 years, 91 (7.7%) were normal, while 53 (4.5%) smears were classified as inadequate (Table 1).

Of the remaining smears, 940 (79.9%) showed non-specific inflammation, i.e. an inflammatory background with no evidence of viral changes or bacteria.

Specific inflammation was found in 81 cases: 56 (4.8%) cases showed abnormal vaginal flora, including *Gardnerella vaginalis*, 14 cases had *Candida albicans* (1.2%), 10 cases (0.9%) had *Trichomonas vaginalis* and 1 case had actinomycosis (0.1%). No cases of HPV infection were found.

Low-grade cervical abnormalities were seen in 11 cases: 9 cases (0.8%) were classified as atypical squamous cells of undetermined significance (ASCUS) and 2 cases (0.2%) were low-grade squamous intraepithelial lesion (LSIL). No malignant cases were reported within this study peri-

Table 1 **Classification of 1176 cervical smears**

Category	No. of smears	%
Inadequate	53	4.5
Normal	91	7.7
Non-specific cervicitis	940	79.9
Specific cervicitis		
Abnormal vaginal flora, including ***Gardnerella vaginalis***	56	4.8
Candida albicans	14	1.2
Trichomonas vaginalis	10	0.9
Actinomycosis	1	0.1
Cervical dysplasia		
ASCUS	9	0.8
LSIL	2	0.2
Cervical carcinoma	0	0
Total	1176	100.0

ASCUS = atypical squamous cells of undetermined significance.
LSIL = low-grade squamous intraepithelial lesions.

od. None of the categories were clustered in any specific age group.

Discussion

The cervical smear is a widely used routine test with many benefits, especially in detecting early cervical changes that can be treated to limit dysplastic processes developing into cancer. Of the cervical smear tests on 1176 women in our hospital, 79.9% showed non-specific inflammation, namely unexplained inflammatory background, thus showing no bacterial or viral features. The remaining cases of inflammation showed 4.8% cases of specific inflammation, 1.2% candida infections, 0.9% trichomonal infections and 1 case of actinomycosis.

The incidence of dysplastic changes in our study (1.0%) was low compared with other studies performed in industrialized countries [*1,13,14*] and we found no cases of cervical carcinoma. This contrasts, for example, with a study in New England in the United States of America (USA) which found that 11.8% of women aged 20–29 years and 8.4% of those over 30 years had infectious processes and 3.5% and 1.3% respectively showed squamous intraepithelial lesions (SIL) [*15*].

No cases of HPV infection were recorded in our hospital during this study period. Statistics from the Centers for Disease Control and Prevention's National Center for HIV, STD, and TB Prevention showed that 5.5 million people in the USA became infected with HPV each year, and infection rates were highest in young women [*12*]. In Jordan, sexual activity typically starts only after marriage where the marital age is over 16 years, and the cultural and religious traditions of our conservative society restrict the likelihood of multiple sexual partners. This may explain why no cases of sexually transmitted HPV, or cervical carcinoma, were found in our study group of women.

References

1. Greenlee RT et al. Cancer statistics, 2000. ***CA: a cancer journal for clinicians***, 2000, 50(1):7–33.
2. McCrory DC et al. ***Evaluation of cervical cytology. Evidence report/technology assessment no.5***. Rockville, Maryland, Agency for Health Care Policy and Research, 1999 (AHCPR publication no.99–E010).
3. Schwartz PE et al. Rapidly progressive cervical cancer: the Connecticut experience. ***American journal of obstetrics and gynecology***, 1996, 175:1105–9.
4. Frame PS, Frame JS. Determinants of cancer screening frequency: the example of screening for cervical cancer. ***Journal of the American Board of Family Practice***, 1998, 11:87–95.
5. Kenter GG et al. The cytological screening history of 469 patients with squamous cell carcinoma of the cervix uteri; does interval carcinoma exist? ***Acta obstetricia et gynecologica scandinavica***, 1996, 75:400–3.
6. IARC Working Group on Evaluation of Cervical Cancer Screening Programmes. Screening for squamous cervical cancer: duration of low risk after negative results of cervical cytology and its implications for screening policies. ***British medical journal***, 1986, 293:659–64.
7. National Institutes of Health Consensus Development Conference statement on cervical cancer. April 1–3, 1996. ***Gynecologic oncology***, 1997, 66:351–61.

8. Schiffman MH, Bauer HM, Hoover RN. Epidemiologic evidence that human papillomavirus infection causes most cervical intraepithelial neoplasia. ***Journal of the National Cancer Institute***, 1993, 85:958–64.

9. Stoler MH. A brief synopsis of the role of human papillomavirus in cervical carcinogenesis. ***American journal of obstetrics and gynecology***, 1996, 175:1091–8.

10. Richart RM et al. Human papillomavirus, IAC Task Force summary. ***Acta cytologica***, 1998, 42:50–8.

11. Stoler MH. Human papillomavirus and cervical neoplasia: a model for carcinogenesis. ***International journal of gynecological pathology***, 2000, 19:16–28.

12. A closer look at HPV infection. In: ***Tracking the hidden epidemics 2000: trends in STDs in the United States***. Atlanta, Georgia, Centers for Disease Control and Prevention, 2000.

13. Johannesson G, Giersson G, Day N. The effect of mass screening in Iceland, 1965–74, on the incidence and mortality of cervical carcinoma. ***International journal of cancer***, 1978, 21:418–25.

14. Hakama M et al. Effect of organized screening on the risk of cervical cancer in the Nordic countries. In: Miller AB et al., eds. ***Cancer screening. UICC project on evaluation of screening for cancer.*** Cambridge, United Kingdom, International Union Against Cancer, 1999:153–62.

15. Mount SL, Papillo JL. A study of 10,296 pediatric and adolescent Papanicoleau smear diagnosis in northern New England. ***Pediatrics***, 1999, 103(3):539–45.

Case report

Glutaric aciduria type 1 in a Kuwaiti infant

H.A. Elsori,[1] K.K. Naguib[2] and M.S. Hammoud[3]

Introduction

Glutaryl-coenzyme A (CoA) dehydrogenase deficiency (MIM 231670) is a recessively inherited neurometabolic disorder associated with encephalopathic crises and severe extra-pyramidal symptoms [*1*]. Macrocephaly, frontotemporal brain atrophy and acute encephalopathic episodes characterize it, with striatal necrosis followed by dystonia [*2*]. However, some patients develop motor disease without overt crisis and other biochemically affected individuals remain asymptomatic [*3–8*].

This is the first report of a Kuwaiti male infant with glutaric aciduria type 1 (GA-1). The clinical picture, the course of the disease, neuro-imaging findings and treatment are discussed.

Case report

F.A. is a Kuwaiti child, aged 3.5 years, who was admitted to hospital at the age of 10 months because of fever, cough and repeated vomiting of 1-week duration. After admission, he developed a series of short left-sided seizures followed a few days later by right-sided seizures. Phenobarbital therapy was started. The seizures continued for 5 days. Shortly after, he developed a left hemiplegia, and he was no longer able to sit or crawl and lost his words.

He is the sixth and youngest child to first-cousin phenotypically normal parents and has 5 healthy sisters. Pregnancy and delivery were normal. Birth weight was 3.6 kg. Macrocephaly was noted at birth, and his head circumference continued to grow parallel to the 98th centile. His development was said to be entirely normal until the age of 10 months. He sat alone at 7.5 months, was crawling and pulling to stand at 8 months and by 10 months he had 1 or 2 words. He was admitted to hospital at the age of 5 months with suspected meningitis excluded by cerebrospinal fluid (CSF) examination.

Examination after the acute episode at 10 months revealed a relatively healthy, mentally normal child, with weight 10 kg and head circumference 51.5 cm. His cranial nerves were normal on examination. He had a dystonia of the left side and left hemiparesis with increased muscle tone and exaggerated tendon reflexes on the same side. There were no abnormal neurological signs in the right limb. Examination of chest, heart, abdomen, skin and genitalia showed that all signs were within normal values. Fundus examination revealed no haemorrhage or other abnormalities. The following

[1]Department of Paediatrics, Adan Hospital, Kuwait.
[2]Medical Genetics Centre, Maternity Hospital, Salmiyah, Kuwait (email: kknaguib@hotmail.com).
[3]Department of Paediatrics, Faculty of Medicine, University of Kuwait, Kuwait.
Received: 25/03/03; accepted: 23/12/03

investigations were normal: plasma sodium, potassium, urea, creatinine, liver enzymes and glucose, haemoglobin, white blood cells and platelets, blood pH (7.36) and serum bicarbonate (21.2 nmol/L), prothrombin time, thrombin time and fibrinogen, and serum ammonia, lactic acid and amino acids. Activated partial thromboplastin time (APTT) was slightly increased at 42 seconds. Plasma ceruloplasmin was slightly elevated. CSF investigations were normal. However, urinary glutaric acid was 67 μmol/mol creatinine (normal < 14) and 3-hydroxy glutaric acid was 85 μmol/mol creatinine (normal range: traces). Glutarylcarnitine levels in urine were elevated and glutaryl-CoA dehydrogenase activity in cultured fibroblasts was low.

Computerized tomography (CT) and magnetic resonance imaging (MRI) scans of the head revealed severe frontotemporal atrophy and bilateral subdural haemorrhage (Figures 1 and 2).

His current therapy consists of carnitine 500 mg 6 hourly, with a low protein diet and carbohydrate drinks to be given during infections and sick days. He is also receiving regular physiotherapy. Phenobarbital was gradually discontinued 5 months after the acute episode. He is generally stable, fit-free, and showing mild improvement with left sided hemiparesis. The child is still alive at the time of writing this report.

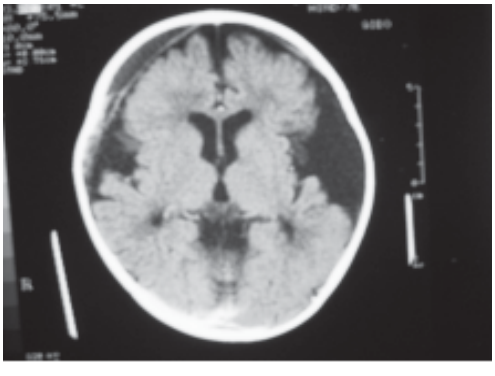


Figure 1 **Computerized tomography scans of the head shows severe fronto-temporal atrophy**

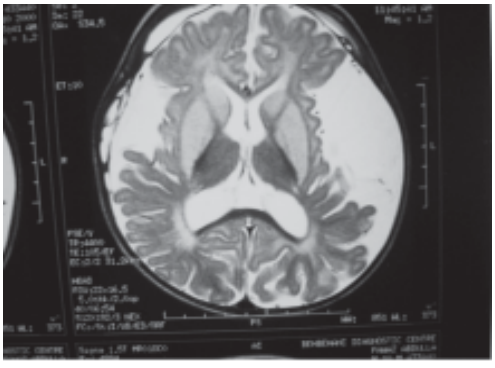


Figure 2 **Magnetic resonance imaging scans of the head shows fronto-temporal atrophy and bilateral subdural haemorrhage**

Discussion

Since the first description of GA-1 by Goodman et al. in 1975 [*9*], several reports have been added to the literature describing one of the more frequent inherited metabolic disorders [*10–12*]. GA-1 is an autosomal recessive disorder caused by deficiency of glutaryl-CoA dehydrogenase, a mitochondrial enzyme involved in the metabolism of lysine, hydroxylysine and tryptophan. The clinical picture typically shows varying degrees of muscular hypotonia, motor delay, dystonia, dysarthria and dyskinesia beginning acutely or gradually in the first few years of life, often in macrocephalic children [*7,13*].

It is difficult to estimate the incidence of GA-1, as the clinical presentation is variable. But the figure of 1:40 000 in Caucasians seems a reasonable approximation [*14–16*]. An incidence as high as 1:30 000 has been suggested [*16,17*]. The disease is particularly frequent in certain communities such as the Amish people in Pennsylvania (1:4000) and Saulteaux/Ojibway Indians in Canada [*1,13–15,18*]. Few patients have been recorded among Arab populations [*19*]. In Kuwait, its incidence has not been estimated so far. However, the frequency of metabolic disorders is common in Kuwait [*20*].

In the present report, the clinical picture, the course of the disease and the biochemical and radiological findings represent the classic presentation of GA-1. Both the onset and the clinical picture of the patient, who had a viral illness followed by encephalopathic crisis, have been considered common features. However, among 100 cases described worldwide, only 4 asymptomatic homozygotes for the disease have been described [*3,11,15*]. This variability in presentation sometimes necessitates a high index of suspicion for diagnosis. Page et al. [*21*] reported a case that presented in the neonatal period with seizures, while Superti-Furga and Hoffmann [*2*] emphasized that presentation may start between the early weeks and the 4th to 5th year of life when intercurrent illnesses, viral infections or gastroenteritis may trigger acute encephalopathy. The biochemical findings of the present case were highly diagnostic. The diagnosis of GA-1 is suggested by the findings of excess 3-hydroxyglutaric acid in the urine and this should be found on a urinary organic acid screen. Blood acylcarnitine profile has also been used as a more sensitive test. However, both tests may show negative results and a strong clinical suspicion is needed [*22*]. Recognition of the biochemical changes before the brain has been injured is essential for a satisfactory outcome. Diagnosis depends on the recognition of relatively non-specific physical findings such as hypotonia, irritability, macrocephaly and urine organic acid quantification [*13*]. The low activity of glutaryl-CoA dehydrogenase in cultured fibroblasts confirms the diagnosis of GA-1. In addition, the radiological finding of fronto-temporal atrophy is typically described in patients with GA-1 [*23*]. It has been suggested that the combination of wide CSF spaces anterior to the temporal lobe and low-density lesions in the basal ganglia are almost diagnostic of this condition [*24*]. In addition, the presence of subdural haemorrhage has been reported [*25*].

Glutaryl-CoA dehydrogenase is a multifunctional enzyme, which exists in the mitochondrial matrix as a homotetramer of 45-kD subunits. The human gene for glutaryl-CoA dehydrogenase has been cloned and mapped to the short arm of chromosome 19p13 [*26*]. More than 63 mutations have been identified so far in GA-1 families, but no one prevalent mutation was detected and little if any relationship between genotype and clinical phenotype could be recognized. The mutations were widely distributed through the gene, with the largest number in exon 10 [*27*]. Recessive inheritance of this disorder is confirmed.

In conclusion, this report is the first of GA-1 from Kuwait. The clinical, biochemical and radiological findings confirm the diagnosis. Our patient is now stable but has only minor improvement, which agrees with most of the reported cases in the literature. We hope that continued therapy with carnitine and low protein diet together with emergency regimen with carbohydrate drinks will at least prevent further deterioration and encephalopathic crisis. Coordinated research is needed to understand the

pathogenesis of the brain pathology, to define the role of dietary therapy and to explore the possibility of neonatal screening. Multi-centre studies are needed to establish the best method for diagnosis and the optimal therapy of this disorder.

References

1. Hoffmann GF et al. Clinical course, early diagnosis, treatment and prevention of disease in glutaryl-CoA dehydrogenase deficiency. ***Neuropediatrics***, 1996, 27:115–23.
2. Superti-Furga A, Hoffman G. Glutaric aciduria type 1 (glutaryl-CoA-dehydrogenase deficiency): advances and unanswered questions. ***European journal of paediatrics***, 1997, 156:821–8.
3. Amir N et al. Glutaric aciduria type 1: enzymatic and neuroradiologic investigations of two kindred. ***Journal of pediatrics***, 1989, 114:983–9.
4. Lipkin PH et al. A case of glutaric acidemia type I: effect of riboflavin and carnitine. ***Journal of pediatrics***, 1988, 112: 62–5.
5. Hoffman GF et al. Early signs and course of disease of glutaryl-CoA dehydrogenase deficiency. ***Journal of inherited metabolic disease***, 1995, 18:173–6.
6. Woelfle J et al. Subdural hemorrhage as an initial sign of glutaric aciduria type 1: a diagnostic pitfall. ***Pediatric radiology***, 1996, 26:779–81.
7. Renner C et al. Clinically asymptomatic glutaric aciduria type I in a 4 5/12-year-old girl with bilateral temporal arachnoid cysts. ***Journal of inherited metabolic disease***, 1997, 20:840–1.
8. Pineda M et al. Glutaric aciduria type I with high residual glutaryl-CoA dehydrogenase activity. ***Developmental medicine and child neurology***, 1998, 40: 840–2.
9. Goodman S et al. Glutaric aciduria: a “new” disorder of amino acid metabolism. ***Biochemical medicine***, 1975, 12: 12–21.
10. Gregersen N et al. Glutaric aciduria: clinical and laboratory findings in two brothers. ***Journal of pediatrics***, 1977, 90: 740–5.
11. Kyllerman M et al. Dystonia and dyskinesia in glutaric aciduria type I: clinical heterogeneity and therapeutic considerations. ***Movement disorders***, 1994, 9: 22–30.
12. Hgberg B, Kyllerman M, Steen G. Dyskinesia and dystonia in neurometabolic disorders. ***Neuropediatrics***, 1979, 10: 305–20.
13. Baric I et al. Diagnosis and management of glutaric aciduria type I. ***Journal of inherited metabolic disease***, 1998, 21: 326–40.
14. Haworth J et al. Phenotypic variabilities in glutaric aciduria type I: report of fourteen cases in five Canadian kindred. ***Journal of pediatrics***, 1991, 118:52–8.
15. Morton DH et al. Glutaric aciduria type I: a common cause of episodic encephalopathy and spastic paralysis in the Amish of Lancaster county, Pennsylvania. ***American journal of medical genetics***, 1991, 41:89–95.
16. Ziadeh R, Naylor E, Ginegold D. ***Identification of two cases of glutaric aciduria type I through routine neonatal screening using liquid secondary ionization tandem mass spectrometry.*** Abstracts of the 6th International Congress on Inborn Errors of Metabolism, Milan, Italy, May 27–31, 1994: WS–2.

17. Kyllerman M, Steen G. Glutaric aciduria. A "common" metabolic disorder? ***Archives francaises de pediatrie***, 1980, 37:279.

18. Goodman S, Freeman F. Organic acidemias due to defects in lysine oxidation: 2-ketoadipic academia and glutaric academia. In: Scriver CR et al., eds. ***The metabolic and molecular bases of inherited disease***, 7th ed. New York, McGraw–Hill, 1995:1451–60.

19. Al-Essa M et al. Glutaric aciduria type 11: observations in seven patients with neonatal- and late-onset disease. ***Journal of perinatology***, 2000, 20(2):120–8.

20. Teebi AS et al. Phenylketonuria in Kuwait and Arab countries. ***European journal of pediatrics***, 1987, 146:59–60.

21. Page A et al. Early clinical manifestation of glutaric aciduria type I and nephritic syndrome during the first months of life. ***Acta paediatrica***, 1997, 86(10):1144–7.

22. Hauser S, Peters H. Glutaric aciduria type I: an undiagnosed cause of encephalopathy and dystonia-dyskinesia syndrome in children. ***Journal of pediatrics and child health***, 1998, 34(3):302–4.

23. Martinez-Lage J et al. Macrocephaly dystonia and bilateral temporal arachnoid cysts: glutaric aciduria type 1. ***Child's nervous system***, 1994, 10:198–203.

24. Brisman J, Ozand P. CT and MRI of the brain in glutaric aciduria type I. A review of 59 published cases and a report of 5 new patients. ***American journal of neuroradiology***, 1995, 16:675–83.

25. Greenberg C et al. Assignment of human glutaryl-CoA-dehydrogenase gene (GCDH) to the short arm of chromosome 19, 19p13.2, by ***in situ*** hybridization and somatic cell hybrid analysis. ***Genomics***, 1994, 21:289–90.

26. Biery BJ et al. Gene structure and mutation of glutaryl-coenzyme A dehydrogenase: impaired association of enzyme subunits that is due to an A421V substitution causes glutaric acidemia type 1 in the Amish. ***American journal of human genetics***, 1996, 59(5):1006–11.

27. Goodman S et al. Glutaryl-coA dehydrogenase mutations in glutaric acidemia (type 1): review and report of thirty novel mutations. ***Human mutation***, 1998, 12: 141–4.

Case report

Maternal death due to severe pulmonary oedema caused by falciparum malaria: a case report

I. Adam[1] and M.I. Elbashir[2]

Introduction

Pregnancy increases susceptibility to falciparum malaria, and the level of disease transmission in an area influences the manifestations of the disease during pregnancy. In areas of low and unstable transmission, malaria during pregnancy is usually symptomatic, unlike the situation in areas of high endemicity, where patients are usually asymptomatic or present with severe anaemia [*1,2*]. There is some degree of immune suppression during pregnancy, with sequestration of infected red blood cells in the placenta through binding to chondroitin sulfate [*3,4*].

Malaria constitutes 40% of the infectious disease burden and approximately 50%–70% of all outpatient visits to hospitals in Sudan [*5*]. In eastern Sudan, malaria is mesoendemic and the predominant malaria species is *Plasmodium falciparum* [*6,7*]. We have previously observed different forms of clinical presentations of severe malaria among pregnant Sudanese women, including cerebral malaria, and that all parities were infected [*8*]. Antimalarial drug resistance is also a growing threat in Sudan [*6*].

We report a young pregnant woman with severe chloroquine-resistant falciparum malaria and pulmonary oedema who died of respiratory failure in spite of adequate treatment with quinine in hospital.

Case report

A 24-year-old primigravida presented to New Halfa Teaching Hospital (eastern Sudan) on 28 December 2002 with amenorrhoea for 34 weeks, fever, headache, productive cough and vomiting for 5 days. Two days before admission she had received 5 injections of chloroquine after confirmation of *P. falciparum* infection without improvement.

The following findings were recorded on presentation: weight 73 kg, temperature 39.2 °C, pulse 95 beats/minute, blood pressure 110/70 mmHg, respiratory rate 30 breaths/minute, haemoglobin 9 g/dL, total white blood cells 8500 cells/µL, blood glucose 110 mg/dL, blood urea 25 mg/dL, serum creatinine 0.9 mg/dL. Her chest was clear clinically, with no crepitations or rhonchi. Examination of the baby showed a fundal height that correlated with the mother's dates, cephalic presentation and audible heartbeat.

The diagnosis of chloroquine-resistant falciparum malaria with or without chest

[1]New Halfa Teaching Hospital, New Halfa, Sudan.
[2]Faculty of Medicine, University of Khartoum, Khartoum, Sudan.
Received: 12/10/03; accepted: 23/12/03

infection was suspected initially. Thick blood films confirmed parasitaemia and the patient was put on quinine hydrochloride infusion in 5% dextrose 600 mg 3 times daily and also given benzyl penicillin 1 million IU intravenously every 4 hours.

After 24 hours the woman's axillary temperature was slightly lower at 38.8 °C, respiratory rate had risen to 50 breaths/minute and the blood film was still positive, but she was cyanosed. Pulmonary oedema was suspected and the diagnosis was confirmed by chest X-ray. The patient was put on intermittent oxygen, furosemide 40 mg/kg twice daily and 15 mg of morphine was given intramuscularly. Quinine and penicillin were continued but there was no improvement.

On the third day the patient's blood films were negative but she was deeply cyanosed, respiratory rate was 54 breaths/minute, temperature was 38.4 °C and she had chest crepitations. She died on the third day from respiratory failure.

Discussion

This report draws the attention to the threat caused by falciparum malaria in pregnant women in areas of low and unstable malaria transmission such as that in eastern Sudan. However, complications of falciparum malaria in adults, especially lung injury and renal failure, can occur after several days of treatment when the parasites have decreased from baseline or even when parasites disappear from the peripheral blood [*9*]. This patient presented with manifestations of malaria after 5 days of treatment with chloroquine, a drug that is showing increasingly high failure rates in Sudan [*6*].

In many Asian and African countries, malaria is reported as one of the main causes of maternal mortality [*10–14*], and in central Sudan it was the leading cause of maternal mortality over the 15 years 1985–99, accounting for 37% of maternal deaths [*12*]. Therefore, the utmost care and prompt early treatment with effective drugs is recommended in pregnant women, due to high susceptibility to severe complications in areas of low and unstable transmission, and the rising rate of multi-drug resistance in all malaria-endemic areas. The World Health Organization recommends quinine as the drug of choice for severe falciparum malaria [*15*]. However, it should not be relied upon as the sole treatment, but attention should be also directed to good monitoring of blood pH and gases (services lacking in our centre) and of venous pressure to avoid over-hydration that may cause or exacerbate pulmonary oedema. Likewise, intensive care units with a ventilator are of paramount importance for patients with pulmonary oedema. As in over-hydration, heart failure, renal failure and pulmonary irritants, falciparum malaria should be remembered as a cause of pulmonary oedema.

References

1. Brabin BJ et al. A study of the consequences of malaria infection in pregnant women and their infants. ***Parassitologia***, 1993, 35(suppl.):9–11.

2. Nosten F et al. Malaria during pregnancy in an area of unstable endemicity. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1991, 85:424–9.

3. Fievet N et al. Immune response to ***Plasmodium falciparum*** antigens in Cameroonian primigravidae: evolution after delivery and during second pregnancy. ***Clinical experimental immunology***, 1997, 107:462–7.

4. Fried M, Duffy PE. Adherence of ***plasmodium falciparum*** to chondroitin sulfate A

in human placenta. ***Science***, 1996, 272: 1502–4.

5. El Gaddal AA. The experience of the Blue Nile Health Project in the control of malaria and other water associated diseases. In: American Association for Advancement of Science. ***Malaria and development in Africa. A cross-sectoral approach***. Washington DC, AAAS, 1991.

6. Adam I et al. In the Sudan: chloroquine resistance is worsening and quinine resistance is emerging. ***Sudan medical journal***, 2001, 39:5–11.

7. El Gadal AA. Malaria in the Sudan. In: Buck AA, ed. ***Proceedings of the conference on malaria in Africa.*** Washington, DC, American Institute of Biological Sciences/USAID, 1986:156–9***.***

8. Adam I et al. Quinine therapy in severe ***Plasmodium falciparum*** malaria during pregnancy in Sudan. ***Eastern Mediterranean health journal***, 2004, 10(1/2):159–66.

9. World Health Organization, Communicable Diseases Cluster. Severe falciparum malaria. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 2000, 94(suppl. 1):S1–90.

10. Wickramasuriya GAW. ***Malaria and ankylostomiasis in the pregnant woman. Their more serious complications and sequelae.*** Oxford, Oxford University Press, 1937.

11. Menon R. Pregnancy and malaria. ***Medical journal of Malaysia***, 1972, 27:115–9.

12. Dafallah SE, El Agib FH, Bushra GO. Maternal mortality in a teaching hospital in Sudan. ***Saudi medical journal***, 2003, 24:369–73.

13. Fawcus S et al. Community based study cause of maternal mortality in rural and urban Zimbabwe. ***Central African journal of medicine***, 1995, 41:105–13.

14. Urassa E et al. Female mortality in the reproductive ages in Dar es Salam, Tanzania. ***East African medical journal***, 1994, 71:226–31***.***

15. World Health Organization, Division of Control of Tropical Diseases. Severe and complicated malaria. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 1990, 84(suppl. 2):1–65.

Letter to the Editor

Sir,

We refer to our paper entitled *Epidemiological study in a new focus of cutaneous leishmaniasis in the Islamic Republic of Iran* published in the *Eastern Mediterranean Health Journal*, 2003, Vol. 9 No. 4, pages 816–826.

In this paper we reported that in Jovein district, Sabzevar county in the north-east of the Islamic Republic of Iran, 7 of 45 (15.6%) *R. opimus* were found to be infected with *Leishmania* and these isolates were identified as *L. major*. These were identified by Professor K.P. Chang (University of Health Science/Chicago Medical School, United Sates of America) using a restriction fragment length polymorphism (RFLP)–PCR technique with *NAGT* gene.

However, subsequent to publication of the above-mentioned paper, characterization was made of one further isolate from an eighth case of *Rhombomys opimus* found to be infected with *Leishmaia* in the same area. This isolate was identified as *L. turanica.*

Thus of a total of 8 of 45 (17.8%) *R. opimus* found to be infected with *Leishmania*, 7 were infected with *L major* and 1 with *L. turanica*.

It has, until recently, been assumed that *Leishmania* parasites circulating in the *R. opimus* population in the Islamic Republic of Iran are *L. major*. This finding is the first report of the isolation and characterization of *L. turanica* from *R. opimus* from an area where there are many active colonies of the great gerbils. It is most probable that this is a continuation of the distribution of *L. turanica* in Turkmenistan which has now extended to the Islamic Republic of Iran.

M.R. Yaghoobi-Ershadi, A.A. Akhavan, M.R. Abai, B. Ebrahimi
School of Public Health and Institute of Public Health Research
Tehran University of Medical Sciences,
Tehran, Islamic Republic of Iran

A.R. Zahraei-Ramazani
Isfahan Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

R. Vafaei-Nezhad
Department of Public Health
Sabzevar University of Medical Sciences
Sabzevar, Islamic Republic of Iran

A.A. Hanafi-Bojd
Bandar Abbas Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

R. Jafari
Yazd Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

Letter to the Editor

Sir,

We refer to our paper entitled *Epidemiological study in a new focus of cutaneous leishmaniasis in the Islamic Republic of Iran* published in the *Eastern Mediterranean Health Journal*, 2003, Vol. 9 No. 4, pages 816–826.

In this paper we reported that in Jovein district, Sabzevar county in the north-east of the Islamic Republic of Iran, 7 of 45 (15.6%) *R. opimus* were found to be infected with *Leishmania* and these isolates were identified as *L. major*. These were identified by Professor K.P. Chang (University of Health Science/Chicago Medical School, United Sates of America) using a restriction fragment length polymorphism (RFLP)–PCR technique with *NAGT* gene.

However, subsequent to publication of the above-mentioned paper, characterization was made of one further isolate from an eighth case of *Rhombomys opimus* found to be infected with *Leishmaia* in the same area. This isolate was identified as *L. turanica*.

Thus of a total of 8 of 45 (17.8%) *R. opimus* found to be infected with *Leishmania*, 7 were infected with *L major* and 1 with *L. turanica*.

It has, until recently, been assumed that *Leishmania* parasites circulating in the *R. opimus* population in the Islamic Republic of Iran are *L. major*. This finding is the first report of the isolation and characterization of *L. turanica* from *R. opimus* from an area where there are many active colonies of the great gerbils. It is most probable that this is a continuation of the distribution of *L. turanica* in Turkmenistan which has now extended to the Islamic Republic of Iran.

M.R. Yaghoobi-Ershadi, A.A. Akhavan, M.R. Abai, B. Ebrahimi
School of Public Health and Institute of Public Health Research
Tehran University of Medical Sciences,
Tehran, Islamic Republic of Iran

A.R. Zahraei-Ramazani
Isfahan Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

R. Vafaei-Nezhad
Department of Public Health
Sabzevar University of Medical Sciences
Sabzevar, Islamic Republic of Iran

A.A. Hanafi-Bojd
Bandar Abbas Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

R. Jafari
Yazd Training and Health Research Centre
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

Guidelines for authors

1. Papers submitted for publication must not have been published or accepted for publication elsewhere. The Eastern Mediterranean Regional Office reserves all rights of reproduction and republication of material that appears in the *Eastern Mediterranean health journal* (EMHJ).

2. Original papers written in Arabic, English or French may be sent for consideration to the Editor-in-chief, *Eastern Mediterranean health journal*, WHO Regional Office for the Eastern Mediterranean, PO Box 7608, Nasr City (11371), Cairo, Egypt. Papers can also be submitted by email to EMHJ@emro.who.int. Papers will be abstracted in all three languages.

3. The subject of the paper should pertain to public health or some other related technical and scientific subject within the field of interest of the World Health Organization, with special reference to the Eastern Mediterranean Region.

4. Three copies of each manuscript should be provided. The text, together with the accompanying tables and figures, should not exceed 15 double-spaced typewritten or printed A4 pages (4500 words) and should be printed on one side only. When the manuscript is accepted or conditionally accepted, the author will be requested to submit a 3.5 inch computer diskette containing the text, tables, graphs and illustrations. For English and French papers, please provide the text, upon the editor's request, in both wordprocessed format (we prefer Microsoft Word for the PC but can translate most other formats) and also saved as a text/ASCII file. Papers submitted in Arabic should follow the same guidelines as papers written in English or French. If the paper is a translation of all or part of another unpublished work, a copy in the original language should be submitted too. Where possible, graphs should be provided in Harvard Graphics under Windows or Excel, and the illustrations and photographs should be provided in EPS or TIFF format. However, it is necessary to provide three sets of original photographs and figures with the background data. If there is any text or lettering on the photographs, an additional clean set should be provided without the text/lettering.

5. All papers received will be peer reviewed, and on the basis of the reviewer's comments, the Editorial Board reserves the right to accept or reject any paper. Papers are accepted on the understanding that they are subject to statistical and editorial revision as deemed necessary, including abridgement of the text and omission of tabular or graphic material.

6. The title of the paper should be as concise as possible, preferably around 10 words, and should be placed on a separate sheet, together with the full name(s) of the author(s), institutional affiliations(s) and highest scientific degrees obtained. The mailing address, as well as any other contact information (email address, fax, telephone) of the corresponding author should be provided. The number of authors should not exceed five. All authors should have made material contribution to either the design, analysis or writing of the study and have approved the final version submitted. Authors may be asked to verify their contribution. Other names may be included in the acknowledgements.

7. To facilitate the translation of abstracts and authors' names, authors whose mother tongue is written in Arabic characters and writing in English or French should supply their full names in Arabic script and provide transliterations.

8. Papers reporting original research findings should follow the IMRAD format: Introduction; Materials (subjects) and methods; Results; Analysis; and Discussion. An abstract of no more than 100 words should be supplied, clearly and briefly stating the objectives, context, results and conclusions.

9. Authors should verify where appropriate that all persons on whom research has been carried out have given their informed consent, and where participants (living or dead) were unable to give such consent, that surrogate consent was obtained.

10. Review articles should contain sections dealing with objectives, sources, methods of selection, compilation and interpretation of data and conclusions.

11. In-text citations of published works should be limited to essential up-to-date references. Apart from review articles, a maximum of 25 references is advisable. They should be numbered separately as they occur in the text with sequential Arabic numerals in parentheses [square brackets]. These references should appear in a numbered list on a separate page at the end of the paper. They should contain the following elements of information as appropriate: name(s) and initial(s) of author(s); title of paper or book in its original language plus translation; complete name of journal plus volume number and page range; name of publisher (commercial or institutional) and place of publication (city and country); and date of publication. Papers with inadequate references or references not arranged according to these principles will be returned to the author for correction. The following are examples of the Journal's preferred style:

Book:
Al Hamza B, Smith A. *The fifth sign of identity*. Cairo, American University Press, 1990.

Journal article:
Jones A et al. One day in Tibet. *Journal of tautology*, 1993, 13(5):23–7.

Document:
Al-Itneen M, ed. *The principles of uncertainty*. Geneva, World Health Organization, 1985 (document WHO/DOC/537).

12. Figures and tables with appropriate captions should each be on a separate sheet, numbered sequentially with arabic numerals and attached to the end of the paper. Each figure and table should be referred to in the text and its placement in the text should be clearly indicated where appropriate. Where appropriate, sources should be given for each figure or table. If any figures, tables or other materials have been copied from other sources, authors have the sole responsibility for securing the necessary permission. In order to avoid layout problems in final production tables and figures should be limited as far as possible. Not more than one table or figure per 1000 words is preferable. Figures derived from data must be accompanied by those data to enable redrawing if necessary.

13. Original papers and diskettes will not be returned except upon request by the principal author.

14. On publication the authors will receive one copy each of the issue in which the article appears and the principal author will receive 50 reprints. Requests for further reprints and pricing information may be obtained from the Editor-in-chief.

المجلة الصحية لشرق المتوسط
دلائل إرشادية للمؤلفين

١. ينبغي أن لا تكون الورقات المقدَّمة للنشر، قد نشرت أو قبلت للنشر في أي مكان آخر. ويحتفظ المكتب الإقليمي لمنظمة الصحة العالمية لشرق المتوسط بجميع حقوق استنساخ أو إعادة نشر المواد التي تنشر في *المجلة الصحية لشرق المتوسط*.

٢. يمكن أن ترسل الورقات الأصلية، المكتوبة بالعربية، أو الإنكليزية، أو الفرنسية، للنظر فيها من قِبَل رئيس تحرير *المجلة الصحية لشرق المتوسط*، بالمكتب الإقليمي لمنظمة الصحة العالمية لشرق المتوسط، ص. ب. (٧٦٠٨)، بمدينة نصر (١١٣٧١)، بالقاهرة، في مصر. ويتم تقديم خلاصات للورقات، باللغات الثلاث.

٣. ينبغي أن يكون موضوع الورقات منتمياً لمجال الصحة العمومية، أو أي ميدان تقني وعلمي آخر، له صلة بالمجالات ذات الأهمية لمنظمة الصحة العالمية، مع الإشارة بشكل خاص إلى إقليم شرق المتوسط.

٤. ينبغي تقديم ثلاث نسخ من كل مخطوطة أو مطبوعة. كما ينبغي أن لا يتعدى النص، مع الجداول، والرسومات المرافقة، ١٥ صفحة مطبوعة على الآلة الكاتبة مع ترك فاصلين بين كل سطر، من القطع A4 (٤٥٠٠ كلمة)، وأن تكون الطباعة على وجه واحد فقط من الصفحة. وعندما يتم إعلان المؤلف بأن المطبوعة التي قدَّمها قد تم قبولها من دون شرط، أو قبولها بشروط، ينبغي أن يقدِّم قرص حاسوبي (٣,٥ بوصة)، يتضمن النص، والجداول، والرسوم البيانية والتوضيحية. وبالنسبة للورقات المقدَّمة باللغتين الإنكليزية والفرنسية، يرجى، بناءً على طلب رئيس التحرير، أن يتم تقديم النص، في كلٍّ من، صيغة معالجة الكلمات (وحبَّذا لو أمكن استخدام برنامج الكلمات اللينة الدقيقة Microsoft Word، بالنسبة للحاسوب الشخصي، غير أننا يمكن أن نترجم غالبية الصيغ الأخرى)، وفي شكل محفوظ كنص/ملف الكود الأمريكي القياسي لتبادل المعلومات ASCII (أسكي). وينبغي اتباع نفس الإرشادات في ما يتعلق بالورقات المقدمة باللغة العربية. وإذا كانت الورقة المقدمة، هي ترجمة كلية أو جزئية لعمل آخر لم ينشر، فينبغي تقديم نسخة من هذا العمل، في لغته الأصلية. وحيثما أمكن، يفضل أن تكون الرسوم البيانية في شكل رسوم هارفارد البيانية، مع استخدام برنامج النوافذ Windows أو إكسل Excel، وتقديم الرسوم التوضيحية والصور الفوتوغرافية في صيغة EPS أو TIFF. كما أنه من الضروري تقديم ثلاث مجموعات من الصور الفوتوغرافية والرسومات الأصلية، مع المعطيات الأساسية. وفي حالة وجود أي نص أو حروف مكتوبة على الصور، فينبغي تقديم نسخة إضافية خالية من أي نص مطبوع أوأي حروف مكتوبة .

٥. يتم مراجعة جميع الورقات المقدَّمة مراجعة دقيقة من قِبَل الزملاء، وفي ضوء هذه المراجعة، تحتفظ هيئة التحرير بحق قبول أو رفض أي ورقة. ومن المتفق عليه أن جميع الورقات التي يتم قبولها، تخضع للمراجعة الإحصائية والتحريرية، بحسب ما يلزم، بما في ذلك اختصار النص، أو حذف بعض الجداول أو الرسوم البيانية.

٦. ينبغي أن يكون عنوان الورقة مختصراً على قدر المستطاع، وحبَّذا لو كان حوالي ١٠ كلمات، وأن يكتب على ورقة منفصلة، مع تحديد اسم المؤلف (أو أسماء المؤلفين)، وعضويتهم في المؤسسات المختلفة، وأعلى الدرجات العلمية التي حصلوا عليها. كذلك، ينبغي ذكر العنوان البريدي، والمعلومات الأخرى اللازمة للاتصال بالمؤلف (بريد إلكتروني، فاكس، هاتف). ويجب أن لا يزيد عدد المؤلفين على خمسة. ولابد أن يكونوا قد ساهموا جميعاً في تصميم البحث أو تحليل نتائجه أو كتابته، وأن يكونوا قد وافقوا، جميعاً على النسخة النهائية المقدَّمة. وقد يطلب من المؤلفين إثبات الإسهام الذي قدَّموه. ويمكن إدراج أسماء أخرى إلى عبارات الشكر التي تكون في مقدِّمة الورقة.

٧. ومن أجل تيسير ترجمة الخلاصات وأسماء المؤلفين، على المؤلفين الذين تكون لغتهم الأم تكتب بحروف عربية، ويكتبون مؤلفاتهم بالإنكليزية أو الفرنسية، أن يزودوا رئيسي التحرير بأسمائهم كاملة، مكتوبة بالحروف العربية، ثم بالحروف اللاتينية.

٨. الورقات التي تمثّل تقارير حول نتائج البحوث الجديدة، ينبغي أن تكتب بالترتيب التالي: المقدمة؛ المواد (المواضيع) والطرق؛ النتائج؛ التحليل؛ والمناقشة. وينبغي أن تشفع هذه الورقات بخلاصة لكل منها، لا تزيد على ١٠٠ كلمة، تبيّن بوضوح، وبإيجاز، الأهداف، والسياق، والنتائج، والاستنتاجات.

٩. ينبغي أن يثبت المؤلفون، بحسب ما يلزم، أن جميع الأشخاص الذين أجري عليهم البحث، قد وافقوا موافقة واعية على ذلك، وفي حالة تعذر الحصول على موافقة المشاركين (أحياء أو أموات)، ينبغي أن يثبت المؤلفون أنه قد تم الحصول على موافقة وكلائهم أو ورثتهم.

١٠. ينبغي أن تتناول مقالات الاستعراض والمراجعة الماضية، النقاط التالية: الأهداف، المصادر، طرق الانتقاء، تجميع المعطيات وتفسيرها والاستنتاجات.

١١. ينبغي أن يقتصر الاستشهاد من أي أعمال منشورة، في النص، على المراجع الحديثة الأساسية. ولا ينصح بزيادة المراجع على ٢٥ مرجعاً على الأكثر، باستثناء المقالات النقدية. ويلزم ترقيم المراجع، كلما ظهرت في النص، وأن يليها أعداد عربية بين أقواس [أقواس مربعة]. كما ينبغي تدوين هذه المراجع في قائمة مرقمة، في صفحة منفصلة، في نهاية الورقة، وأن تتضمن المعلومات التالية، إن أمكن: اسم المؤلف أو أسماء المؤلفين، والحروف الأولى من أسمائهم، وعنوان الورقة أو الكتاب في اللغة الأصلية، إضافة إلى ترجمته؛ واسم المجلة بالكامل، مع رقم المجلد، وعدد الصفحات؛ واسم الناشر (التجاري أو المؤسسي)؛ ومكان النشر (المدينة والبلد)؛ وتاريخ النشر. وسوف يتم إعادة الورقات التي تكون فيها المراجع غير كاملة، أو غير مرتبة بحسب هذه المبادئ، إلى المؤلف، لتصحيحها. وفي ما يلي أمثلة للأسلوب الذي تفضل المجلة الصحية لشرق المتوسط أن يتبع:

كتاب:

Al Hamza B, Smith A. *The fifth sign of identity*. Cairo, American University Press, 1990.

مقالة في مجلة:

Jones A et al. One day in Tibet. *Journal Of tautology*, 1993,13(5): 23-7.

وثيقة:

Al-Itneen M, ed. *The principles of uncertainty*. Geneva, World Health Organization, 1985 (document WHO/DOC/537).

١٢. وفي ما يتعلق بالرسومات والجداول، المشفوعة بالشروح الملائمة، فإنه ينبغي أن ترد كل منها في صفحة منفصلة، ومرقمة على التوالي بالأعداد العربية، وملحقة في نهاية الورقة. كما ينبغي الإشارة إلى كل رسم وكل جدول يشار إليه في النص، وتحديد مكانه بوضوح، بحسب ما يلزم، وحبّذا لو أمكن تحديد مصدر كل رسم وكل جدول. وفي حالة نقل أي رسومات أو جداول من مواد أخرى، فإنه تقع على عاتق المؤلف، أو المؤلفين، المسؤولية الكاملة عن الحصول على الأذون اللازمة. وبُغْيَةَ تجنُّب أي مشكلات في طريقة تنسيق المنتج النهائي، فإنه ينبغي الاقتصار على قدر الإمكان في إدراج الجداول والرسومات. وحبّذا لو أمكن الاقتصار على جدول واحد أو رسم واحد لكل ١٠٠٠ كلمة. علماً بأن الرسومات المتعلقة ببعض المعطيات، ينبغي أن تصاحب هذه المعطيات، وأن يتسنّى إعادة رسمها، إذا تطلّب الأمر.

١٣. لا ترد الورقات والقريصات الأصلية، إلا بناءً على طلب من المؤلف الرئيسي.

١٤. بعد النشر، يحصل المؤلفون على نسخة من العدد الذي ترد فيه المقالة، بينما يحصل المؤلف الرئيسي على ٥٠ نسخة من البحث المنشور. وتقدّم الطلبات للحصول على المزيد من النسخ، أو على معلومات حول الأسعار، إلى رئيس التحرير.

WHO sales and discount policy

Objective

Within the financial obligations of the publishing and distribution process, prices of WHO publications are kept as low as possible in order to maximize their dissemination and reach readers for whom they are intended.

The price and discount policies for WHO/EMRO and WHO/HQ publications are as follows:

Price and discount policy for WHO/EMRO publications

- EMRO publications are priced in US dollars.
- Sales agents receive a 40% discount and 30 days credit. Credit limit is US$ 500.00.
- Bulk orders of individual books, i.e. 1000 copies per title, qualify the agent for a 50% discount instead of a 40% discount; however, payment of total value must be made before dispatch of publications is effected.
- Dispatch charges are calculated at 25% of cover prices.
- Present delivery time average is two weeks from date of receipt of firm order.

Price and discount policy for WHO/HQ publications

- WHO/HQ publications and subscriptions are priced in Swiss francs. Clients in developing countries are eligible for a special tariff which in all cases is 30% less than the Swiss francs regular prices.
- Sales agents receive a 40% discount for book orders and 20% for subscription orders. Credit limit is Swiss francs 1000.00.
- Bulk orders qualify the agents for a special higher discount, provided the dispatch of the whole order is done to the same consignee. In this case, a proforma invoice will be issued by WHO/HQ, and the order will be dispatched only upon receipt of payment. No return of books or periodicals will be accepted.
- Payment of invoices may be made in US dollars at the official rate of exchange at the date of payment.
- Present delivery time average is four weeks from date of receipt of orders.

A WHO/EMRO Publications Price List is available on request.

البلدان أعضاء إقليم منظمة الصحة العالمية لشرق المتوسط

الأردن أفغانستان الإمارات العربية المتحدة باكستان البحرين
تونس الجماهيرية العربية الليبية جمهورية إيران الإسلامية الجمهورية العربية السورية
الجمهورية اليمنية جيبوتي السودان الصومال العراق عُمان
قطر الكويت لبنان مصر المغرب المملكة العربية السعودية

Member States of the World Health Organization
Eastern Mediterranean Region

Afghanistan Bahrain Djibouti Egypt Islamic Republic of Iran
Iraq Jordan Kuwait Lebanon Libyan Arab Jamahiriya Morocco
Oman Pakistan Qatar Saudi Arabia Somalia Sudan
Syrian Arab Republic Tunisia United Arab Emirates Republic of Yemen

Etats Membres de l'Organisation mondiale de la Santé
Région de la Méditerranée orientale

Afghanistan Arabie saoudite Bahreïn Djibouti Egypte
Emirats arabes unis République islamique d'Iran Iraq
Jamahiriya arabe libyenne Jordanie Koweït Liban Maroc
Oman Pakistan Qatar République arabe syrienne Somalie
Soudan Tunisie République du Yémen

Correspondence

Editor-in-chief
WHO Eastern Mediterranean Regional Office

P.O. Box 7608
Nasr City, Cairo 11371
Arab Republic of Egypt

Tel: (202) 670 2535
email: khayat@emro.who.int
emhj@emro.who.int

Fax: (202) 670 2492
(202) 670 2494

Subscription details
Individual copies: US$ 15.00
Annual subscription: US$ 60.00
There is a 50% discount for orders from developing countries
Prices include cost of dispatch
Subscription orders should be sent to the Editor-in-chief

Contents