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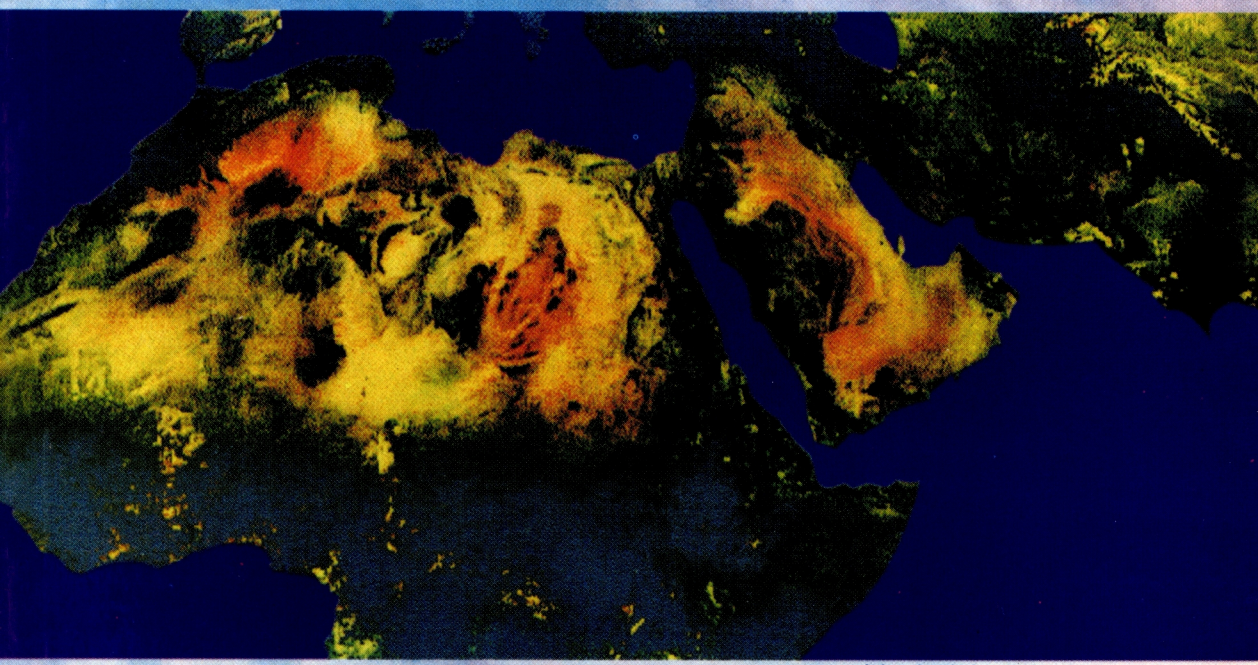

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Regional Office for the Eastern Mediterranean
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المجلة الصحية لشرق المتوسط

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، وخاصةً ما يتعلق منها بإقليم شرق المتوسط. وهي موجَّهة 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

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LA REVUE DE SANTÉ DE LA MÉDITERRANÉE 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.

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Eastern Mediterranean Health Journal

Letter from the Editor

The 60th Session of the World Health Assembly meets from 14 to 23 May 2007 in Geneva. The main function of the Assembly is to determine the policies of the World Health Organization. Among the issues being discussed this year are poliomyelitis eradication, tuberculosis, health systems and emergency-care systems, oral health, gender strategy, and avian and pandemic influenza. The Assembly will consider resolutions on these and other issues agreed at the 120th Session of the WHO Executive Board in January this year.

Infectious diseases remain high on the list of priorities but the considerable burden of noncommunicable diseases is addressed in a resolution passed by the Executive Board for the prevention and control of noncommunicable diseases and the implementation of the global strategy (EB120.R17). As noted in this resolution, mortality due to noncommunicable diseases is expected to rise by 17% by 2015, with serious economic consequences for all. In addition, the 11th General Programme of Work (2006–15) of WHO included the target of reducing death rates from all noncommunicable diseases by 2% annually during the next 10 years. Thus, in the resolution, Member States are urged to strengthen national and political will to prevent and control noncommunicable diseases as part of the commitment to achieving the target set by the 11th Programme of Work and to develop and implement a national multisectoral evidence-based action plan for their prevention and control. The Executive Board also requests the Director-General of WHO to prepare an action plan to be submitted to the Sixty-First Session of the World Health Assembly in 2008 that would set out priorities, actions, a time frame and performance indicators for prevention and control of noncommunicable diseases between 2008 and 2013.

This issue of EMHJ contains a considerable number of papers concerned with noncommunicable diseases. For example, several papers on diabetes and cardiovascular diseases are presented, which are among the most prominent noncommunicable diseases. Other papers included relate to mental health and nutrition, and also to hearing, vision and oral health in children. These papers indicate the extent and diversity of the problems of noncommunicable diseases and the pressing need to tackle them. Research, such as that presented in the papers in this issue, can provide decision-makers with the much-needed data and evidence to identify the extent of health problems, set priorities and monitor the progress of actions developed to address these problems.

رسالة من المحرِّر

من المقرَّر أن تنعقد جمعية الصحة العالمية في جنيف خلال المدة من 14 إلى 23 أيار/مايو 2007. والوظيفة الأساسية لجمعية الصحة العالمية هي تقرير سياسات منظمة الصحة العالمية. ومن القضايا التي تدور حولها المناقشات هذا العام: استئصال شلل الأطفال، ومكافحة السل، والنُظُم الصحية ونُظُم الرعاية في حالات الطوارئ، وصحة الفم، واستراتيجية الجندر، وإنفلونزا الطيور وجائحة الإنفلونزا البشرية. وسوف تنظر الجمعية في اعتماد قرارات حول هذه القضايا وغيرها من القضايا التي اتُّفق عليها في الدورة العشرين بعد المئة للمجلس التنفيذي، التي انعقدت في كانون الثاني/يناير من هذا العام.

ولاتـزال الأمراض الـمُعْدِية في صدر قائمة الأولويات، غير أن العبء الهائل للأمراض غير السارية قد تناولـه قرار صدر عن المجلس التنفيذي حول الوقاية من الأمراض غير السارية ومكافحتها، وحول تنفيذ الاستراتيجية العالمية في هذا الصدد (القرار EB120.R12). ويشير هذا القرار إلى أن الوفيات الناجمة عن الأمراض غير السارية يُتوقَّع أن ترتفع بنسبة 17% بحلول عام 2015، وأن تتسبَّب في عواقب اقتصادية خطيرة للجميع. كما انطوى برنامج العمل العام الحادي عشر (للفترة 2006 – 2015) على هدف خفض معدَّل الوفيات الناجمة عن جميع الأمراض غير السارية بنسبة 2% سنوياً خلال السنوات العشر القادمة. وبذلك، فإن هذا القرار يحثّ الدول الأعضاء على تقوية إرادتها الوطنية والسياسية من أجل اتِّقاء الأمراض السارية ومكافحتها، في إطار التزامها بتحقيق الهدف الـمُدْرَج في برنامج العمل العام الحادي عشر، كما يحثّها على وضع خطة عمل وطنية مُرْتَكِزة على البيِّنات وتشارك فيها عدَّة قطاعات، من أجل الوقاية من هذه الأمراض ومكافحتها.

كما طلب المجلس التنفيذي إلى المدير العام للمنظمة وضع خطة عمل تُعْرَض على الدورة الحادية والستين لجمعية الصحة العالمية في عام 2008، حيث من المقرَّر أن تحدِّد هذه الدورة الأولويات، والأنشطة، والإطار الزمني لها، ومؤشِّرات الأداء المتعلِّقة بالوقاية من الأمراض السارية ومكافحتها في الفترة من عام 2008 إلى عام 2013.

إن هذا العدد من المجلة الصحية يضم بين دفتَيْه عدداً كبيراً من الورقات البحثية حول الأمراض غير السارية. فهو يحتوي على عدَّة ورقات حول مرض السكَّري والأمراض القلبية الوعائية، وهي من أهم الأمراض غير السارية. وثَـمَّة ورقات أخرى في هذا العدد تتصل بالصحة النفسية والتغذية، وبصحة السمع والبصر والفم لدى الأطفال. وتشير هذه الورقات إلى نطاق وتنوُّع مشاكل الأمراض غير السارية، والحاجة الـمُلحَّة إلى التصدِّي لها. فالبحوث، من أمثلة ما يعرضه هذا العدد من ورقات، يمكنها أن تقدِّم لأصحاب القرار المعطيات والبيِّنات التي تمسّ الحاجة إليها لتحديد مدى ونطاق المشاكل الصحية، كما أنها تحدِّد الأولويات، وترصُد التقدُّم الـمُحْرَز نحو التصدِّي لهذه المشاكل.

Quality improvement programme for diabetes care in family practice settings in Dubai

M.S. Khattab,[1] A.M. Swidan,[1] M.N. Farghaly,[1] H.M. Swidan,[1] M.S. Ashtar,[1] E.A. Darwish,[1] A.K. Al Mazrooei[1] and A.A. Mohammad[1]

برامج تحسين جودة رعاية مرضى السكَّري في مرافق رعاية صحة الأسرة في دبيّ

ماجد خطاب، أشرف سويدان، محمد فرغلي، هاني سويدان، ملهم أشتر، ابتهال درويش، آمنة المزروعي، أشرف أحمد محمد

الخلاصة: بدأ تنفيذ برنامج مستمر لتحسين جودة الرعاية المقدَّمة لمرضى السكَّري المسجَّلين، وذلك في 16 مركزاً للرعاية الصحية الأولية في دبيّ. وقد شُكِّلت الفِرَق المعنيَّة بتحسين الجودة، وأُعِدَّت الدلائل الإرشادية السريرية ونُظُم المعلومات، وبُدئ في تنفيذ نظام الممرضة الممارسة لرعاية مرضى السكَّري، وفي تطبيق أسلوب الفِرَق. وقد بيَّنت المراجعات التي أُجريت قبل تنفيذ هذا النظام وبعد تنفيذه، تحسُّناً ملموساً في معدلات تسجيل المؤشرات السريرية الرئيسية وفي حصائلها. فعلى سبيل المثال، ارتفعت من 20.6% إلى 31.7%، نسبة المرضى الذين تقل مستويات الهيموغلوبين المرتبط بالغليكوزيل لديهم عن 7%، كما ارتفعت من 20.8% إلى 33.6% نسبة المرضى الذين تقل نسبة كوليستيرول البروتين الشحمي المنخفض الكثافة لديهم عن 100 مغ/ديسي لتر. في حين انخفض متوسط ضغط الدم الانقباضي في المرضى المسجَّلين من 135.3 مم زئبق إلى 133.2 مم زئبق.

ABSTRACT A continuous quality improvement programme for the care of registered diabetes patients was introduced in 16 government-affiliated primary health care centres in Dubai. Quality improvement teams were formed, clinical guidelines and information systems were developed, diabetes nurse practitioners were introduced and a team approach was mobilized. Audits before and after the introduction of the scheme showed significant improvements in rates of recording key clinical indicators and in their outcomes. For example, the proportion of patients with glycosylated haemoglobin levels < 7% increased from 20.6% to 31.7% and with LDL cholesterol < 100 mg/dL increased from 20.8% to 33.6%. Mean systolic blood pressure of registered patients fell from 135.3 mmHg to 133.2 mmHg.

Programme d'amélioration de la qualité de la prise en charge du diabète en médecine générale à Dubaï

RÉSUMÉ Un programme d'amélioration continue de la qualité de la prise en charge des patients diabétiques enregistrés a été lancé à Dubaï dans 16 centres de soins de santé primaires affiliés au gouvernement. Des équipes pour l'amélioration de la qualité ont été constituées, des directives cliniques élaborées et des systèmes d'information clinique déployés ; des infirmiers praticiens spécialisés en diabétologie ont été mobilisés, de même qu'une véritable stratégie d'équipe. Des audits conduits avant et après la mise en place de ce programme ont mis en évidence une amélioration significative du taux d'enregistrement des indicateurs cliniques clés et de leur évolution. Par exemple, le pourcentage de patients présentant un taux d'hémoglobine glyquée < 7 % a augmenté, passant de 20,6 % à 31,7 %, tandis que pour une LDL cholestérolémie < 100 mg/dL ce pourcentage est passé de 20,8 % à 33,6 %. Chez les patients enregistrés, la pression systolique moyenne est tombée de 135,3 mmHg à 133,2 mmHg.

[1]Primary Health Care Sector, Department of Health and Medical Services, Dubai, United Arab Emirates (Correspondence to M.S. Khattab: msKhattab@dohms.gov.ae).
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Introduction

Dubai is the second largest of the 7 Emirates of the United Arab Emirates (UAE) with almost 700 000 inhabitants. Like other Gulf countries, this Emirate is currently undergoing rapid socioeconomic development with the concomitant lifestyle changes of increasing use of "fast foods" and increasingly sedentary life, leading to health problems such as increasing rates of obesity and type 2 diabetes, which has emerged as an epidemic problem in this region [*1*]. Type 2 diabetes represents a real challenge to the health planners in UAE due to its high prevalence and increased economic cost to society [*2*]. The latter includes its effect on morbidity, employment, productivity, premature mortality and the increased use of health services. At the moment, evidence-based interventions and models are available to continuously improve the quality of diabetes programmes at the community level based on principles of chronic disease management [*3–8*].

Parallel to the economic reforms underway in Dubai, the health sector is also undergoing a process of reform. Since the year 2002, a new leadership for the health system in the Department of Health and Medical Services (DOHMS) in Dubai has been applying its vision to develop the system to international standards and pursue excellence in health care. Dubai is not only moving forward on reform of the health care system but also for international accreditation of this system. To this end, the principles, concepts and tools of total quality improvement have been applied as a core business in the organization of health care in this emirate [*9*]. Great investments have been made in developing the health care system at all levels by applying total quality improvement.

Improving the quality of health care provided to diabetes patients has been identified as a priority area for the continuous quality improvement programme endorsed by the DOHMS. The aims of this study were to conduct a baseline assessment of the quality of diabetes care in primary health care (PHC) settings in Dubai before the implementation of the diabetes quality improvement programme and to measure the impact of the programme on key clinical indicators of diabetes care.

Methods

The present study was carried out in 16 of 18 family practice centres affiliated to the PHC sector of DOHMS in 2004. Two clinics were excluded from the study as they only provide primary medical services to expatriates at Dubai airport and Port Rashid.

Quality performance improvement scheme

Model used

The FOCUS PEDSA quality performance improvement model was used as a framework for the PHC system development. The steps of the 1st phase of this model (FOCUS) depends on Finding an opportunity for improvement, Organizing a quality improvement team, Clarifying the process, Understanding the problem and Selecting an area for improvement. The 2nd phase of the model (PEDSA) stands for Plan, Do, Study and Act [*10*].

Strategic planning

In applying this model a strategic planning workshop was conducted in April 2003 to identify priority areas for improvement in PHC. The participants were representatives from all PHC sections: doctors, nurses, health educators, pharmacists, administrators and customer services. At the workshop, diabetes mellitus fulfilled the criteria

for a priority area for implementing a quality improvement disease management programme due to its high prevalence, high cost, high variability in practice patterns, high risk of clinical outcomes, inefficient delivery system, potential for changes in patients' lifestyle to improve outcomes, the availability of clinical and other expertise to develop the programme and the considerable impact of the disease on the burden of illness in this region [*1,2*].

One doctor from each PHC centre was invited to attend focus group discussions about current problems of diabetes care in PHC settings and barriers to good diabetes care practice. Three focus discussion groups were formed, each of 5–6 participants, led by a facilitator. Each of the 3 groups independently reached a consensus about the identified problems and barriers. The 3 groups then met to establish a unified list, suggested solutions and a quality agenda to overcome the current problems and barriers concerning diabetes care and to continuously improve the PHC diabetes programme based on principles and an evidence-based care model of chronic disease management [*3–8*].

A multidisciplinary quality improvement team of 12 members was formed as a task group at the central level to set priorities for implementing the quality agenda set by the focus groups discussions. Strategic directions for improving quality of care included developing decision support, clinical information systems, mobilizing teamwork and delivery systems. Goals and specific objectives were then set to achieve each of these strategic directions.

Table 1 shows the obstacles to practising good diabetes care as perceived by the doctors in the focus group discussion sessions and the solutions implemented during the quality improvement process.

Diabetes care guidelines

Diabetes care guidelines were formulated based on the most up-to-date clinical evidence in order to develop the decision support system [*3–8*]. Measurements of body weight, body mass index (BMI) and blood pressure were undertaken in accordance with National Health and Nutrition Examination Survey (NHANES) procedures [*11*]. Glycosylated haemoglobin (HbA1c) levels were measured in accordance with USA standard methods [*12*] (normal range 4.2%–6.3%). Serum total cholesterol and triglycerides were measured using a colorimetric assay, serum high-density lipoprotein (HDL) cholesterol was measured using a direct enzymatic method and low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula [*13*]. The goals mentioned in this study were in accordance with those specified by the American Diabetes Association (ADA) guidelines [*8*]: HbA1c < 7.2%, LDL cholesterol < 100 mg/dL, HDL cholesterol > 45 mg/dL, triglycerides < 150 mg/dL, and systolic blood pressure < 130 mmHg and diastolic pressure < 80 mmHg.

Processes in the health centres

The clinical information system of the diabetes programme was developed through establishing a computerized diabetes register in each PHC centre, and developing key clinical indicators of best practice. Medical records were also developed through introducing colour coding of records, problem lists, drug lists, special follow-up cards for diabetes patients and special forms for annual checkups and health education.

Developing the delivery system was undertaken through establishing diabetes quality improvement teams at the grassroots level in each of the 16 family practice centres. Each health centre team was composed

Table 1 **Obstacles to organization of diabetes care in the 1st practice audit and the solutions identified by focus group discussions with doctors**

Obstacles identified	Solutions/agenda implemented
No structural system of care	
Lack of a diabetes register	Establish a diabetes register
Lack of a system for recall of defaulters	Establish a system for recall of defaulters
Poor continuity of care	
Lack of clinical guidelines	Establish clinical guidelines and clinical pathways
Lack of shared care scheme	Establish shared care policy with the hospital
Poor medical records	
–Poor documentation	Improve documentation
–Lack of diabetes follow-up card	Design diabetes follow-up cards
–Lack of problem and drug lists	Introduce problem and drug lists
Poor teamwork and lack of some staff experience	
Unavailability of diabetes specialized nurse	Train cadre of specialized nurses in diabetes
Unavailability of staff job descriptions	Establish staff job descriptions
Absence of multidisciplinary technical staff meetings	Instigate regular multidisciplinary team meetings and staff training and education
Lack of training of medical record staff and administrators	Introduce the concept of nursing diabetes case management
Lack of time	
Short consultation time	Increase consultation time to 15 minutes
Staff shortage	Appoint more staff
Absence of a system for continuous performance improvement	
Absence of agreed clinical indicators and standards of care	Introduce concepts and tools of total quality improvement
Absence of peer review system	Establish clinical indicators and standards
Patients' problems	Conduct regular audit cycles and feedback
–Lack of compliance	Consider patients' ideas, concerns and expectations
–Polypharmacy	Patient and family education
–Multiple problems	Improve continuity of care

of a doctor, a nurse, a health educator, a dietician and an administrator. The purpose of establishing these teams was to develop a team approach to diabetes care based on the established guidelines; to develop the role of nurse practitioners in diabetes; and to train the team on methods and tools of performance measurements. Nurses were trained as case managers and clinical auditors of diabetes care.

Before and after audits

A list of all the patients with their file numbers was obtained from the diabetes register

in each PHC centre. The 1st practice audit and the establishment of comprehensive baseline data about diabetes patients started in June 2003. A retrospective analysis of all files identified from the diabetes register was performed by the clinical auditors for the period between May 2002 to May 2003. Files included in this study were only active diabetes files for diabetes patients who attended the PHC centres for consultation about diabetes at least once during the study period (n = 2548) and the analysis was undertaken manually by the clinical auditors. This analysis included a comprehensive assessment of variables related to socioeconomic status (age, sex, education, occupation, marital status and employment), profile of diabetes (type of diabetes, type of treatment, duration of diabetes, family history of diabetes and family history of coronary heart disease, and several variables related to process and outcome of care.

The 2nd audit started in January 2005. Due to shortage of time and staff, only certain key clinical performance indicators of process and outcome of diabetes care were audited. The 16 PHC centres were asked to review active files for all diabetes patients attending for diabetes-related visits over a 1-month period. The files were reviewed retrospectively over 12 months by the nurse clinical auditors and included data collection for the key clinical indicators, which were: HbA1c, blood pressure, LDL cholesterol, BMI, smoking status and referral for funduscopy examination. The data regarding laboratory investigations were extracted from the computerized laboratory electronic system which was operating by the time of the 2nd audit, while analysis of the remaining variables was still undertaken manually through extracting and analysing data available in medical records.

Analysis

Data analysis was undertaken using *SPSS*, version 12. Appropriate tests of significance were performed; unpaired *t*-test was performed to compare independent sample means and the chi-squared test was performed to compare categorical variables. The data for the continuous variables, HbA1c, blood pressure and LDL cholesterol were converted into categorical data to be benchmarked with other practices regarding best practice standards set by the ADA [*8*].

Results

Prevalence of diabetes

The population of the catchment areas of the 16 family practice centres affiliated to DOHMS, Dubai is 614 210 people. However, the total number of registered files in these centres for people who are utilizing the service is 319 197, representing a 52% utilization rate. The total number of registered diabetes patients in these PHC centres is 4903 patients giving a point prevalence of 1.6% of the total registered population in the 16 PHC centres. The total number of active files included in the current study was 2548, representing 51% of registered diabetes patients.

Demographic characteristics

Table 2 shows the sociodemographic characteristics of the patients with diabetes based on available information from the medical records. The mean (standard deviation) age was 55.3 (11.6) years and 90.3% were ≥ 40 years of age, with nearly equal sex distribution, and the majority (66.0%) were of UAE nationality. Table 2 also shows that 94.3% of the diabetes patients were married, 2.7% were single or divorced and 3.0% widowed.

Table 2 **Sociodemographic characteristics of diabetes patients in primary health care centres in Dubai in the 1st practice audit**

Variable	No. of records	% of records
Age (years)		
Total recorded	2340	91.8[a]
< 40	222	9.5
≥ 40	2118	90.5
Sex		
Total recorded	2548	100.0[a]
Male	1320	51.8
Female	1228	48.2
Nationality		
Total recorded	2548	100.0
UAE	1680	66.0
Non-UAE	868	34.0
Marital status		
Total recorded	1143	44.9[a]
Married	1078	94.3
Single	22	1.9
Divorced	9	0.8
Widowed	34	3.0
Education		
Total recorded	527	20.7[a]
Illiterate	159	30.2
Primary school	109	20.7
Secondary school	148	28.1
University or above	111	21.1
Employment		
Total recorded	1142	44.8[a]
Employed	602	52.7
Unemployed/housewife	540	47.3

[a]*Percentages calculated from total number of eligible records reviewed in 1st audit (*n = *2548 records). UAE = United Arab Emirates.*

Of the patients, 30.2% were illiterate and 47.3% unemployed. It was noted that 79.3% of the records had missing data regarding education level and more than 50% of the records were missing information regarding the employment and marital status of the diabetes patients.

Profile of diabetes

Table 3 shows the profile of diabetes in the patients. The table shows that 90.0% of diabetes patients were diagnosed with type 2 diabetes, 74.5% were on oral hypoglycaemic medication only, 30.7% had had

Table 3 **Characteristics of diabetes patients recorded in primary health care centres in Dubai in the 1st practice audit**

Characteristic	No. of records	% of records
Type of diabetes		
Total recorded	2408	94.5[a]
Type 1	241	10.0
Type 2	2167	90.0
Type of treatment		
Total recorded	2396	94.0[a]
Oral drugs	1785	74.5
Insulin	278	11.6
Combination	161	6.7
Diet only	172	7.2
Duration of diabetes (years)		
Total recorded	1562	61.3[a]
< 5	610	39.1
5–10	472	30.2
> 10	480	30.7
Body mass index (kg/m²)		
Total recorded	1405	58.0[a]
< 25	373	25.3
25–< 30	556	39.6
≥ 30	547	33.9
Family history of diabetes		
Total recorded	830	32.6[a]
Positive	513	61.8
Negative	317	38.2
Family history of coronary heart disease		
Total recorded	548	21.5[a]
Positive	144	26.3
Negative	404	73.7

[a]*Percentages calculated from total number of eligible records reviewed in 1st audit (*n = *2548 records).*

diabetes for > 10 years, 61.8% had a family history of diabetes and 26.3% had a positive history of ischaemic heart disease. Three-quarters of the patients with diabetes were overweight or obese (BMI ≥ 25 kg/m^2). Missing data were mainly in recording the history of coronary heart disease (67.4%) and family history of diabetes (78.5%).

Performance indicators

Table 4 compares the key performance clinical indicators of process and outcome of diabetes care in the 16 PHC centres between the 1st and 2nd audit cycles. There were significant improvements in the process of care for the key clinical performance indicators studied: HbA1c, blood pressure

Table 4 **Comparison of some key performance indicators of process and outcome of care between 2 audit cycles for diabetes patients attending 16 primary health care centres in Dubai**

Clinical indicator	1st audit			2nd audit			95% CI[c]
	No. of records	%	Mean value (SD)	No. of records	%	Mean value (SD)	
HbA1c level			8.7% (2.1)			8.1% (2.5)	0.4–0.8***
Total performed***	1589	62.4[a]		1039	84.2[b]		
< 7%	328	20.6		329	31.7		
7.0%–8.4%***	492	31.0		331	31.9		
8.5%–9.5%	269	16.9		158	15.2		
> 9.5%	500	31.5		221	21.3		
Systolic blood pressure			135.3 mmHg (20.5)			133.2 mmHg (20.0)	0.6–3.6*
Total performed***	2183	85.7[a]		1165	94.4[b]		
< 130 mmHg***	891	40.8		466	40.9		
130–159 mmHg	1020	46.7		560	48.0		
≥ 160 mmHg	272	12.9		128	10.5		
LDL-cholesterol			129.2 mg/dL (38.3)			115.4 mg/dL (36.8)	10.8–16.8***
Total performed***	1655	65.0[a]		966	78.3[b]		
< 100 mg/dL	344	20.8		325	33.6		
100–130 mg/dL***	575	34.7		316	32.7		
> 130 mg/dL	736	44.5		298	30.8		
Body mass index				(*n* = 622)			
Total recorded***	1405	55.1[a]		621	99.8[b]		
Referral for funduscopy				(*n* = 622)			
Total performed***	738	29.0[a]		349	53.0[b]		
Smoking status				(*n* = 748)			
Total recorded***	629	24.7[a]		568	76.0[b]		

**Statistically significant difference between 1st and 2nd audit at* P < *0.05.*
****Statistically significant difference between 1st and 2nd audit at* P < *0.001.*
[a]*Percentages calculated from total number of eligible files reviewed in 1st audit (*n = *2548 records).*
[b]*Percentages calculated from total number of eligible files reviewed in 2nd audit (*n = *1234 records).*
[c]*95% confidence interval for difference in means.*
n = *total number of eligible files reviewed.*
SD = standard deviation; HbA1c = glycosylated haemoglobin; LDL = low-density lipoprotein.

and LDL-cholesterol, recording of BMI and smoking status and referral for funduscopy ($P < 0.001$).

Table 4 also demonstrates a significant improvement in outcome variables of diabetes care. Mean HbA1c was reduced from 8.7% to 8.1% ($P < 0.001$; 95% CI: 0.4–0.8) and the proportion of patients achieving the audit target level of HbA1c < 7% increased significantly from 20.6% to 31.7% ($P < 0.001$).

The mean systolic blood pressure fell from 135.3 mmHg to 133.2 mmHg ($P < 0.05$; 95% CI: 0.6–3.6). While the proportion of patients achieving the audit target of systolic blood pressure control < 130 mmHg did not significantly improve, there were significant decreases in the other categories ($P < 0.001$).

The mean LDL-cholesterol decreased from 129.2 mg/dL to 115.4 mg/dL ($P < 0.001$, 95% CI: 10.8–16.8) and the proportion of patients with the audit target < 100 mg/dL increased from 20.8% to 33.6% ($P < 0.001$).

Fewer files were reviewed for the different clinical indicators of the 2nd audit. This was due to manpower shortages affecting the availability of clinical auditors in each of the 16 PHC centres to submit the required data on time.

Table 5 **Diabetes patients reaching target levels of some key clinical indicators according to certain socioeconomic variables in 1st practice audit in primary health care centres in Dubai**

Variable	HbA1c < 7%			Systolic BP < 130 mmHg			LDL-chol < 100 mg/dL		
	No. of records	%	OR (95% CI)	No. of records	%	OR (95% CI)	No. of records	%	OR (95% CI)
Age (years)									
< 40	17	13.9	0.6 (0.3–1.0)*	112	64.7	3.0 (2.1–4.1)*	18	18.1	0.8 (0.5–1.4)
≥ 40	274	21.0		686	37.9		293	20.9	
Sex									
Male	166	20.3	0.9 (0.7–1.2)	480	41.8	1.1 (0.9–1.3)	180	21.7	1.2 (0.9–1.4)
Female	162	21.0		411	39.7		164	19.9	
Marital status									
Married	150	20.9	1.0 (0.4–2.4)	390	41.9	0.9 (0.5–1.7)	163	21.2	0.6 (0.3–1.4)
Unmarried	7	20.6		22	45.8		12	27.9	
Nationality									
UAE	203	19.8	0.8 (0.7–1.1)	546	38.3	0.7 (0.6–0.9)*	221	20.1	0.9 (0.7–1.1)
Non-UAE	125	22.2		345	45.5		123	22.0	
Education									
Illiterate	28	25.9	1.2 (0.7–2.1)	48	31.4	0.4 (0.3–0.6)*	28	24.1	1.1 (0.6–1.9)
Literate	60	21.9		177	51.0		62	28.1	
Occupation									
Employed	77	18.9	0.8 (0.5–1.2)	358	46.8	1.4 (1.1–1.8)*	94	22.7	1.5 (0.8–1.6)
Unemployed	82	22.3		173	37.7		81	20.3	

**Significant at P < 0.05.*
HbA1c = glycosylated haemoglobin; BP = blood pressure; LDL-chol = low-density lipoprotein cholesterol.
OR = odds ratio; CI = confidence interval; UAE = United Arab Emirates.

Outcome of diabetes care

Table 5 shows the relationship of outcome of diabetes care with some socioeconomic variables in the 1st audit. No significant relationships were observed between the proportion of patients achieving a target of HbA1c < 7% and LDL target < 100 mg/dL and the socioeconomic variables studied, except age ≥ 40 years which was significantly associated with a higher proportion of diabetes subjects achieving the target ($P < 0.05$). On the other hand there was a significant relationship between the proportion of patients achieving a target of systolic blood pressure < 130 mg/dL and age < 40 years, nationality, literacy and employment ($P < 0.05$) with higher proportions of non-UAE nationals, literate and employed patients achieving the target.

Discussion

This study documents the impact of implementing the quality agenda for improvement of the diabetes care programme in light of principles and evidence-based models of chronic disease management [*4–8*]. Several areas for system improvement were identified based on the care model, and quality improvement teams were formed to undertake such improvements. The main areas identified for system improvements were information systems, decision support and systems delivery. The main outcome measures were to monitor and document the extent of improvement in glycaemic, blood pressure and lipid control.

Prevalence of diabetes in the registered practices population

The current study showed that the prevalence of diabetes in the registered practice population in the 16 PHC centres was 1.6%, while community-based studies in the UAE have reported a rate of 10% [*2*]. This gap could be explained by the multiplicity of health systems in Dubai, as DOHMS is not the only provider of health services in Dubai. In addition to the private sector, the Ministry of Health has its own health premises and some governmental organizations provide health services for their own employees. Some patients could have more than one health card and have access to more than one health care provider. This gap could be also a reflection of the low detection rate of diabetes in the community and the need to establish screening programmes for the early detection of undiagnosed cases of diabetes in the community. Research evidence has shown that cases of type 2 diabetes can be missed in elderly patients with vascular problems of sufficient severity to warrant amputation. It has been suggested that selective screening of high-risk groups is one solution to the problem of reducing the level of undiagnosed diabetes [*10*].

Utilization of diabetes care services

The present study showed that only 52% of the registered diabetes patients were actively utilizing the PHC services. This could be because patients with type 1 diabetes receive their care mostly from the hospitals and because the health system in the UAE allows citizens with UAE nationality to register in more than one health system, acquire more than one health card and choose to receive medical services from any of the available health systems. In addition, the recently introduced fee-for-service scheme for non-UAE citizens may have also contributed to the low utilization rate of the diabetes services.

Registered diabetes population in PHC

The present study showed that most of diabetes population had type 2 diabetes, were taking oral hypoglycaemic medications,

were married and were UAE nationals. The illiteracy rate was 44%, compared with 48% in Saudi Arabia, and the unemployment rate was 47%, compared with 44% in Saudi Arabia [*11*]. The study also showed that about three-quarters of the diabetes patients were overweight, with BMI > 25 kg/m^2 compared with 56% in a report from Saudi Arabia [*12*]. This means that nearly half of the diabetes population are illiterate, unemployed and mostly overweight. This information reflects the need to use appropriate methods of health education for the illiterate group and give more attention to assess activity levels and promote exercise programmes.

Information systems

Information about age, sex and nationality of the patients could be found easily in almost all the PHC records. On the other hand, in the 1st audit cycle documentation about marital status, education and employment was poor. This is comparable to some other reports from the Gulf area which found low rates of documentation regarding education and employment status [*14*] and other reports that demonstrated a marked improvement in documentation of these variables in a diabetes care follow-up audit [*15*]. The degree of improvement in the documentation of socioeconomic variables was not assessed in the 2nd audit cycle of the current study as it needs a major investment in time to undertake such tasks manually. Nevertheless, staff training programmes following the recommendations emerging from the 1st audit emphasized the importance of documenting such variables.

As noted by the doctors in the focus group discussions, the structure of the PHC medical records did not facilitate the process of providing adequate diabetes care due to the lack of diabetes follow-up cards. The latter are considered to be one of the essential items of providing good diabetes care [*11*]. The introduction of a problem-oriented medical record system is an ideal solution to improve the quality of medical records for chronic conditions. Also the introduction of drug lists, problem lists and diabetes follow-up cards can help time wasted during the consultation for diabetes patients, who usually have multiple problems and polypharmacy needs. In addition, establishing simple clinical indicators of care will help audit coordinators retrieve relevant information quickly from the records. Considerable time was devoted to conducting the 1st audit cycle manually; nevertheless, in 2004, DOHMS introduced a new computer-based information system with computerized laboratory, radiology and billing systems. This saved time as it was possible in the 2nd audit cycle to conduct the audit of laboratory results electronically. A full electronic medical record system is planned to be in action by late 2006, which will greatly facilitate the audit process for all the studied variables.

Process of diabetes care

Glycosylated haemoglobin levels are an objective measure of metabolic control of diabetes. This study showed a significant improvement in the rate of performing this test from 62% to 82% between the 1st and 2nd audit cycle. This can be compared with rates of performing glycosylated haemoglobin tests ranging from 0% to 60% from Saudi Arabia [*14,15*], from 83.0% to 93.0% from studies in the United Kingdom (UK) [*16,17*] and 15%, 44% and 81% from the United States of America (USA) [*18–20*].

The current study was also able to document a significant improvement in the rate of measuring blood pressure from 84% to 98%. This compares with rates of blood pressure recording ranging from 66% to 100% in Saudi Arabia [*14,15,21*], 83% in the UK [*16*] and 86% in the USA [*18*].

Lipid disorders are a common source of co-morbidity in diabetes patients and treating such disorders is important as cardiovascular diseases are currently among the main causes of morbidity and mortality in the Eastern Mediterranean Region [*2*]. The current study showed a significant improvement in the rate of performing lipid profiles from 64% in the 1st audit to 75% in the 2nd audit. This compares with a testing rate of 73.8% in Saudi Arabia [*13*] and rates ranging from 31%, 45% to 66% in reports from the USA [*18–20*].

Our study showed a significant improvement in referral rates for funduscopy examination between the 2 surveys from 28.9% to 53.0%. Studies from Saudi Arabia reported referral rates of 33% [*15*] and 61.5% [*21*], from the UK of 64.4% to 86% [*16,17*], and from the USA of 22%, 66% and 28% [*18–20*].

Outcomes of diabetes care

This study in Dubai showed that the proportion of patients with good glycaemic control (i.e. HbA1c levels < 7%) improved from 20.6% to 31.7% in the 2nd audit cycle. A report from Australia showed an increase from 18% to 25% in the 2nd audit [*22*], while another Australian report demonstrated a rate of 57% [*23*], reaching ADA targets. By comparison, data from the USA showed rates between 37% and 44% [*24,25*]. Another study from the USA demonstrated an improvement in patients' mean HbA1c level from 7.8% to 7.4% [*26*] which is comparable with the improvement in our study from 8.7% to 8.2%.

In the present study, the mean systolic blood pressure dropped from 135.3 mmHg to 133.2 mmHg, while the proportion of diabetes patients reaching the ADA target of systolic blood pressure < 130 mmHg remained the same. In a study from the USA [*19*] the mean blood pressure was found to be 134.1 mmHg and in another study [*24*] the proportion of patients achieving the ADA target were 41%. In a study from the UK the mean systolic blood pressure fell from 147 mmHg to 140 mmHg between 2 audits [*27*].

The current audit showed significant improvements in control of LDL-cholesterol, as the proportion of diabetes patients with LDL-cholesterol level < 100 mg/dL increased from 20.8% to 33.6%. By comparison, 23% of patients in the USA [*24*] and 52.8% in Australia [*23*] achieved ADA targets.

Conclusion

This study demonstrated the impact of improving some aspects of the system and organization of diabetes care on improving key clinical indicators of the diabetes programme in Dubai. The study focused on mobilizing decision support, teamwork, developing role of nurses in diabetes care and improving information systems.

The results suggest that many opportunities for cardiovascular disease risk reduction are still missed in spite of efforts to improve the system of care for diabetes in Dubai Emirate. The extent of improvement that has taken place is still not sufficient to meet the challenge, as a significant proportion of individuals were not meeting the targets of the key clinical indicators. Control of weight and glycaemia are complex processes that require efforts beyond health system service development. There is also still a need to monitor and study the impact on outcome of care of socioeconomic variables in Dubai.

Further studies are needed to measure the impact on diabetes outcome measures of increasing the interaction of the health care team with diabetes patients, mobilizing self-

care efforts and community involvement in the diabetes programme.

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Connaissances des patients diabétiques de type 2 sur leur maladie à Sousse (Tunisie)

A. Ben Abdelaziz,[1] H. Thabet,[2] I. Soltane,[2] K. Gaha,[3] R. Gaha,[2] H. Tlili[4] et H. Ghannem[2]

معرفة مرضى السكّري من النمط الثاني بطبيعة حالاتهم، في سوسة، بتونس

أحمد بن عبد العزيز، حبيبة ثابت، ابتسام سلطان، خالد قحة، رفيقة قحة، هندة التليلي، حسن غنَّام

الخلاصة: قيَّم الباحثون معارف 404 مريضاً بالسكّري من النمط الثاني حول طبيعة مرضهم، وذلك بغرض تقييم جودة أنشطة التوعية والتثقيف في مجال السكّري؛ في وحدات الرعاية الصحية الأولية، في سوسة، عام 2003. وتبيَّن للباحثين أن مستوى معرفة المرضى بحالاتهم كان مقبولاً في 59% فقط من المرضى. وكانت الدراية بتعريف داء السكّري والفيزيولوجيا المرضية له هما المجالَيْن الرئيسَيْن اللذين تنقص فيهما المعلومات. وكانت نسبة الإجابات الصحيحة 62.6% و50.3% على التوالي. ولذلك ينبغي إيلاء مزيد من الاهتمام لتوعية وتثقيف مرضى السكّري، في إطار البرنامج الوطني لرعاية المرضى المصابين بأمراض مزمنة.

RÉSUMÉ Nous avons évalué les connaissances de 404 patients diabétiques de type 2 à l'égard de leur problème de santé dans les structures de soins de première ligne à Sousse en 2003. Il ressort de ce travail que seulement 59 % des diabétiques ont un niveau de connaissances satisfaisant. La définition et l'origine du diabète représentaient les deux principales lacunes dans les connaissances des patients interrogés, avec un pourcentage de réponses correctes de 62,6 % et 50,3 % respectivement. Une attention accrue devrait être portée à l'éducation des patients diabétiques dans le cadre du Programme national de prise en charge des maladies chroniques.

Knowledge of patients with type 2 diabetes about their condition in Sousse, Tunisia

ABSTRACT We assessed the knowledge of 404 type 2 diabetic patients about their condition in order to evaluate the quality of diabetes education in primary health care units in Sousse in 2003. We found that knowledge was satisfactory in only 59% of the patients. Their knowledge about the definition of diabetes and its pathophysiology were the 2 main areas where knowledge was lacking: the proportion of correct answers were 62.6% and 50.3% respectively. More attention should be paid to educating diabetic patients within the chronic disease care national programme.

[1]*Département de Santé communautaire, Faculté de Médecine de Sousse, Sousse (Tunisie) (Correspondance à adresser à A. Ben Abdelaziz : ahmed_epidemio@yahoo.fr).*
[2]*Service d'Épidémiologie, CHU Farhat Hached de Sousse, Sousse (Tunisie).*
[3]*Service de Néphrologie, CHU Fattouma Bourguiba, Monastir (Tunisie).*
[4]*Groupement de Santé de Base de Sousse, Sousse (Tunisie).*
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Introduction

Le diabète de type 2, maladie chronique en pleine expansion mondiale, pose un problème majeur de santé publique [*1*] en Tunisie. Sa prévalence est passée de 2,3 % en 1977 [*2*] à 10,2 % en 1995 [*3*]. Cette augmentation est due à la transition épidémiologique [*4*], caractérisée par une occidentalisation du style de vie, l'augmentation de l'obésité et du stress [*5*], ainsi qu'à une adoption rapide de nouvelles habitudes alimentaires et d'un mode de vie sédentaire [*6*]. Du fait de sa prévalence en accroissement continu et de sa morbi-mortalité menaçante [*7*], le diabète de type 2 pose aussi un problème de coût non négligeable pour le système de soins [*8*].

Il est démontré par différentes études qu'une approche globale et agressive de cette maladie est efficiente en termes de coût et d'efficacité [*9,10*]. En effet, l'éducation thérapeutique du patient diabétique fait partie intégrante du traitement comme dans toutes les autres maladies chroniques [*11*]. Pour gérer leur traitement, les patients diabétiques de type 2 doivent réaliser eux-mêmes des actes techniques et prendre des décisions d'ordre thérapeutique, l'ensemble étant désigné par le terme de « comportements de soins » [*5*]. Or l'adhésion à ces comportements de soins dépend de nombreux facteurs : psychologiques, affectifs, familiaux et socioculturels, dont les connaissances nécessaires à la gestion du traitement. Un des rôles des soignants est donc d'intégrer l'enseignement des connaissances de la maladie à un processus d'éducation thérapeutique du patient, axée sur la gestion de sa pathologie. Plusieurs études ont montré que les diabétiques de type 2 ayant bénéficié d'une éducation thérapeutique non seulement connaissaient mieux leur maladie, mais aussi savaient mieux se traiter, étaient mieux équilibrés, faisaient moins de complications et étaient moins longtemps et moins souvent hospitalisés [*11*].

Cependant, la pratique d'une éducation thérapeutique fondée sur des données probantes et adaptée aussi bien à la culture locale qu'à la personnalité du patient est encore peu généralisée dans les structures de soins de première ligne en Tunisie assurant la prise en charge des maladies chroniques, dont le diabète de type 2. D'où l'intérêt de ce travail qui se propose de décrire le niveau des connaissances d'un échantillon représentatif des diabétiques de type 2, suivis en première ligne, à propos de leur problème de santé et de relever par conséquent les éventuelles lacunes dans la pratique de cette dimension thérapeutique primordiale : l'éducation pour la santé.

Méthodes

Il s'agit d'une étude épidémiologique descriptive et transversale ayant porté sur un échantillon représentatif des patients diabétiques de type 2 suivis dans la région sanitaire de Sousse pendant la période allant de janvier à avril 2003. Cet échantillon a été stratifié selon le niveau de prise en charge : centres de santé de base et consultations de diabétologie. Le calcul de la taille de l'échantillon a été basé sur l'hypothèse que la prévalence estimée de l'éducation diabétique a été de 50 % avec une précision de 5 % et un niveau de confiance de 95 %. Cette taille a été majorée de 5 % pour remédier à d'éventuelles données manquantes.

Les structures de soins participant à l'étude ont été identifiées à travers un échantillonnage stratifié selon les deux échelons de soins de la première ligne afin d'assurer la représentativité de la population de l'étude et de pouvoir approfondir l'analyse statistique des données. Ainsi,

l'enquête s'est déroulée dans deux centres spécialisés de diabétologie et trois centres de santé de base. Dans ces structures de santé de première ligne, aucune éducation thérapeutique structurée et systématique n'est organisée pour les patients chroniques dont les diabétiques de type 2, en dehors d'une éducation pour la santé souvent individualisée, rapide et aléatoire dans le cadre des consultations médicales.

L'éducation du diabétique de type 2 a été évaluée à travers les connaissances que celui-ci avait sur sa maladie. Ainsi, 20 questions à réponses fermées axées sur cinq chapitres ont été posées : la définition du diabète, l'origine du diabète, l'évolution du diabète, les interférences avec la vie courante et les instructions thérapeutiques. Chaque dimension étudiée a été composée de quatre items. Nous avons supposé que les différents items ont été égaux dans leur importance. Une réponse correcte a été cotée 1, une réponse fausse ou l'aveu d'une non-connaissance « ne sait pas » a été coté(e) 0. Ainsi, chaque dimension prenait un score allant de 0 à 4. Un patient était considéré éduqué à propos d'une dimension de la maladie diabétique s'il avait correctement répondu au moins à 3 items correspondants. Un score global des connaissances a été donc établi, allant de 0 à 20.

Pour faciliter l'interprétation des résultats, nous avons procédé à la transformation linéaire des scores des cinq dimensions et du score global selon la formule suivante [*12*] : score final = [(score d'origine – plus petit score d'origine) × 100] / étendue possible des scores d'origine. Ainsi, les nouveaux scores obtenus variaient de 0 à 100. Le niveau des connaissances d'un patient a été considéré « satisfaisant » si le patient avait obtenu un score global ≥ 75 %, « moyen » si le score global a été compris entre 50 % et 75 %, et enfin « insuffisant » s'il a obtenu un score global < 50 %. Le traitement statistique des données a été effectué au Service d'Épidémiologie et de Statistiques médicales du CHU Farhat Hached de Sousse sur le logiciel Epi Info 6,04 FR.

Résultats

Caractéristiques de la population étudiée

Cette enquête a porté sur un échantillon représentatif de 404 patients diabétiques de type 2 suivis dans la région sanitaire de Sousse. La population étudiée, avec une moyenne d'âge de 60 ans (E.T. 10,9) était constituée de 66,6 % de femmes. Un patient sur cinq bénéficiait de l'assurance médicale gratuite. Le pourcentage des patients inactifs sur le plan professionnel était de 64,4 %.

Le profil clinique de ces diabétiques de type 2 est caractérisé par une ancienneté moyenne de diabète de 8 ans (E.T. 6,1), une fréquence élevée de l'obésité (37,6 %), une co-morbidité importante, particulièrement l'hypertension artérielle (71,3 %) ainsi que des complications dégénératives fréquentes essentiellement neurologiques (47,5 %) et oculaires (28,7 %).

Évaluation des dimensions des connaissances

Connaissance de la définition du diabète

Le signe majeur du diabète (polyurie nocturne) a été reconnu par la quasi-totalité des patients. Cependant, la connaissance de la macrosomie fœtale comme signe de suspicion de diabète chez la femme enceinte a été l'item le moins connu par les patients diabétiques de type 2 (Tableau 1). En effet, la moyenne globale de cette dimension de l'éducation diabétique a été de 66 (E.T. 23,7). Le pourcentage des patients qui avaient une bonne connaissance de la

Tableau 1 **Connaissance de la définition du diabète chez les patients diabétiques de type 2**

Savez-vous que	Nbre (n = 404)	%	IC 95 %
La glycémie moyenne d'une personne saine est de 1 g/100 mL	335	82,9	78,8 - 86,4
À partir d'une glycémie de 1,20 g/L, la personne pourrait être considérée diabétique	215	53,2	48,2 - 58,2
Une femme qui accouche d'un bébé de plus de 4 kg est à haut risque de diabète	164	40,6	35,8 - 45,6
Se lever souvent la nuit pour uriner est un signe majeur du diabète	385	95,3	92,6 - 97,1

IC 95 % : intervalle de confiance à 95 %.

définition du diabète (connaissent au moins trois items) était de 62,6 %.

Connaissance de l'origine du diabète
Le tableau 2 montre que la connaissance de l'obésité comme facteur de risque pour le diabète a été mentionnée par 80,9 % des patients diabétiques de type 2 et que seulement 35,1 % des patients savaient que l'hypertension artérielle n'entraînait pas le diabète. La connaissance de l'origine de la maladie diabétique (connaissance de 3 items ou plus) a été reconnue par la moitié des patients (50,3 %). En effet, la moyenne globale de cette dimension de l'éducation diabétique était de 54 (E.T. 28,7).

Connaissance de l'évolution du diabète
Il ressort du tableau 3 que la majorité des patients diabétiques de type 2 connaissaient le caractère chronique de leur maladie ainsi que les complications dégénératives du diabète. Cependant, seulement 64,9 % des patients interrogés savaient répondre correctement aux quatre items concernant l'évolution du diabète. La moyenne globale de cette dimension de l'éducation diabétique était de 85 (E.T. 20,0). Les complications oculaires étaient les plus connues (97,3 %).

Connaissance des interférences du diabète
D'après le tableau 4, la connaissance de l'interférence du diabète avec la grossesse est l'item le moins connu ; par contre, les soins des pieds ainsi que l'importance des activités physiques sont connus par presque la totalité des patients (> 90 %). En plus, 89,1 % des patients connaissaient plus de trois items des interférences de la

Tableau 2 **Connaissance de l'origine du diabète chez les patients diabétiques de type 2**

Savez-vous que	Nbre (n = 404)	%	IC 95 %
Le type de diabète que vous avez (type 2) est héréditaire	244	60,4	55,4 - 65,2
L'obésité peut entraîner le diabète	327	80,9	76,7 - 84,6
L'hypertension artérielle n'entraîne pas le diabète	142	35,1	30,5 - 40,1
Chez le diabétique, le sucre ingéré n'est pas bien utilisé par le corps	207	51,2	46,3 - 56,2

IC 95 % : intervalle de confiance à 95 %.

Tableau 3 **Connaissance de l'évolution du diabète chez les patients diabétiques de type 2**

Savez-vous que	Nbre (n = 404)	%	IC 95 %
Le diabète est une maladie chronique qui évolue pendant toute la vie	356	88,1	84,5 - 91,0
Le diabète non traité pourrait entraîner une maladie cardiaque	320	79,2	74,9 - 83,0
Le diabète non équilibré pourrait entraîner une maladie des yeux	393	97,3	95,0 - 98,6
Le diabète mal équilibré pourrait entraîner une maladie des reins	321	79,5	75,1 - 83,2

IC 95 % : intervalle de confiance à 95 %.

maladie diabétique avec la vie quotidienne. La moyenne globale de cette dimension de l'éducation diabétique était de 87 (E.T. 17,5).

Connaissance des instructions du diabète
Les signes de l'hypoglycémie étaient connus par les trois quarts des patients interrogés et 96,3 % des diabétiques de type 2 étaient convaincus de la nécessité d'un traitement à vie sous surveillance médicale (Tableau 5). En plus, 91,6 % des patients connaissaient au moins trois items des instructions imposées par la maladie diabétique. La moyenne globale de cette dimension de l'éducation diabétique était de 85 (E.T. 16,2).

Score global des connaissances

Seulement 58,9 % (IC 95 % : 53,9 - 63,7) de la population étudiée ont été considérés « bien informés » à propos de leur maladie contre 35,9 % (IC 95 % : 31,2 - 40,8) ayant un niveau de connaissances « moyen ». Le taux des patients diabétiques considérés non éduqués (niveau global des connaissances moyen ou mauvais) vis-à-vis de leur maladie était de 41,1 %. La moyenne du score global des connaissances était de 75 (E.T. 15,5).

La figure 1 illustre la répartition des connaissances des patients diabétiques de type 2 en fonction des cinq dimensions ; les insuffisances majeures des connaissances intéressaient les deux dimensions suivantes : l'origine du diabète et sa définition.

Discussion

Le concept d'éducation des patients diabétiques a été développé depuis de longues années [*13*]. C'est l'ensemble des activités

Tableau 4 **Connaissance des interférences du diabète chez les patients diabétiques de type 2**

Savez-vous que	Nbre (n = 404)	%	IC 95 %
Un diabétique traité par des médicaments doit avoir des activités physiques	391	96,8	94,4 - 98,2
Un diabétique ne doit pas manger comme tous les membres de sa famille	360	89,1	85,6 - 91,9
Une femme diabétique doit surveiller beaucoup plus ses grossesses qu'une femme non diabétique	309	76,5	72,0 - 80,5
Le diabétique doit accorder plus d'attention au choix de ses souliers et de ses chaussettes	370	91,6	88,3 - 94,0

IC 95 % : intervalle de confiance à 95 %.

Tableau 5 **Connaissance des instructions du diabète chez les patients diabétiques de type 2**

Savez-vous que	Nbre (n = 404)	%	IC 95 %
Le patient diabétique doit toujours manger lors de la prise de ses médicaments du diabète	369	91,3	88,0 - 93,8
Des sueurs apparues brutalement chez un diabétique traité par des médicaments signifient la chute de la glycémie	286	70,8	66,1 - 75,1
Le diabétique traité par des médicaments peut faire le jeûne (ramadan) après accord du médecin	363	89,9	86,4 - 92,5
Le diabétique doit prendre son traitement à vie sous surveillance médicale	389	96,3	93,8 - 97,8

IC 95 % : intervalle de confiance à 95 %.

pédagogiques conçues pour aider le patient à acquérir des compétences concernant sa santé, alliant son information et par conséquent, l'adoption et le maintien volontaire d'attitudes positives et de comportements favorables. Cette participation active du patient aide à la réussite du contrôle glycémique et retarde l'apparition des complications de la maladie.

Ce travail n'a pas été à l'abri de quelques insuffisances méthodologiques limitant partiellement sa validité interne et externe. D'une part, l'évaluation de l'éducation thérapeutique repose classiquement sur l'exploration des trois axes : les connaissances, les attitudes et les pratiques des patients. Or dans notre étude, seule la composante « connaissances » a été décrite étant donné

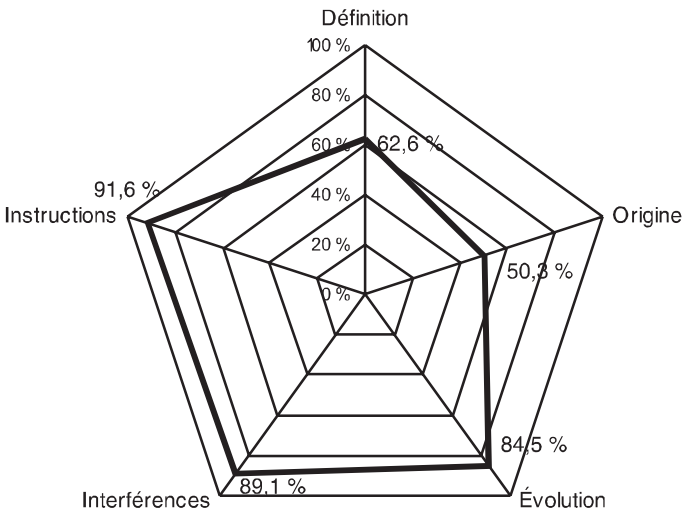

Figure 1 **Proportion des connaissances des cinq dimensions de l'éducation diabétique (connaissance de trois items ou plus par dimension) chez les patients diabétiques de type 2**

la facilité de son étude [*14,15*]. Par ailleurs, il existe une corrélation positive entre les connaissances et les attitudes et les comportements : mieux un patient connaît sa pathologie, plus il adoptera de bonnes attitudes et des pratiques correctes dans la gestion de sa maladie. D'autre part, le recueil des données a été fait au moyen d'un questionnaire spécialement conçu pour ce travail dont la validité est en cours d'étude. Dans la littérature, il existe d'autres questionnaires anglo-saxons, largement utilisés et validés par les équipes de recherche, mais spécifiquement conçus pour les diabétiques de type 1.

Cette étude a permis de conclure que seulement 59 % de notre population de diabétiques de type 2 avaient un niveau de connaissances « satisfaisant ». Ce résultat a été décevant puisque des notions élémentaires de la maladie diabétique (ex. : savoir qu'elle est chronique et que le patient diabétique peut s'exposer à des complications cardio-vasculaires, oculaires et rénales, savoir que l'apparition des sueurs chez un diabétique signifie une hypoglycémie) étaient mal connues par les diabétiques qui avaient en plus beaucoup d'idées erronées.

Ce manque d'information des diabétiques a été confirmé par d'autres études tunisiennes. En effet, le pourcentage des patients diabétiques, bien informés concernant leur maladie, étudiés dans des différentes régions de notre pays variait de 14,7 % à 51 % [*16-18*]. D'autres études étrangères ont rapporté aussi cette insuffisance d'information chez les diabétiques de type 2 [*19-22*]. Les différences des méthodes de mesure et d'échantillonnage font que les comparaisons entre les études, particulièrement l'estimation des taux des patients éduqués, doivent être interprétées avec précaution. Pourtant, l'insuffisance de l'éducation diabétique paraît évidente dans toutes ces études et intéressait l'ensemble des dimensions des connaissances : définition de la maladie, son origine, son évolution, ses interférences avec la vie et enfin les instructions pour sa bonne gestion par le patient. Selon notre étude, les items portant sur la définition de la maladie et sur son origine représentaient les deux principales lacunes dans les connaissances des patients diabétiques de type 2 interrogés, avec un pourcentage de réponses correctes de 62,6 % et 50,3 % respectivement.

Définition et origine de la maladie

En effet, seulement la moitié des patients avait une notion correcte de la définition du seuil à partir duquel une personne est considérée diabétique et 40 % savaient que la macrosomie foetale pouvait être un signe de diabète. L'insuffisance d'information sur l'association diabète et grossesse peut être expliquée par le fait que la plupart des patients interrogés étaient des personnes âgées, devenues diabétiques après avoir dépassé l'âge de procréation. Le mécanisme ainsi que les facteurs de risque du diabète n'étaient pas clairs à l'esprit des patients. L'obésité était de loin le facteur de risque le plus connu (80,9 %) ; par contre, 64,9 % des diabétiques interrogés croyaient abusivement à la responsabilité de l'hypertension artérielle dans la genèse du diabète de type 2. Cette information erronée est due probablement à la fréquence de l'association de ces deux problèmes de santé. Ces insuffisances des connaissances concernant la définition et l'origine du diabète pourraient être expliquées par le fait que les médecins croyaient que les notions de définition et d'origine de la maladie font partie de leur savoir sacré et par conséquent, ils ne s'efforçaient pas d'expliquer ces notions aux patients.

Évolution de la maladie

Les causes de la morbidité et de la mortalité des diabétiques sont dominées par les

complications à long terme, représentées essentiellement par les accidents de l'angiopathie et de la microangiopathie [*23,24*] ; pour les combattre, une bonne coopération du patient aux mesures préventives et thérapeutiques est nécessaire. Dans notre étude, le caractère chronique du diabète de type 2 a été rapporté par 88 % des patients et les signes de complications aiguës telles que l'hypoglycémie n'étaient rapportés que par 71 % des patients. Cette défaillance dans les connaissances des patients concernant les complications aiguës du diabète a été retrouvée également dans l'enquête de Ben Ammar [*16*] ; les signes révélateurs d'une hypoglycémie n'ont été cités que par 4,2 % des patients interrogés. Une étude anglaise [*25*] a montré qu'il existait des lacunes dans les connaissances des diabétiques interrogés concernant les complications aiguës de la maladie telles que l'hypoglycémie et l'acidocétose. Les résultats de l'étude américaine du groupe de Médecine préventive [*26*] et ceux de l'étude espagnole [*20*] sur l'évaluation du degré des connaissances des diabétiques de type 2 suivis en première ligne rejoignent les nôtres en montrant la méconnaissance des complications cardiaques.

Cette méconnaissance des complications dégénératives de la maladie diabétique pourrait tenir, d'une part, à la longueur de la période asymptomatique qui précède leur apparition et d'autre part, à un déficit d'information de la part du médecin qui ne donne des explications aux complications d'une maladie que lorsqu'elles sont installées. Ce contexte favorise vraisemblablement l'ambivalence du patient et du médecin, même s'ils sont correctement informés des risques de complications graves et invalidantes.

Interférences de la maladie et instructions

L'interférence du diabète avec la grossesse est l'item le moins connu ; par contre, les soins des pieds ainsi que l'importance des activités physiques et d'un régime adéquat sont connus par presque la totalité de l'échantillon (> 90 %).

Les résultats de notre étude concordent avec ceux des autres enquêtes [*16,24,27-29*]. Les patients savent qu'il est recommandé de pratiquer des exercices physiques, qu'il faut respecter un régime limitant l'apport de glucides et de graisses, cependant ils ne mettent pas systématiquement ces recommandations en pratique. En effet, la modification de l'alimentation par exemple nécessite un changement de comportement, très difficile à obtenir chez le diabétique de type 2, compte tenu de son âge, de l'ancienneté de ses habitudes, de son surpoids, de son faible niveau socio-économique et de la place importante de la diététique dans la vie de tous les jours [*30,31*].

Conclusion

Cette étude a permis de quantifier l'ampleur du problème de l'insuffisance des connaissances des diabétiques de type 2 suivis en première ligne dans la région sanitaire de Sousse à l'égard de leur problème de santé. Par conséquent, il est primordial de renforcer la formation des médecins en matière d'éducation thérapeutique en introduisant davantage les sciences humaines lors de la formation initiale (psychologie, pédagogie, communication, etc.), en sensibilisant très tôt les étudiants à la prise en charge des pathologies chroniques et en incluant le thème de l'éducation diabétique dans le certificat de « Pratique médicale ». En plus, il nous paraît important d'institutionnaliser la pratique de l'éducation thérapeutique pour les patients diabétiques dans les structures de soins de première ligne sous forme de séances d'éducation diabétique en groupe dans les Centres de Santé de Base et d'un séjour éducatif hospitalier en « hôpital de

jour » dans les hôpitaux de circonscription pour permettre aux diabétiques d'apprendre convenablement la gestion de leur maladie et d'acquérir des attitudes positives et valides face à leur problème de santé.

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Relation between hypercholesterolaemia and vascular endothelial microinflammation

A.S. Elwakkad,[1] S.I. Mohamed[1] and M. Fathalla[2]

العلاقة بين فرط كوليستيرول الدم وبين الالتهابات الدقيقة في الخلايا البطانية للأوعية الدموية

أماني الوقاد، سعدية محمد، محمد فتح الله

الخلاصة: تم في إطار هذه الدراسة بحث علاقة الترابط بين فرط كوليستيرول الدم وزيادة الأكسدة من جانب، وبين مستوى ب — سيليكتين والانترلوكين — 6، من جانب آخر بوصفها من العلامات التي تميز الوضع الراهن للخلايا البطانية. وأُجريت الدراسة على 40 من المصريين البالغين الذين لا تظهر عليهم أعراض فرط كوليستيرول الدم، و20 من الشواهد المماثلين لهم في العمر والجنس. ولوحظ ارتفاع يُعتدّ به إحصائياً في مستوى أكسدة الشحوم (P<0.001) في مجموعة الدراسة، كما لوحظ ترابط إيجابي بينه وبين مستوى الكوليستيرول (P<0.001) والبروتين الشحمي المنخفض الكثافة LDL (P<0.002). وكان مستوى نشاط إنزيم بيروكسيداز الغلوتاثيون مرتفعاً أيضاً بشكل يُعتدّ به إحصائياً (P<0.001)، وترابط نشاطه ترابطاً إيجابياً مع مستوى الكوليستيرول (P<0.001) ومستوى البروتين الشحمي المنخفض الكثافة (P<0.001). ولوحظ أيضاً ارتفاع واسمات وظائف الخلايا البطانية بشكل يُعتدّ به إحصائياً في المجموعة الخاضعة للدراسة (P<0.001) مع ترابط إيجابي بمستوى الكوليستيرول (P<0.001) ومستوى البروتين الشحمي المنخفض الكثافة (P<0.001). وخلصت الدراسة إلى أن فرط كوليستيرول الدم يسبِّب الالتهابات الدقيقة في الخلايا البطانية للأوعية الدموية، وأن ب — سيليكتين والإنترلوكين — 6 قد يكونان من عوامل اختطار الإصابة بمرض القلب الوعائي.

ABSTRACT We investigated the correlation between hypercholesterolaemia and oxidative stress and P-selectin and interleukin-6 (IL-6) as markers for endothelial status. We studied 40 Egyptian adults with asymptomatic hypercholesterolaemia and 20 age- and sex-matched controls. Lipid peroxidation was significantly higher ($P < 0.001$) in the study group and positively correlated with cholesterol ($P < 0.001$) and low-density lipoprotein (LDL) ($P < 0.002$). Glutathione peroxidase activity was also significantly higher ($P < 0.001$) with positive correlation with cholesterol ($P < 0.001$) and LDL ($P < 0.001$). Markers for endothelial cell function were significantly higher in the study group ($P < 0.001$) with a positive correlation with cholesterol ($P < 0.001$) and LDL ($P < 0.001$). Hypercholesterolaemia causes endothelial microinflammation, and P-selectin and IL-6 may also be risk factors for cardiovascular disease.

Relation entre l'hypercholestérolémie et la micro-inflammation de l'endothélium vasculaire

RÉSUMÉ Nous avons exploré la corrélation entre l'hypercholestérolémie, le stress oxydatif et les marqueurs de la fonction endothéliale que sont la P sélectine et l'interleukine 6 (IL-6). Nous avons étudié 40 Égyptiens adultes présentant une hypercholestérolémie asymptomatique et 20 témoins appariés selon l'âge et le sexe. La peroxydation lipidique est apparue significativement plus intense ($p < 0,001$) dans le groupe expérimental et corrélée positivement au cholestérol ($p < 0,001$) et aux lipoprotéines de basse densité (LDL) ($p < 0,002$). De même, l'activité glutathione peroxidase était significativement supérieure ($p < 0,001$), avec une corrélation positive avec le cholestérol ($p < 0,001$) et les LDL ($p < 0,001$). Les marqueurs de la fonction des cellules endothéliales se sont avérés significativement plus élevés dans le groupe expérimental ($p < 0,001$), en corrélation positive avec le cholestérol ($p < 0,001$) et les LDL ($p < 0,001$). L'hypercholestérolémie génère une micro-inflammation de l'endothélium vasculaire, tandis que la P sélectine et l'IL-6 peuvent également être des facteurs de risque de maladie cardio-vasculaire.

[1]Department of Medical Physiology; [2]Department of Internal Medicine, National Research Centre, Giza, Egypt. (Correspondence to A.S. Elwakkad: amanyse@hotmail.com)
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Introduction

The vascular endothelium is a dynamic endocrine organ that regulates vascular tone, local homeostasis, and the fibro-inflammatory-proliferative process. Many studies have demonstrate that endothelial dysfunction and activation is one of the earliest markers in patients with atherogenic risk factors (e.g. male sex, ageing, hypertension, diabetes mellitus, smoking, family history) in the absence of angiographic evidence of atherosclerosis [*1*].

Oxidative stress to the vascular endothelium is a serious causative factor of vascular endothelial dysfunction, and plays an important role in the pathophysiology of several vascular diseases, including atherosclerosis, diabetes, neuronal disorders, and ischaemia-reperfusion injury [*2*]. It was noted that some of the patients attending 6th October national insurance clinic for annual routine laboratory and clinical examinations were diagnosed as hypercholesterolaemic without any clinical symptoms. A few years later, vascular injury was noted during the annual medical examination. Thus, we carried out this study to confirm the relationship between hypercholesterolaemia and vascular injury.

Hypercholesterolaemia is frequently associated with enhanced lipid peroxidation [*3*]. We therefore aimed to investigate the correlation between hypercholesterolaemia and oxidative stress on the one hand and P-selectin and interleukin-6 (IL-6) (pro-inflammatory cytokine) as markers of endothelial functional status on the other.

Methods

We contacted asymptomatic Egyptian adult employees of the National Research Centre (males and females) who had been examined at the health insurance outpatient clinic between the beginning of October 2004 and the end of December 2004 and who had been identified as having hypercholesterolaemia (total cholesterol > 200 mg/dL). We excluded any patient with cardiovascular disease. Of those we invited to take part in our study 65% refused to participate and 35% agreed (40 patients). During the same period, 20 healthy age- and sex-matched personnel whose medical records showed total cholesterol and triglycerides were within normal levels and who had no cardiovascular disease were selected from the medical staff of the National Research Centre to participate in the study as controls. This group was retested to confirm their blood lipid status before participating in the study.

After taking verbal agreement, all participants (patients and controls) underwent the following investigations.

Blood samples (10 mL) were collected from each participant at the health insurance clinic or the clinic in the National Research Centre, as convenient for the participant. Each sample was divided into 2 × 5 mL portions: in the first portion, serum was separated, divided into aliquots and preserved at –20 °C until used; the blood in the second portion was collected over EDTA and assayed on the same day for the determination of glutathione peroxidase activity and lipid peroxidation, measured as thiobarbituric acid-reactive substance (TBARS).

Lipid peroxidation was determined as TBARS value according to the method of Mitsura and Midori. The TBARS value was measured as the difference in optical density read at 535 nm and 520 nm [*4*].

Glutathione-peroxidase activity in whole blood was determined using Ransel kit (Randox Laboratories, Crumlin, UK) according to the manufacturer's instructions.

Total serum cholesterol was determined using a commercial kit (catalogue number

07986B-07/98BioMérieux, Marcy l'Etoile, France) according to the manufacturer's instructions].

Serum high-density lipoprotein (HDL) cholesterol was determined using a BioMérieux kit (catalogue number 00232B-04/96) according to the manufacturer's instructions.

Serum low-density lipoprotein (LDL) cholesterol was measured directly using a BioMérieux kit (catalogue number 00238 B-04/96) according to the manufacturer's instructions. It was read at wavelength 500 nm and calculated using the formula: $A_{sample}/A_{standard} \times n$ mg/dL (dilution coefficient n = 387).

Human P-selectin was measured by enzyme-linked immunosorbent assay kit for quantitative detection of soluble human P-selectin (Bender MedSystems, Vienna, Austria) according to the manufacturer's instructions.

IL-6 was measured using an immunoenzymometric assay kit (IL-6 EASIA, Biosource, Nivelles, Belgium) for the quantitative measurement of human IL-6 in serum according to the manufacturer's instructions.

Results were expressed as mean and standard deviation (SD). Data were analysed using *SPSS*, version 10. Data were compared using a paired *t*-test for independent variables. Values of $P < 0.05$ were considered significant.

Pearson correlations between different variables were done. Values of $P < 0.01$ were considered significant (2-tailed).

Results

Levels of lipid peroxidation (TBARS) ($P < 0.001$) and glutathione peroxidase activity as markers for oxidative stress were statistically significantly higher in the hypercholesterolaemic (patient) group ($P < 0.001$). P-selectin (marker for endothelial cell function) and IL-6 (pro-inflammatory cytokine) were also markedly higher in the patient group ($P < 0.001$) (Table 1).

Table 2 shows the correlation (Pearson coefficient, *r*) between total cholesterol

Table 1 **Comparison between hypercholesterolaemic patients (total cholesterol > 200 mg/dL) and controls (total cholesterol ≤ 200 mg/dL) for total cholesterol and markers of oxidative stress and endothelial function**

Variable	Patients Mean (SD)	Controls Mean (SD)
Cholesterol (mg/dL)	291.85 (73.35)	115.3 (20.58)
Oxidative stress marker		
TBARS difference between OD (535–520 nm)	0.8705 (8.488E-02)	0.3111 (4.977E-02)
Glutathione peroxidase activity (units/L whole blood)	132.37 (24.38)	41.25 (12.319)
Endothelial function marker		
P-selectin (ng/mL)	791.5 (322.57)	184.88 (114.98)
Interleukin-6 (pg/mL)	66.35 (39.69)	4.1 (2.3722)

TBARS = thiobarbituric acid-reactive substance, indicator of lipid peroxidation, indicated as difference in optical density read at 535 nm and 520 nm.
P < *0.001 for all variables.*
SD = standard deviation.

level and LDL-cholesterol level and oxidative stress, expressed by lipid peroxidation (TBARS) and glutathione peroxidase activity. Also shown is the correlation with endothelial function, expressed by P-selectin and the pro-inflammatory cytokine IL-6.

Table 3 shows the correlation between oxidative stress, expressed by lipid peroxidation and glutathione peroxidase activity, and markers of endothelial function, expressed by P-selectin and pro-inflammatory cytokine IL-6 ($P < 0.001$). Correlation between Il-6 and P-selectin was also statistically significant.

There was a negative, but not statistically significant, correlation between HDL cholesterol and the markers of oxidative stress and endothelial function (Table 3).

Discussion

Hypercholesterolaemia has frequently been associated with enhanced lipid peroxidation [*3*]. In this study we examined the relation between hypercholesterolaemia and increased oxidative stress. We found a very high positive correlation between cholesterol level, LDL cholesterol and raised oxidative stress, expressed as high lipid peroxidation and glutathione peroxidase activity. This is consistent with the result of Davi et al., who stated that they had obtained evidence of enhanced lipid peroxidation (*in vivo*) in hypercholesterolaemic patients [*3*].

Desideri et al. stated that hypercholesterolaemia was associated with endothelial activation and increased lipid peroxidation [*5*]. Lewis et al. showed that oxidative stress stimulates the production and release of platelet-activating factor (PAF) in endothelial cells [*6*]. Other reports from Marathe et al. and Tokumura et al. indicated that PAF as well as PAF-like phospholipids are critical factors in the pathophysiology of vascular endothelial dysfunction under oxidative stress conditions [*7,8*].

According to Lum and Roebuck, oxidative stress to the vascular endothelium is a serious causative factor of vascular endothelial dysfunction and plays an important role in the pathophysiology of several vascular diseases [*2*]. LDL is the cholesterol

Table 2 **Correlation between cholesterol and low-density lipoprotein (LDL) and markers of oxidative stress and endothelial function**

Variable	Cholesterol		LDL	
	r	*P*	*r*	*P*
Oxidative stress marker				
TBARS	0.772	< 0.001	0.665	< 0.002
Glutathione peroxidase activity	0.735	< 0.001	0.759	< 0.001
Endothelial function marker				
P-selectin	0.879	< 0.001	0.876	< 0.001
IL-6	0.782	< 0.001	0.775	< 0.001

Correlation significant at the 0.01 level (2-tailed).
TBARS = thiobarbituric acid-reactive substance, indicator of lipid peroxidation.
IL-6 = interleukin-6.

Table 3 **Correlation between markers for oxidative stress and endothelial function markers and high-density lipoprotein (HDL) cholesterol**

Variable	Oxidative stress marker				Endothelial function marker			
	TBARS		Glutathione peroxidase activity		P-selectin		IL-6	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
P-selectin	0.750	< 0.001	0.812	< 0.001	–		–	
IL-6	0.717	< 0.001	0.805	< 0.001	0.913	< 0.001	–	
HDL cholesterol[a]	–0.217	0.372	–0.097	0.68	–0.113	0.636	–0.086	0.78

Correlation significant at the 0.01 level (2-tailed).
[a]*Not significant.*
TBARS = thiobarbituric acid-reactive substance, indicator of lipid peroxidation.
IL-6 = interleukin-6.

component that is more directly involved in the pathogeneses of vascular dysfunction in hypercholesterolaemic patients.

In our study there was increased level of LDL cholesterol and increased oxidative stress. LDL becomes pathogenic when subjected to oxidation (increase in oxidative stress) and becomes ox-LDL [*9*]. Ox-LDL is, in fact, no longer recognized by the LDL receptors; instead it is taken up by scavenger receptors. These are not subjected to regulation by the intracellular cholesterol level in the subendothelial macrophages which transform to foam cells [*10*]. Egashira showed that LDL, especially oxidized LDL, inhibits endothelial function through inhibition of NO (nitric oxide) activity by down-regulation of endothelial NO synthase expression, decreased receptor-mediated release of NO, and activation of NO via superoxide anion production [*1*].

Aikawa et al. concluded that lipid lowering reduced production of reactive oxygen species, ox-LDL accumulation and plasma level of anti-ox-LDL IgG; VCAM-1 and MCP-1 expression decreased and NO synthase expression increased, and endothelial cells exhibited more normal ultrastructure [*11*].

P-selectin level was much higher in the hypercholesterolaemic group, with a strong positive correlation with cholesterol and LDL-cholesterol levels. This is in agreement with Johnson-Tidey et al., who stated that high P-selectin plasma level in symptomatic hypercholesterolaemic patients may represent an index of the presence of atherosclerotic vascular lesions P-selectin expression is endothelial cells overlying atherosclerotic plaques [*12*].

Davi et al. observed that plasma P-selectin concentration was directly correlated with LDL levels, which suggests that LDL might have an impact on the series of events that lead to P-selectin expression and release *in vivo*. They also found that hypercholesterolaemia was associated with elevated plasma P-selectin [*13*]. P-selectin level may be proposed as a marker of endothelial dysfunction in hypercholesterolaemic patients. This agreed with the results of our study as we found a strong positive correlation between P-selectin and markers of oxidative stress expressed by lipid peroxidation and glutathione peroxidase activity.

Levels of the proinflammatory cytokine IL-6 were significantly higher in the hyperc-

holesterolaemic group compared to healthy controls. There was a positive correlation with cholesterol, LDL, oxidative stress and endothelial function. This result agreed with that of Nawawi et al., who observed that hypercholesterol-aemia caused endothelial dysfunction, leading to increased production of adhesion molecules and cytokines (IL-6) [*14*]. Desai et al. concluded that the inflammatory cytokine IL-6 was an important mediator of increased endothelial permeability via alterations in ultra-structural distribution of tight junctions and morphologic changes in shape causing endothelial barrier dysfunction [*15*].

Blood levels of inflammatory markers have been associated with hypercholesterolaemia [*16*]. Cytokines (IL-6, Il-1B) and soluble adhesion molecules have been associated with both hypercholesterolaemia and atherosclerotic diseases. Soluble intercellular adhesion molecule-1 and IL-6 have been found to reflect endothelial dysfunction in patients with primary hypercholesterolaemia [*17*].

IL-6 has been found to induce oxidative stress and endothelial dysfunction by over-expression of the angiotensin II type I receptor [*18*]. Pro-inflammatory cytokines such as tumour necrosis factor alpha and IL-6 are important mediators of immune response, associated with endothelial dysfunction [*19*].

Conclusion

Hypercholesterolaemia causes endothelial microinflammation. IL-6 and P-selectin were also identified as risk factors for cardiovascular disorders.

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Diagnostic value of homocysteine, C-reactive protein and bilirubin for coronary artery disease

N. Yilmaz,[1] H.K. Çiçek,[1] A. Çelik,[1] I. Meram,[1] R. Kocabas[1] and V. Davutoglu[2]

القيمة التشخيصية للهوموسيستئين، والبروتين المتفاعل سي، والبيليروبين، في أمراض الشرايين التاجية

نجاة يلماز، هليا كابنورجيجك، أحمد جلك، إجلال مريم، رمضان قوجه باش، وداد داود أوغلو

الخلاصة: أجرى الباحثون تقييماً لثلاث محدِّدات مميّزة جديدة خاصة بأمراض الشرايين التاجية (البيليروبين، والهوموسيستئين الكلي (t-Hcy)، والبروتين المتفاعل سي العالي الحساسية (hs-CRP)، على 319 مريضاً يعانون من آلام بالصدر، قُسِّموا إلى فئتَيْن وفقاً لنتائج تصوير الأوعية التاجية: فئة المصابين بأمراض الشرايين التاجية (262)، وفئة غير المصابين بهذه الأمراض (57) وكانت هناك فئة شاهدة قوامها 50 شخصاً من الأصحاء. وتبيَّن أن أعلى قيمة تشخيصية قد تحقَّقت لدى الفئة التي خضعت لاختبار الهوموسيستئين الكلي من بين المرضى الموثَّق مرضهم بصور الأوعية التاجية، في حين كانت أقل قيمة تشخيصية لدى الفئة التي خضعت لاختبار البيليروبين. وكانت معدلات الحساسية والنوعية للبيليروبين، والبروتين المتفاعل سي العالي الحساسية، والهوموسيستئين الكلي (وفقاً لمنحنيات الخاصية العاملة في المتلقّي): 70.09%، و50%، و76.8% على التوالي، و40.4%، و80.7%، و70.2% على التوالي. ويستنتج من ذلك أنه من غير الممكن التعرُّف على المرضى المُختَطَرين بأمراض الشرايين التاجية من خلال قياس مستويات البيليروبين المصلي، في حين قد تمثِّل اختبارات الهوموسيستئين الكلي، والبروتين المتفاعل سي العالي الحساسية، واسمات أفضل.

ABSTRACT We evaluated 3 new markers for coronary artery disease (CAD) [bilirubin, total homocysteine (t-Hcy) and high-sensitivity C-reactive protein (hs-CRP)] in 319 patients with chest pains divided into 2 groups based on coronary angiography: CAD group (*n* = 262) and non-CAD group (*n* = 57). A control group consisted of 50 healthy subjects. t-Hcy had the highest diagnostic value for diagnosis of angiographically documented patients; bilirubin had the lowest. The sensitivities and specificities (based on ROC curves) of bilirubin, hs-CRP and t-Hcy were 70.9%, 50% and 76.8% respectively, and 40.4%, 80.7% and 70.2% respectively. We conclude that serum bilirubin levels cannot identify people at risk of CAD and t-Hcy and hs-CRP may be stronger markers.

Valeur diagnostique de l'homocystéine, de la protéine C réactive et de la bilirubine dans la maladie coronarienne

RÉSUMÉ Nous avons évalué 3 nouveaux marqueurs de la maladie coronarienne (MC), à savoir la bilirubine, l'homocystéine totale (HcyT) et la protéine C réactive ultrasensible (CRPus) [ou hautement sensible (CRPhs)], chez 319 patients se plaignant de douleurs thoraciques répartis en 2 groupes en fonction des résultats de la coronarographie : le groupe avec MC (n = 262) et le groupe sans MC (n = 57). Un groupe témoin était constitué de 50 sujets sains. En présence d'une MC confirmée par l'angiographie, l'HcyT s'est avérée avoir la plus haute valeur diagnostique, la bilirubine ayant la plus faible. Les courbes ROC (pour *Receiver Operating Characteristic*) montrent pour chacun des trois marqueurs, bilirubine, CRPus et HcyT, respectivement une sensibilité de 70,9 %, 50 % et 76,8 % et une spécificité de 40,4 %, 80,7 % et 70,2 %. Nous en concluons que la bilirubinémie est dans l'incapacité d'identifier les sujets à risque de MC et que l'HcyT et la CRPus peuvent être des marqueurs plus puissants.

[1]Department of Biochemistry; [2]Department of Cardiology, Gaziantep University Medical School, Gaziantep, Turkey (Correspondence to N. Yilmaz: necatyilmaz@hotmail.com).
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Introduction

Coronary artery disease (CAD) often occurs in the absence of traditional risk factors. This study evaluated 3 promising new markers for cardiovascular risk: bilirubin, total homocysteine (t-Hcy) and high-sensitivity C-reactive protein (hs-CRP) [*1,2*]. Natural antioxidant defences have evolved to protect humans against deleterious effects of free radicals. The primary enzymatic defences are intracellular, but other antioxidant defences are largely extracellular, including antioxidative substrates such as uric acid and unconjugated bilirubin, the predominant bile pigment in the intravascular compartment. For many years, the bile pigment was considered as a toxic waste product formed during haem catabolism. However, more recent evidence suggests that bilirubin is a potent physiological antioxidant that may provide important protection against atherosclerosis, CAD and inflammation. In 1994, Schwertner et al. were the first to observe a significant inverse correlation between total bilirubin plasma concentrations and the prevalence of CAD [*3*]. Subsequently, Hopkins et al. noted that patients with early familial CAD had a mean total serum bilirubin of 8.9 (SD 6.1) μmol/L compared with 12.4 (SD 8.1) μmol/L in healthy control subjects [*4*]. Low serum bilirubin concentrations have been shown to be independently and inversely associated with an increased risk for CAD [*3*]. The strength of the association between bilirubin and CAD appears to be similar to that of high-density lipoprotein-cholesterol (HDL-C). The antioxidant capacity of bilirubin and its ability to provide potent scavenging of peroxyl radicals have led to suggestions that mildly increased circulatory bilirubin may have a physiological function to protect against disease processes that involve oxygen and peroxyl radicals [*5,6*]. Antioxidant activity and cardioprotective potential may be attributable to any of the bilirubin forms, including free unconjugated bilirubin, protein-bound unconjugated bilirubin, delta bilirubin or mono- or di-conjugated bilirubin. Under physiological conditions, the predominant circulatory form of bilirubin is the unconjugated, albumin-bound form [*7–9*].

In recent years, "non-traditional factors" such as hs-CRP, total homocysteine, as well as oxidative stress, have been proposed as risk factors for the development and progression of atherosclerosis and atherothrombotic cardiovascular disease [*10–13*]. The purpose of this study was to examine the relationship between traditional and non-traditional biomarkers of CAD in coronary angiography patients and in apparently healthy control subjects.

Methods

Subjects

All patients referred to the Department of Cardiology, University of Gaziantep between March 2003 and August 2003 for whom clinical data were available were included in our study. Thus 319 subjects were included who were admitted to hospital with chest pain and underwent coronary angiography. These patients were divided into 2 groups: the CAD group which consisted of 262 patients (63 females and 199 males) with stenosis of the coronary arteries and the non-CAD group (57 patients; 4 females and 53 males) which consisted of patients in whom CAD was excluded by coronary angiography (degree of stenosis < 20% indicating the absence of clinically relevant coronary stenosis). A third group was recruited which consisted of 50 apparently healthy control subjects (17 females and 23 males). The controls underwent physical

examination and routine laboratory investigation to verify their health status and that they were not taking any drugs. Age- and sex-matched individuals without any clearly evident chronic disease were recruited as control subjects.

Each angiogram was read jointly by at least 2 cardiologists. Coronary artery lesions were magnified, traced and measured with calipers to determine the percentage of diameter narrowing of the artery. All coronary angiographies were performed in the same centre. Patients with CAD were further divided into groups according to the maximum coronary stenosis at angiography: 0%–20% (no detectable CAD), 20%–49% (mild disease), 50%–70% (moderate disease, and 70%–100% (severe disease). Further classification of severity of the disease was done by counting the number of diseased vessels (0 to 3).

All participants were weighed and measured, gave blood samples and were questioned about established cardiovascular risk factors, including diabetes, smoking and hypertension. Although the healthy subjects did not undergo coronary angiograms they had a comprehensive physical examination by a physician, completed the World Health Organization standard Rose questionnaire on chest pain, and answered other questions about their past medical history [*14*]. None of the individuals in the healthy group had angina or a prior history of CAD. All of them had normal electrocardiograms according to the Minnesota Coding Criteria [*14*]. Obesity was defined as a body mass index (BMI) greater than 27.8 kg/m² as proposed by the National Institutes of Health Consensus Statement [*15*]. Diabetes mellitus was considered present in patients with a known history of diabetes and in patients with a fasting glucose ≥ 126 mg/dL (7.0 mmol/L) according to the American Diabetes Association criteria [*16*].

All 50 control subjects were monitored for somatic illness throughout the investigation period and were excluded if symptoms of infection or systemic illness were present (acute or chronic liver disease, cancer, renal disorder, rheumatic disease, etc.). Patients diagnosed with acute coronary syndrome 6 months prior to the study were excluded. Additional exclusion criteria included the use of aspirin, S-adenosyl-methionine, vitamin supplements, alcohol, anticonvulsants, estrogen, lipid-lowering therapy and other medications that might affect bilirubin, CRP and homocysteine metabolism. Thus 319 individuals were included in our patient group after these exclusions.

The study was approved by the Ethics Committee of Gaziantep University, and the individuals participating in the study gave their informed consent.

Laboratory methods

Blood samples of 319 patients and 50 controls (in EDTA tubes and tubes without additives) were taken at the time of admission between 08:00 and 10:00 after an overnight fast. Blood was centrifuged at 3000 g for 10 minutes at 4 ºC. After separation, the aliquots were frozen at –70 °C until analysis.

We measured serum total bilirubin by a diazo method with a detergent to accelerate azo-coupling and to prevent the precipitation of protein. The test was performed by means of an autoanalyser (Hitachi Modular DP Systems, Roche Diagnostics, and Mannheim, Germany). Total bilirubin levels below 1.1 mg/dL are normal for adults. Measurement is linear from 0.1 to 30 mg/dL. The intra-assay imprecision (coefficient of variation) was 1.3% and inter-assay imprecision (coefficient of variation) was 1.9% at a bilirubin concentration of 2.1 mg/dL.

Serum hs-CRP and t-Hcy concentrations were determined with the Immulite® one

analyser and Immulite® reagent (DPC, Los Angeles, USA) according to the manufacturer's instructions. The assays were linear from 2 to 50 μmol/L (t-Hcy) and 10 to 160 mg/L (hs-CRP); calibrators and controls were supplied by manufacturers. Specifications of intra-assay and inter-assay coefficients of variation of hs-CRP and t-Hcy assays were assessed from quality control data of the laboratory, which were 5.3% and 6.0% (intra-assay for hs-CRP), 9.1% and 9.9% (inter-assay for hs-CRP), 1.5% to 3.0% (intra-assay for t-Hcy) and 1.7% to 3.2% (inter-assay for t-Hcy).

Statistical analysis

Summary statistics were evaluated for all variables. Differences between the 3 groups were tested with a *t*-test for independent samples or Mann–Whitney test for continuous variables and a chi-squared test for categorical variables. The difference in current smoking frequency between the groups was tested by the Fisher exact test. Spearman correlation coefficients were obtained for biomarkers and each study variable for CAD patients. To determine independent predictors of the presence of CAD, multivariate logistic regression analysis was done using a model including all variables with a *P*-value < 0.15 on univariate analysis.

None of the results changed if the log of bilirubin and t-Hcy was used instead of the untransformed values. Because the distribution of hs-CRP is rightward skewed, values derived from log-transformed means were used as means for this variable throughout the study; these values virtually coincided with median values. Area under the curve (AUC) values in receiving operating characteristics (ROC) curve (as a measure of discriminating efficacy) were used for comparison of the diagnostic values of different analyses (including only the CAD and non-CAD groups, using angiography as the gold standard). Optimal cut-off levels, sensitivity and specificity of CRP were selected based on the ROC curves. Only 11 women were under age 50 years and there was no difference in bilirubin, hs-CRP and t-Hcy levels between pre- and postmenopausal women. Therefore, these variables were not further considered in the analysis. Two-tailed $P < 0.05$ values were considered. All statistical analyses and illustrations were obtained with *SPSS*, version 9.0 and MedCalc statistical software.

Results

Summary statistics are given for patients with CAD, without CAD (patients with normal angiogram) and for apparently healthy subjects in Table 1. There was no significant difference between the groups in BMI, waist/hip ratio and age. Mean [standard deviation (SD)] serum bilirubin levels were significantly higher in apparently healthy subjects [0.81 (SD 0.32) mg/dL] than patients without CAD [0.52 (SD 0.25) mg/dL] and the patients with CAD [0.55 (SD 0.39) mg/dL] who underwent coronary angiography ($P < 0.01$). However, t-Hcy [10.7 (SD 5.14) μmol/L] and hs-CRP [0.43 (SD 0.61) mg/dL] levels were significantly lower in individuals in the apparently healthy group and the groups undergoing coronary angiography; without CAD [13.0 (SD 8.61) μmol/L, 1.27 (SD 2.78) mg/dL, $P < 0.01$] and CAD [19.4 (SD 8.73) μmol/L, 1.54 (SD 0.87) mg/dL, $P < 0.01$] respectively. Additionally, serum t-Hcy and hs-CRP were significantly higher in patients with CAD compared to those without CAD ($P < 0.05$). Mean serum levels of hs-CRP [1.7 (SD 2.1) mg/dL] and t-Hcy [19.8 (SD 9.6) μmol/L] were highest in the patients who smoked (not shown in the table).

Table 1 **Summary statistics of the groups**

Variable	Healthy controls (*n* = 50)	Patients without CAD (*n* = 57)	Patients with CAD (*n* = 262)
Female (%)[a,b]	34	6	24
Age (years)	50 (8.74)	50 (8.54)	53 (8.48)
Smoking (%)[a,b]	16	19	42
Hypertension (No.)[d]	20	34	39
Diabetes (No.)[c]	0	2	18
Body mass index (kg/m^2)	27.8 (4.96)	28.1 (5.34)	27.8 (3.96)
Waist/hip ratio	0.91	0.92	0.95
Total bilirubina (mg/dL)	0.81 (0.32)	0.52 (0.25)	0.55 (0.39)
Total homocysteine (μmol/L)[a,b]	10.7 (5.14)	13.0 (8.61)	19.4 (8.73)
High-sensitivity C-reactive protein (mg/dL)[a,b]	0.43 (0.61)	1.27 (2.78)	1.54 (0.87)
Lipoprotein little A antigen (g/L)[a,b]	0.23 (0.24)	0.31 (0.32)	0.43 (0.33)
White blood cells (10^3/μL)[d]	7219 (1768)	7903 (1997)	8316 (2527)
Total cholesterol (mg/dL)[b]	174 (42.12)	170 (36.95)	188 (42.88)
Triglycerides (mg/dL)[b]	170 (87.13)	156 (69.25)	199 (113.33)
High-density lipoprotein cholesterol (mg/dL)[c,a]	43 (11.12)	34 (8.31)	31 (7.93)
Uric acid (mg/dL)[d]	5.5 (1.24)	6.1 (49.06)	6.4 (1.81)
Glucose (mg/dL)[d]	86 (13.27)	103 (20.21)	113 (58.50)
Aspartate aminotransferase (U/L)	32 (12.55)	34 (11.27)	39 (39.58)
Creatine kinase-MB (U/L)	26 (24.29)	26 (17.67)	32 (26.39)
Urea (mg/dL)	35 (9.78)	34 (11.27)	38 (17.81)
Platelets(10^3/μL)	263 (86.53)	249 (63.87)	268 (66.33)
Haemoglobin (g/dL)	13.9 (1.76)	13.5 (1.55)	13.9 (1.39)
Haematocrit (%)	40.7 (4.34)	39.9 (4.70)	40.8 (3.80)

[a]*Healthy control group versus patients without CAD and those with CAD;* P < *0.01.*
[b]*Patients without CAD versus patients with CAD;* P < *0.05.*
[c]*Healthy control group versus patients with CAD;* P < *0.001.*
[d]*Patients with CAD versus healthy control group;* P < *0.05.*
Values are means (standard deviations) except where indicated otherwise.
CAD = coronary artery disease.

Correlation coefficients of biomarkers of CAD in patients in whom CAD was angiographically documented are given in Table 2. There was a negative correlation between bilirubin and sex (male) (r = –0.183, P < 0.01 and r = –0.199, P < 0.01 respectively); in contrast, a significant positive correlation between bilirubin and serum t-Hcy concentrations was found (r = 0.330, P < 0.001). Bilirubin was also significantly correlated with triglycerides (r = –0.183, P < 0.01) and uric acid (r = 0.127, P < 0.05), but was not significantly correlated with any other study variable.

Table 2 **Correlation coefficients of biomarkers of coronary artery disease (CAD) in patients diagnosed by angiography (Spearman coefficients)**

Variable	Bilirubin	Total homocysteine	High-sensitivity C-reactive protein
Body mass index (kg/m^2)	NS	NS	NS
Sex (male/female)	r = –0.199**	r = 0.219***	r = 0.145**
Age (years)	NS	r = 0.158**	r = 0.267***
Smoking	NS	r =0.136*	NS
High-sensitivity C-reactive protein (mg/dL)	NS	r = 0.466***	–
Total homocysteine (μmol/L)	r = 0.330***	–	r = 0.466***
Bilirubin (mg/dL)	–	r = 0.330***	NS
Lipoprotein little A antigen (g/L)	NS	NS	r = 0.200***
White blood cells (10^3/μL)	NS	r = 0.138*	r = 0.250***
Total cholesterol (mg/dL)	NS	r = 0.129*	NS
Triglycerides (mg/dL)	r = –0.183**	NS	NS
High-density lipoprotein cholesterol (mg/dL)	NS	NS	r = 0.140**
Uric acid (mg/dL)	r = 0.127*	r = 0.150**	r = 0.150**
Stenotic vessels (No.)	NS	r = 0.450***	NS

**Significant at* P < *0.05; **Significant at* P < *0.01; ***Significant at* P < *0.001.*
NS = not significant.

Total Hcy and hs-CRP concentrations showed many correlations with other study parameters (Table 2). There was a positive correlation between serum t-Hcy and sex, age, smoking, hs-CRP and number of stenotic vessels. In addition there was positive correlation between hs-CRP and sex, age and t-Hcy.

The predictor variables obtained by regression analysis for the number of stenotic vessels in CAD patients are given in Table 3. Sex (male, P = 0.001), age (P = 0.004) and t-Hcy (P = 0.0001) were strongly correlated with the number of stenotic vessels (severity of disease); hypertension (P = 0.019) was moderately associated, and HDL-C (P = 0.022), glucose (P = 0.028), total cholesterol (P = 0.047) were weakly associated. Bilirubin, hs-CRP and other parameters were not related to the number of diseased vessels and the degree of occlusion (P > 0.05).

Optimal cut-off levels and the associated diagnostic performances (sensitivity, specificity and diagnostic value) of serum bilirubin, hs-CRP, t-Hcy, based on ROC analysis, are given in Table 4. Optimal cut-off levels for bilirubin, hs-CRP and t-Hcy providing the maximum efficiency found in patients (n = 319) with CAD were 0.59 mg/dL, 1.09 mg/dL and 12.1 μmol/L respectively. ROC curve-based sensitivities

Table 3 **Regression analysis: predictor variables for the number of stenotic vessels in patients with coronary artery disease**

Variable	Beta	Standard error of the mean	*P*-value
Sex (male)	0.396	0.163	0.0001
Age (years)	0.166	0.008	0.004
Smoking	0.018	0.153	0.782
Body mass index (kg/m^2)	–0.007	0.015	0.894
Hypertension	0.141	0.142	0.019
Total bilirubin (mg/dL)	–0.057	0.177	0.336
Total homocysteine (μmol/L)	0.213	0.213	0.0001
High-sensitivity C-reactive protein (mg/dL)	0.028	0.032	0.631
Lipoprotein little A antigen (g/L)	0.083	0.200	0.152
Uric acid (mg/dL)	–0.033	0.038	0.587
Triglycerides (mg/dL)	0.097	0.001	0.130
Total cholesterol (mg/dL)	0.122	0.002	0.047
High-density lipoprotein cholesterol (mg/dL)	0.172	0.000	0.022
Glucose (mg/dL)	0.128	0.001	0.028
White blood cells (10^3/μL)	0.007	0.000	0.906

of bilirubin, hs-CRP and t-Hcy levels were 70.9%, 50.0%, 76.8% respectively. The specificities of bilirubin, hs-CRP and t-Hcy were 40.4%, 80.7% and 70.2% respectively (data of ROC curves are shown in Figures 1–3).

Discussion

To the best of our knowledge, the present study is the first to assess the diagnostic performance and relationship of bilirubin with hs-CRP and t-Hcy for cardiovascular disease in men and women in an angiographically documented design. The study demonstrated that patients with angiographically confirmed CAD had significantly higher serum hs-CRP and t-Hcy levels than non-stenotic patients (patients with normal angiogram) and the apparently healthy control group. These data strongly suggest that serum t-Hcy helps to identify individuals at risk of atherosclerosis (AUC value 0.781), especially among those with elevated hs-CRP and decreased bilirubin levels. t-Hcy showed the highest AUC value (0.781) compared to hs-CRP (0.648) and bilirubin (0.507).

In agreement with previous reports, we found that the bilirubin levels in serum were significantly lower in the patients with CAD than in age- and sex-matched controls [*3,17,18*]. We found that a serum bilirubin concentration of 10.0 μmol/L (0.58 mg/dL) discriminated between high and low cardiovascular risks. This association was

Table 4 **Optimal cut-off levels and associated specificity, sensitivity and diagnostic value of concentrations of biomarkers for the diagnosis of angiographically documented coronary artery disease**

Variable	Cut-off level	Sensitivity (%)	Specificity (%)	Diagnostic value (area under the curve)	+LR	–LR
Bilirubin	0.59 mg/dL	70.9	40.4	0.507	1.19	0.72
White blood cells	6700 $10^3/\mu L$	70.0	38.8	0.535	1.14	0.77
Uric acid	4.5 mg/dL	88.7	28.1	0.578	1.23	0.45
High-density lipoprotein cholesterol (female)	31 mg/dL	64.9	47.1	0.598	1.22	0.75
High-density lipoprotein cholesterol (male)	25 mg/dL	28.5	95.0	0.599	5.70	0.75
Total cholesterol	184 mg/dL	52.6	73.6	0.630	1.99	0.64
Lipoprotein little A antigen	0.24 g/L	59.5	64.9	0.630	1.70	0.62
Triglycerides	144 mg/dL	65.4	58.2	0.631	1.56	0.59
High-sensitivity C-reactive protein	1.09 mg/dL	50.0	80.7	0.648	2.59	0.62
Total homocysteine	12.1 μmol/L	76.8	70.2	0.781	2.67	0.29

+LR = positive likelihood ratio.
–LR = negative likelihood ratio.

independent of the extent of CAD, BMI, diabetes, hypertension and smoking. Individuals in the top quintile of serum bilirubin concentration had an 80% reduction of the CAD risk compared with individuals in the lowest quintile [*4*]. In 1995, Breimer et al. performed a prospective study of 7685 middle-aged men enrolled in the British Regional Heart Study and found that both low and high bilirubin concentrations were associated with an increased risk of CAD [*7*]. More recently, Vitek et al. reported on the prevalence of CAD in individuals with Gilbert syndrome who were found to have a CAD prevalence of 2% compared with 12.1% in the general population [*18*]. A meta-analysis of 11 studies has shown a negative relationship between serum bilirubin concentration and severity of atherosclerosis in men ($r = –0.31$, $P < 0.0001$) [*19*] but we did not find such an association in either men or women. However, we found that the number of stenotic coronary arteries was significantly associated with elevated serum t-Hcy and hs-CRP concentration. Several researchers have investigated the risk of myocardial infection in individuals with the *UGT1A1*28* allele [*20,21*]. According to the "oxidative modification hypothesis", which suggests atherogenesis is initiated by oxidization of low-density lipoprotein particles, it has been suggested that increased physiological concentrations of serum bilirubin may reduce atherogenic risk by reducing oxidation. An involvement of bilirubin in immune reactions and inflammatory processes has also been documented [*22–24*]. Smoking causes oxidative stress and production of acute phase reactants, such as CRP, temporary ischaemia, repeti-

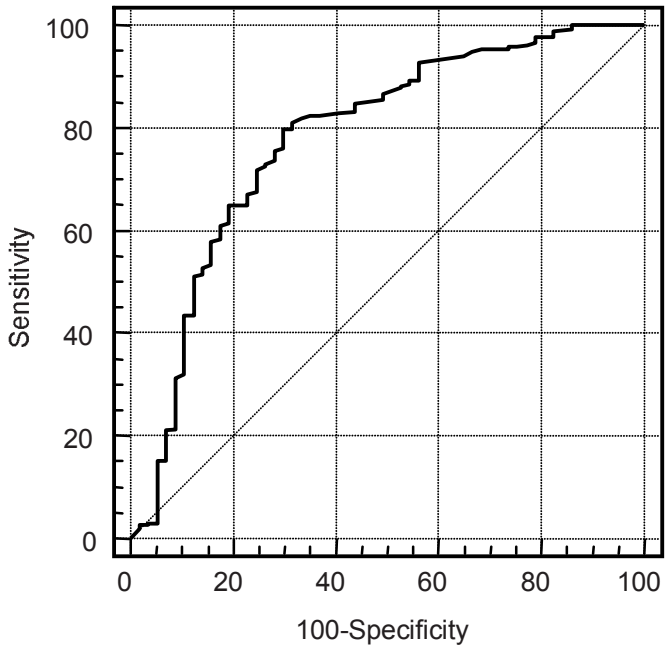

Figure 1 **ROC curve of total homocysteine**

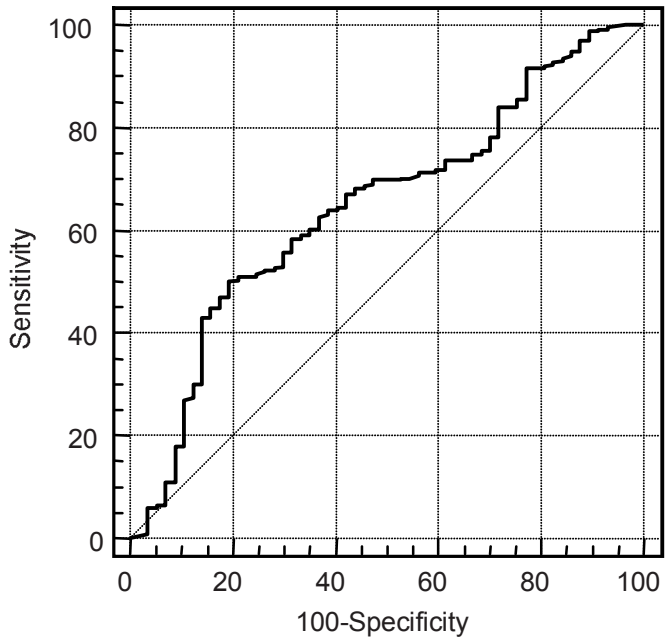

Figure 2 **ROC curve of high-sensitivity C-reactive protein**

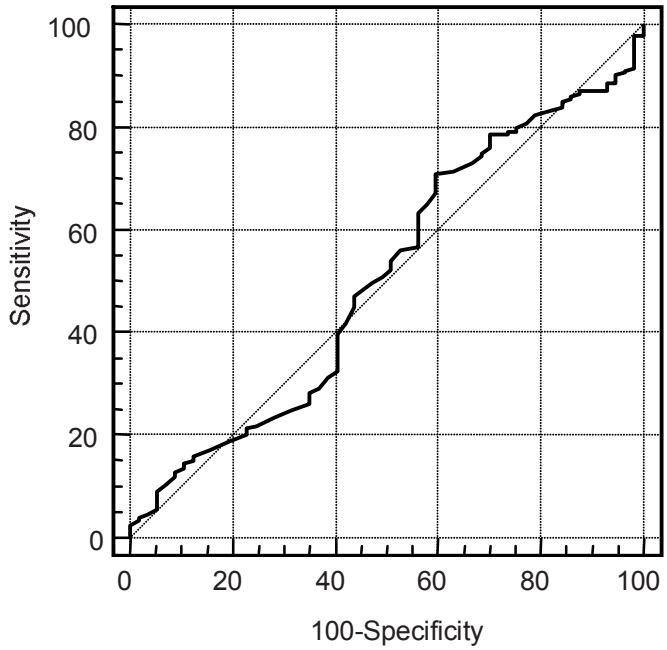

Figure 3 **ROC curve of total bilirubin**

tion of inflammation and reactive oxygen species. Thus, these factors constitute endothelial injury, which increases platelet aggregation, abnormalities of fibrinolysis and smooth muscle cell proliferation, and accelerate the development of thrombosis and atherosclerosis [*25,26*].

Earlier studies have reported differences in the levels of t-Hcy, ranging from 13.9–20.1 μmol/L in persons with CAD [*27,28*]. We found a mean t-Hcy level of 19.4 (SD 8.73) μmol/L in the CAD group, 10.7 (SD 5.14) μmol/L in the healthy group and 13.0 (SD 8.61) μmol/L in the non-CAD group. Some differences between reported serum t-Hcy levels may be related to analytical methods and ethnic differences. Bortolotto et al. grouped patients as hypertensive and hypertensive plus CAD. When compared, the plasma t-Hcy levels were significantly higher in the hypertensive plus CAD group [*29*]. Our study agrees with this study in that we obtained a similar association. The regression coefficient of hypertension with arterial blood pressure was 0.141 (SEM 0.142), $P = 0.019$. Also, homocysteine enhances oxidative stress. A study in 19 centres in Europe reported high homocysteine levels and increased risk of CAD in smokers [*30*]. We found that the t-Hcy levels tended to increase in the presence of more cardiovascular risk factors, i.e. male gender, older age, diabetes mellitus, hyperlipidaemia and certain chronic diseases. As expected, traditional coronary risk factors were more prevalent among those participants with elevated levels of t-Hcy and hs-CRP in our study, as in other studies [*31–33*]. More recently, McConnell et al. [*34*] and Lear et al. [*35*] have reported gender differences in C-reactive protein. The observed gender differences have important

implications for the establishment of cut-off points for cardiovascular risk stratification [*36*]. We found that lower total serum bilirubin was associated with a higher risk of CAD among men, but the pattern was much clearer in women (Table 2). Contrary to the findings of Djoussé et al. [*13*], our study provides only suggestive evidence for a lower risk for women. However, the relatively small number of CAD cases in women means that our study had less statistical power in women. Women may be more susceptible to low levels of bilirubin. The fact that the median age at baseline was 50 years in women indicates that most of the women in our study were postmenopausal. It is possible that in this older age group, the effects of bilirubin are not off-set by those of estrogen.

A plausible biological mechanism is necessary to support a causal association between serum bilirubin and CAD outcome. The levels of bilirubin may be related to an inflammatory condition in patients with CAD [*37,38*]. Another possibility is that low bilirubin concentration is not *per se* a major causative factor in the development of CAD, but rather a reflection of the presence of this ailment. According to this view, low bilirubin is a result of increased oxidative activity in CAD-prone individuals, leading to consumption of a natural antioxidant such as bilirubin [*39–41*]. Our data suggest that serum bilirubin concentration is more closely associated with the oxidative stress marker serum uric acid level [–0.033 (SEM 0.038), $P < 0.587$] than smoking. These findings conflict with those that have found subjects who smoke and have low serum bilirubin antioxidant concentrations [*20*]. Problems in risk assessment also arise from overlapping properties (shared pathophysiological pathway) of traditional risk factors such as hypertension, obesity, age, gender, smoking and diabetes [*42–49*].

To conclude, we found little evidence of an association between the serum concentration of bilirubin and atherosclerosis. In contrast, the concentration of novel (t-Hcy and hs-CRP) and traditional risk markers may be stronger markers for atherosclerosis in CAD patients.

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Regional consultation on establishing guidelines on management and care for acute coronary conditions

The World Health Organization Regional Office for the Eastern Mediterranean organized the above-mentioned regional consultation to establish guidelines on the management and care for acute coronary conditions, in Cairo, Egypt, from 27 to 29 March 2007.

The objectives of the consultation were:

- to review the progress made in the management and care of acute coronary conditions among countries of the Regions; and
- to set regional strategies for the management and care of acute coronary conditions.

Experts from Egypt, Islamic Republic of Iran, Lebanon, Pakistan, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates, United Kingdom, as well as WHO concerned staff, participated in the consultation.

Distribution des facteurs de risque cardio-vasculaire chez des patients coronariens dans le Sahel tunisien

M. Lihioui,[1] E. Boughzala,[2] M. Ben Farhat,[3] H. Ammar,[4] A. Chaouech,[5] R. Jemaa[1] et N. Kaabachi[1]

توزُّع عوامل اختطار الإصابة بالأمراض القلبية الوعائية لدى مرضى الشرايين التاجية في منطقة الساحل، بتونس

مراد لحيوي، آسية بوغزالة، محمد بن فرحات، حبيب عمار، عبد الرزاق شاوش، رياض جمعة، نزيهة كعباشي

الخلاصة: قام الباحثون بتقييم عوامل اختطار الإصابة بالأمراض القلبية الوعائية وارتباطها بحالات المرضى الذين أدخلوا إلى المستشفى للعلاج من أمراض تاجية، خلال الفترة ما بين عامَيْ 1994 و1998. وأُجري، لدى الدخول إلى المستشفى، تحليل للسمات السريرية (الإكلينيكية) لـ 3455 مريضاً (72.4% منهم من الرجال؛ 1741 منهم مصابون باحتشاء عضلة القلب، و1714 يعانون من ذبحة غير مستقرة). وتبيّن انتشار التدخين، وخلل استقلاب البروتينات الشحمية، وارتفاع ضغط الدم، والسكّري، والبدانة، بمعدل 77.4%، 39.4%، 28.5%، 42.5%، 25.1% على التوالي، بين الرجال، و2.9%، 43.7%، 59.2%، 56.6%، 31.9% على التوالي، بين النساء. واستناداً إلى هذا المُرْتَسَم المتعلق بعوامل الاختطار، فإن الحاجة قائمة لوضع استراتيجية وطنية للوقاية الأوَّلية من هذه الأمراض وتعزيز صحة القلب، في تونس.

RÉSUMÉ Le but de ce travail était de déterminer la distribution des facteurs de risque cardio-vasculaire dans la région du Sahel chez des malades hospitalisés pour maladie coronaire entre 1994 et 1998. Les caractéristiques à l'entrée à l'hôpital de 3455 patients (72,4 % d'hommes ; 1741 infarctus du myocarde et 1714 angors instables) ont été étudiées. La fréquence du tabagisme, de la dyslipidémie, de l'hypertension artérielle, du diabète et de l'obésité était respectivement de 77,4 %, 39,4 %, 28,5 %, 42,5 % et 25,1 % chez les hommes et de 2,9 %, 43,7 %, 59,2 %, 56,6 % et 31,9 % chez les femmes. Avec ce profil de risque cardio-vasculaire, la Tunisie devrait conforter davantage son programme global de prévention primaire et de promotion de la santé cardio-vasculaire.

Distribution of cardiovascular risk factors in coronary patients in Sahel Tunisia

ABSTRACT We evaluated cardiovascular risk factors and their association in patients in Sahel, hospitalized for coronary disease over the period 1994–1998. The clinical features of 3455 patients (72.4% men, 1741 with myocardial infarction, 1714 with unstable angina) were analysed on hospital admission. The prevalence of smoking, dyslipidaemia, hypertension, diabetes and obesity was 77.4%, 39.4%, 28.5%, 42.5% and 25.1% respectively in men and 2.9%, 43.7%, 59.2%, 56.6% and 31.9% respectively in women. With this risk factor profile a national strategy of primary prevention and heart health promotion is needed in Tunisia.

[1]Laboratoire de recherche LAB-SM-01, Service de Biochimie, Hôpital La Rabta, Tunis (Tunisie). (Correspondance à adresser à R. Jemaa : jemaa_riadh@yahoo.fr).
[2]Service de cardiologie, Hôpital Sahloul, Sousse (Tunisie).
[3]Service de cardiologie, Hôpital Fattouma Bourguiba, Monastir (Tunisie).
[4]Service de cardiologie, Hôpital Farhat Hached, Sousse (Tunisie).
[5]Service de cardiologie, Hôpital Tahar Sfar, Mahdia (Tunisie).
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Introduction

Les maladies cardio-vasculaires sont la cause principale de morbidité et de mortalité dans les pays industrialisés. Elles sont à l'origine de 41 % de décès [*1,2*] et la majorité des décès d'origine cardio-vasculaire est due à l'insuffisance coronaire : la pathologie coronaire est la première cause de mortalité chez les hommes de plus de 45 ans et chez les femmes de plus de 65 ans [*3*]. Pour permettre d'importants progrès en matière de traitement et de prévention des maladies cardio-vasculaires, il faut axer la recherche sur la compréhension des mécanismes qui sont à la base du développement de ces maladies et s'appuyer sur des études épidémiologiques de grande ampleur pour identifier les facteurs de risque internes et externes.

Avec le développement socioéconomique et de l'infrastructure sanitaire, la Tunisie est en pleine phase de transition épidémiologique [*4*]. Cette transition est caractérisée par une baisse des taux de mortalité, une augmentation de l'espérance de vie, une modification des causes de mortalité au profit des maladies chroniques non transmissibles, les maladies cardio-vasculaires en particulier. Un diagnostic de situation s'impose pour quantifier l'ampleur du problème et étudier la meilleure stratégie de prévention. Nous avons entrepris une étude populationnelle en milieu hospitalier pour décrire la fréquence de différentes pathologies cardio-vasculaires et leurs facteurs de risque associés.

Dans cette partie du travail, qui implique tous les services hospitalo-universitaires de cardiologie situés dans la région du Sahel en Tunisie et qui regroupe les gouvernorats de Sousse, Monastir et Mahdia, nous avons étudié la fréquence et la distribution des principaux facteurs de risque cardio-vasculaire chez des sujets coronariens hospitalisés entre 1994 et 1998.

Méthodes

Cette étude s'est adressée à tous les patients ayant fait un infarctus du myocarde (IDM) ou un angor instable et admis en unités de soins intensifs cardiologiques (USIC) des hôpitaux Sahloul et Farhat Hached à Sousse, de l'hôpital Fattouma Bourguiba à Monastir et de l'hôpital Tahar Sfar à Mahdia entre 1994 et 1998. Un patient était considéré comme atteint d'un infarctus du myocarde s'il avait au moins 2 des éléments suivants : douleur angineuse typique au repos pendant au moins 30 min ; élévation du segment ST $\geq$ 0.1 mV dans 2 dérivations contiguës frontales ou $\geq$ 0.2 mV dans 2 dérivations précordiales contiguës à l'électrocardiogramme (ECG) ; apparition d'une onde Q de nécrose au décours de la douleur ; élévation des créatines phosphokinases (CPK) à plus de deux fois la normale.

Un patient était considéré comme ayant un angor instable s'il avait un des éléments suivants : angor de repos ; angor d'effort accéléré, brutalement aggravé ; angor d'effort de novo.

Les données cliniques, biologiques et familiales des patients (sexe, âge, poids, taille, hypertension artérielle, diabète, tabac, alcool, antécédents familiaux et personnels de cardiopathie ischémique, profession, lieu de naissance, lieu de résidence) ont été analysées de façon rétrospective à partir des dossiers médicaux.

L'obésité a été définie par un indice de masse corporelle (IMC) $\geq$ 25,8 kg/m^2 chez la femme et 26,4 kg/m^2 chez l'homme, soit un surpoids supérieur ou égal à 20 % d'après les tables de 1959 de la *Metropolitan Life Insurance Company* [*5*], déterminé sur les valeurs du poids et de la taille mesurés pendant l'hospitalisation. Les autres facteurs de risque (diabète, hypertension, dyslipidémie et tabagisme) étaient déterminés d'après les informations contenues dans l'observation médicale ainsi que par l'analyse des médi-

caments prescrits. L'hypertension artérielle (HTA) a été définie par l'existence d'un traitement antihypertenseur en cours ou en fonction des recommandations de l'OMS [*6*], comme l'existence d'une pression artérielle systolique ≥ 140 mmHg ou d'une pression artérielle diastolique ≥ 90 mmHg notées à plusieurs reprises jusqu'à la fin de l'hospitalisation. L'existence d'un diabète était déterminée par une glycémie à jeun ≥ 1,26 g/L ou un traitement antidiabétique en cours [*7*]. La dyslipidémie était définie par une valeur du cholestérol total > 2 g/L et/ou des triglycérides > 1,5 g/L et une valeur du LDL-cholestérol > 1,6 g/L ou un traitement hypolipémiant en cours. Les valeurs lipidiques étaient élevées dans tous les bilans pratiqués régulièrement au cours de l'hospitalisation. Le tabagisme a été défini à partir de l'interrogatoire lors de l'admission ou du dossier médical préexistant.

Les données ont été saisies et analysées sur SYSTAT (*System for statistics*, version 5). Les données ont été exprimées en moyenne ± écart réduit ou en nombre de sujets et pourcentage (%). L'analyse des variables qualitatives a été réalisée par le test du χ^2, alors que l'analyse des données quantitatives a fait appel au test *t* de Student ou à l'analyse de variance. Dans tous les cas, un seuil de significativité de 5 % a été utilisé.

Résultats

L'échantillon représentait la totalité des patients admis entre 1994 et 1998 pour insuffisance coronaire aiguë dans les services de cardiologie des quatre centres hospitalo-universitaires de la région du Sahel en Tunisie, soit environ le tiers de l'ensemble des patients hospitalisés pour cette pathologie en Tunisie. Les données de 3455 patients (1741 IDM et 1723 angors instables) ont été analysées. Leur description selon le type de pathologie (IDM ou angor instable) et en fonction de l'âge est indiquée au tableau 1. Les hommes qui représentent 72,4 % de la population totale sont âgés en moyenne de 59,9 ans (E.T. 12,3) (extrêmes : 20 et 97 ans) et les femmes de 63,1 ans (E.T. 10,7) (extrêmes : 24 et 100 ans).

La figure 1 montre les principaux facteurs de risque cardio-vasculaire dans l'ensemble de l'échantillon et par sexe. Il y a une différence statistiquement significative de la prévalence de l'HTA entre les femmes (59,2 %) et les hommes (28,5 %), $p < 0,001$. Le diabète est retrouvé chez 46,4 % et les femmes sont significativement plus souvent atteintes (56,4 %) que les hommes (42,5 %), $p < 0,001$. L'obésité a été retrouvée dans 27 % des cas. Elle est significativement plus fréquente chez les femmes (31,9 %) que chez les hommes (25,1 %), $p < 0,001$. La dyslipidémie a été retrouvée dans 40,6 % des cas, avec une prévalence plus élevée chez les femmes (43,7 %) par rapport aux hommes (39,4 %), $p < 0,025$.

Tableau 1 **Caractéristiques des sujets selon le diagnostic et l'âge**

Caractéristique	IDM (n = 1741)		Angor instable (n = 1714)	
	Nbre	%	Nbre	%
Sexe				
Hommes	1404	80,6	1097	64
Femmes	337	19,4	617	36
Classe d'âge (ans)				
< 35	22	1,3	37	2,2
35-44	135	7,7	192	11,2
45-54	304	17,5	374	21,8
55-64	519	29,8	531	30,9
65-74	508	29,2	441	25,7
75 -84	230	13,2	116	6,8
≥ 85	23	1,3	23	1,3
Âge (ans)				
Moyenne (E.T.)	61,8	(11,8)	58,7	(11,9)

IDM = infarctus du myocarde.

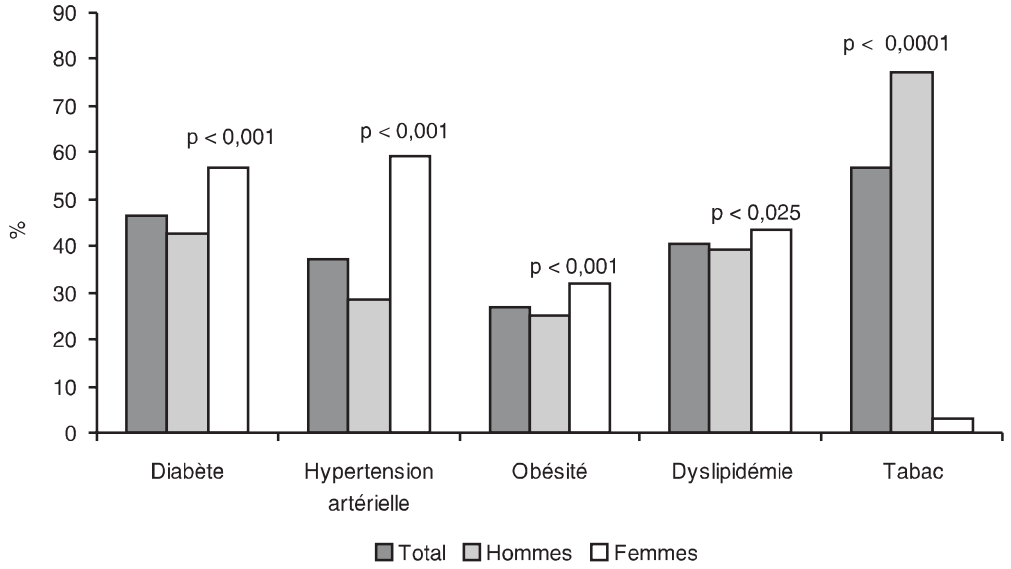

Figure 1 **Prévalence (%) des principaux facteurs de risque cardio-vasculaire dans la population totale et selon le sexe**

L'hypercholestérolémie se retrouve chez 15,8 % des sujets, l'hypertriglycéridémie chez 8,5 % et la dyslipidémie mixte chez 16,3 %.

Le tabagisme a été retrouvé dans 56,8 % des cas. Les hommes sont significativement plus souvent fumeurs (77,4 %) que les femmes (2,9 %), $p < 0,0001$; 8,2 % des sujets fument entre 1 et 10 paquets/année, 18,8 % fument entre 11 et 20 paquets/année, 54,8 % fument entre 21 et 50 paquets/année et 18,1 % fument plus de 50 paquets/année.

L'association chez la même personne entre les facteurs de risque étudiés a montré que 7,7 % des sujets coronariens n'ont aucun facteur de risque, 26,3 % ont un seul facteur de risque, 30,5 % en ont deux, 23,9 % en ont trois, 9,9 % en ont quatre et 1,5 % ont cinq facteurs de risque. La distribution des facteurs de risque chez l'homme et selon l'âge est indiquée au tableau 2. La prévalence du tabagisme est élevée à tous les âges, variant de 81,8 % pour la tranche d'âge inférieure à 35 ans à 62,5 % pour la tranche d'âge supérieure à 85 ans. Le pourcentage de coronariens hypertendus augmente avec l'âge, passant de 1,8 % chez les moins de 35 ans à plus de 35 % lorsqu'on dépasse les 75 ans. Il en est de même pour la prévalence du diabète, qui représente moins de 10 % chez les moins de 35 ans, pour atteindre 49,8 % dans la tranche d'âge 55-64 ans et baisse ensuite à 25,0 % chez les plus de 85 ans. Pour la dyslipidémie, les valeurs sont élevées et croissantes jusqu'à 54 ans pour décroître ensuite progressivement au delà de cet âge. Il en est de même pour l'obésité qui suit la même évolution que la dyslipidémie. La distribution des facteurs de risque chez la femme selon l'âge est indiquée au tableau 3.

Tableau 2 **Distribution des facteurs de risque selon l'âge chez les hommes**

Facteur de risque	< 35 ans (n = 55) Nbre (%)	35-44 ans (n = 285) Nbre (%)	45-54 ans (n = 526) Nbre (%)	55-64 ans (n = 735) Nbre (%)	65-74 ans (n = 644) Nbre (%)	75-84 ans (n = 232) Nbre (%)	≥ 85 ans (n = 24) Nbre (%)	Total (n = 2501) Nbre (%)
Tabagisme	45 (81,8)	234 (82,1)	433 (82,3)	567 (77,1)	477 (74,0)	166 (71,5)	15 (62,5)	1937 (77,4)
Hypertension	1 (1,8)	20 (7,0)	107 (20,3)	247 (33,6)	250 (38,8)	82 (35,3)	6 (25,0)	713 (28,5)
Diabète	5 (9,1)	75 (26,3)	227 (43,1)	366 (49,8)	294 (45,6)	90 (38,8)	6 (25,0)	1063 (42,5)
Obésité	15 (23,8)	71 (24,9)	179 (34,0)	220 (29,9)	118 (18,3)	23 (9,9)	2 (13,3)	628 (25,1)
Dyslipidémie	14 (25,4)	125 (43,8)	247 (46,9)	325 (44,2)	217 (33,7)	54 (23,2)	4 (16,6)	986 (39,4)

Les résultats sont exprimés sur deux lignes : la première correspond au nombre de sujets présentant le facteur de risque, la deuxième ligne correspond au pourcentage dans la classe d'âge considérée.

Tableau 3 **Distribution des facteurs de risque selon l'âge chez les femmes**

Facteur de risque	< 35 ans (n = 4) Nbre (%)	35-44 ans (n = 42) Nbre (%)	45-54 ans (n = 152) Nbre (%)	55-64 ans (n = 315) Nbre (%)	65-74 ans (n = 305) Nbre (%)	75-84 ans (n =114) Nbre (%)	≥ 85 ans (n = 22) Nbre (%)	Total (n = 954) Nbre (%)
Tabagisme	0 (0,0)	5 (8,4)	7 (4,6)	5 (1,6)	6 (2,0)	4 (3,5)	1 (4,5)	28 (2,9)
Hypertension	1 (25,0)	16 (38,1)	71 (46,7)	199 (63,2)	191 (62,6)	75 (65,8)	13 (59,1)	565 (59,2)
Diabète	0 (0,0)	16 (38,1)	75 (49,3)	198 (62,8)	177 (58,1)	65 (57,0)	9 (40,9)	540 (56,6)
Obésité	0 (0,0)	16 (38,1)	65 (42,7)	127 (40,3)	80 (26,2)	15 (13,2)	2 (9,1)	305 (32,0)
Dyslipidémie	0 (0,0)	14 (33,3)	73 (48,0)	154 (48,8)	128 (42,0)	42 (36,8)	6 (27,3)	417 (43,7)

Les résultats sont exprimés sur deux lignes : la première correspond au nombre de sujets présentant le facteur de risque, la deuxième ligne correspond au pourcentage dans la classe d'âge considérée.

Chez les femmes du groupe d'âge 35-44 ans, la prévalence de l'hypertension artérielle (38,1 % vs 7,0 %), du diabète (38,1 % vs 26,3 %), et de l'obésité (38,1 % vs 24,9 %) est plus élevée que celle observée chez les hommes pour la même tranche d'âge, alors que la prévalence du tabagisme (8,4 % vs 82,1 %) et de la dyslipidémie (33,3 % vs 43,8 %) est plus basse. Toutefois, l'évolution de la prévalence des différents facteurs de risque reste croissante avec l'âge chez les deux sexes.

Discussion

Pendant longtemps, l'étude des maladies cardio-vasculaires et leurs facteurs de risque ne concernaient que les sociétés développées [*8,9*], puisqu'il n'existe pas de données fiables sur la fréquence, en termes de morbidité et de mortalité, des maladies cardio-vasculaires dans les pays en développement. L'étude des maladies cardio-vasculaires et des facteurs de risque associés en Tunisie est intéressante à plus d'un titre. D'abord, très peu de données épidémiologiques sont disponibles pour quantifier le problème en Tunisie, à part quelques études en milieu semi-urbain [*10*] et urbain [*4,11*] et touchant un nombre réduit de sujets ou s'intéressant à un seul facteur de risque [*12*] comme le diabète ou l'hypertension artérielle. Ensuite, des données de ce type confirment le phénomène de transition épidémiologique, ce qui devrait permettre au pays de mieux organiser son système de santé pour faire face à cette nouvelle pathologie chronique et coûteuse et d'entreprendre des actions de prévention efficaces à l'échelle du pays entier, comme cela a été le cas pour les pays à forte mortalité cardio-vasculaire [*13,14*]. Par ailleurs, très peu de données publiées existent à ce jour sur la prévalence en milieu hospitalier des différentes pathologies cardio-vasculaires et de leurs facteurs de risque. Notre étude, qui porte sur une cohorte de 3455 patients originaires de la région du Sahel en Tunisie et hospitalisés pour maladie coronaire, montre un profil de risque cardio-vasculaire qui rappelle, et dépasse pour certains facteurs comme le diabète ou le tabagisme, celui des pays développés et traditionnellement exposés au fléau des maladies cardio-vasculaires comme la France (HTA 49,9 %, diabète 17,6 % chez des patients angineux [*15*], ou encore HTA 42,1 %, diabète 19,2 % chez des sujets coronariens [*16*]). Aux États-Unis, la prévalence du diabète était de 26 % chez les hommes et de 21 % chez les femmes [*17*]. Dans une autre étude décrivant des patients angineux suivis au Royaume-Uni, l'HTA y est rapportée chez 48 % des malades, le diabète chez seulement 9 % des patients [*18*].

Le pourcentage des malades hypercholestérolémiques (12,4 %) est nettement inférieur à celui de l'étude américaine où 34 % des patients étaient concernés, sans différence entre les hommes et les femmes. Il l'est encore davantage, comparé aux études françaises ELAN (Étude longitudinale dans l'ANgor) [*15*] et CORALI [*19*] (57 %) et à l'étude européenne EUROASPIRE (*European Action on Secondary Prevention through Intervention to Reduce Events*) [*20*] où il atteint 71 % des patients européens et 73 % des patients français. Cette différence avec nos propres résultats est partiellement liée aux particularités alimentaires de chaque population.

L'obésité est retrouvée chez 18,7 % des patients, pourcentage supérieur à celui de l'étude ELAN (14,8 %) et l'étude PREVENIR (10,9 %). Quant au tabagisme, il est noté chez 68,3 % des malades ; ce pourcentage est nettement supérieur à celui de l'étude PREVENIR (48,8 %), à celui de l'étude ELAN et de l'étude EUROASPIRE (18 %) et à celui de l'étude CORALI. Dans cette dernière étude datant des années

1987-89, 59 % des patients fumaient plus de 10 cigarettes par jour. La fréquence particulièrement élevée du tabagisme chez les hommes (77,4 % vs 2,9 %) explique en grande partie leur plus grande susceptibilité à développer des cardiopathies ischémiques surtout par rapport aux femmes post-ménopausées. Le taux de tabagisme chez les hommes (77,4 %) excède en effet celui des États-Unis (43 %) [*21*] et celui de la plupart des pays de la communauté européenne (41 %), à l'exception de la Grèce (61 %) [*22*]. La femme demeure encore préservée, contrairement aux pays développés.

Conclusion

Les résultats de notre étude sur la région du Sahel en Tunisie confirment les résultats déjà publiés et portant sur la région du grand Tunis [*23*], et montrent que la prévalence des facteurs de risque cardio-vasculaire chez des patients hospitalisés pour maladie coronaire est élevée. Ces données descriptives mettent en évidence un profil à haut risque cardio-vasculaire de ce type de patients, nécessitant une prise en charge et un suivi régulier dans un contexte de prévalence élevée de facteurs de risque cardio-vasculaire.

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Does the number of previous caesarean deliveries affect maternal outcome and complication rates?

H.A. Alchalabi,[1] Z.O. Amarin,[1] L.F. Badria[1] and F.F. Zayed[1]

هل يؤثّر عدد الولادات القيصرية السابقة في حصيلة الولادة وفي معدل المضاعفات؟

هيفاء علي الجلبي، زهير عودة عمارين، ليلى فرنسيس بدرية، فهيم فرج زايد

الخلاصة: قام الباحثون بتقييم مضاعفات الولادة بالنظر إلى عدد الولادات القيصرية السابقة، وذلك في مستشفى الأميرة بديعة التعليمي، في إربد، بالأردن. وأُجري تحليل للسجلات الطبية للسيدات اللاتي وُلِّدن قيصرياً وعددهن 1739 امرأة. وكشف التحليل عن زيادة نسبتها 14 ضعفاً في احتمال التعرُّض لاستئصال الرحم القيصري لدى من يعانين من المشيمة المنزاحة ممَّن تعرَّضن لولادة قيصرية سابقة، بالمقارنة مع من يعانين من المشيمة المنزاحة دون التعرُّض لولادة قيصرية سابقة. ولوحظ ازدياد مخاطر استئصال الرحم القيصري كلما ازداد عدد الولادات القيصرية السابقة. وكانت السيدات اللاتي ولدن بالجراحة القيصرية 3 مرات أو تزيد، أكثر تعرُّضاً لمخاطر نقل الدم. كما لوحظ أن معدل الإصابة بالحمى التالية للجراحة أكثر شيوعاً لدى السيدات اللاتي وُلِّدن بالجراحة القيصرية ثلاث مرات أو أكثر، بالمقارنة مع السيدات اللاتي وُلِّدْنَ بالجراحة القيصرية لأول مرة.

ABSTRACT We evaluated maternal complications in relation to number of previous caesarean sections in Princess Badea Teaching Hospital, Irbid, Jordan. Analysis of the medical records of 1739 patients delivered by caesarean section was conducted. It revealed a 14-fold increase in the risk of caesarean hysterectomy in patients with placenta praevia and previous caesarean section compared to patients with placenta praevia and no previous caesarean section. The risk of caesarean hysterectomy increased with increasing number of previous caesarean sections. Those with 3 or more previous caesarean sections were at significantly higher risk of blood transfusion. Post-operative pyrexia was commoner in women with 3 or more previous caesarean sections compared to those undergoing their first one.

Le nombre d'antécédents d'accouchements par césarienne a-t-il un impact sur l'état de la mère et/ou sur le taux de complications post-partum ?

RÉSUMÉ Nous avons évalué les complications maternelles en fonction du nombre d'antécédents d'accouchements par césarienne au centre hospitalo-universitaire Princesse Badea à Irbid en Jordanie. Les dossiers médicaux de 1739 parturientes césarisées ont été analysés. Cette analyse a révélé une multiplication par un facteur 14 du risque d'hystérectomie d'hémostase chez les parturientes présentant un placenta praevia et ayant accouché par césarienne par rapport aux parturientes avec placenta praevia non césarisées. Le risque d'hystérectomie d'hémostase augmente parallèlement au nombre d'antécédents d'accouchements par césarienne. Les femmes ayant déjà subi au moins 3 césariennes s'avèrent significativement plus susceptibles de nécessiter une transfusion sanguine. On a constaté une plus grande fréquence de la pyrexie post-opératoire chez les parturientes ayant subi au moins 3 césariennes par rapport aux primocésarisées.

[1]*Department of Obstetrics and Gynaecology, Jordan University of Science and Technology, Irbid, Jordan (Correspondence to H.A. Alchalabi: halchalabi@yahoo.com).*
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Introduction

Caesarean section is considered a safe surgical procedure. Better anaesthesia, improved surgical techniques, more efficacious preventive and therapeutic measures against infections and thromboprophylaxis have contributed to the advancement of safety. Despite this, caesarean section remains associated with higher maternal morbidity and mortality than vaginal delivery [*1,2*]. Although anaesthesia and surgery carry their inherent risks, maternal morbidity and mortality at caesarean section is more a consequence of either a disease predating pregnancy or induced by pregnancy [*3*].

About one-third of performed caesarean sections are repeat procedures [*4*]. Repeat caesarean sections are associated with an increased incidence of placenta praevia and placenta praevia accreta [*5–7*], scar dehiscence and rupture [*3,8,9*]. Health workers in developing countries in general, and Middle Eastern countries in particular, may face different problems. Large families are the desired norm and sterilization is not readily acceptable so the prevalence of women with multiple previous caesarean sections is high.

Most studies compare patients delivered by caesarean section with those delivered vaginally. The aim of our study, however, was to evaluate maternal complications during the peripartum period in relation to the number of previous caesarean sections and the risks of maternal morbidity and mortality. The ultimate goal being the provision of evidence-based information that can be used in planning antenatal care and admission for elective or emergency deliveries to units that are well equipped to deal with potential complications. Such evidence would have added benefit in counselling couples regarding the advisability of performing tubal ligation in cases of multiple previous caesarean sections.

Methods

Out of 2209 patients delivered by caesarean section at Princess Badea Teaching Hospital between January 2000 and June 2001, the complete medical records of 1739 patients (80%) were reviewed. The review of this large number of files to retrieve the necessary data after the patients were discharged was done manually and was time consuming. During the period since the data were collected no change in policies or practice occurred in the management of patients delivered by caesarean and so the situation in the hospital is believed to be the same now.

The rate of caesarean section was 18% of all deliveries. The surgical procedure involved a "standard" transverse lower segment caesarean section under general anaesthesia. These operations were performed by fourth-year obstetric residents or specialists and tubal ligation only performed if the patient and her husband gave their consent. Cephalosporins were routinely prescribed and anticoagulant prophylaxis was administered to patients with high thromboembolic risk profiles. Patients were divided into those with no previous caesarean section and those with 1, 2, and 3 or more previous caesarean sections (groups 0, 1, 2 and 3 respectively).

In addition to demographic data, parity and gestational age, details of any maternal intra-operative, postoperative and puerperal morbidity and mortality were extracted. Placenta praevia accreta was diagnosed intraoperatively. The following information was extracted from the records: peripartum hysterectomy including hysterectomy for placenta praevia accreta, bowel and bladder injury and any intra- or postoperative blood transfusion due to excessive blood loss during the operation. Puerperal complications in each of the designated groups were

also recorded, such as fever (> 38 °C on 2 consecutive measurements, 6 hours apart other than in the first 24 hours) and wound infection presenting as induration, erythema and or purulent discharge. Wound seromas were not included.

Descriptive statistics were generated and significance of statistical comparison was determined by the chi-squared test. The Fisher exact test was used for smaller groups. Odds ratios (OR) and 95 confidence intervals (CI) were calculated to identify the association between number of caesarean sections and certain complications. $P < 0.05$ was considered statistically significant.

Results

Of the 1739 patient records reviewed, 1060 (61%) had no previous caesarean section and were undergoing the procedure for the first time, 351 (20%) had 1 previous caesarean section, 204 (12%) had 2 and 124 (7%) had 3 or more previous (the highest was 6 caesarean sections).

As expected, maternal age and parity were higher in patients with more previous caesarean sections, but this was not the case for gestational age. Tubal ligation was performed in 64 (3.7%) patients (Table 1). Of these, 49 (76.6%) were in high parity patients (36 patients had no previous caesarean section, 6 with 1 previous caesarean section, 6 with 2 previous caesarean sections and 1 with 3 previous caesarean sections). Only 15 (23.4%) patients had tubal ligation because of high number caesarean sections (3–6 previous caesarean sections).

Table 2 shows the maternal complications recorded according to the presence or absence of previous caesarean sections. Twelve (12) patients required caesarean hysterectomy. Of these, 7 were because of placenta praevia accreta, all of which were anterior. One patient had a hysterectomy with a normally sited placenta that was adherent. Two patients had bowel injury; 1 with history of 2 previous caesarean sections, the other with history of 4. Bladder injury was recorded in 3 women, the first in combination with uterine rupture and no previous caesarean section, the second had 1 previous caesarean section and was delivered in the second stage, the third patient had had 6 previous caesarean sections and was delivered at 37 weeks of gestation and found to have incomplete rupture and extensive adhesions. There was 1 death who was a mother with 3 previous caesarean sections and placenta praevia accreta. She died a few hours after undergoing caesarean hysterectomy because of prolonged shock and multiple organ failure.

Generally women with no previous caesarean section and those with previous

Table1 **Characteristics of patients in the study groups**

Characteristic	Number of previous caesarean sections			
	0 (*n* = 1060)	1 (*n* = 351)	2 (n = 204)	3 (*n* = 124)
Maternal age[a] (years)	29.3 (6.5)	30.2 (5.2)	31.5 (5.3)	33.4 (4.8)
Parity[a]	2.4 (2.8)	2.4 (2.2)	3.2 (1.7)	4.2 (1.7)
Gestational age[a] (weeks)	38.8 (2.3)	38.4 (2.2)	37.5 (1.9)	37.1 (2.0)
Tubal ligation [No. (%)]	36 (3.4)	6 (1.7)	6 (2.9)	16 (12.9)

[a]*Values are means (standard deviations) except where otherwise stated.*

Table 2 **Maternal complications in patients with and without history of previous caesarean section**

Maternal complication	No previous caesarean section (*n* = 1060)		Previous caesarean section (*n* = 679)		*P*-value
	No.	%	No.	%	
Blood transfusion	80	7.6	56	8.2	0.6608
Hysterectomy	5	0.5	7	1.0	0.2709
Placenta praevia/ hysterectomy	1	0.1	6	0.9	0.0307*
Bladder injury	1	0.1	2	0.3	0.6941
Bowel injury	0	0.0	2	0.3	0.3060
Fever	31	2.9	15	2.1	0.3642
Wound infection	35	3.3	14	2.1	0.1687
Maternal death	0	0.0	1	0.2	0.8060

**Significant at* P < *0.05.*

caesarean sections had a similar rate of complications apart from hysterectomy for placenta praevia accreta, which was significantly higher in patients with previous caesarean section ($P = 0.03$) (Table 2).

The rates of maternal complications were compared between the 4 groups according to the number of previous caesarean sections (Table 3). The risk for blood transfusion as a result of intra-operative blood loss was similar in patients with no previous caesarean section and those with 1 previous caesarean section. Women with 2 previous caesarean sections were at lower risk of transfusion (OR = 0.31, 95% CI: 0.12–0.77, $P = 0.01$), while women with 3 previous caesarean sections were at a higher risk of blood transfusion (OR = 1.96, 95% CI: 1.12–3.44, $P = 0.02$).

There was an increased risk of placenta praevia accreta in relation to previous caesarean scar. In patients with placenta praevia, 6 out of 20 (30%) women with previous caesarean section needed a hysterectomy compared to 1 out of 33 (3%) of those with no previous caesarean section (OR = 14.14, 95% CI: 1.65–128.56, $P = 0.02$). When the study groups were analysed separately, the risk of hysterectomy increased with increasing number of previous caesarean sections (OR = 1.50, 33.00, 132.00 for groups1, 2 and 3 respectively) (Table 3). The risk of scar rupture was not significantly affected by the number of previous caesarean sections. Women with 1 or 2 previous caesarean sections had the same risk of developing post-operative fever as women without previous caesarean section, but the risk of fever in women with 3 or more previous caesarean sections was higher (OR = 2.31, 95% CI: 1.04–5.14, $P = 0.04$) (Table 3). No significant correlation was found between having had any number of previous caesarean sections and the risk of developing wound infection. There were no cases of anaesthetic complications or thromboembolic events in the records reviewed.

Table 3 **Complications in patients delivered by caesarean section in relation to number of previous caesarean sections**

Complication	Previous caesarean sections	Complications Present	Absent	OR (95% CI)	*P*-value
Blood transfusion	0[a]	80	980	1	
	1	34	317	1.31 (0.86–2.0)	0.209
	2	5	199	0.31 (0.12–0.77)	0.012*
	≥ 3	17	106	1.96 (1.12–3.44)	0.018*
Placenta praevia/ hysterectomy	0[a]	1	33	1	
	1	0	11	1.50 (0.05–47.84)	0.819
	2	2	2	33.00 (2.02–538.64)	0.014*
	≥ 3	4	1	132.00 (6.84–2546.02)	0.001*
	All[b]	6	14	14.14 (1.65–128.56)	0.019*
Dehiscence/rupture	1[a]	1	3348	1	
	2	3	201	1.74 (0.35–8.68)	0.502
	≥ 3	4	119	3.91 (0.86–17.71)	0.077
Fever	0[a]	31	1029	1	
	1	7	344	0.67 (0.26–1.35)	0.216
	2	0	204	0.08 (0.005–1.33)	0.079
	≥ 3	8	115	2.31 (1.04–5.14)	0.041*
Wound infection	0[a]	35	1025	1	
	1	7	344	0.59 (0.26–1.35)	0.216
	2	2	202	0.29 (0.07–1.33)	0.090
	≥ 3	5	118	1.24 (0.48–3.23)	0.658

**Significant at* P < *0.05.*
[a]*Reference group.*
[b]*Total number of patients with previous caesarean sections.*
Due to the small numbers in some categories and the wide confidence intervals, the statistical values are not strong.
OR = odds ratio, CI = confidence interval.

Discussion

When undergoing an abdominal delivery, patients with previous 1 or more caesarean sections are exposed to specific problems that are directly related to this mode of delivery [*2*]. Despite the improvement in technical skills and preventive measures of various potential complications, maternal morbidity and mortality at caesarean section are still encountered [*1,2*]. When counselling patients with previous caesarean sections regarding future pregnancies, evidence-based advice is advantageous, which is why we conducted the study.

Analysis revealed that blood transfusion was required for 7.6% of patients with no previous caesarean section and for 8.2% of those with previous caesarean section. This

is higher than the 1.9% reported by Loverro [*5*]. The group with 2 previous caesarean sections needed fewer blood transfusions, which is mostly due to the fact that these patients had elective deliveries while those with no or 1 previous caesarean section were mostly emergency deliveries. The significantly higher frequency of blood transfusion in patients with 3 or more previous caesarean sections ($P = 0.018$) cannot be clearly explained but may be related to associated problems in this group, such as placenta praevia, uterine atony due to twin pregnancy and atony due to grand multiparity.

Placenta praevia accreta is a serious problem that is strongly associated with the presence of previous caesarean section scar [*8–11*]. Our study revealed a 14-fold increase in the risk of peripartum hysterectomy for this indication in patients with previous caesarean section compared to those with placenta praevia and no previous caesarean section. This risk of hysterectomy increased with increasing number of previous caesarean section. This corroborates data from other surveys which showed a linear correlation between the risk of caesarean hysterectomy in cases of placenta praevia accreta and the number of previous caesarean sections [*7,12*].

Peripartum hysterectomy is an operation that is almost always performed as an emergency and is associated with significant blood loss as suggested by Castaneda et al. [*13*]. This makes it essential that patients with previous caesarean section and placenta praevia should be properly counselled and operated on by senior staff members. Enough blood products must be readily available. Prenatal diagnosis of placenta praevia accreta by transabdominal colour Doppler ultrasound may have an impact on the peripartum clinical management [*14,15*]

Regarding postoperative pyrexia, there was a lower overall incidence of fever in patients undergoing their first caesarean section and those with previous caesarean sections compared with the report of Chazotte and Cohen (2.9% and 2.1% respectively versus 5.1%) [*8*]. Women with 3 or more previous caesarean sections had a significantly higher risk of postoperative fever than those with no history of previous caesarean section. Variable degrees of adhesions, extensive tissue handling and longer operative time are possible contributors to this discrepancy. These variables should be the subject of further investigation. Analysis of the difference in wound infection between the subgroups did not reveal any significant differences.

The number of women with multiple previous cesarean sections who had opted for tubal ligation was very small which perhaps reflects the desire for large families in the community.

Given the risk of complications associated with repeat caesarean delivery, women likely to face this situation should be counselled about these risks and encouraged to consider avoiding large families. To minimize maternal risk, women with placenta praevia and previous caesarean section should be delivered by the most senior members of staff in adequately equipped hospitals.

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Preterm delivery risk factors: a prevention strategy in Shiraz, Islamic Republic of Iran

A. Rajaeefard,[1] M. Mohammadi[1] and A. Choobineh[2]

استراتيجية للوقاية من عوامل اختطار ولادة الخدَّج (المبتسرين) في مدينة شيراز الإيرانية

عبد الرضا رجايي فرد، مهدي محمدي، علي رضا جوبينه

الخلاصة: تم خلال المدَّة من 3 شباط/فبراير إلى 5 آذار/مارس 2000 تصنيف 1177 من الحوامل المترددات على 36 مركزاً صحياً في مدينة شيراز، إلى متعرِّضات لاختطار مرتفع (519 امرأة)، أو لاختطار منخفض (598 امرأة)، وذلك على أساس وجود عوامل اختطار ولادة الخدَّج (المبتسرين). وتلقَّت الحوامل المتعرِّضات لاختطار مرتفع تدريباً على استراتيجيات تستهدف الحد من ولادة المبتسرين. وكان معدل تواتُر ولادة المبتسرين 3% لدى المجموعة المنخفضة الاختطار، و14.6% لدى المجموعة المرتفعة الاختطار (P<0.001). وتمثَّلت العوامل المهمة المسبِّبة لولادة الخدَّج (المبتسرين) في ما يلي: توسُّع عنق الرحم أكثر من 1 سم، والتقلُّصات الرحمية قبل الأوان، والحمل بأكثر من جنين واحد، والتدخين. ولوحظ أن ولادة الخدَّج (المبتسرين) كانت أقل بدرجة يُعتدُّ بها إحصائياً لدى المجموعة المرتفعة الاختطار التي تلقَّت التدريب، بالمقارنة مع مجموعة مماثلة في دراسة سابقة لم تحصل على تدريب.

ABSTRACT From 3 February–5 March, 2000, 1117 pregnant women attending 36 health centres in Shiraz were categorized as high risk (*n* = 519) and low risk (*n* = 598) based on the presence of preterm delivery risk factors. High-risk women received training on strategies to reduce the risk of premature delivery. The frequencies of preterm delivery in the low- and the high-risk groups were 3.0% and 14.6% respectively (*P* < 0.001). The significant factors for preterm delivery were cervical dilation > 1 cm, premature uterine contractions, multifetal gestation and smoking. Premature delivery was significantly lower in the high-risk group compared with a similar group in a previous study who had not received training.

Les facteurs de risque de prématurité : la stratégie de prévention à Chiraz en République islamique d'Iran

RÉSUMÉ Du 3 février au 5 mars 2000, 1117 femmes enceintes suivies par 36 centres de santé de Chiraz ont été classées respectivement dans les catégories à haut risque (n = 519) et à risque faible (n = 598) en fonction de la présence de facteurs de risque de prématurité. Les femmes à haut risque ont été sensibilisées aux stratégies visant à réduire le risque d'accouchement prématuré et ont reçu une formation *ad hoc*. Dans les groupes à faible et haut risque de prématurité, la fréquence des accouchements prématurés était respectivement de 3,0 % et de 14,6 % (p < 0,001). Les facteurs de prématurité les plus significatifs étaient la dilatation du col > 1 cm, la précocité des contractions utérines, les grossesses multiples et le tabagisme. La prématurité s'est avérée significativement plus faible dans notre groupe à haut risque que dans un groupe comparable ayant participé à une autre étude sans avoir reçu de formation appropriée.

[1]Department of Epidemiology and Biostatistics; [2]Department of Occupational Health, School of Health, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran (Correspondence to A. Rajaeefard: rajaeefard@sums.ac.ir).

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Introduction

Every year around the world some 13 million premature children are born. Most of these children are born in developing countries, and they account for the largest share of prenatal morbidity and mortality [*1–7*]. The consequences of preterm delivery for children are extremely serious and a preterm neonate might be affected by them throughout his/her life. Infants born too soon die and suffer disability and other morbidity more frequently than infants born at full gestation [*6*]. They also represent a large economic burden; extremely preterm neonates might have to stay in the neonatal intensive care unit for 90 days and each day can cost approximately 750 EUR (US$ 1 = 0.76 EUR) [*4*]. In developed countries, 35% of expenses for treating diseases in children result from preterm delivery [*8*]. A study in the United Kingdom showed that 62% of mortality in neonates < 1 month and 85% of mortality in infants < 1 year occurred in those born prematurely (gestational age between 22 and 36 weeks) [*9*]. For women, preterm birth may be the tip of the iceberg of other potentially preventable morbidities and may have its own long-term physiological and psychological consequences for the mother.

Data suggest that preterm delivery has not decreased in the last decade in spite of all known risk factors [*4*]. In the United States, for instance, preterm birth has risen steadily from 9.4% in 1981 to 11.4% in 1997 [*6*].

The main causes of preterm deliveries are preterm uterine contractions, > 1 cm dilation or more than 70% effacement of cervix and abnormalities in the uterus or cervix [*8*]. Research in Finland showed that unmarried status, smoking, low education, age above 35 years and first pregnancy were the most important risk factors for preterm deliveries [*10*]. Although there are many maternal characteristics associated with preterm delivery, the etiology in most cases is not clear. Research to study risks, etiology and prevention of preterm delivery is therefore necessary in order to reduce the rate of preterm delivery and its adverse health and economic outcomes.

In the Islamic Republic of Iran, there are no extensive data about preterm delivery. A controlled trial conducted by Makiabadi in 2 hospitals of Shiraz in which 806 pregnant women were divided into 3 groups (low risk, high risk with training and high risk without training) showed that the incidence of preterm delivery in these groups was 3.1%, 8.6% and 30.4% respectively [*11*].

The objectives of the present study were to investigate and provide data on the risk factors of preterm delivery in Shiraz city and to introduce a preventive strategy to be integrated in the maternal health care programme in order to reduce the rate of preterm delivery.

Methods

In this study, all 36 health care centres of Shiraz city were involved. In the first phase of the study, a midwife from the family planning division from each centre was invited to take part in a one-week workshop (conducted by a gynaecologist) to introduce the known preterm delivery risk factors and common prevention strategies and also the study structure, objectives and data collection instrument (Table 1).

In the second phase, the health care providers trained at the workshop started collecting data on the pregnant women attending their centres. A questionnaire was used for data collection and as a screening instrument. The questionnaire devised was based on that of Holbrook et al. [*12*] and

Table 1 **Contents of the one-week workshop for training health care providers**

Content
Risk factors of preterm delivery
Items indicated in Table 2
Alcohol consumption
Hypertension
Diabetes
Bleeding
Preterm delivery prevention methods
Refraining from intensive physical activity
Resting
Employment outside the home
Care of genital health
Avoiding sexual relations
Increasing fluid intake
Avoiding anxiety and stress
Preventing and treating anaemia and malnutrition
Awareness general risk factors in pregnancy period
Preventing labour progression

contained 14 items for major risk factors, 14 items for minor risk factors and 12 items for background risk factors (Table 2). Each major, minor and background risk factor scored 10, 5 and 2.5 respectively. If the risk score for a pregnant woman exceeded 10, she was categorized in the high-risk group, otherwise in the low-risk group. The reason for taking a risk score of 10 as the cut-point was based on Makiabadi's study [*11*] indicating a score of 10 would give > 90% sensitivity. A high sensitivity would result in including a larger number of pregnant women into the high-risk group, which would have no harmful effects on the women. Additionally, a score of 10 has been used as the cut-point in similar studies by other researchers, for instance Main et al. [*13*].

Thus, all pregnant women attending the 36 health care centres during 3 February to

Table 2 **Risk factors included in the questionnaire used as the screening instruments**

Risk factor
Major risk factors
Multifetal gestation
History of preterm delivery
History of preterm uterine contraction in previous pregnancies
History of preterm pain in previous pregnancies
History of cervical cone biopsy
History of more than one abortion in the 2nd trimester
History of at least 2 stillbirths
History of at least 2 neonatal deaths
Surgical procedures during pregnancy
Abnormalities of the uterus or cervix
Premature contractions
> 1 cm dilation or > 70% effacement
Injury or trauma to the mother
Gestational hypertension
Hydramnios
Minor risk factors
Febrile disease during pregnancy
Urinary tract infection
Liver disease
Cardiac disease
Lung disease
History of bleeding in the 2nd trimester
Smoking > 10 cigarettes a day
Smoking water-pipe 2 times a day
Pregnancy lost in the 2nd trimester
> 2 pregnancies lost in the 1st trimester
History of 1 stillbirth
Drug addiction
Essential hypertension
Hyperthyroidism
Background risk factors
Maternal age < 18 and > 35 years
Maternal height < 150 cm
Maternal haemoglobin < 11 g/dL
Maternal weight < 48 kg at the beginning of pregnancy
Weight loss of ≥ 2 kg at the 18th week of gestation
Weight gain of < 5 kg at the 32nd week of gestation

Table 2 **Risk factors included in the questionnaire used as the screening instruments** *(concluded)*

Risk factor
≤ 1 year pregnancy interval
History of 1 pregnancy lost in the 1st trimester
First pregnancy or 5th and more pregnancy
Severe physical stress
Severe emotional stress
Low socioeconomic status

5 March, 2000 with gestational age less and 36 weeks were screened for the presence of preterm delivery risk factors using the questionnaire and were divided into 2 groups; low risk for preterm delivery and high risk.

In the third phase of the study, the high-risk pregnant women were divided into subgroups of 5 to 10 persons. As an intervention activity, to detect and reduce the preterm delivery risk factors, a training programme was devised by the researchers and was given by the trained health care providers to the subgroups. The programme consisted of a 4-hour training session followed by several routine consulting sessions. The contents of the training were nearly the same as those of the workshop conducted for the health care providers (Table 1). In the routine consulting sessions, previous training was briefly repeated and, if needed, clinical interventions, such as hospitalization or treatment, were prescribed.

For ethical reasons we did not to include a control group (high-risk pregnant without training) in the study. Since the protocol of health care services given to pregnant women in governmental health care centres remained the same from 1992 to 2000, and the criteria for categorizing pregnant women remained the same, the control group of Makiabadi's study (high risk without training) [*11*] was used as the control group of this study to assess the effectiveness of the prevention strategy.

All the women were followed to delivery and their delivery status was recorded (preterm or full term).

Statistical analysis

As preterm delivery has a complex etiology with several associated variables, we used a multivariate regression model to analyse the data. Statistical analyses were performed using *SPSS*, version 11 and *SYSTAT*. The chi-squared test was used as criteria for introducing independent variables into the regression models. Logistic regression (binary and polytomous response) and Cox regression model were used to analyse factors associated with preterm delivery. Polytomous response logistic regression with the following 3 levels was applied for categorizing the outcomes of the pregnant women studied:

- Level 1: Preterm delivery
- Level 2: Full term (≥ 37 weeks) delivery with intervention
- Level 3: Full term delivery without intervention (reference level) (Makiabadi's group)

In the Cox regression model, the gestational age was considered a continuous variable and was not dichotomized to < 37 and ≥ 37 weeks.

Results

There were 1117 pregnant women included in the study; 519 (46.5%) and 598 (53.5%) of the pregnant women were labeled as high risk and low risk respectively. The total number of preterm deliveries was 94 (8.4%). The number of preterm deliveries in the low-risk group was 18 (3.0%) and

in the high-risk group was 76 (14.6%); the difference was statistically significant ($P < 0.001$). Comparison of the preterm delivery rate in the high-risk group of this study (14.6%) with that of the control group of the previous study (30.4%) [*11*] showed the significant effect of the training programme ($P < 0.001$).

Table 3 presents the distribution of some risk factors in the 2 groups. The only significant differences found between the high- and low-risk groups were in education level ($P = 0.03$) and number of pregnancies ($P = 0.002$).

Table 4 shows the distribution of the main risk factors in the high-risk pregnant women. Based on the scoring procedure, women with at least 1 of these main factors were categorized in the high-risk group.

Table 3 **Sociodemographic and pregnancy data of the pregnant women by risk group**

Variable	Group				*P*-value
	Low risk		High risk		
	No.	%	No.	%	
Age(years)					0.18
≤ 21	171	29.1	166	32.3	
22–29	305	52.0	241	46.9	
≥ 30	111	18.9	107	20.8	
Total	587	100.0	514	100.0	
Education					0.03*
Illiterate	25	4.3	36	7.1	
Elementary (1–5 years)	180	30.6	169	33.5	
Guidance school (6–8 years)	197	33.5	182	36.0	
High school (9–12 years)	166	28.2	101	20.0	
University education (> 12 years)	20	3.4	17	3.4	
Total	588	100.0	505	100.0	
Occupation					0.45
Housewife	550	94.8	493	95.5	
Employed outside the home	30	5.2	23	4.5	
Total	580	100.0	516	100.0	
Number of pregnancies					0.002**
1	229	38.4	192	37.1	
2–4	331	55.4	262	50.6	
≥ 5	37	6.2	64	12.4	
Total	597	100.0	518	100.0	
Duration of pregnancy at the entry into the programme (weeks)					0.2
< 22	166	30.6	168	36.0	
22–27	208	38.4	171	36.6	
≥ 28	168	31.0	128	27.4	
Total	542	100.0	467	100.0	

*Chi-squared homogeneity test: *significant at* P < *0.05; **significant at* P < *0.01.*
The totals do not sum to 519 and 598 because data were missing for some women.

Table 4 **Distribution of the major risk factors in the pregnant women**

Risk factor	No. (*n* = 1117)	%
History of preterm uterine contraction	119	10.7
History of preterm delivery	52	4.7
History of preterm pain in the previous pregnancy	32	2.9
Gestational hypertension	30	2.7
Injury or trauma during pregnancy	25	2.2
Smoking > 10 cigarettes a day[a]	24	2.2
> 1 abortion in the second trimester	11	1.0
Multifetal gestation	19	1.7
> 1 cm dilation of cervix	13	1.2
> 70% thinning of the amnion	11	1.0
Hydramnios	7	0.6
Abnormalities of the uterus or cervix	6	0.5
Surgery during pregnancy	3	0.3
2 stillbirths and 2 neonatal deaths	3	0.3
Cone biopsy from cervix	1	0.1

[a]Because of the high frequency of smoking this was included with the major risk factors.

Polytomous logistic regression analysis is presented in Tables 5. The table presents the odds ratios of the outcome of delivery in level 1 in reference to level 3. As indicated in Table 5, presence of > 1 cm dilation, smoking > 10 cigarettes a day, multifetal gestation and other factors were significantly associated with preterm delivery. The regression models also showed that when comparing the delivery outcome between level 2 (full-term delivery with intervention) and level 3 (full-term delivery without intervention as the reference level), the only factor retained in the model was smoking > 10 cigarettes a day (odds ratio = 4).

Table 6 presents odds ratios from the Cox regression models. In this analysis, more factors were significantly associated with preterm delivery (presence of > 1 cm dilation, multifetal gestation, smoking > 10 cigarettes a day, other factors, injury or trauma during pregnancy, preterm uterine contractions and period of training).

Discussion

In this study, based on the risk factors of preterm delivery, the pregnant women

Table 5 **Polytomous logistic regression models indicating factors most strongly associated with preterm delivery**

Factors retained in the model	Odds ratio[a]	95% confidence interval	*P*-value
> 1 cm dilation of cervix	54.5	6.6–447.6	< 0.001
Smoking > 10 cigarettes a day	6.7	2.2–20.5	0.001
Multifetal gestational pregnancy	6.5	2.1–19.7	0.001
Other factors[b]	4.6	1.5–14.7	0.01
Training for more than 98 days	0.45	0.26–0.79	0.005

Goodness of fit for the model: D = 64.58, df = 10, P < *0.001.*
[a]Reference group: level 3 (full term delivery without intervention).
[b]Including: positive history of at least 2 stillbirths or 2 neonatal deaths; surgical procedures during pregnancy; hydramnios; abnormalities in uterus or cervix; cone biopsy from cervix.

Table 6 **Cox regression models indicating factors most strongly associated with preterm delivery**

Factors retained in the model	Odds ratio[a]	95% confidence interval	*P*-value
> 1 cm dilation of cervix	2.79	1.58–4.92	< 0.001
Multifetal gestational pregnancy	2.27	1.42–3.63	< 0.001
Other factors[b]	1.92	1.20–3.10	0.008
Smoking > 10 cigarettes a day	1.53	1.00–2.35	0.05
Injury or trauma during pregnancy	1.41	0.94–2.11	0.09
Preterm uterine contractions	1.26	1.04–1.53	0.02
Logarithm of period of training	0.67	0.55–0.82	< 0.001

Goodness of fit for the model: D = 55.15, df = 7, P < *0.001.*
[a]*Reference group: level 3 (full term delivery without intervention).*
[b]*Including: at least 2 stillbirths or 2 neonatal deaths; surgical procedures during pregnancy; hydramnios; abnormalities of the uterus or cervix; cone biopsy from cervix.*

were categorized as low- and the high-risk groups. The frequency of preterm delivery in the study group was 8.4%; 3.0% for the low-risk and 14.6% for the high-risk group. As expected, the difference between the frequencies of preterm delivery in the 2 groups was statistically significant ($P < 0.0001$). The frequency of preterm delivery in our study was higher than that of preterm delivery found in Denmark with the rate of 3.1% [*14*] and lower than that of preterm delivery in the United States with the rate of 15.2% [*15,16*].

The preterm delivery rate in the low-risk group of Makiabadi's study [*11*] was not significantly different from the frequency in the low-risk group of our study ($P > 0.05$). The frequency of preterm delivery among the high-risk group of Makiabadi's study who had not received training, considered as the control group (30.4%), was significantly higher than that of the high-risk group of the present study who had received training (14.6%) ($P < 0.0001$). This indicates the effectiveness of combining a training programme with the routine health care given to high-risk pregnant women. The results of our study are in agreement with previous reports [*2,3,17*] that suggest that participation in an organized preterm delivery prevention programme that emphasizes patient education and frequent provider contact can significantly decrease the incidence of preterm birth. Based on this, the training programme for preterm delivery prevention devised in our study was integrated into the routine health care programme for high-risk pregnant women in all health centres in the Islamic Republic of Iran.

Our results show that cervical dilation more than 1 cm increases the risk of preterm delivery about 54 fold. Other strong risk factors retained in the regression models were smoking and multifetal gestational pregnancy which increased the risk of preterm delivery over 6 fold. This concurs with the findings of other studies [*3,8,10*]. It was also found that training pregnant

women for more than 98 days (14 weeks) could decrease the risk of preterm delivery by approximately 50%. Considering this period as a continuous variable in the Cox regression gave a better result in decreasing the risk of preterm delivery.

Comparing the results of the 2 regression models showed that although the first 4 risk factors were nearly the same, the Cox regression model also revealed an association between preterm delivery and injury or trauma during pregnancy, preterm uterine contractions and the period of training. Thus Cox regression seems to provide a more comprehensive statistical analysis.

Conclusion

Our study indicates that the following risk factors increased the risk of preterm delivery among our study population: > 1 cm dilation of the cervix; smoking > 10 cigarettes a day; multifetal gestational pregnancy; injury or trauma during pregnancy; preterm uterine contractions.

Training high-risk pregnant women about the risk factors for preterm delivery and preventive strategies could be an effective way to lower the incidence of preterm delivery and consequently prenatal mortality.

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Epidemiology of neural tube defects in northern Iran, 1998–2003

M.J. Golalipour,[1] E. Mobasheri,[2] M.A. Vakili[3] and A.A. Keshtkar[3]

وبائيات عيوب الأنبوب العصبي في شمال إيران، 1998 – 2003

محمد جعفر كلعلي بور، إلهام مبشِّري، محمد علي وكيلي، عباسعلي كشتكار

الخلاصة: تم في إطار هذا البحث تقدير معدلات عيوب الأنبوب العصبي في مستشفى للإحالة في مدينة غورغان، بشمال جمهورية إيران الإسلامية، وعلاقة هذه العيوب بالجنس، والأصل الاثني للأم، وعمر الأم، والفصل. ولوحظت 109 حالات من بين 951 37 ولادة في الفترة 1998 – 2003، أي بمعدل انتشار 28.7 حالة لكل 000 10 ولادة (24.8 حالة لكل 000 10 من الذكور، و32.8 حالة لكل 000 10 من الإناث). وبلغ هذا المعدل 40.5 لكل 000 10 من المنتمين للعِرْق التركماني، 25.2 بين المنتمين للعِرْق الفارسي، و30.8 بين المنتمين للعِرْق السيستاني. وكان معدل حدوث السنسنة المشقوقة 16.3، وانعدام الدماغ 11.3 لكل 000 10 شخص. وكان معدل المصابين من حديثي الولادة أعلى ما يكون في حالة زيادة عمر الأم على 35 عاماً (50.7 لكل 000 10). وكانت ذروة الانتشار في شهر كانون الأول/ديسمبر.

ABSTRACT We determined the rates of neural tube defects at a referral hospital in Gorgan, north Islamic Republic of Iran, and the relations of these abnormalities to sex, maternal ethnicity, maternal age and season. During 1998–2003, there were 109 cases among 37 951 births, a prevalence of 28.7 per 10 000 (24.8 and 32.8 per 10 000 among males and females respectively). The rates in Turkmen, native Fars and Sistani ethnic groups were 40.5, 25.2 and 30.8 per 10 000 respectively. The rates of spina bifida and anencephaly were 16.3 and 11.3 per 10 000 respectively. The rate of affected newborns was highest in mothers aged over 35 years (50.7 per 10 000). The peak prevalence was in December.

Épidémiologie des malformations du tube neural dans la région Nord de l'Iran, 1998-2003

RÉSUMÉ Nous avons déterminé le taux de malformations du tube neural dans un hôpital de recours de Gorgan, ville située au nord de la République islamique d'Iran, et caractérisé la relation entre ces malformations et des paramètres tels que le sexe de l'enfant, l'origine ethnique de la mère, l'âge maternel et la saison. Au cours de la période 1998-2003, sur les 37 951 naissances enregistrées, il a été recensé 109 cas de malformations du tube neural, soit une prévalence de 28,7 pour 10 000 naissances (à savoir respectivement 24,8 et 32,8 cas pour 10 000 naissances de sexe masculin et féminin). Dans les trois groupes ethniques Turkmène, Farsi et *Sistani*, ces taux étaient respectivement de 40,5, 25,2 et 30,8 pour 10 000 naissances. Le spina bifida et l'anencéphalie représentaient respectivement 16,3 et 11,3 cas pour 10 000 naissances. La fréquence des malformations du tube neural s'est avérée plus importante chez les nouveau-nés de mères âgées de plus de 35 ans (50,7/10 000 naissances). La prévalence maximale a été observée en décembre.

[1]Gorgan Congenital Malformations Research Centre; [2]Department of Gynaecology; [3]Department of Health, Gorgan University of Medical Sciences, Gorgan, Islamic Republic of Iran (Correspondence to M.J. Golalipour: mjgolalipour@yahoo.com).
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Introduction

Neural tube defects (NTD) result in congenital malformations of the nervous system, the most common of which are anencephaly, spina bifida and encephalocele. They are the result of multifactorial disturbances in embryonic neurulation [*1*]. Numerous risk factors have been identified for NTD. Exposure to methotrexate, valproic acid or aminopterin, maternal diabetes, hyperthermia, low socioeconomic status, and lack of folate have been shown to increase the risk of NTD. Also, genetic factors are believed to be important [*2–5*].

The prevalence of NTD at birth varies considerably by country, geographic zone, and ethnic and racial group; it ranges from as high as 1 case in 100 births in some regions of China to about 1 case in 2000 or less in some Scandinavian countries. In many countries the prevalence is approximately 1 in 1000 births [*5–8*].

Previous studies on NTD have been carried out in some parts of the Islamic Republic of Iran. In a study on 13 037 births in the capital, Tehran (1969–78), 17.6/10 000 newborns had NTD [*9*]. In another study of 8585 deliveries in Hamadan (1991–97) (a north-west province), the prevalence of NTD was 50.1/10 000 [*10*] and in Cannadajh–Kordestan (another north-west province), out of 14 915 births, 55.0/10 000 newborns had NTD [*11*].

NTD may lead to spontaneous abortion, stillbirth, death in early infancy or a lifetime of disability. In view of the significant health costs of NTD it important to have baseline data of the prevalence of NTD in every region. This study was done in a referral hospital in the north of the Islamic Republic of Iran during 6 years (1998–2003) to determine the prevalence of different types of NTD and the relations of these abnormalities to factors including sex, maternal ethnicity, maternal age and season.

Methods

This descriptive cross-sectional study was carried out in Dezyani teaching hospital in Gorgan, the capital city of Golestan province, north Islamic Republic of Iran. The hospital serves as a referral centre for obstetric and gynaecologic problems and a prenatal intensive care unit for all other hospitals and clinics in the south-east of the Caspian Sea border (Golestan province). The region has a population of about 1.5 million and covers an area of about 20 460 km^2. Dezyani hospital is one of 17 hospitals and there are more than 500 primary health centres in the region. As a result, patients in this catchment area requiring transfer for the purpose of specialized investigations and treatment (obstetrics and gynaecology) must be referred to Dezyani hospital.

All live and stillbirth newborns delivered in the hospital from January 1998 through December 2003 from mothers residing in Gorgan province were screened for congenital malformations. NTD were defined according to the *International classification of diseases*, version 10. Stillbirths referred to all fetal deaths after 24 weeks or longer gestation. It was not possible in this study to record data about abortions. All NTD rates were calculated per 10 000 births.

Demographic characteristics and general information of all of the neonates and their parents—sex, date of birth, kind of NTD, mother's age and ethnicity—were recorded in the medical chart. Other variables such as consanguineous marriage and residence of parents were recorded only for neonates with NTD. Three ethnic groups (native Fars, Turkmen and Sistani) were defined. The native Fars groups are

the predominant inhabitants of the region. The Turkmen migrated from other parts of central Asia around 250 years ago and have a rate of interracial marriage of nearly 100%. The Sistani are immigrants from the Iran–Pakistan–Afghanistan border from half a century ago.

All data were analysed with *SPSS* software and were evaluated and compared with the chi-squared test. A *P*-value of 0.05 or less was considered statistically significant.

Results

Between 1998 and 2003 there were 37 951 births in Dezyani teaching hospital, Gorgan, with 109 newborns and stillbirths recorded with NTD. The prevalence at birth of NTD during the 6-year period was therefore 28.7 per 10 000 births. There were 48 males and 61 females; the rate of NTD was 24.8/10 000 and 32.8/10 000 in males and females respectively (no significant difference) (Table 1).

Out of the 109 NTD cases, 62 had spina bifida, 43 were anencephalic and 4 had encephalocele. The corresponding prevalence for spina bifida was 16.3/10 000 births (13.9 and 18.8/10 000 for males and females respectively), for anencephaly 11.3/10 000 (9.3 and 13.5/10 000 for males and females) and for encephalocele 1.1/10 000 (1.5 and 0.5/10 000 for males and females).

Table 1 shows the rate of NTD by mother's age; the highest rate of NTD was 50.7/10 000 in newborns with mothers aged ≥ 35 years.

The NTD rates were 40.5/10 000, 25.2/10 000 and 30.8/10 000 for mothers of Turkmen, native Fars and Sistani ethnic groups respectively (no significant difference). This study shows 36 (33.0%) of the parents with affected newborns had consanguineous marriages. Also 63% of the parents resided in rural areas and 37% in urban areas.

Table 1 **Prevalence of neural tube defects (per 10 000 births) by sex, mother's age and ethic group, 1998–2003**

Variable	Total no. of births	Type of defect						Total		χ^2	*P*-value
		Spina bifida		Anencephaly		Encephalocele					
		No.	/10 000	No.	/10 000	No.	/10 000	No.	/10 000		
Sex											
Male	19 370	27	13.9	18	9.3	3	1.5	48	24.8	2.13	0.14
Female	18 581	35	18.8	25	13.5	1	0.5	61	32.8		
Mother's age (years)											
15–19	5 161	4	7.8	6	11.6	2	3.9	12	23.3	3.86	0.15
20–34	30 817	52	16.9	33	10.7	2	0.6	87	28.2		
≥ 35	1 973	6	30.4	4	20.3	–	–	10	50.7		
Mother's ethnic group											
Native Fars	25 439	36	–	25	–	3	–	64	25.2	3.96	0.14
Turkmen	5 686	12	–	11	–	–	–	23	40.5		
Sistani	6 826	13	–	7	–	1	–	21	30.8		
Total	37 951	62[a]	16.3	43	11.3	4	1.1	109	28.7		

[a] *The ethnicity of one newborn was not recorded.*

Figure 1 shows the rate of NTD each year. The highest rate was in the year 2000 (36.0/10 000). Seasonal variations during the 6-year period were observed. The rate of NTD in October to March (33.0/10 000 births) was higher than July to June (24.0/10 000 births) ($\chi^2 = 2.42$, df = 1, $P > 0.05$). The peak prevalence occurred in December.

Discussion

Our study showed a rate of NTD in this referral hospital in the Islamic Republic of Iran of 28.7/10 000 births. In this research we could not study abortions and therefore our results may be underestimated. Our rate is higher than studies in other countries such as Canada where it was 1.41/1000 [*8*], in South Africa 1.74/1000 [*12*], in Germany 15.0/10 000 [*13*], in the north of England 17.9/10 000 [*14*], in the north of France 10.9/10 000 [*15*] and in the United States of America (USA) 9.3 to 14.6/10 000 [*5*]. The rate is lower than that of China which was 6.0/1000 [*16*], in Turkey 30.1/10 000 [*3*] and in north-west of the Islamic Republic of Iran (Hamadan) 50.1/10 000 [*10*]. These variations in different studies could be explained by the influence of racial, ethnic and social factors in various parts of the world, which are commonly explained as genetic disorders. Geographical, nutritional and socioeconomic and biological factors could also be involved. Other reasons for these variations in birth defect prevalence are the type of sample (referral hospitals would be expected to have higher rates) and method of diagnosis).

The rates of NTD in different ethnic groups showed that the Turkmen had the highest rate at 40.5/10 000 but among native Fars it was 25.2/10 000 and among Sistani it was 31.0/10 000. Studies by other researchers also show different NTD rates among different races [*5,17,18*], suggesting that race and ethnicity may be a factor in the rate of NTD [*19*].

Spina bifida was the most common NTD in our study, which agrees with

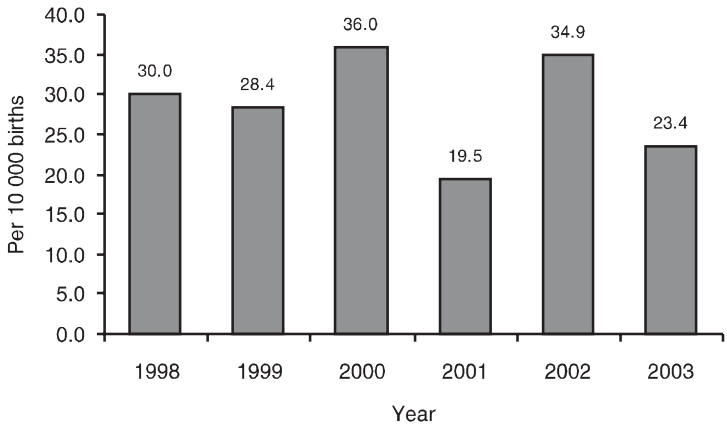

Figure 1 **Annual rates of neural tube defects (/10 000 births)**

other studies [*20,21*], followed by anencephaly and encephalocele. The rate of cystic spina bifida in our study population was 16.3/10 000, which is higher than 6.2/10 000 in France [*22*], 7.1/10 000 in Texas [*5*] and 1.09/10 000 in Saudi Arabia [*23*]. It should also be mentioned that our rate is higher than another study in Tehran (central Islamic Republic of Iran) with 3.8/10 000 [*9*] and in Hamadan (north-west province) with 6.98/10 000 [*10*]. The rate of anencephaly in our study was 11.3/10 000, which is higher than the other studies such as 6.0/10 000 in South America [*24*], 6.4/10 000 in Texas [*5*] and 8.0/10 000 in Tehran [*9*]. But the rate in our study was lower than in Hamedan with 15.6/10 000, China with 87.0/10 000 and Turkey with 16.4/10 000 [*10*]. The rate of encephalocele (1.1/10 000) was similar to a study in the USA (1.03/10 000) [*5*].

Regarding sex differences, our results indicate that the rate of NTD was higher in females than males (male to female ratio = 0.76), as reported by other researchers [*5,25,26*]. The male to female ratio was 0.69 for anencephaly and 0.74 for spina bifida, which is also comparable to other studies [*5,9,17,22–24*]. For example, in the USA the ratio for all NTD was 0.62, for anencephaly 0.54 and for spina bifida 0.68 [*5*].

Our research showed that the highest rate of affected newborns was in mothers aged ≥ 35 years (50.7/10 000), with 23.3/10 000 in mothers aged 15–19 years and 28.2/10 000 aged 20–34 years. Our observation of a linear relation between the rate of NTD and increasing maternal age is different from other studies which show a higher risk among younger mothers [*27*] or, more commonly, a U-shaped curve with higher rates in mothers aged under 19/20 years and over 35 years [*5,12,22,28*]. Thus age is a complex risk factor in NTD and this issue needs more investigation.

In this study a seasonal variation was observed and the rate of NTD was higher in the October to March period with a peak in December. In a study in Ireland [*27*] the rate was higher in January–June (28.0/10 000) compared with July–December (23.2/10 000). Also in Ireland the peak was in April [*27*].

Some research has shown that the rate of consanguineous marriage is high in NTD births [*21,23*]. In our study 33% of parents with affected newborns had consanguineous marriage, although this rate is lower than in Saudi Arabia (89% of the spina bifida parents) [*23*] and higher than in South Africa [*12*]. Another study in the north-west of the Islamic Republic of Iran indicated that the rate of consanguinity among parents with healthy infants was 23% [*29*]. The possibility that consanguinity could be a risk factor for NTD in a population requires further research.

In this study 63% and 37% of parents with affected newborns lived in rural and urban areas respectively. A greater prevalence of NTDs at birth has been shown for rural areas compared with urban areas [*30,31*]. A report from China (1988–1991) indicated the prevalence of NTD in rural areas (44.3/10 000) was 3 times higher than urban areas (14.4/10 000) [*32*]. It may be due to factors such as high population growth rates and socioeconomic factors.

According to our findings ethnicity and interfamilial marriage may play a role in the NTD rate in this region of the Islamic Republic of Iran, although there could also be effects of environmental factors such as exposure to toxic agricultural substances and nutritional factors such as folate deficiency. So further investigations are needed, and we recommend that a central registry be set up to record NTD occurring in the south-east Caspian Sea region of the country.

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Parental consanguinity among parents of neonates with congenital hypothyroidism in Isfahan

M. Hashemipour,[1] M. Amini,[1] M. Talaie,[1] R. Kelishadi,[1] S. Hovespian,[1] R. Iranpour,[1] M. Salek,[1] S. Haghigh[1] and K.H. Khatibi[1]

قرابة العَصَبَات بين آباء الوِلْدان المصابين بقصور الدرقية الخلقي في إصفهان

مهين هاشمي بور، مسعود أميني، مجتبى طلائي، رؤيا كليشادي، سيلوا هوسبيان، رامين إيرانبور، مهدي سالك، ساسان حقيقي، خسرو خطيبي

الخلاصة: حدَّد الباحثون مدى انتشار قصور الدرقية الخلقي، ومعدل انتشار قرابة العَصَبَات بين آباء الوِلْدان المصابين بقصور الدرقية لدى 93 381 وليداً، وُلدوا في 17 مستشفى في إصفهان، خلال الفترة من أيار/مايو 2002 إلى نيسان/إبريل 2005. وقيست مستويات ثيروكسين المصل (T4)، والهرمون المنبِّه للدرقية (TSH)، خلال المدة من اليوم الثالث إلى اليوم السابع من الولادة. واستُدعي الوِلْدان الذين وجدت مستويات القياس لديهم غير طبيعية، لإعادة تقييمها. واعتبر الوِلْدان الذين كان مستوى الهرمون المنبِّه للدرقية لديهم 10 ميلي وحدة دولية/ل أو أكثر، وثيروكسين المصل أقل من 6.5 ميكروغرام/دل، في المقايسة الثانية، مصابين بقصور الدرقية. وبلغ مجموع من استُدعي 1038 وليداً، شخصت الإصابة بقصور الدرقية لدى 274 منهم. وتبيَّن أن هنالك ترابطاً يُعتدُّ به إحصائياً بين قرابة الوالدين وبين الإصابة بقصور الدرقية الخلقي (P = 0.006). وكان قصور الدرقية الخلقي أكثر شيوعاً لدى الوِلْدان الذين آباؤهم أبناء عمومة من الدرجة الأولى، منه لدى الوِلْدان الذين آباؤهم أبناء عمومة من الدرجة الثانية (P = 0.008).

ABSTRACT We determined the prevalence of congenital hypothyroidism and the rate of consanguinity among parents of hypothyroid neonates among 93 381 neonates born in 17 hospitals in Isfahan from May 2002 to April 2005. Serum thyroxine (T_4) and thyroid stimulating hormone (TSH) levels were measured on the 3rd–7th day of birth and neonates with abnormal levels were recalled and the levels reassessed. Those with TSH ≥ 10 mIU/L and T_4 < 6.5 µg/dL on the second assay were considered hypothyroid. In all, 1038 neonates were recalled and 274 were diagnosed as hypothyroid. There was a significant association between parental consanguinity and congenital hypothyroidism (*P* = 0.006); congenital hypothyroidism was commoner in neonates with 1st cousin parental consanguinity than 2nd cousin parental consanguinity (*P* = 0.008).

Consanguinité parentale chez les parents de nouveau-nés présentant une hypothyroïdie congénitale à Ispahan

RÉSUMÉ Nous avons évalué la prévalence de l'hypothyroïdie congénitale et le taux de consanguinité chez les parents de nouveau-nés hypothyroïdiens dans un échantillon de 93 381 enfants nés dans 17 hôpitaux d'Ispahan entre mai 2002 et avril 2005. La thyroxine (T_4) et la thyréostimuline, ou TSH (*pour thyroid stimulating hormone*), sériques ont été mesurées entre les 3e et 7e jours de vie, les nouveau-nés présentant des taux anormaux étant alors rappelés pour un nouveau dosage hormonal. En présence d'une TSH ≥ 10 mUI/L et d'une T_4 < 6,5 µg/dL, le diagnostic d'hypothyroïdie était alors confirmé. Nous avons recensé au total 1038 rappels de nouveau-nés et 274 cas d'hypothyroïdie avérée. L'association entre consanguinité parentale et hypothyroïdie congénitale est apparue significative (p = 0,006). Nous avons constaté une plus grande fréquence de l'hypothyroïdie congénitale chez les nouveau-nés issus de mariages entre cousins germains que chez les enfants nés de mariages entre cousins issus de germains (p = 0,008).

[1]*Isfahan Endocrine and Metabolism Research Centre, Isfahan, Islamic Republic of Iran (Correspondence to M. Hashemipour: emrc@mui.ac.ir).*

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Introduction

Congenital hypothyroidism is one of the most preventable causes of mental retardation. Its prevalence is reported to be 1 in 3000–4000 live births. Early diagnosis and treatment of congenital hypothyroidism can prevent its hazards [*1*].

The prevalence of congenital hypothyroidism varies in different areas and among different races. Previous studies have shown that congenital hypothyroidism was more prevalent among Asian neonates than others and parental consanguinity was considered as a cause [*2,3*]. Besides familial factors, other risk factors, such as environmental, genetic and autoimmune factors, affect the prevalence of congenital hypothyroidism [*4–7*].

Congenital hypothyroidism has been reported to be more prevalent in the Islamic Republic of Iran than other communities. Three studies in our country, in Fars province, Tehran and Isfahan, have reported a high prevalence of congenital hypothyroidism [*8–10*]. Moreover, recently Ordookhani et al. reported a high prevalence of permanent congenital hypothyroidism and parental consanguinity among patients with congenital hypothyroidism in Tehran [*11*].

The aim of our study was to determine the prevalence of congenital hypothyroidism in our region by screening for the disorder in Isfahan. According to the preliminary findings of the study of Hashemipour and colleagues [*10*], the prevalence of congenital hypothyroidism is high in our region. Therefore, as well as determining the prevalence of congenital hypothyroidism, we compared parental consanguinity of all referred neonates with that of neonates with confirmed congenital hypothyroidism to determine if this factor plays a role in the disorder.

Methods

This was a descriptive study carried out from May 2002 to April 2005 and all neonates referred from the 17 maternity hospitals in Isfahan were evaluated. The study was designed in collaboration with paediatric endocrinologists, the head of the Isfahan Endocrine and Metabolism Research Centre, the head of the Social Medicine Department of Isfahan University of Medical Sciences and Health Services and carried out with the research assistance of Isfahan University of Medical Sciences & Health Services. The Research Bureau of Isfahan University of Medical Science and Health Services gave ethical approval for the study.

The deans of all the 17 hospitals and the heads of their neonatal sections were informed of the study, and the importance of screening for congenital hypothyroidism was explained. With their approval, we approached all newly delivered mothers in the hospitals and explained to them the disorder, its complications and the method of screening. The coverage percentage of this project was derived by calculating the ratio of the number of referred neonates to live births.

Trained nurses in the hospitals completed a questionnaire with mothers which recorded gestational age, neonate's sex, weight, height, head circumference and nationality and parental consanguinity (1st and 2nd cousin). We recommended that the mothers attend the Isfahan Endocrine and Metabolism Research Centre for screening after discharge from hospitals on the 3rd–7th day of delivery. They were requested to give the questionnaire to the executive committee of congenital hypothyroidism screening in the Centre. This committee consisted of a trained general practitioner and nurses who received the referred women.

Venous blood samples of the neonates were obtained by trained nurses in the Centre on the 3rd–7th day of birth and serum thyroxine (T_4) and thyroid stimulating hormone (TSH) levels were measured in Isfahan Endocrine and Metabolism Research Centre. An endocrinologist and collaborating general practitioner evaluated the laboratory results, the status of parental consanguinity and determined the neonates who needed to be recalled.

Recalls were determined based on the levels of T_4 and TSH in neonates born at term who weighed over 2500 g. Neonates born at term with $T_4 < 6.5$ μg/dL or TSH ≥ 20 mIU/L [*12,13*], and premature neonates with a low level of T_4 for their weight or high TSH level for their age were selected for recall [*14*]. Neonates who were referred after the 7th day of birth were recalled based on a T_4 level < 6.5 μg/dL or TSH level > 10 mIU/L [*15*].

If the TSH level was between 20 and 39 mIU/L then a second laboratory test, including T_4, was carried out. If the TSH level was > 40 mIU/L then as well as carrying out a second laboratory tests, treatment was initiated [*16*]. The second measurement from recalled neonates was performed on the 7th–28th day of birth. According to the 2nd laboratory test, if the levels of TSH and T_4 were in the normal range, the neonate was considered to have hyperthyrotropinaemia. If the level of T_4 was < 6.5 μg/dL or TSH > 10 mIU/L [*12*] then the neonate was considered to have congenital hypothyroidism.

The physician performed physical examinations of the neonates and evaluated the laboratory tests and finally, based on the findings, prescribed levothyroxin 10–15 g per kg per day for hypothyroid neonates.

In addition to measurement of TSH level, if term or premature neonates had low levels of T_4 according to their weight, additional laboratory tests, such as T_3 resin uptake (T_3RU) and free T_4 index (FT_4I), were carried out. According to these results, congenital hypothyroidism was diagnosed and patients underwent treatment. Patients with confirmed congenital hypothyroidism were recommended to undergo thyroid scintigraphy before starting treatment.

Laboratory methods

The levels of TSH and T_4 were measured using Iran Kavoshyar kits. The level of TSH and T_4 were measured using immunoradiometric assay and radioimmunoassay respectively with the gamma counter of the Endocrine and Metabolism Research Centre (Berthold LB 12-2111). Sensitivity of the kits was 0.05 mIU/L for TSH and 0.38 μg/dL for T_4.

Thyroid scintigraphy was performed using technetium pertechnetate.

Statistics

Data were analysed using *SPSS*, version 13 and *Epi-Info*, 2002. Differences in the frequency of parental consanguinity between screened neonates without congenital hypothyroidism and those with congenital hypothyroidism were compared using the chi-squared test. The odds ratios (OR) and confidence intervals (CI) for parental consanguinity in neonates with congenital hypothyroidism and those without were calculated. $P < 0.05$ was considered significant.

Results

This study included 93 381 neonates from 17 private and public maternity hospitals in Isfahan which represented 82.8% of live births. Of the neonates, 51.7% were female and 48.3% male, 97% were born at term and 3% premature, and 97.3%, 2.6% and 0.1% were respectively Iranian, Afghan and oth-

er nationalities (Armenian, Iraqi, Libyan, Yemeni); the nationality of 136 neonates was not determined.

Of all the studied neonates, 27.7% had parental consanguinity (both 1st and 2nd cousin); the parents of 61.6% of this group had a consanguineous marriage with a 1st degree relative. Of the 93 381 referred neonates, 1038 (1.1%) were recalled; 971 (93.5%) of these underwent laboratory tests and 274 were diagnosed with congenital hypothyroidism and received medical treatment.

The prevalence of congenital hypothyroidism was 2.9 per 1000 live births or 1 in 341 live births; 4 neonates had secondary hypothyroidism. As regards sex, 161 (58.8%) of hypothyroid neonates were female and 113 (41.2%) male, giving a female to male ratio of 1.4:1. Of the hypothyroid neonates, 251 (91.2%) were born at term and 23 (8.4%) were premature.

The rate of parental consanguinity (1st and 2nd cousin) is shown in Table 1; 101 (36.9%) neonates with congenital hypothyroidism had consanguineous parents (both 1st and 2nd degree relation) and of these, 75 (74.3%) had parental consanguinity with a 1st degree relation.

Only 121 (44.1%) of the hypothyroid neonates underwent thyroid scintigraphy (most of them were the patients with primary high TSH levels); the remainder did not undergo the procedure because of poor compliance of their parents. According to the results of the thyroid scan, 82 (68.3%) of the patients with congenital hypothyroidism had a normal thyroid scan, 1 had goitre, 7 (5.8%) had ectopia and 31 (25.8%) had agenesia. Therefore 31.6% of our patients with congenital hypothyroidism had dysgenesia.

The overall prevalence of parental consanguinity among normal, goitrous, ectopic and agenetic congenital hypothyroidism patients was 46.3, 0.0%, 57.1% and 45.1% respectively. Data about 1st and 2nd cousin parental consanguinity among these patients are presented in Table 2.

There was significant association between parental consanguinity (both 1st and 2nd degree relation) and the prevalence of congenital hypothyroidism. Consanguinity was more prevalent among neonates with hypothyroidism (OR = 1.53, 95% CI: 0.51–0.85, $\chi^2 = 11.33$, $P = 0.0007$). In addition, congenital hypothyroidism was more prevalent in neonates with 1st cousin parental consanguinity as compared with 2nd cousin parental consanguinity (OR = 1.8, 95% CI: 1.13–2.88, $\chi^2 = 6.83$, $P = 0.008$).

Discussion

The prevalence of congenital hypothyroidism worldwide is reported to be 1 in 3000–4000 live births [*1*]. In our study of 93 381 referred neonates the prevalence of congenital hypothyroidism was 1 in 349 live

Table 1 **Parental consanguinity in all studied newborns and those with congenital hypothyroidism**

	1st cousin parental consanguinity	2nd cousin parental consanguinity	No familial marriage	Total[a]
Total unaffected neonates	15 900	9916	67 251	93 067
Hypothyroid neonates	75	26	173	274

[a]*For 40 infants it was not known if the there was parental consanguinity or not.*

Table 2 **Parental consanguinity among patients who performed thyroid scintigraphy**

Parental consanguinity	Thyroid scintigraphy							
	Normal (*n* = 82)		Goitre (*n* = 1)		Agenesia (*n* = 31)		Ectopia (*n* = 7)	
	No.	%	No.	%	No.	%	No.	%
1st cousin	31	37.8	0	0.0	12	38.7	3	42.9
2nd cousin	7	8.5	0	0.0	2	6.4	1	14.3
Overall	38	46.3	0	0.9	14	45.1	4	57.1

births, which is high. Previous studies have reported a high prevalence of congenital hypothyroidism in our country (1 in 1433, 1 in 914 and 1 in 370 live birth in Fars province, Tehran and Isfahan respectively) [*8–10*]. Rates for nearby countries differ. The prevalence of congenital hypothyroidism in Pakistan was reported to be 1 in 1000 live births [*17*], while in Saudi Arabia urban areas it was 1 in 2759 live births and in the rural areas it was 1 in 1538 live births [*18*].

Our study shows that among neonates with congenital hypothyroidism, parental consanguinity was 1.5 times higher than among neonates without congenital hypothyroidism. Various studies have reported that congenital hypothyroidism is more prevalent among Asian families than non-Asian ones. Rosenthal et al. evaluated the prevalence of congenital hypothyroidism in the north-west of the United Kingdom (UK) among different races, nationalities and minorities, especially Muslims and Asians [*2*]. They found that the prevalence rates of congenital hypothyroidism among Asians and non-Asian families were 1 in 918 and 1 in 3391 live births respectively. This significant difference may be a result of parental consanguinity among the Asian population. Congenital anomalies, mortality and morbidity were also more prevalent in hypothyroid neonates [*2*]. Another study in the UK, from 1981 to 1991 showed that the prevalence of congenital hypothyroidism among Pakistani families with consanguineous parents (1 in 781 live births) was significantly higher than the total prevalence of congenital hypothyroidism in the UK (1 in 2154 live births) [*3*]. In addition, congenital hypothyroidism prevalence among Indian neonates without consanguinity was 1 in 5540 live births.

A study in Israel showed that the incidence of congenital hypothyroidism was higher in Arab families with familial marriage than those reported from industrialized countries, but was similar to those found in Saudi Arabia [*19*]. This may be due to the high degree of consanguineous marriages among Arab populations. Also a study in Saudi Arabia found that congenital hypothyroidism was 1.8 times more common in rural areas and they believed that consanguinity was the cause [*18*]. Ordookhani and colleagues have shown high prevalence of familial marriage among cases of congenital hypothyroidism [*11*]. Only a few studies have shown no significant relationship between consanguinity and congenital hypothyroidism [*20*]. Overall these findings suggest a role of consanguinity in congenital hypothyroidism and other congenital anomalies.

Recently Ordookhani and colleagues reported a high prevalence of consanguinity among patients with permanent congenital

hypothyroidism [*21*]. They concluded that parental consanguinity may be considered a causative factor for the high prevalence of thyroid dysgenesia, which was the commonest cause of permanent congenital hypothyroidism in their study. Overall, 28.6% of all screened neonates and 47.1% of hypothyroid patients had parental consanguinity. Our findings (27.7% of all studied neonates and 36.9% of congenital hypothyroidism patients with consanguineous parents) are similar to these.

In our study, parental consanguinity, especially with 1st cousin relation, was more prevalent among hypothyroid neonates. We did not study the prevalence of transient and permanent hypothyroidism because our patients with congenital hypothyroidism had not reached 3 years of age which is necessary for determination of transient and permanent forms of congenital hypothyroidism. Nonetheless, our findings support the role of consanguinity in the high prevalence of overall congenital hypothyroidism.

According to our study, overall parental consanguinity and 1st cousin parental consanguinity were present in 47.4% and 39.5% of all infants with dysgenesia (agenetic and ectopic), which is in line with the results of a recent study in Tehran [*10*] which reported overall and 1st cousin parental consanguinity of 55.6% and 33% among congenital hypothyroidism patients with dysgenesia. Although the rate of transient and permanent congenital hypothyroidism has not yet been determined, patients diagnosed with dysgenesia are considered permanent congenital hypothyroid. The remainder with normal thyroid scan can be considered transient pending additional studies that will be performed at 3 years of age.

Considering different etiologies of congenital hypothyroidism, dyshormonogenesis is inherited through an autosomal recessive pattern but dysgenesia is a sporadic disorder. The causes of thyroid dysgenesia are unclear, but are believed to be multifactorial, including environmental and complex gene interactions [*22*]. A recent study has reported that familial factors affect 2% of all dysgenesis cases [*23*].

As with the study of Ordookhani et al., nearly half of our patients with congenital hypothyroidism with dysgenesia had parental consanguinity which has not been reported by other studies. This may reflect the presence of some unknown mutations in the genes involved in thyroid ontogeny in our population.

Considering the high prevalence of congenital hypothyroidism in our country, consanguinity, especially with first degree relatives, clearly appears to have a role in this increased prevalence. More studies are needed in this area. At the same time, interventions are needed to try and reduce the rate, such as public awareness activities to increase people's knowledge about the condition and the risk of familial marriage.

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Child and Adolescent Health and Development website

This website aims at sharing information on the work on the health and psychosocial development of children under-5 carried out by the WHO Regional Office for the Eastern Mediterranean and related activities and initiatives promoted and carried out in countries in the Region. It is intended for public health and programme managers, academia, civil organizations and nongovernmental organizations, students and anyone interested in public child health issues, with special focus on the Eastern Mediterranean Region.

The CAH website provides detailed information on the coverage of child health activities at different levels in countries in the Region, especially the implementation of the Integrated Management of Child Health (IMCI) strategy. Specific sections describe the evolution of IMCI over the years in the Region, the process and guidelines to develop national child health policies, work carried out in the area of preservice education related to child health, health systems issues, the community component, the child health-related Millennium Development Goals, research work, and advocacy initiatives.

The website can be accessed at: http://www.emro.who.int/cah/

Prevalence of refractive error and low vision among schoolchildren in Cairo

B.M. El-Bayoumy,[1] A. Saad[2] and A.H. Choudhury[3]

معدَّل انتشار العيوب الانكسارية وضَعْف الرؤية بين تلاميذ المدارس في القاهرة

بشرى محمد البيومي، أمل سعد، عبد الحنان شودري

الخلاصة: أُجري مسح أوَّلي للوقوف على معدَّل انتشار العيوب الانكسارية وضَعْف الرؤية، لدى 5839 من تلاميذ المدارس في الفئة العمرية 7 – 14 عاماً، في العاصمة المصرية، القاهرة. واستخدمت في التحرِّي لوحة لاندولت لاختبار حدة الإبصار، واختبار الثقب. وتبيَّن من الدراسة أن معدل انتشار العيوب الانكسارية (حدة الإبصار ≤ 12/6) بين تلاميذ المدارس يبلغ 22.1%، وأن معدل انتشار ضعف الرؤية (حدة الإبصار ≤ 18/6) يبلغ 12.5%. وكان معدل انتشار ضَعْف الرؤية أعلى ما يكون بين تلاميذ المدارس الإعدادية الذين يزيد عمرهم على 12 عاماً. وكانت العيوب الانكسارية أعلى بين الإناث (21.4 للإناث، مقابل 13.6% للذكور). ويوصي الباحثون بإجراء مسح وطني لتحرِّي مشكلات الإبصار لدى الأطفال في سن المدرسة وما قبل سن المدرسة.

ABSTRACT A preliminary survey was conducted to detect the prevalence of refractive error (RE) and low vision among 5839 schoolchildren aged 7–14 years in Cairo, Egypt. Screening was done using Landolt broken ring chart and pinhole test. The prevalence of RE (visual acuity ≤ 6/12) among the schoolchildren was 22.1% and low vision (visual acuity ≤ 6/18) was 12.5%. The prevalence of low vision was greatest among the preparatory schoolchildren aged 12+ years. RE was higher among the female students than males (21.4% and 13.6% respectively). Development of a national survey for detection of visual problems for both preschool and school-aged children is recommended.

Prévalence des troubles de la réfraction oculaire et de la déficience visuelle chez les écoliers du Caire

RÉSUMÉ Une enquête préliminaire a été menée au Caire (Égypte) afin de déterminer la prévalence des troubles de la réfraction oculaire et de la déficience visuelle chez 5839 enfants scolarisés âgés de 7 à 14 ans. Le dépistage a reposé sur le test optométrique de Landolt, dit test de vision de loin (anneau brisé), et le test de la lampe à fente (ou sténopé, dit également *pinhole*). La prévalence des troubles de la réfraction oculaire (acuité visuelle ≤ 6/12) chez les écoliers était de 22,1 % et celle de la déficience visuelle (acuité visuelle ≤ 6/18) de 12,5 %. La prévalence de la déficience visuelle était la plus élevée parmi les écoliers de 12 ans et plus. Les troubles de la réfraction oculaire étaient plus fréquents chez les filles que chez les garçons (21,4 % contre 13,6 %). Il est recommandé de mettre en place une enquête nationale de dépistage des problèmes visuels chez les enfants d'âge préscolaire et scolaire.

[1]*Memorial Institute for Ophthalmic Research, Cairo, Egypt.*
[2]*National Research Centre, Cairo, Egypt (Correspondence to A. Saad: amel_h3@yahoo.com).*
[3]*Regional Office for the Eastern Mediterranean, World Health Organization, Cairo, Egypt.*
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Introduction

Refractive error (RE) leading to low vision is one of the most common problems of visual impairment, especially among schoolchildren, and frequently remains undiagnosed for long periods. The World Health Organization (WHO) has grouped uncorrected RE with cataract, glaucoma, trachoma and macular degeneration, infectious disease, and vitamin A deficiency among the leading causes of blindness and vision impairment in the world [*1*]. In Egypt, a preliminary national survey done in the Helwan area of Cairo reported that 34% of the recorded disabilities were visual disability [*2*].

Correction of RE and low vision are one of the priorities of global initiatives for Vision 2020 [*3*]. In Egypt there are few studies showing the prevalence of errors of refraction. The present study is a preliminary survey to determine the prevalence of RE and low vision among schoolchildren in Cairo, which is the capital of Egypt, with the highest population density in the country. It is the first study on a large sample (6000 students) in 4 educational sectors of different socioeconomic level. Studies have been done in different governorates with smaller populations and in smaller samples (not more that 1000–1500) students [*4–8*]. This is also the first study to train school doctors and school nurses (as all the schools are covered by the Medical Insurance Organization, the governmental organization that funds the medical services of all school-age children in primary, preparatory and secondary schools).

Methods

Selection of the target population

This was a cross-sectional descriptive study of a cluster random sample of 12 government schools. The schools were chosen using a multistage random sampling technique. The schools of Cairo governorate were divided into clusters based on Ministry of Education geographic divisions. Four educational geographic divisions were chosen randomly (El-Waiely, Mataria, Heliopolis and Nozha).

The schools of each of the selected educational geographic divisions were stratified into primary schools, preparatory schools for males and preparatory schools for females. Subsets of school clusters were randomly selected from the 3 school strata of the chosen educational areas, i.e. 1 primary school, 1 male preparatory school and 1 female preparatory school independent of their numbers. All the students of the selected schools were included in the screening (age range 7–15 years). Private schools were excluded from the study as their health systems are different from that of the government schools and there is a private school doctor for each school.

Information on parents' education, occupation and employment status was also obtained from the parents of each child by questionnaire, to estimate the socioeconomic status according to Park and Park [*9*].

Ophthalmic examination

The health insurance school health physician and the school nurse of each school included in the study were trained by the authors how to measure the visual acuity (VA) of the students. Assessment of VA of all the students was done with a Landolt broken ring chart at 6 metres in a well-illuminated room. VA was measured with and without glasses. Children with VA 6/12 or less with or without correction were examined by pinhole test to evaluate the improvement of VA. The school doctors were also trained to evaluate ocular balance, strabismus by cov-

ered and uncovered test, and ocular motility in the 6 cardinal positions.

The children with VA ≤ 6/18 in both eyes with best correction were categorized as low vision. Children with uncorrected VA were referred to the medical insurance clinics. The type of RE was obtained from the ophthalmic prescription.

Statistical analysis

The collected data were analysed using *SPSS*, version 7.5. The prevalence of RE among the screened students was estimated. Pearson chi-squared test was applied and differences were considered significant at $P < 0.05$.

Results

From the school records, 6000 students aged from 7 to 15 years were selected to be included in the study; 161 students (2.7%) refused to participate. The remaining 5839 students (3113 females and 2726 males) were screened.

The screening revealed that 1292 of the 5839 students (22.1%) had RE (VA ≤ 6/12), and 728 (12.5%) had low vision (VA ≤ 6/18) (Table 1). Strabismus was found in only 42 students (0.7%). Of the children with RE, 55.7% were myopic, 27.3% hypermetropic and 17.0% astigmatic.

Table 1 **Visual acuity of the 5839 children screened in Cairo governorate**

Visual acuity	No.	%
6/6	2840	48.6
6/9	1707	29.2
6/12	564	9.7
6/18	336	5.8
6/24	201	3.4
6/36	125	2.1
6/60	66	1.1
Total	5839	100.0

Table 2 shows the age distribution of the children with RE: 85.4% were aged 12+ years. Figure 1 shows that the prevalence of RE and low vision were significantly higher among female students compared with males ($P < 0.05$).

Among the students with RE, 42.3% wore glasses and 57.7% had no glasses. The proportion of students with RE and without glasses was slightly higher among families of low socioeconomic status (55.0%), than among families of middle socioeconomic status (52.7%), but this was not significantly different ($P > 0.05$).

Discussion

A preliminary national survey of disabilities in Egypt in Helwan, Cairo, reported that 34% of the recorded disabilities were visual disability [*2*].

The present study was a preliminary screening to determine the prevalence of refractive error (RE) among schoolchildren from 4 different randomly selected educational geographic divisions. We found the prevalence of RE (VA ≤ 6/12) was high—22.1% of school students aged 7–14 years—and 12.5% of them had low vision (VA ≤ 6/18). The frequency of students with low vision was mostly among the preparatory-school students.

A previous study of primary-school children in one area of Cairo (Shubra) diagnosed RE in 21.8% of all examined children [*5*], whereas another study detected a higher prevalence of RE (36.8%) among primary-school children in Giza governorate [*6*]. In Menofiya governorate it was reported that 17.5% of primary-school children had RE [*4*]. In Tanta governorate, RE was found in about 39% of 511 primary-school students,

Table 2 **Distribution of visual acuity by age for children with refractive errors**

Age (years)	No. screened	Visual acuity 6/18		6/24		6/36		6/60		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%
7–	359	10	2.8	3	0.8	0	0	0	0	13	3.6
8–	395	10	2.5	2	0.5	1	0.3	1	0.3	14	3.5
9–	294	5	1.7	5	1.7	6	2.0	0	0	16	5.4
10–	428	10	2.3	8	1.9	3	0.7	1	0.2	22	5.1
11–	401	23	5.7	8	2.0	8	2.0	2	0.5	41	10.2
12–	1570	111	7.1	70	4.5	40	2.5	17	1.1	238	15.2
13–	1086	65	6.0	53	4.9	26	2.4	20	1.8	164	15.1
14–15	1303	102	7.8	52	4.0	41	3.1	25	1.9	220	16.9
Total	5836	336	5.8	201	3.4	125	2.1	66	1.1	728	12.5

amblyopia in 0.8% and strabismus in 0.6% [*7*]. In Al-Minya governorate a study on a random sample of 1588 schoolchildren aged 7–15 years found RE in 11.9%, amblyopia in 3.6% and strabismus in 1.6% [*8*].

RE may be viewed as resulting from a combination of genetic and environmental factors [*10*]. Myopia has reached epidemic proportions in many countries such as Japan, Hong Kong, Taiwan and Singapore [*11*]. The present study found that myopia was the most prevalent type of RE among the screened schoolchildren (55.7%), followed by hypermetropia (27.3%), and astigmatism (17.0%); strabismus was found in only 0.7%.

Figure 1 **Prevalence of refractive error and low vision by sex**

In a previous study, only 9.2% of the children with RE wore glasses [*7*]. But the present screening revealed that 42.3% had glasses, although family income had no significant effect. Not wearing glasses may lead to a greater deterioration in VA of the affected children. Thus, awareness about the importance of visual correction may play a significant role in proper management of RE cases. Further study about the public awareness of early detection of RE and proper management is suggested.

Recommendations

The main recommendations from this study are:

- Development of national programme for early detection of visual impairment,

involving both preschoolers and schoolchildren.

- Establishment of a school screening programme and follow-up for RE and low vision involving both preschoolers and schoolchildren.
- Governmental support for providing low-cost spectacles and school support to encourage children to wear their glasses.

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Prevalence and causes of childhood blindness in camps for displaced persons in Khartoum: results of a household survey

Z. Zeidan,[1] K. Hashim,[2] M.A. Muhit[3] and C. Gilbert[3]

انتشار العمى بين الأطفال في مخيّمات النازحين في الخرطوم وأسبابه: نتائج مسح أسري

زيدان عبده زيدان، خالد هاشم، محمد موهيت، كلير قلبرت

الخلاصة: حُدِّدت أسباب، ومدى انتشار العمى بين 29 048 طفلاً تقلّ أعمارهم عن 16 عاماً، ينتمون إلى جميع الأُسَر التي تضمُّها خمسة مخيّمات للنازحين داخلياً في الخرطوم، بالسودان. وفي أعقاب زيارات قام بها عاملون صحيون مدرَّبون من منزل إلى منزل، خضع 916 طفلاً لإجراءات تقييم إضافية، تبيَّن من خلالها إصابة 2.7% منهم بالعمى، و1.6% بضَعْف وخيم في البصر، و5.5% بضَعْف في البصر، وفق معايير منظمة الصحة العالمية. وقُدِّر انتشار العمى بين الأطفال في المخيمات بـ 1.4 لكل 1000 من الأطفال، وتبيَّن أن الأسباب الرئيسية للإصابة بالعمى هي عتامات القرنية (40%) الناجمة بشكل أساسي، عن عَوَز الفيتامين A، يليها الغَمَش amblyopia (32.5%).

ABSTRACT The prevalence and causes of visual impairment and blindness were determined in 29 048 children < 16 years in all households of 5 camps for internally displaced people in Khartoum State, Sudan. After house-to-house visits by trained health care workers, 916 children received further assessment, 2.7% of whom were found to be blind, 1.6% to be severely visually impaired and 5.5% to be visually impaired, according to World Health Organization criteria. The prevalence of blindness in children in the camps was estimated as 1.4 per 1000 children. The leading causes of blindness were found to be corneal opacities (40.0%), mainly due to vitamin A deficiency, followed by amblyopia (32.5%).

Prévalence et causes de la cécité infantile dans les camps pour personnes déplacées de Khartoum : résultats d'une enquête auprès des ménages

RÉSUMÉ La prévalence et les causes des déficiences visuelles et de la cécité ont été déterminées chez 29 048 enfants de moins de 16 ans dans chacun des foyers hébergés dans 5 camps pour personnes déplacées situés dans l'État de Khartoum au Soudan. À la suite d'une enquête porte à porte effectuée par des personnels de santé dûment formés, 916 enfants ont fait l'objet d'une évaluation approfondie : 2,7 % d'entre eux étaient atteints de cécité, 5,5 % de déficience visuelle partielle et 1,6 % de déficience visuelle grave, selon les critères de l'Organisation mondiale de la Santé. La prévalence de la cécité chez les enfants logés dans ces camps a été estimée à 1,4 pour 1000 enfants. Les principales causes de cécité identifiées étaient l'opacité cornéenne (40,0 %), essentiellement due à une carence en vitamine A, suivie de l'amblyopie (32,5 %).

[1]Department of Community Medicine, Faculty of Medicine, University of Khartoum, Khartoum, Sudan (Correspondence to Z. Zeidan: drziedan61@hotmail.com).
[2]Walidain Eye Hospital, Khartoum, Sudan
[3]London School of Hygiene and Tropical Medicine, London, United Kingdom.
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Introduction

Five per cent of worldwide blindness involves children younger than 15 years of age; in developing countries this age group constitutes 50% of the population. By World Health Organization (WHO) criteria, there are 1.5 million children worldwide who are blind: 1.0 million in Asia, 0.3 million in Africa, 0.1 million in Latin America and 0.1 million in the rest of the world. There are marked differences in the causes of childhood blindness in different regions due to different socioeconomic factors. In developing countries, 30% to 72% of such blindness is avoidable: 9% to 58% is preventable and 14% to 31% is treatable. The leading cause of blindness in children in developing countries is corneal opacification caused by a combination of measles, xerophthalmia and the use of traditional eye medicine [*1*]. Infectious diseases, malnutrition, vitamin A deficiency and measles are the main causes of avoidable blindness in children of poor countries [*2*].

In Sudan there is an absence of population data on the prevalence of blindness in children. However, the prevalence of blindness in all ages in Sudan was found to be 1.78%, the major causes being cataract, corneal opacities, uncorrected refractive errors, trachoma and onchocerciasis [*3*].

It has been found that the causes of blindness in children are the same as the causes of under-5 mortality (e.g. premature birth, measles, vitamin A deficiency, congenital rubella syndrome and meningitis) [*4*]. Therefore the under-5 mortality rate can be taken as a proxy indicator to estimate the prevalence of child blindness. In Sudan, the under-5 child mortality rate was found to be 104/1000 live births.

The number of displaced people in Sudan has been estimated to be about 4 million [*5*]. The primary reason for leaving their origin was war, followed by food insecurity, economic opportunities and employment. Approximately 340 000 internally displaced persons (IDPs) live in the 5 official camps, which are located at the peripheries of 3 large cities (Khartoum, Khartoum North and Omdurman). They live in cardboard or mud houses in poor hygiene conditions and with a lack of water supply [*3*]. The results of an interagency household survey in displaced camps in Khartoum indicate that the crude mortality rate for children under 5 years is near the emergency threshold of 1 per 10 000 per day. The main cause of death in all areas is diarrhoea. Other causes included chest infections, pneumonia and measles [*6*]. Clearly living conditions are poor in the camps and child mortality is high, which suggests visual impairment may also be high among such children.

We aimed to determine the prevalence and leading causes of visual impairment and blindness in children in the above-mentioned camps. The outcome of this study will provide baseline information that may assist in measuring the progress of the VISION 2020 programme in fighting causes of childhood blindness in the country.

Methods

Subjects

Children under 16 years who were living in the IDP camps around Khartoum for at least a 6-month period before the study were the target population.

The 5 IDP camps in Khartoum State are Mayo Farms, Jebel Awlia, El Salaam, Wad el Bashier and Karton Kassala with a total populations of 72 621 during the study period (5–10 October 2003). Each camp was divided into 30 clusters, each having between 34 and 66 households, i.e. average population per cluster ranged between 408

and 792 individuals. Every 7th household in each cluster was visited.

The eligible children were those under 16 years who had been living in these households for a minimum period of 6 months before the survey and contracted eye problems from birth until the time of the study. Health workers who were trained in conducting field surveys to detect eligible children with eye problems or defective vision were involved in the house-to-house surveys. The health worker asked the parents whether their children had recent or previous eye problems, or if they had noticed any change in the eyesight of their children. Visual acuity was not measured during household interviews, but children with eye problems were registered and the heads of the households were given a card and requested to be present with their children on pre-determined days in the camp clinics to see the ophthalmic medical assistants and optometrists to assess their eye problems and visual acuity.

Examination in the field

Children found by the field health workers to have eye problems were later examined in the camp clinics by an examination team using portable equipment. The examining team in each camp consisted of 4 ophthalmic medical assistants, 1 optometrist, 2 medical officers, who were trained in the eye hospital, 2 health workers from the local health units of the camps, 5 medical students, a records clerk and a driver. At the camp clinic, each child was first registered by the health workers and a history was taken from each child or their parents by the health workers or medical students. Visual acuity was measured in each eye separately at 6 m and 3 m using a Snellen E chart. Impairment in visual acuity in children under 5 years was determined by showing bright objects. The following WHO categories of visual loss were used for visual acuity in the better eye: 6/18 or better – not impaired; < 6/18–6/60 – visual impairment; < 6/60–3/60 – severe visual impairment; < 3/60 – blind [*7*]. Trained ophthalmic medical assistants using a 4× magnifying loupe and a hand-held flashlight examined the anterior segment of the child's eye. Posterior segments were not examined at this level.

Acute eye problems were treated free of charge. Children with complicated eye diseases or visual acuity < 6/18 were referred to Alwaldain Eye Hospital, Omdurman Province. Transport was offered free of charge.

Examination in eye hospital

At the referral eye hospital, the ophthalmologist reviewed the field results. In children aged 5 years or more the external eye and anterior segment were examined using a slit lamp and posterior segments were examined with a direct ophthalmoscope after dilating the pupils, if necessary. A diagnosis of glaucoma was made on the basis of anterior and posterior segment signs, as visual testing was not possible. Glaucoma cases were assessed using a Schiotz tonometer to assess intraocular pressure.

Visual acuity was measured again and refraction was performed for all children. If there was difficulty measuring visual acuity in children under the age of 3 years of age, they were examined and refracted under local anaesthesia.

For each child with a visual acuity of < 6/18 in the better eye, the examining ophthalmologist sought to identify the reasons for visual loss.

All the findings were recorded on a data sheet and were entered into a database. The data were analysed using *SPSS*, version 10.

Results

The target population included 29 048 children under 16 years of age. Of these, 1115 children were registered by the health workers as having a history of recent or previous eye problems during the house-to-house interviews. Of these, 916 came to the camp clinics where they were examined and treated by the field team; 105 of them were found to have visual acuity < 6/18 and were referred to the eye hospital for further refraction and examination.

Out of the 105 referred to the eye hospital, 15 were found to be severely visually impaired (visual acuity < 6/60 in the better eye) and 25 blind (visual < 3/60). The prevalence of severe visual impairment among the referred children was 1.6% whereas the prevalence of blindness was 2.7% and the prevalence of blindness and severe visual impairment together was 4.4% (Table 1).

The prevalence of blindness was higher in males compared to females although this difference was not statistically significant, but it was significantly higher in the older age group than in the younger age groups in males ($P < 0.05$) (Table 2).

The commonest anatomical sites of visual loss in the 40 blind and severely visually impaired children were the corneas in 40% (corneal scaring), the higher centre of the brain in 32.5% (amblyopia), the lens (cataract) in 12.5%, retina in 7.5%, the whole globe in 2.5%, optic nerve in 2.5% and uvea (glaucoma) in 2.5% (Table 3).

In all, 35 (87.5%) of the blind or severely visually impaired children presented with avoidable causes of blindness and vision loss: vitamin A deficiency (22.5%), trauma (10.0%) and measles (7.5%), which are preventable causes, and amblyopia (32.5%) and cataract (12.5%), which are treatable causes (Table 4), although amblyopia is only treatable up to 9 years of age.

Of the 40 children with severe visual impairment and blindness, 23 were referred for surgery, 10/23 (43.4%) for corneal scaring and 8/23 (34.8%) for cataract surgery (Table 5).

Table 1 **Visual acuity of 916 children in camps for internally displaced people, Khartoum 2003**

Category of visual loss	Presenting acuity in the field		After refraction in the clinic	
	No.	%	No.	%
6/6–6/18	811	88.5	826	90.2
< 6/18–6/60	65	7.1	50	5.5
< 6/60–3/60	0	0.0	15	1.6
< 3/60	40	4.4	25	2.7
Total	916	100.0	916	100.0

Discussion

The prevalence of blindness in children varies between countries as it is influenced by socioeconomic status, and it is reflected by the childhood mortality rate. While eye lesions are the main causes in high-income countries, corneal scarring due to measles and vitamin A deficiency are the main causes in low-income countries [*1*]. In our study the prevalence of blindness and severe visual impairment in children in displaced camps in Sudan was 1.4/1000, which is consistent with the prevalence of childhood blindness in low income countries with low under-5 mortality rates, where the prevalence may be as high as 1.5 per 1000 children [*8*]

Our rate is similar to some population-based studies in other countries. For example, the prevalence of blindness was 1.5/1000 in the age group of 5–15 years in Chile but the main causes of blindness were not available [*9*]. In India it was found to be 1.2/1000 in the age group of 7–15 years,

Table 2 **Prevalence of blindness in children according to age and sex at camps for internally displaced people, Khartoum 2003**

Age group (years)	Males			Females			Total			95% CI
	No. examined	No. blind	%	No. examined	No. blind	%	No. examined	No. blind	%	
0–5	174	4	2.3	185	5	2.7	359	9	2.5	0.9–4.1
6–16	264	10	3.8	256	6	2.3	520	16	3.1	2.3–3.9
Unknown	11	0	0.0	026	0	0.0	37	0	0.0	–
Total	449	14	3.1	467	11	2.4	916	25	2.7	0.7–4.7

Blindness indicated by visual acuity < 3/60.
CI = confidence interval.

where retinal disorders, corneal opacities, congenital anomaly and amblyopia were the main causes of blindness [*9*]. In Nepal the prevalence of blindness was found to be 1.5/1000 in the age group of 5–15 years, but the main causes of blindness were not available [*9*].

Examining the main causes showed that corneal scarring (mostly related to vitamin A deficiency disorders) and lens opacity (cataract) were responsible for 40% and 13% of childhood blindness and severe visual impairment respectively. These 2 conditions are entirely avoidable (prevention for vitamin A deficiency disorders and early diagnosis and surgical treatment for cataract). Our result is consistent with the recommendations and priorities of WHO VISION 2020 initiative which identifies corneal scarring and cataract as the major causes of childhood blindness in most developing countries [*7*].

The majority of surgical operations that were done at the eye hospital were for corneal opacities and cataract, which suggests

Table 3 **Anatomical sites and causes of blindness or severe visual impairment in the 40 children with visual acuity of < 6/60 in the better eye, Khartoum 2003**

Anatomical classification	No. (*n* = 40)	%
Corneal opacity	16	40.0
Vitamin A deficiency	9	22.5
Trauma	4	10.0
Measles	3	7.5
Higher centre of the brain (amblyopia)	13	32.5
Lens (cataract)	5	12.5
Retina	3	7.5
Retinitis pigmentosa	2	5.0
Vascular abnormality	1	2.5
Uvea (glaucoma)	1	2.5
Whole globe anomaly (microphthalmos)	1	2.5
Optic nerve (optic nerve atrophy due to unknown cause)	1	2.5

Table 4 **Avoidable causes of severe visual impairment and blindness among the 40 children with visual acuity < 6/60 in the better eye, Khartoum 2003**

Avoidable causes	No. (*n* = 40)	%
Preventable		
Vitamin A deficiency	9	22.5
Autosomal dominant	2	5.0
Trauma	4	10.0
Measles	3	7.5
Treatable[a]		
Cataract	5	12.5
Glaucoma	1	2.5
Total avoidable	24	60.0

[a]*Amblyopia (32.5%) was not included as it is only treatable up to 9 years of age.*

Table 5 **Distribution of the children referred for surgery by type of eye disease, Khartoum 2003**

Type of eye disease	No.	%
Corneal opacities	10	43.5
Cataract	8	34.8
Divergent squint	3	13.0
Others	2	8.7
Total	23	100.0

the need to initiate a training programme on paediatric eye surgery for the doctors, so as to prevent further complication to blindness.

Although 25 blind cases and 15 with severe visual impairment are a small number, not all cases were determined by initial screening and thus these figures are an underestimate of the number of cases. Nonetheless out data provide useful baseline information for programme planners involved in addressing childhood blindness in Sudan.

Improving vaccination for measles and distribution of vitamin A supplements will assist in prevention of severe visual impairment and blindness in the majority of children in these camps. A public health eye programme based on VISION 2020 should be established to combat childhood blindness problems focusing on the primary health care level.

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Prevalence and risk factors for hearing disorders in secondary school students in Ismailia, Egypt

A.G. Abdel-Rahman,[1] F.A.S. Meky,[2] M.F. Allam,[2] M. El-Tabakh[3] and M.M. El-Gaafary[3]

انتشار اضطرابات السمع وعوامل اختطارها بين طلاب المدارس الثانوية في الإسماعيلية، بمصر

أميرة جمال عبد الرحمن، فاطمة عبد السلام مكي، محمد فاروق علام، محمد الطباخ، مها محمد الجعفري

الخلاصة: أُجري من خلال هذه الدراسة تقدير لمدى انتشار اضطرابات السمع وعوامل اختطارها في عيِّنة تمثِّل 10% من جميع طلاب المدارس الثانوية في مدينة الإسماعيلية، بمصر. وأعطي استبيان لجميع المشاركين، كما خضعوا لاختبارات «ويبر» و«ريني» لقياس العجز السمعي. وأوضحت الدراسة انتشار الصَّمَم بنسبة 22.2% بين الطلاب الـ 2633 الذين أُجري عليهم البحث، كان أغلبُه صمَّما حسياً عصبياً. وتبيَّن وجود مزيج من الصمم الحسي العصبي والصمم التوصيلي بنسبة أكبر لدى طلاب المدارس التقنية (46.2%) منها لدى طلاب المدارس العامة (28.6%) أو التجارية (25.3%). وتَمَّ بتحليل التحوُّف اللوجستي العديد المتغيِّرات، تحديد عدد نوبات التهاب الأذن الوسطى، وسوابق معالجة أمراض الأذن، وسوابق الإدخال إلى مستشفى الحميات، وسوابق جراحات الأذن، كعوامل اختطار مستقلة للإصابة بالصمم الحسي العصبي.

ABSTRACT This study estimated the prevalence of hearing disorders and associated risk factors in a 10% sample of all secondary-school students in Ismailia city, Egypt. All participants were given a questionnaire and Weber and Rinne tests for hearing disabilities. Among 2633 students, the prevalence of hearing loss was 22.2%, mostly sensorineural hearing loss. More students at technical schools had mixed sensorineural and conductive hearing loss (46.2%) than students at general (28.6%) or commercial (25.3%) schools. Multivariate logistic regression analysis identified the number of attacks of otitis media, history of ear disease treatment, history of admission to fever hospital and history of ear surgery as independent risk factors for sensorineural hearing loss.

Prévalence et facteurs de risque des troubles auditifs chez les élèves du secondaire à Ismaïlia en Égypte

RÉSUMÉ Cette étude a évalué la prévalence des troubles auditifs et des facteurs de risque associés dans un échantillon représentant 10 % de la population des élèves du secondaire de la ville d'Ismaïlia (Égypte). Tous les participants se sont vu remettre un questionnaire et ont subi les tests d'acuité auditive de Weber et de Rinne. Dans cet échantillon de 2633 élèves, la prévalence de la perte d'audition s'élevait à 22,2 %, consistant majoritairement en une surdité neurosensorielle. Les élèves des collèges et lycées d'enseignement technique étaient plus nombreux à présenter une surdité mixte de transmission et neurosensorielle (46,2 %) que les élèves des collèges et lycées d'enseignement général (28,6 %) ou commercial (25,3 %). L'analyse de régression logistique multivariée a permis d'identifier comme facteurs de risque indépendants de surdité neurosensorielle le nombre d'épisodes d'otite moyenne, d'antécédents de traitement d'une pathologie auriculaire, d'hospitalisations pour épisodes fébriles et d'otochirurgie.

[1]Department of Community, Environmental and Occupational Medicine; [3]Department of Ear, Nose and Throat, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.
[2]Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt (Correspondence to M.F. Allam: fm2faahm@uco.es).
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Introduction

Hearing loss in infants and children may be sensorineural, conductive, or mixed unilateral or bilateral and symmetric or asymmetric. It can also be syndromic (involving other identifiable features) or nonsyndromic (isolated hearing loss); congenital or postnatal; prelingual, perilingual or postlingual (i.e. onset before, during, or after speech or language acquisition); and genetic or nongenetic [*1*]. Sensorineural hearing loss is an extremely common disorder, with a spectrum of effect ranging from an almost undetectable degree of disability to a profound alteration in the ability to function in the society. Because its onset is frequently insidious and accompanied by subtle compensatory strategies, hearing loss is usually overlooked by physicians and patients [*2*].

The prevalence of hearing loss in several countries has been estimated as 4%, 7.9% 15% and 10.8% in Saudi Arabia, Pakistan, Kenya and the United States of America respectively [*3–6*]. It was estimated that 3.9 million children in Africa had mild hearing loss and 1.2 million had moderate to severe hearing loss [*7*]. In Egypt, there is a scarcity of studies estimating the prevalence of hearing loss.

The risk factors for conductive and sensorineural hearing loss are mutually exclusive. Risk factors for the former include middle ear infection, trauma to the tympanic membrane, foreign body impaction in the external canal and consanguineous marriages, while those for sensorineural include viral neuritis, fracture base, ototoxic drugs, noise exposure and tumours of the cerebello–pontine angle [*3,8*]. In Europe, as in sub-Saharan Africa, the most prevalent causes of hearing impairment are chronic and suppurative otitis media [*7,9,10*].

There is a paucity of data regarding the risk factors of hearing loss in Egyptian adolescents. Thus, epidemiologic studies are needed to assess hearing loss in this important age category for setting priorities and designing efficient interventions.

The main objective of this study was to estimate the prevalence of hearing loss among secondary-school students in an Egyptian city, and to identify the risk factors associated with it, in order to enable specific preventive measures to be targeted at students with these risk factors.

Methods

There are around 1.5 million inhabitants of Ismailia city. All secondary schools in the city (19 schools) were included in the study: 10 general schools, 5 commercial schools and 4 technical schools. From 2 classes per school year, 10% of the students in each school year were randomly selected. Over the period September 2003 to July 2004, 2750 students were invited to participate in this study, of whom 2633 accepted (response rate 95.7%). No significant difference was found between participants and non-participants regarding their age or sex.

Students were asked to complete a standardized interview questionnaire, whom included demographic data (age, sex, school type, number of siblings and order of birth), clinical symptoms and the main risk factors for hearing loss. These factors included family history of consanguinity between parents or hearing problems, and history of ear surgery, infections, trauma, admission to fever hospital and intramuscular injection of antibiotics.

All participants were subjected to Weber and Rinne tests for assessment of hearing disabilities. According to the findings of these tests, a student was considered to have normal hearing, conductive hearing loss, sensorineural hearing loss or mixed

conductive and sensorineural hearing loss. Only 44 (1.7%) students had an ambiguous diagnosis and were excluded from our analysis. Comparative analysis between students with coherent and incoherent diagnoses showed no statistically significant differences regarding their demographic data or medical and family past history.

Analysis

Initial comparisons between students with different hearing loss and those with normal hearing tests were done using the Pearson chi-squared test for categorical variables. Risk factors for conductive hearing loss are completely different from those for sensorineural hearing loss. Thus, conductive and sensorineural hearing loss were considered as 2 distinct pathologies and we conducted a separate multivariate model for each of them.

The multivariable models to describe the risk factors for conductive and sensorineural hearing loss were obtained using stepwise logistic regression analysis initially with a conservative significance level of 0.25. Our dependent variable for this analysis was the state of hearing (whether normal or abnormal) according to Weber and Rinne tests findings. Subsequently, the resulting model was reduced using a likelihood ratio test with a significance level of 0.05. The calibration of the final model was assessed using the Pearson chi-squared goodness-of-fit test, and its discrimination was assessed by the area under the receiver-operating curve. All statistical analyses were performed using *SPSS*, version 11.0.

Results

Demographic data

A total of 2589 secondary-school students were included in our study; 1713 (66.2%) were from the 1st grade school year, 430 (16.6%) from the 2nd grade and 446 (17.2%) from the 3rd grade. Nearly half of the students (49.8%) were from general secondary school and the rest were from commercial (24.8%) or technical school (25.4%). The mean (standard deviation) age of the students was 15.4 (SD 1.2) years (range 13 to 21 years) with a female to male ratio of 1.3:1. The mean number of siblings of the students was 3.2 (SD 1.6) and only 632 students (24.4%) reported consanguinity between parents.

Prevalence of types of hearing loss

A total of 576 students out of 2589 (22.2%) had hearing loss. Of these, 403 (70.0%) had sensorineural hearing loss, 82 (14.2%) bilateral conductive hearing loss, 91 (15.8%) mixed sensorineural and conductive hearing loss.

Tinnitus, vertigo and hearing difficulty while talking to friends were the 3 commonest symptoms related to the different diagnoses of hearing loss. The percentage of students diagnosed as sensorineural, conductive, and mixed sensorineural and conductive hearing loss and complaining of tinnitus were 71.7%, 58.5% and 71.5% respectively. Meanwhile, vertigo and hearing difficulties while talking to friends were reported in 51.9% and 50.1% of students diagnosed as sensorineural, 53.6% and 48.7% of conductive and 64.9% and 57.2% of mixed hearing loss respectively.

Risk factors for hearing loss

Table 1 shows the association between the sociodemographic characteristics of the studied groups and different types of hearing loss. Mixed sensorineural and conductive hearing loss was higher in females (82.4%) than males (17.6%) compared with those with normal hearing and this difference was highly statistically significant ($P < 0.001$). Otherwise, no sex differences were

Table 1 **Association between different diagnoses of hearing loss and sociodemographic characteristics**

Variable	Normal hearing		Sensorineural hearing loss		Bilateral conductive hearing loss		Mixed sensorineural and conductive hearing loss	
	(*n* = 2013)		(*n* = 403)		(*n* = 82)		(*n* = 91)	
	No.	%	No.	%	No.	%	No.	%
Female sex	1111	55.2	225	55.8	40	48.8	75	82.4[b]
School type								
General	1027	51.0	183	45.4	54	65.9[a]	26	28.6
Commercial	490	24.3	109	27.0	20	24.4	23	25.3
Technical	496	24.6	111	27.5	8	9.8	42	46.2[b]
Consanguinity between parents	481	23.9	102	25.3	21	25.6	28	30.8
Family history of hearing problems	450	22.4	106	26.3	19	23.2	22	24.2

n = *total number of students.*
[a]P < *0.01 versus normal hearing;* [b]P < *0.05 versus normal hearing (Pearson chi-squared test was used for categorical variables).*

noticed in both sensorineural and bilateral conductive hearing loss. The percentage of students at general school diagnosed with bilateral conductive hearing loss (65.9%) was higher than that of students at commercial (24.4%) and technical schools (9.8%) compared to those with normal hearing. Moreover, the percentage of students at technical school diagnosed as mixed sensorineural and conductive hearing loss (46.2%) was higher than that of students at other school types (28.6% at general schools and 25.3% at commercial schools). The mean number of siblings was only significantly higher in mixed sensorineural and conductive hearing loss compared to those with normal hearing. No association between order of birth and any type of hearing loss was found (data not shown).

Past history of ear surgery, otitis media, admission to fever hospital, intramuscular injection of antibiotics and ear disease treatment were statistically associated with the presence of sensorineural hearing loss (Table 2). Similarly, history of ear surgery, ear disease treatment, postnasal discharge and trauma were statistically associated with the presence of bilateral conductive hearing loss. Mixed sensorineural and bilateral conductive hearing loss was significantly associated with a history of postnasal discharge, otitis media, measles and mumps, intramuscular injection of antibiotics and ear disease treatment. No association of consanguinity was found between family history of hearing problems and the presence of hearing loss.

Multivariate analysis

The multivariate logistic regression model identified the number of attacks of otitis media, history of ear disease treatment, history of admission to fever hospital and history of ear surgery as the independent risk factors for sensorineural hearing loss (Table 3).

The risk factors possibly associated with conductive hearing loss in the final mul-

Table 2 **Association between different diagnoses of hearing loss and history of different risk factors**

History of:	Normal hearing (*n* = 2013)		Sensorineural hearing loss (*n* = 403)		Bilateral conductive hearing loss (*n* = 82)		Mixed sensorineural and conductive hearing loss (*n* = 91)	
	No.	%	No.	%	No.	%	No.	%
Postnasal discharge	601	29.9	135	33.5	36	43.9[a]	38	41.8[c]
Ear surgery	17	0.8	10	2.5[a]	4	4.9[b]	1	1.1
Otitis media	132	6.6	50	12.4[b]	9	11.0	16	17.6[b]
Measles or mumps	572	28.4	109	27.0	25	30.5	43	47.3[b]
Trauma	69	3.4	14	3.5	8	9.8[a]	5	5.5
Admission to fever hospital	253	12.6	70	17.4[c]	13	15.9	16	17.6
Intramuscular antibiotics	236	11.7	64	15.9[c]	9	11.0	18	19.8[c]
Ear disease treatment	157	7.8	67	16.6[b]	20	24.4[b]	13	14.3[c]

n = *total number of students.*
[a]P < *0.01 versus normal hearing;* [b]P < *0.001 versus normal hearing;* [c]P < *0.05 versus normal hearing (Pearson chi-squared test was used for categorical variables).*

tivariate analysis model are presented in Table 4. A history of ear surgery carried the highest risk for conductive hearing loss (odds ratio = 4.06).

Discussion

The importance of early detection of hearing loss that may interfere with the process of learning has been repeatedly reported [*11–13*].

Our study aimed to estimate the prevalence of hearing loss among secondary-school students, and to identify the risk factors associated with it. Before reaching conclusions based on the present results, it is necessary to consider a number of potential objections to our procedures. Simple tools such as questionnaires and tuning fork tests were used (Rinne and Weber test). These tools are characterized by high specificity and low sensitivity. For instance,

Table 3 **Factors associated with sensorineural hearing loss in the multivariate analysis**

Variable	Odds ratio	95% confidence interval	*P*-value
Number of attacks of otitis media	1.21	1.04–1.42	0.014
History of ear disease treatment	1.98	1.27–3.09	0.003
History of admission to fever hospital	1.55	1.04–2.29	0.029
History of ear surgery	2.79	1.07–7.28	0.035

Hosmer–Lemeshow goodness-of-fit test: P = *0.672.*
Discrimination (area under the receiver operating characteristics curve): 0.590.

Table 4 **Factors associated with conductive hearing loss in the multivariate analysis**

Variable	Odds ratio	95% confidence interval	*P*-value
History of postnasal discharge	1.52	1.18–1.96	0.001
History of ear disease treatment	3.25	1.88–5.61	0.000
History of ear surgery	4.06	1.28–12.84	0.017
General school (reference category)	–	–	–
Commercial school	3.62	1.70–7.73	0.001
Technical school	2.81	1.21–6.49	0.016

Hosmer–Lemeshow goodness-of-fit test: P = *0.831.*
Discrimination (area under the receiver operating characteristics curve): 0.711.

the specificity of a questionnaire to detect hearing loss is 94%, compared with 62.4% for otoscopy and 84% for tympanometry. However, its sensitivity is 5 times less than the 2 previously mentioned methods [*14*]. Tuning fork tests are the traditional methods of differentiating conductive from sensorineural hearing impairments prior to the advent of pure tone audiometry. However, they cannot substitute for a correctly done pure tone audiometry with a full masking. The Rinne tuning fork tests have high specificity and low sensitivity to detect conductive hearing loss. Thus, when a Rinne test becomes negative it should be a reliable indicator [*15–17*]. Also, in about 25% of cases, the results of the Weber test do not agree with the results of pure tone audiometry. Its interpretation is sometimes difficult in the presence of bilaterally affected ears and it should be applied to unilateral hearing loss [*15,16*]. The results arising from these tools must be treated as provisional diagnoses that need confirmation by a more sophisticated battery of tests including pure tone audiometry and tympanometry, otoacoustic emissions and augmented brainstem response. Of course, from the history and tuning fork examination we could suspect that a student may have conductive or sensorineural hearing loss, and they will be referred to audiological evaluation.

The present study revealed a prevalence of all types of hearing loss of 22.2%. This prevalence is higher than the prevalences reported in other developing countries such as Kenya (15%) and Pakistan (8%) [*3,6*]. This could reflect different environmental exposures as there is a greater exposure to portable music devices, cell-phone use and high-powered output music speakers among young people in our environment. Segal and his coworkers [*18,19*] reported that up to 70% of hearing loss was sensorineural. This high proportion agrees with the results of the present study, where sensorineural hearing loss was the most prevalent loss, constituting 70% of the cases.

A previous English study has shown that there is no effect of sex on hearing loss until age 31 to 40 years [*20*]. Similarly, our study showed that sex has no effect on either sensorineural or conductive hearing loss. However, it did have an effect on mixed sensorineural and conductive deafness especially in females. There is no clear explanation for this and it could be due to a subgroup anomaly.

Regarding the risk factors associated with hearing loss, we found that positive

consanguinity and presence of family history of hearing problems among parents of the children were not significantly associated with suspected sensorineural hearing loss. Similarly, O'Hara et al. reported that consanguineous marriages were not associated with hearing impairment [*21*]. However, consanguinity was the major factor in other studies [*22,23*]. In our study, family history was not associated with the presence of sensorineural or conductive hearing loss. Billings and Kenna found a family history of sensorineural hearing loss or prematurity and/or complicated perinatal course in 28.6% of their patients [*24*].

Otitis media seems to have an impact on the development of hearing loss in schoolchildren. In the present study a highly significant association was found between history of otitis media and the presence of sensorineural or mixed sensorineural and conductive hearing loss. These findings agree with the results of a recent survey conducted in schoolchildren in Greenland [*25*]. Similarly, previous studies in other developing countries, such as Brazil and Nigeria, have shown that a history of chronic otitis media in schoolchildren carried a higher risk for hearing loss [*26,27*]. Sensorineural hearing loss is found to be significantly associated with episodes of otitis media. These findings are in accordance with reports from Alaska, Canada, Greenland and Pakistan [*3,25*].

In our study, as in the study of Elahi et al. [*3*], no cases of hearing loss were attributable to viral infections such as measles and mumps. A retrospective study carried out in Turkey has shown that febrile illness was the major cause of hearing loss [*28*]. Similarly, the present study has demonstrated that previous admission to fever hospital was significantly associated with sensorineural hearing loss.

In the univariate analysis, trauma was significantly associated with conductive hearing loss. In accordance with this finding, Cummings considered head trauma as one of the important risk factors for hearing loss [*29*].

The univariate and the multivariate analyses have shown that a history of otolaryngologic surgery carried a higher risk for sensorineural and conductive hearing loss. Previous studies have also showen a high risk of otolaryngologic surgery for different types of hearing loss [*26,30*].

The multivariate model in the present study showed that commercial school type was highly associated with conductive hearing loss. This might be due to the activities related to this school type, which include noise levels that may exceed the permissible values [*31*]. If students are being exposed, for example, to hazardous noise levels there is a need to obtain measurements of noise levels and supply students with ear protection in the classrooms.

The prevalence of the mixed type of hearing loss was almost the same as the conductive type. In the univariate analysis, in the group with mixed hearing loss, females represented 82% of the sample, although sex differences were not noticed in either of the other 2 types of hearing loss (conductive or sensorineural). Again, almost half of the students with mixed type of hearing loss were from technical schools. A factor that affects exclusively girls in technical schools should be explored. A history of measles or mumps was associated with the mixed type of hearing loss; an association that was not evident in the other groups with hearing loss.

In conclusion, audiometric screening is highly recommended to detect hearing loss among secondary-school students. Notwithstanding the limitations of the tools

used in our study, the administration of a well-structured questionnaire at school entry, complemented by tuning fork tests may be a practical option for an early detection programme in any developing country.

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Evaluation of the Ministry of Health school oral health programme in the West Bank region of Palestine

E. Kateeb[1]

تقييم برنامج وزارة الصحة المدرسي المعني بصحة الفم، في الضفة الغربية، بفلسطين

إلهام طالب الخطيب

الخلاصة: تقدِّم هذه الدراسة تقييماً لأنشطة ونتائج البرنامج المدرسي لصحة الفم الذي أجرته وزارة الصحة في المدارس العمومية في الضفة الغربية بفلسطين خلال الفترة من 1997 – 1998 إلى 2003 – 2004. وقد تَرَكَّزَ التحليل الاستعادي الذي أُجري للسجلات الرسمية على مَنَاسب صحة الفم وإحالات الطلاب. وكان وجود تحسُّن طفيف في معدلات الأسنان المنخورة، والمقلوعة، والمحشوة في بعض المحافظات خلال السنتَيْن الأخيرتَيْن، بمثابة مؤشِّر على بعض التقدُّم في مجال مكافحة التسوُّس. ومع ذلك، فإن هناك حاجة لاستمرار الجهود للحفاظ على معدَّل التسوُّس عند هذا الحد وضمان عدم ارتفاعه في مناطق استقرار المرض، وزيادة الجهود الاستراتيجية للتعاطي مع معدلات التسوُّس المرتفعة في المناطق العالية الاختطار. وأظهرت المقابَلات المتعمِّقة التي تمت مع أصحاب الشأن، نقاطَ القوة ومواطنَ الضَعْف في برنامج التحرِّي، وساعدت في وضع التوصيات الرامية إلى تحسين ذلك.

ABSTRACT This paper reports an evaluation of the activities and outcomes of the school oral health programme conducted by the Ministry of Health in public schools in the West Bank region of Palestine from 1997–98 to 2003–04. Retrospective analysis of official records focused on oral health indices and student referrals. A slight improvement in DMFT scores in students in some governorates in the last 2 years showed some progress in caries control. However, maintenance efforts are required to ensure that caries level does not rise in disease-stable areas, and an increase in strategic effort is required to address the high caries level in high-risk areas. In-depth interviews with stakeholders identified the strengths and weaknesses of the screening programme and recommendations for improvements.

Évaluation du programme de santé bucco-dentaire en milieu scolaire du Ministère palestinien de la Santé en Cisjordanie

RÉSUMÉ Cet article se fait l'écho d'une évaluation des activités et des résultats du programme de santé bucco-dentaire en milieu scolaire conduit par le Ministère palestinien de la Santé dans les écoles publiques cisjordaniennes de 1997-1998 à 2003-2004. L'analyse rétrospective des dossiers médicaux officiels a essentiellement reposé sur les indices de santé bucco-dentaire et le nombre de consultations chez le dentiste. Une légère amélioration de l'indice CAO (nombre de dents cariées, absentes ou obturées) observée ces 2 dernières années chez les élèves résidant dans certains gouvernorats traduisait un progrès dans la maîtrise des atteintes carieuses. Toutefois, des efforts sont nécessaires en termes de surveillance bucco-dentaire si l'on veut éviter une augmentation du taux de caries dans les zones de stabilité de la pathologie, de même qu'est indispensable un renforcement des démarches stratégiques visant à limiter le pourcentage élevé d'atteintes carieuses dans les zones à haut risque. Des entretiens approfondis avec les différents acteurs ont permis d'identifier les atouts et les faiblesses du programme de dépistage et d'élaborer un certain nombre de recommandations destinées à améliorer ce dernier.

[1]*University of Massachusetts Amherst, Amherst, United States of America; Department of Community and Preventive Dentistry, Al Quds University, East Jerusalem (Correspondence to E. Kateeb: elhame20@hotmail.com).*
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Introduction

Most childhood tooth decay could be avoided through simple preventive measures such as screening, monitoring, combined use of fluorides and dental sealants and regular professional care. These measures can save children pain, complicated procedures and high dental treatment costs. In order to apply the measures effectively, public health care administrators and decision-makers need the tools, the capacity and the information to assess and monitor oral health needs, choose intervention strategies, design policy options appropriate to their own circumstances and improve the performance of the oral health system [*1*]. Dental screening data can be used to identify trends and to assist in allocating scarce resources [*2*] and are an important indicator of a community's health status [*3*].

One successful model of oral health programmes is school-based screening and education. School-based programmes are increasingly being seen as a strategic way to identify children who need dental care the most and thus improve access to health and social support services for vulnerable populations. Studies show that school dental screening is capable of stimulating dental attendance among children with a treatment need [*4*,*5*] and improving the dental health status of schoolchildren [*6*].

However, there are inherent problems and challenges with school-based screening programmes. Al-Tannir discussed the importance of outreach activities in promoting awareness of a dental screening programme and highlighted the need for personal contact by programme staff to ensure that children get the necessary follow-up [*7*]. Cooperative relationships between dental practitioners and the schools are required [*8*]. Furthermore, school-based dental screening programmes can be very time- and labour-intensive [*9,10*]. Other challenges include developing a standardized screening protocol, including both the establishment of standardized criteria for referral [*11*] and sufficient training and calibration of screeners [*12*]. It is important, however, to highlight that training does not fully resolve problems with consistent identification of dental needs between screeners [*13*]. Another question is who should carry out the screening: dentists and dental hygienists [*9*] or primary care providers or paediatric dentists [*14*].

This paper outlines the oral screening programme that has been set up in public schools in 9 governorates in the West Bank region of Palestine, and details the evaluation of the effectiveness of the programme in minimizing oral health diseases, particularly caries.

West Bank oral health screening programme

As a global concern, in 1979 The World Health Organization (WHO) announced that by the year 2000, the global average for dental caries was to be no more than 3 decayed, missing or filled teeth (DMFT) at 12 years of age [*15*] and in 1989 WHO endorsed the promotion of oral health as an integral part of health for all by the year 2000 [*1*]. To achieve this, WHO urged Member States to establish oral health information systems and offered assistance in efforts to develop these systems and provide them with core standardized methods but with flexibility to expand by adding information relevant to the local situation.

To meet national needs and international requests, an oral health screening programme was launched in West Bank public schools of the Palestinian Authority in 1997, aiming to screen schoolchildren

in the 3rd, 7th and 10th grades. It is a part of the national school health programme conducted by the Palestinian Ministry of Health (MOH) in collaboration with other international organizations. The programme is carried out and operated by the MOH's 17 dental clinics that are distributed all over the West Bank and report to the central office in Ramallah.

The programme started with oral screening, educational seminars and students' referrals to oral clinics operated by the MOH. After that, the programme developed into offering some necessary preventive procedures, such as fluoride gel application and fissure sealants for selected schools in school years 2002–03 and 2003–04. The programme uses WHO models and criteria [*16*] in screening for dental decay using the DMFT index and for gingival health using the CPITN index [community periodontal index of treatment needs]. Later, programme operators added fluorosis and malocclusion assessment to the screening programme.

Although the dental screening programme does not have specific objectives, the school health programme aims to improve the general and oral health of school students and increase their access to health services.

Programme effectiveness was measured in 2 stages: short-term and long-term. Short-term outcomes can be demonstrated by increasing coverage rate, increasing FT component and care experience index (i.e. more services delivered and more follow-ups made), and increasing the percentage of referred students who actually attended oral clinics (i.e. success in raising awareness of oral health care, increasing follow-up and stimulus for seeking treatment). Long-term outcomes can be demonstrated by lower DMFT values, especially the DT component. This outcome needs more time to be apparent, because caries progression is a relatively slow process; it takes about 2 years from the initial attack of caries to be clinically evident and be counted as D in the DMFT index.

Methods

Two methods of evaluation were used: quantitative (retrospective analysis of official records) and qualitative (in-depth interviews).

Retrospective analysis of official records

Data for the evaluation were drawn from 7 annual oral health reports organized by the central oral health department in the Palestinian Authority MOH (school years 1997–98 until 2003–04). These data provide a means for tracking changes in quantifiable behaviours. The oral health offices in the 9 Palestinian governorates send their monthly school oral health screening results to the central office in Ramallah, where they are organized and analysed into the final report. Each school in the designated governorate has the chance to be screened once a year. DMFT data (among other oral health indicators) are collected for each student in the selected grades.

The data presented here were derived from routine dental examination conducted by the MOH dentists using visual methods without radiography or fibro-optic transillumination. In school year 2003–04 a grant from the United Nations Children's Fund (UNICEF) supplied all the governorates with WHO standardized examination sets for oral screening. The methods used for the diagnosis and reporting of caries experience followed those published by the WHO for oral epidemiological studies [*16*].

The dental screening programme targeted public school students in 3rd, 7th and 10th grades in all the 10 governorates. In

this evaluation, only data for 7th and 10th grades were used, because for the first 5 years 3rd graders were screened then substituted by 1st graders. The 7th grade (12-year-olds) and 10th grade (15-year-olds) are global monitoring cohorts; this allowed more permanent teeth to be included in the examination, and would facilitate international comparisons [*17*]. Only 9 governorates were used in this evaluation, because the 10th (Jerusalem) was added only in the last 4 years.

Five indicators were used [*18*]:

1. *DMFT index*: the mean number of teeth decayed, missing or filled because of decay among schoolchildren. The index may refer to permanent teeth or baby teeth. It is a general indicator of dental health status among children and is felt to be extremely reliable; the lower the index, the better the dental health of the population. The index records past history and is cumulative [*19*]. To be recorded as decayed, teeth must have evidence of carious cavitations to the level of the dentine.
2. *DT index*: the number of decayed teeth divided by the number of examined students. This shows the caries experience by population.
3. *Care experience index*: the number of filled teeth divided by the number of examined students [(FT/DMFT) ×100/100]. This indicator assesses the delivery of dental services to the population.
4. *Coverage rate*: the number of students examined in each governorate divided by the number of students in that governorate.
5. *Percentage of MOH oral clinic visits*: the percentage of oral clinic visits by referred students (referred by screening teams). This shows the effect of oral school health programmes in stimulating students and their parents to seek dental care and the amount of follow-up by the programme itself. This is a valuable indicator to measure programme effectiveness.

Analysis of the data extracted from the MOH's 7 annual reports was carried out using *SPSS* software package.

In-depth interviews

The second method used in this report was in-depth interviews with programme administrators, dentists who conducted the oral screening and staff involved in interpreting and analysing data. Interviews comprised a series of questions, typically semi-structured or unstructured, conducted in person. A trained dentist with dental public health experience prepared and conducted those interviews.

The advantages and disadvantages of the programme and other programmes operating in the region, concerns about the implementation of the programme, suggestions and recommendations to improve it and general oral health policy in the Palestinian Authority areas were discussed.

Results

Oral health indicators

The analysis of the data revealed the following outcomes for the 5 indicators.

Coverage rate: All governorates showed a steady increase in coverage rates in the first 4 years and a boost in the last 3 years of the evaluation. Overall, the rate increased from 22.8% in 7th grade and 14.5% in 10th grade in 1997–98 to 92.4% and 88.2% respectively in 2003–04. The highest rates were obtained in school year 2003–04; coverage rates in 7th grade were consistently higher than 10th grade, as shown in

Figure 1. A major increase in coverage rates after year 2000–01 occurred after the school oral health administration assigned local dental staff for each region to screen school students, saving time and cost of dentists' travelling from one region to another.

DMFT index: Trends in DMFT over time demonstrated a slight decrease in DMFT scores for the West Bank in the last 2 years (Figure 2). The mean West Bank DMFT scores for 7th grade ranged from 1.35 in 1997–98 to 2.17 in 2001 and from 1.6 in 1997–98 to 2.9 in 2000–01 for 10th graders. In school year 2003–04 the mean DMFT was 1.49 for 7th grade and 1.9 for 10th grade.

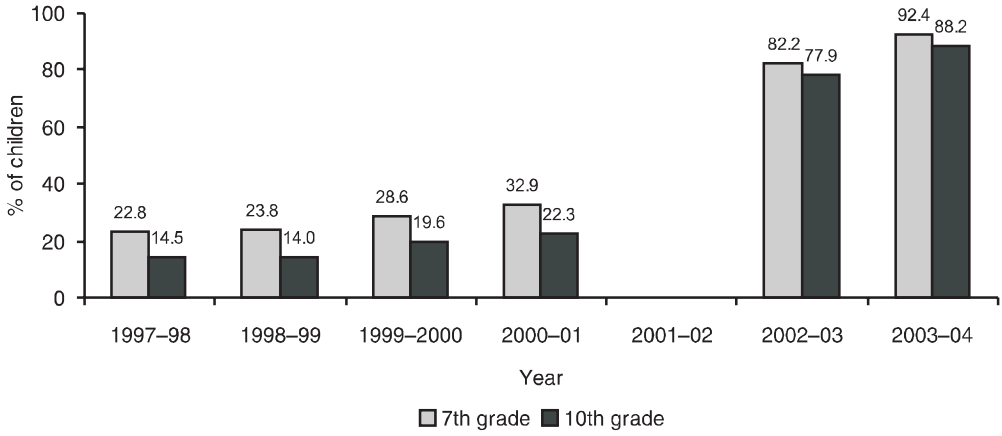

Figure 1 **Coverage rate of oral health screening for schoolchildren in grades 7 and 10 of West Bank schools**

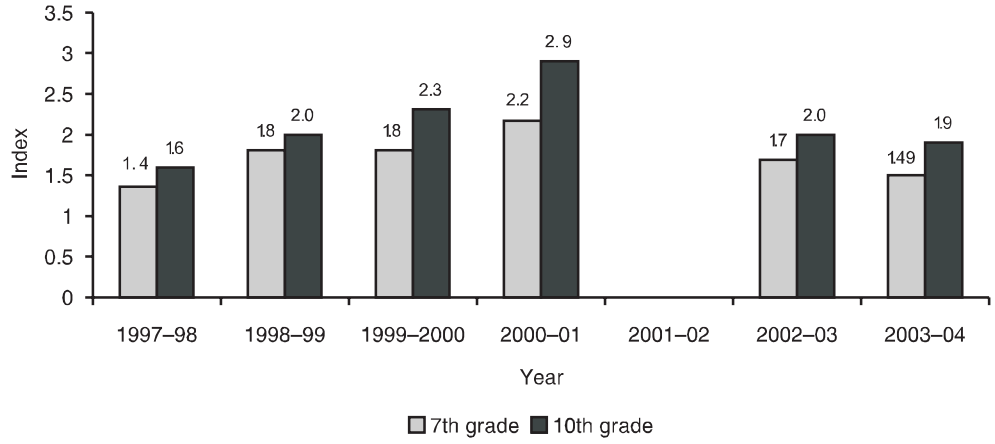

Figure 2 **Decayed, missing filled teeth (DMFT) index for schoolchildren in grades 7 and 10 of West Bank schools**

The lowest recorded mean DMFT for all areas of the West Bank was 1.35 in 7th grade students and 1.6 in 10th grade in school year 1997–98. The highest DMFT was 2.17 in 7th grade and 2.9 in 10th grade in school year 2000–01. In general, 10th graders had higher DMFT scores than 7th graders.

DT index: When the components of DMFT were examined separately, however, we can see that DT was the major contributor to the DMFT scores; FT was the smallest contributor. This was true in both 7th and 10th grades (Figure 3). Thus, although DMFT scores slightly improved over the 7-year period, the DT component had increased while FT and care index remained low. The measure of DT was higher in 10th grade than 7th grade children.

Care experience index: The care index ranged from 11.9% to 15.5% for the 7th grade children over the 7-year period of the programme. Care experience indices were higher in 10th grade than 7th grade children (Figure 4). The 7th grade children had a care experience index of 14.8% in school year 2003/04 and 10th graders scored 20% in the same year.

Percentage of referred students visiting oral clinics: The analysis showed that a small percentage of referred students attended dental clinics in school years 2002–03 and 2003–04 (Figure 5). The percentage was lowest in Salfit and highest in Jericho. School year 2003–04 had lower values than the preceding year, 2002–03. The mean percentage of students who attended dental clinics increased from 9% in 2002/03 to 11% in 2003/04 school year.

Regional variations

A wide range of DMFT values were seen across the 9 individual governorates. When analysed by governorate, the highest DMFT was recorded in Salfit (7.8 in 7th grade in school year 2002–03 and 7.0 in 10th grade in school year 2001–02), and the lowest DMFT was recorded in Jericho (0.7 in 1999–2000) and Nablus (0.62 in 1998–99 in 7th grade).

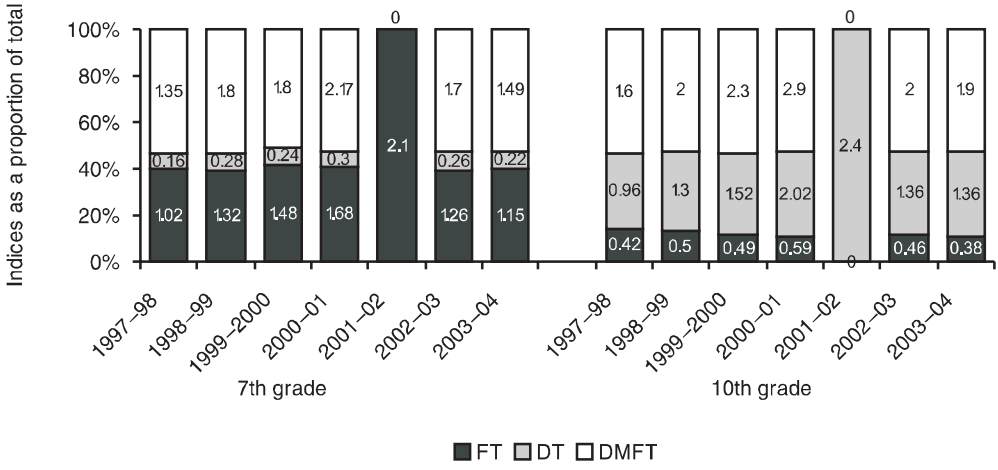

Figure 3 **Proportions of decayed, missing or filled teeth (DMFT), filled teeth (FT) and decayed teeth (DT) for schoolchildren in grade 7 and 10 of West Bank schools**

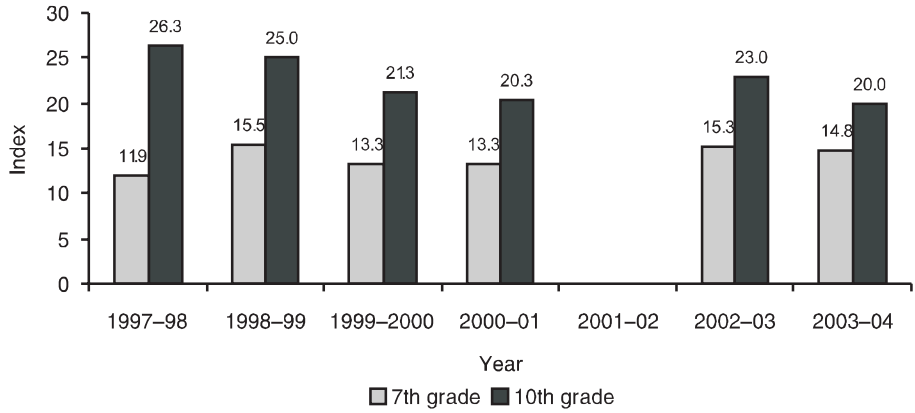

Figure 4 **Care experience index for schoolchildren in grades 7 and 10 of West Bank schools**

Issues and recommendations identified in interviews

Comments on the programme performance, administration and equipment extracted from the in-depth interviews with the stakeholders highlighted a number of concerns. These are summarized on Table 1, together with recommendations to address the issues.

Discussion

Dental outcome indicators

The 92% coverage rate in the 7th grade cohort (12-years-olds) in 2003/04 could be considered a high figure when compared with an industrialized country such as the United Kingdom (UK). On average, 16% of the total population of children aged 14

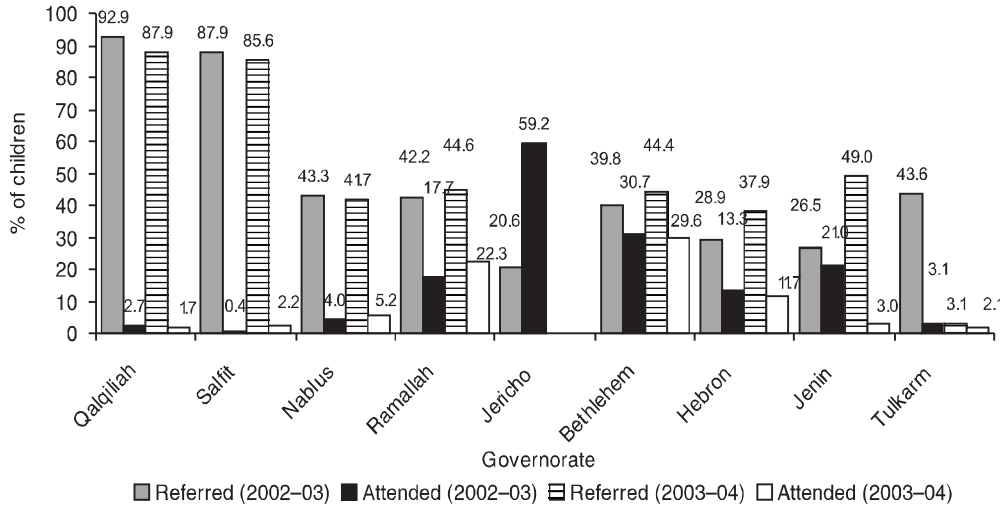

Figure 5 **Percentage of screened children who were referred, and who attended clinics, in grades 7 and 10 of West Bank schools**

Table 1 **Issues raised in the interviews with participants and stakeholders**

Issues raised	Recommendations
Validity and reliability	
Poor diagnostic conformity among dental staff in different screening sites over the 10 governorates. Poor validity and reliability of the screening form.	Set up staff orientation and adequate training; peer/support monitoring; regular discussion forums, to discuss any issues arising during the programme implementation; field observations; random check-ups; and calibration sessions.
Large variations in lighting conditions for the visual examination among different screening sites.	Provide a source of light and a head rest to all screening teams.
Workforce and transportation	
Difficulties in conducting the screening and delivering community dental services due to workforce shortages in oral health in the public sector.	Expand the role and scope of practice of dental auxiliaries. With ongoing support and appropriate training, dental hygienists and auxiliaries can offer preventive and curative oral care at lower costs.
Difficulties in accessing schools due to transport problems for doctors and patients.	Use portable dental clinics to reach rural areas that lack dental clinics.
Follow-up	
No follow-up for students who need treatment.	Give more emphasis to follow-up of students at least twice a year after the students' initial dental screening.
Care offered in the MOH's dental clinics is mainly service-on-demand in nature (curative and not preventive) and is largely concentrated on the extraction of teeth.	Change the emphasis of the clinical component of the programme from restorative treatment services to preventive services, especially dental sealant applications.
Cooperation and coordination	
Lack of cooperation and coordination among programme operators, school administrations, students' parents and private clinics to document treatments in the provided referrals forms.	Establish effective channels of communication between ministries of health and education, local health and education authorities, schools, communities, teachers and students. Schools can be a focal point for dissemination of results, particularly to students, school staff, parents, families and community members and in establishing referral and follow-up systems.
Collaboration and partnership	
Need for collaboration and partnership among different national and international nongovernmental organizations (NGOs) and the MOH.	Foster stronger partnerships with local communities, such as dental schools, health-related NGOs and other interested parties will allow collaborators to focus on achieving common goals more firmly and successfully. A validation of the public–private partnership in providing public health dental services will improve quality and accessibility of services. Obtain more funding from government and NGOs for the programme to sustain its activities and objectives.

Table 1 **Issues raised in the interviews with participants and stakeholders** *(concluded)*

Issues raised	Recommendations
Information technology	
Lack of accessible organized information databases, data analysis systems and essential technology requirements.	Use standardized, valid and reliable forms for data collection, with separate research to test the validity and reliability of these forms; staff orientation and training on approved data collection methods; reviewing inconsistent practices; and electronic data entry.
Need for more organized efforts to disseminate screening data and programme results in order to monitor oral health indicators, determine health policy, define the needy populations and create proposals for funding. Awareness about the programme among the key informants interviewed was low.	Disseminate the programme results to all parties involved: policy-makers, sponsors, universities, research entities and other national and international organizations. For example, press releases and articles for local professional publications such as newsletters and journals; presentations at meetings at the local health department, university, national conferences or other settings; listing the reports data in relevant databases and electronic bulletin boards; and sharing the programme experiences and results by phone and meetings with similar programmes.
Distribution of dentists	
Distribution of dentists in Palestinian Authority areas is biased towards urban areas and a preference for working in private clinics rather than the public health sector.	Establish more oral clinics under the supervision of MOH, offering free or low cost treatment for all referred students and expanding the types of treatment modalities that they usually offer (17 oral clinics all over the West Bank operated by MOH). More incentives should be offered for dentists who work in public clinics, especially in rural areas.
Autonomy	
Lack of autonomy in oral health departments makes fund-raising difficult.	Direct available funding towards preventive measures more than curative ones; fissure sealants, fluoride mouth rinses and improving existing screening programmes would be beneficial.
Evaluation	
Need for evaluation of the programme (At the time of the interviews, no evaluation had been documented since the programme launch).	Use evidence-based research to evaluate operating programmes, determine oral health risk factors and define at-risk populations.
Objectives	
Need for well-defined, specific objectives to periodically assess programme progression.	Formulate well-defined, specific, measurable and realistic objectives for the school oral health programme; targets and standards of national oral health to be established to assess activities and outcomes of screening.

years were examined in year 2003–04, 32% less than in the 1998–99 UK survey [*20*]. However, the coverage rate in the Palestinian authority MOH's screening programme was calculated from the ratio of examined students to the total number of students. This ratio did not consider the total population in the same age group, which could include children who attend non-public schools or other forms of independent learning.

The mean DMFT scores were 1.49 and 1.9 in 2003–04 in 7th and 10th grade respectively. The mean DMFT index compares favourably with some other countries in the region. Jordan scored 3.3 in 1999 [*21*], Lebanon scored 5.0 in 1996 [*22*], the Syrian Arab Republic varied between 1.4 and 2.5 in 2004 [*23*], Egypt scored 1.2 in 1991, and Tunisia scored 1.3 in 1994, Algeria scored 2.3 in 1987, and the Islamic Republic of Iran scored 4.0 in 1992 [*24*]. However, the West Bank compared less favourably with more developed countries; DMFT ranged from 0.63 to 1.31 in the UK in different regions [*17*].

Although high DMFT scores indicate high levels of the disease, unchanging DMFT or even a slightly increasing one might indicate a favourable change in care. This is true when all DT components convert to FT components; all the decayed teeth become filled teeth, which points to better treatment services. However, examination of the components of the DMFT index in the 9 governorates of the West Bank did not present this favourable change. DMFT scores in all areas over the 7-year period were largely attributable to the DT components, not the FT. This was also true in the last 2 years when DMFT showed a small reduction.

In most of the governorates under study, a slight increase in the DMFT scores after a gradual decrease in the last 3 years was noticed; this could be due to altering the examination strategy in school year 2003–04. Examiners switched from visual inspection to tactile inspection, using mirror and explorer, which is considered more accurate in caries detection.

Higher coverage rates demonstrated more representative samples and eventually more accurate DMFT values; this explains the boost in the DMFT index in the 9 governorates in year 2000–01. However, these report results could be more meaningful, if change indicators were weighted according to different coverage rates achieved.

There were regional variations in DMFT values across the 9 governorates. The low caries levels in Jericho are likely to be due to the high natural fluoride content in their water resources. Nablus and Ramallah also demonstrated low DMFT and this could be attributed to 3 factors:

- accessibility: dentists are easier to reach due to the wide availability of public transportation in these urban cities;
- affordability: these 2 cities are important commercial and political centres in the West Bank, which translates into more job opportunities, and thus higher individual incomes;
- availability: a high number of dentists work in private practice in these areas.

Although the DMF scores of these governorates (Nablus, Ramallah and Jericho) were within normal levels or even lower than WHO recommendations (DMF < 3 for 12-year-olds), the percentage of DT was higher than the FT component in these governorates. This indicates the need to enhance dental care measures among students by increasing awareness of good oral hygiene practices. Meanwhile, the school oral health programme should focus on teeth filling at an early stage of caries and application of fissure sealants.

In contrast, Salfit and Qalqiliah presented the highest DMFT scores over the whole programme period; however, due to lack of research, no risk factors have so far been identified in these areas. This great difference in the DMFT values among individual governorates has implications for targeting interventions and services at populations that were identified at risk.

The care index results (11.9% to 15.5%) could be considered very low when compared with UK values. The care index mean in the UK was 12% in 1995/96 then improved to 55% in 2002/2003 [*17*]. Care experience index reflects the restorative care received by those who have suffered disease; it therefore has to be viewed in conjunction with DMFT. These results are of interest in studying the provision of dental services to the age groups under study.

Although the mean percentage of students who attended dental clinics increased (from 9% in 2002/03 to 11% in 2003/04), the results are still considered low, when compared with other regions in the world. In Northern Ireland, the school-based dental screening programme stimulated 45% of the screened students to attend dental clinics, in contrast to 27% of the control group [*4*]. In Davangere, India, the dental screening programme stimulated 31% of screened students to seek dental treatment, compared with only 10% of the control group [*5*]. In the West Bank, the low percentage of referred students who actually visited dental clinics could be due to the following:

- Accessibility problems due to difficulties in transportation and checkpoints, curfews and border closures at the Israeli West Bank barrier, especially for students living in rural areas travelling to the city for care.
- Insufficient oral clinics operated by MOH that offer free treatments (only 17 clinics throughout the West Bank).
- Oral clinics are clustered in urban areas. Suburbs and rural areas lack this type of service.
- Inadequate services are provided in those clinics; very little dental specialties are offered.
- Oral clinics operated by MOH operate only from 08.00 to 14.00 hours, the same time period for school attendance.
- Dentists who carry out curative treatment in the clinics are the same people who are responsible for conducting the school screening; thus they are not always present in the clinics to treat the referred students.

Challenges of the programme

Given the political situation in Palestine, the programme operating teams face a number of critical challenges. Like other Palestinians in the West Bank, they suffered from the direct and indirect consequences of military activities and border closures. It is reported that the dental teams and community health workers are prevented from passing through particular Israeli military checkpoints for days or weeks [*25*]. In addition, checkpoints and road blocks which divide the West Bank into 300 separate clusters cut off 70% of the population from reaching essential health care services for weeks and months [*26,27*].

Some limitations were also encountered in the data collection process:

- One of the most important issues that influenced the quality of data collection was the change in examination methods in school year 2003–04 from visual examination only to the use of examination sets which contain probes and mirrors.
- The percentage of referred students who actually visited oral clinics was available only in the last 2 years. In addition the 10th governorate, Jerusalem, was

added to the screening programme in the last 4 years.

- The available data from the MOH reports were not always complete because of staff changes and resignations.
- Finally, continuous change in staff, different training, and lack of commitment to WHO examination criteria [*16*] make comparability of the data difficult.

Summary and recommendations

The existence of the school oral health programme in the Palestinian Authority areas as a database describing school children's oral health represents the commitment of the MOH to improving the school oral health care and services. The slight improvement in DMFT scores in students in some governorates in the last 2 years can be considered progress in caries control. However, maintenance efforts are required to ensure that caries experience at the population level does not rise in disease-stable areas, and an increase in strategic effort is required to address the high caries level in high-risk areas.

Many of the problems with delivery of the school oral health programme are symptomatic of the need for substantial improvement in programme management. The programme administrators and operating teams have divergent understandings and expectations of their roles and responsibilities. This is particularly so for observing screening sites, control referrals and follow-ups, and for managing and analysing data.

In summary, the MOH strategy for public dental health should use screening data to ensure that priorities for dental health are being properly identified and met, and that responsibilities for policy and operational activities are appropriately assigned and understood between different stakeholders. A national service plan should be developed by the MOH and other collaborators, including a reassessment of the appropriateness of the service planning principles in place, and whether the location and scale of public dental clinics established are meeting the needs of the eligible population. A national oral health promotion strategy should be launched which covers community education, development of an environment supportive of good oral health, facilitation of adequate access to fluoride, support for oral health research and development of a high quality trained workforce.

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Traumatic and non-traumatic coma in children in the referral hospital, Al-Hasa, Saudi Arabia

A.M. Ali,[1] A. Al-Abdulgader,[2] H.M. Kamal[2] and A. Al-Wehedy[2]

الغيبوبة الرضحية وغير الرضحية لدى الأطفال في مستشفى الإحالة، في منطقة الإحساء، بالمملكة العربية السعودية

عبد الفتاح محمود علي، عبد الله العبد القادر، حسام مصطفى كمال، عادل الوهيدي

الخلاصة: قام الباحثون بتحديد معدل حدوث الغيبوبة، وأسبابها، ونتيجتها، بين الأطفال المرضى في مستشفى الملك فهد، وهو مركز الإحالة الوحيد لمنطقة الإحساء، في المملكة العربية السعودية. وبلغ عدد الأطفال الذين أدخلوا المستشفى لإصابتهم بالغيبوبة (في المجال العمري من 28 يوماً إلى 12 عاماً) 91 طفلاً، وذلك خلال المدة من نيسان/إبريل 1999 إلى آذار/مارس 2002. وباستخدام مقياس جلاسجو الرقمي للغيبوبة لتقييم وعي الأطفال، تم تصنيف النتائج العصبية إلى ثلاث فئات: سلامة، واختلال، ووفاة. وبلغ معدل حدوث الغيبوبة 4.77 لكل 100 000 من السكان في السنة. وكانت الرضوح (رضوح الرأس أو الرضوح المتعدِّدة) هي المسبِّب الأكثر شيوعاً للغيبوبة (52.8%)، تليها العدوى (25.3%). وبلغ معدل الوفيات 47.2% (35.4% بين المصابين بالرضوح و60.5% بين الحالات غير الرضحية). ولوحظت نتائج تدل على حدوث اختلال لدى 19.8% من المرضى (22.9% بين المصابين بالغيبوبة الرضحية، و16.3% بين المصابين بالغيبوبة غير الرضحية).

ABSTRACT We determined the incidence, etiology and outcome of paediatric coma patients in King Fahad Hospital, which is the only referral centre for Al-Hasa region, Saudi Arabia. From April 1999 to March 2002, 91 children with coma (age range 28 days to 12 years) were admitted. The Glasgow Coma Scale for children was used for assessment. Neurological outcomes were categorized as intact, impairment or death. Incidence of coma was 4.77 per 100 000 population per year. Trauma (head trauma or polytrauma) was the commonest cause of coma (52.8%), followed by infection (25.3%). Mortality was 47.2% (35.4% among traumatic cases and 60.5% among non-traumatic cases). There was impaired outcome in 19.8% of patients (22.9% with traumatic coma and 16.3% with non-traumatic coma).

Coma post-traumatique et non post-traumatique chez l'enfant à l'hôpital de recours d'Al-Hasa en Arabie saoudite

RÉSUMÉ Nous avons évalué l'incidence, l'étiologie et l'issue du coma en pédiatrie à l'Hôpital King Fahad, seul centre hospitalier de recours pour la région d'Al-Hasa en Arabie saoudite. Entre avril 1999 et mars 2002, 91 enfants en coma (âgés de 28 jours à 12 ans) y ont été admis. L'évaluation a reposé sur le score de Glasgow pédiatrique. Il a été défini trois catégories de pronostic neurologique : bon (récupération complète), incertain (récupération incomplète) ou fatal (décès). L'incidence annuelle du coma pour l'ensemble de la population était de 4,77 cas pour 100 000. Les traumatismes (traumatisme crânien ou polytraumatisme) étaient la cause la plus fréquente de coma (52,8 %), suivis par les infections (25,3 %). La mortalité s'élevait à 47,2 % (35,4 % des cas post-traumatiques et 60,5 % des cas non post-traumatiques). La récupération s'est avérée incomplète chez 19,8 % des patients (22,9 % des comas post-traumatiques et 16,3 % des comas non post-traumatiques).

[1]King Fahad Hospital and Maternity & Children Hospital, Hofuf, Saudi Arabia.
[2]King Fahad Hospital, Hofuf, Saudi Arabia (Correspondence to H.M. Kamal: Hosamyousef90@hotmail.com).
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Introduction

The assessment of patients in coma is a medical emergency. The cause should be identified and, where possible, corrected and the brain provided with appropriate protection to reduce further damage. It then becomes important to identify those patients for whom the prognosis is hopeless and in whom the institution or persistence of resuscitative measures is inappropriate [*1*]. Most epidemiological studies of coma in children have focused on traumatic coma [*2–4*]. In the past few years, there have been an increasing number of studies that have looked at non-traumatic coma of different etiologies [*5,6*].

The aim of this study was to determine the incidence, etiology and outcome of coma, both traumatic and non-traumatic, in paediatric patients in Al-Hassa region, eastern province, Saudi Arabia, a highly populated region, to determine the commonest causes of coma and death in these patients.

Methods

This was a retrospective study of medical records conducted in King Fahad Hospital, Hofuf in Saudi Arabia. This hospital is the only referral centre for the whole of Al-Hassa region, which represents almost one-quarter of the area of Saudi Arabia and is the largest oasis in the world [*7*]. All children, aged 28 days to 12 years, admitted to the paediatric intensive care unit (PICU) with acute alteration of consciousness, between April 1999 and March 2002, were the subjects of the study. Depression of consciousness was assessed by the modified Glasgow Coma Scale for children (GCS) [*8,9*] as shown in Table 1.

Investigations performed for patients of the study were guided by the clinical presentation of the patients and were determined by the consultant in charge of every child. Neurological outcomes [*6*] were determined as: intact (normal or no change from premorbid functioning; seizures, if recorded, are 100% controlled), impaired (alteration of tone, power or reflexes; cranial nerve dysfunction; ataxia; seizures; persistent vegetative states) or death.

Data were collected, computed and statistically analysed using *Epi-Info*, version 6. The chi-squared test was used for comparison between traumatic and non-traumatic coma. The *F*-test was used to assess the significance of the relation between GCS and outcome. Differences were considered significant at $P \leq 0.05$.

Results

During the study period, a total of 91 (10.5%) children out of 870 admissions to PICU were admitted with a diagnosis of coma, an average rate of 2.6 patients per month. There were 59 males and 32 females giving a male to female ratio of 1.8:1. Population census of the region showed that the number of children aged 28 days to 12 years was therefore 635 603 during the study period. The incidence of coma was therefore 4.77 per 100 000 population per year.

Table 2 shows that preschool aged children constituted the greatest proportion of the cases (43.9%) and two-thirds of all the cases had a GCS of 8 or less. Figure 1 indicates that the commonest causes of coma were head trauma (42.9%), followed by infections (25.3%) and polytrauma (9.9%). Figure 2 shows the frequency of different types of infections; gastroenteritis was the commonest cause of sepsis-related coma. *Pseudomonas aeruginosa*, streptococcal pneumonia and *Haemophilus influenzae* were the most frequently isolated microor-

Table 1 **Modified Glasgow coma score**

Score	Response	Response	Response
Eye opening	> 1 year	0–1 year	
4	Opens spontaneously	Opens spontaneously	
3	Opens to a verbal command	Opens to a shout	
2	Opens in response to pain	Opens in response to pain	
1	No response	No response	
Best motor response	> 5 years	2–5 years	0–23 months
5	Oriented and able to converse	Uses appropriate words	Cries appropriately
4	Disoriented and able to converse	Uses inappropriate words	Cries
3	Uses inappropriate words	Cries and/or screams	Cries and/or screams inappropriately
2	Makes incomprehensible sounds	Grunts	Grunts
1	No response	No response	No response
Best verbal response	> 1 year	0–1 year	
6	Obeys command	Spontaneous	
5	Localizes pain	Localizes pain	
4	Flexion withdrawal	Flexion withdrawal	
3	Flexion abnormal (decorticate)	Flexion abnormal (decorticate)	
2	Extension (decerebrate)	Extension (decerebrate)	
1	No response	No response	

Table 2 **Age, type of coma and Glasgow coma score of comatose infants and children**

Variable	No. (*n* = 91)	%
Age group[a]		
Infants (28 days–<1 year)	17	18.7
Preschoolers (1–5 years)	40	43.9
School-aged (6–12 years)	34	37.4
Type of coma		
Traumatic	48	52.7
Non-traumatic	43	47.3
Glasgow coma score		
3–8	61	67.0
9–12	30	33.0

[a]*Mean (standard deviation) = 4.6 (3.5) years, median = 4 years.*

ganism from blood, cerebrospinal fluid or tracheal aspirate.

Tables 3 and 4 show different outcomes (intact, impairment or death) in relation to the cause of coma and GCS score.

Discussion

Most studies on childhood coma have been done in developed countries and there are few comprehensive data from developing countries where 80% of the world's children live [*5*].

Unsupervised activity is a major risk factor for traumatic coma and its age-specific

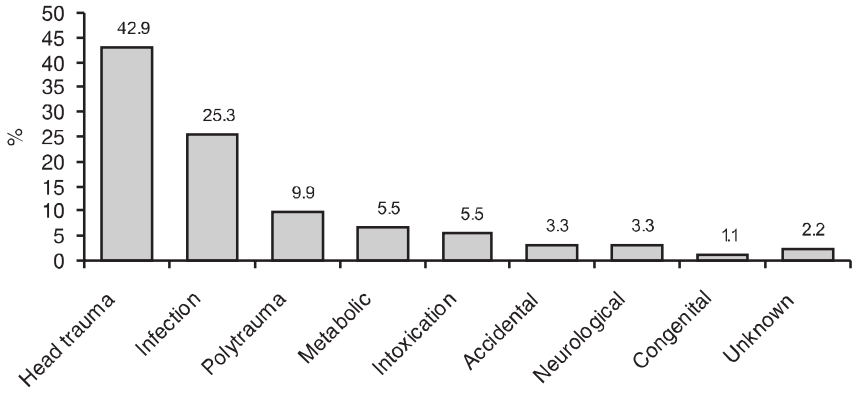

Figure 1 **Etiology of coma in the study patients (*n* = 91)**

incidence rises throughout early childhood with the highest rates in the preschool age group [*10,11*]. In our study, 10.4% of the patients with traumatic coma were in the infant age group compared to 27.9% with non-traumatic coma. Other studies report varying rates for traumatic coma. In an Indian study only 3.2% of the patients were below 2 years [*12*], in a Japanese study 12.5% of patients were infants [*13*] and in a Malaysian study 50% were infants [*5*].

In our study, trauma was the commonest cause of coma during the preschool and school ages and was accompanied by poor outcome (death or impairment) in more than half of the cases. These findings agree with earlier reports on traumatic coma [*3,4,10*]. Acute brain injury has been reported to be the cause of approximately 100 000 paediatric hospital admissions per year in the United States of America [*14*] and it is the leading cause of death in children older than 1 year [*9*]. In a Spanish 1-year study on children, 70% of deaths from traumatic brain injuries occurred within the first 48 hours and mortality ranged between 20% and 35% [*15*]. In another report on head trauma in children, 38% died and the average length of coma in survivors was 15.5 days; 29% of the survivors were unimpaired at follow up, 9% of had motor deficits but normal intellect and 9% had severe intellectual and motor problems [*16*].

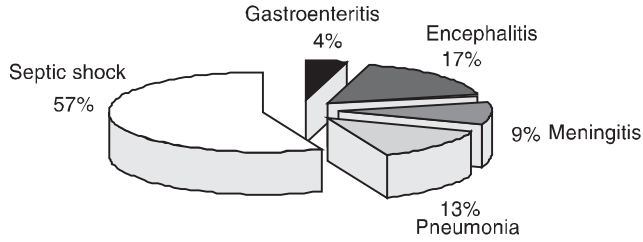

Figure 2 **Infectious causes of coma in the study patients (*n* = 23)**

Table 3 **Etiology of coma by clinical outcome**

Etiology	Total	Intact		Impairment		Death	
		No.	%	No.	%	No.	%
Head trauma	39	16	41.0	11	28.2	12	30.8
Polytrauma	9	4	44.4	0	0.0	5	55.6
Infection	23	2	8.7	3	13.0	18	78.3
Poisoning	5	5	100	0	0.0	0	0.0
Other (accidental)[a]	3	0	0.0	0	0.0	3	100
Metabolic	6	2	33.3	3	50.0	1	16.7
Neurological	3	0	0.0	1	33.3	2	66.7
Congenital	1	0	0.0	0	0.0	1	100
Unknown	2	1	50.0	0	0.0	1	50.0
Total	91	30	33.0	18	19.8	43	47.2

[a] *2 cases of drowning and 1 of electric shock.*

Table 4 **Outcome of cases in relation to mean Glasgow coma score and type of coma**

Outcome	Traumatic (*n* = 48)		Non-traumatic (*n* = 43)		Total (*n* = 91)	
	No.	Mean (SD)	No.	Mean (SD)	No.	Mean (SD)
Intact	20	8.1 (2.5)	10	9.3 (2.2)	30	8.5 (2.1)
Impairment	11	6.6 (2.3)	7	7.0 (2.8)	18	6.7 (2.5)
Death	17	4.2 (1.6)	26	5.8 (3.3)	43	5.1 (2.9)
F-test	14.55		4.90		13.92	
P	< 0.001		< 0.05		< 0.001	

SD = standard deviation.

Infection was the commonest cause of non-traumatic coma in our study and the commonest cause of coma in infants. Our results about infection-induced coma are in agreement with an English study on non-traumatic coma where infections caused 50.5% of coma in infancy, compared to 33.7% and 31.5% in preschool and school-aged children respectively [*6*]. In a Malaysian study, about two-thirds of the total coma cases were due to infection [*5*]. The same study considered infection as the most important cause of childhood coma throughout the world. In a Japanese study, 74% of cases of coma were also due to infection, mostly viral [*13*]. In an Indian study the etiology of coma in 60% of cases with non-traumatic coma was central nervous system (CNS) infection including tubercular meningitis, encephalitis, bacterial meningitis, and others [*17*]. This contradicts some reports from developed counties which stressed the importance of hypoxic ischaemic encephalopathy and toxic/metabolic causes [*11,18,19*].

The pattern of infection varies in different regions. In our study, the commonest infection was septicaemia complicated by septic shock (56.5%) followed by CNS infections (26.1%). The organisms isolated were diverse but the commonest were *Pseudomona*s spp. and *H. influenza*e. Different infective agents predominate in other parts of the world, for example cerebral malaria in Africa [*20*] and dengue haemorrhagic fever in South-east Asia [*21*]. In Japan, measles virus, herpes simplex and rubella are important [*13*]. In Malaysia, *H. influenzae* has been commonly implicated in CNS infection [*22,23*]. In an English study, *Neisseria meningitides* was recovered in 47% of cases where a pathogen was identified [*6*].

Other causes of coma apart from trauma and infection were found in only 21.9% of our patients. They are heterogenous causes but metabolic disorders, poisoning and accidental causes were the commonest. Accidental and neurological causes had the worst outcome in comparison with intoxication, which was followed by complete recovery. Although these findings are similar to previous studies [*5,6*], the small number of cases did not allow for statistical analysis.

In our study the overall mortality rate was 47.2%. The mortality rate was not statistically different in patients with GCS ≤ 8 (47.7%) versus those with GCS > 8 (42.3%). However, patients with lower GCS who survived had less favourable outcomes. Although GCS was lower if coma was due to a traumatic cause, the mortality rate in the non-traumatic group was nearly double that of the traumatic group (60.5% versus 35.4%). The reverse was true regarding the proportion with impaired outcome (16.3% versus 22.9%). This was supported by the finding of a mildly significant relationship between GCS and outcome in the non-traumatic group compared to a highly significant relationship in the traumatic group (Table 4). In non-traumatic coma, etiology rather than GCS was more significantly related to the outcome. Nayana et al. stated that in long-term prediction of outcome in acute non-traumatic coma, GCS is not useful [*24*]. However, verbal response, a component of GCS, correlates well with long-term functional outcome and intelligence quotient. In the Malaysian study, the overall outcome was poor and one-third made a full recovery, one-third recovered with neurological deficit and one-third succumbed to the acute illness [*5*]. In a recent Indian study, 11% achieved full recovery, 54% showed neurological impairment and 35% died [*24*]. Survival was significantly better in patients with CNS infection. In the English study, the mortality rate was 45.7% [*6*].

We conclude that head trauma and infections are the commonest causes of coma. The common reasons for poor outcome included septic shock, severe head trauma, accidental causes and metabolic disorders. GCS in traumatic coma and the specific etiology in non-traumatic coma were the most important prognostic factors for the outcome.

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Effectiveness of cognitive behaviour therapy in schoolchildren with depressive symptoms in Alexandria, Egypt

D. Habib[1] and A. Seif El Din[2]

فعالية معالجة السلوك المعرفي لدى تلاميذ المدارس المصابين بأعراض اكتئابية في الإسكندرية، بمصر

دعاء حبيب، أميرة سيف الدين

الخلاصة: تم في إطار هذه الدراسة تقييم فعَّالية معالجة السلوك المعرفي لدى تلاميذ المدارس في الفئة العمرية 12 – 14 سنة، ممن يعيشون في منطقة ذات مستوى اجتماعي واقتصادي منخفض في مدينة الإسكندرية، بمصر، وذلك خلال العام الدراسي 2003 – 2004. وقد شملت عينة الدراسة 198 من الذكور و136 من الإناث. وتم التقييم التلاميذ باستخدام القائمة التفصيلية لتقدير اكتئاب الأطفال، وقائمة كوبر سميث التفصيلية لتقدير الاعتزاز بالنفس. وبيَّنت الدراسة أن تواتُر (تكرار حدوث) الاكتئاب بلغ 9.6%؛ بواقع 7.1% لدى الذكور، و13.2% لدى الإناث. وقُدِّم علاج للسلوك المعرفي لـ 32 من التلاميذ الذكور المصابين باكتئاب، فقبله 17 تلميذاً منهم فقط حيث تلقّوا 9 جلسات علاجية. وتم تقييم هؤلاء التلاميذ بعد 3 أشهر من تلقّي العلاج باستخدام نفس الأدوات، وبيَّنت وأظهرت فعَّالية قصيرة الأمد للعلاج.

ABSTRACT We evaluated the effectiveness of cognitive behaviour therapy for 12–14-year-old schoolchildren from a low socioeconomic area in Alexandria, Egypt during the academic year 2003–04. Our sample comprised 198 boys and 136 girls. Students were assessed using the Child Depression Inventory and the Coopersmith Self-Esteem Inventory. The frequency of depression was 9.6%; 7.1% in boys and 13.2% in girls. The 32 children with depression were offered cognitive behaviour therapy. Only 17 accepted the offer and received 9 sessions of therapy. They were assessed 3 months after the intervention using the same tools and the results indicate the short-term effectiveness of the therapy.

Efficacité réelle de la thérapie cognitivo-comportementale chez des enfants scolarisés dépressifs d'Alexandrie (Égypte)

RÉSUMÉ Pendant l'année scolaire 2003-2004, nous avons évalué l'efficacité réelle de la thérapie cognitivo-comportementale chez des enfants de 12 à 14 ans scolarisés, issus d'un quartier socialement et économiquement défavorisé d'Alexandrie (Égypte). Notre échantillon se composait de 198 garçons et 136 filles. L'évaluation de ces élèves a reposé sur l'inventaire de dépression de l'enfant (IDE) de Kovacs, également connu sous le nom d'échelle CDI (pour *Child Depression Inventory*) et sur l'inventaire d'estime de soi (*Self-Esteem Inventory*) de Coopersmith. Il a été constaté une fréquence de la dépression de 9,6 %, à savoir 7,1 % chez les garçons et 13,2 % chez les filles. Les 32 enfants dépressifs se sont vu offrir une thérapie cognitivo-comportementale. Seuls 17 d'entre eux ont accueilli favorablement cette offre et ont participé à 9 séances de thérapie. Une évaluation de ces enfants s'appuyant sur les mêmes instruments de mesure et effectuée 3 mois après l'intervention a confirmé l'efficacité réelle à court terme de la thérapie.

[1]Child Mental Health Administrator and Psychiatrist, Alexandria, Egypt (Correspondence to D. Habib: doahabib@yahoo.com).
[2]Department of Community Medicine, Faculty of Medicine, University of Alexandria, Alexandria, Egypt.
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Introduction

Depression in childhood and adolescence is among the commonest and more disabling disorders. It has been reported that childhood depression ranges from 2%–6% among the school-aged population, and it seriously affects childhood and may have serious repercussion in adult life [*1*]. Klerman and Weissman have indicated that the onset of depression is occurring earlier in life today than in the past [*2*]. By the year 2020, depression is expected to become the single leading cause of disease burden worldwide [*3*].

The prevalence of depression in prepubertal children is estimated at approximately 2% and 5%–8% for adolescents [*4,5*]. A community survey of Australian children found that 3.7% of boys and 2.1% of girls at prepubertal age had experienced a depressive episode [*6*]. The gender ratio is 1:1 in prepubertal children and increases to 2:1 female-to-male ratio in adolescents [*7–9*]. In a large study of 1% of total students in preparatory schools in Alexandria, 10% of the students demonstrated depressive scores: 56% of these were girls compared with 44% boys [*10*].

Identifying one specific primary cause for depression among children and adolescents is hard since they are more sensitive to their environment [*11,12*]. Tension and conflicts come together triggering clinical depression with physical symptoms [*13,14*]. In another study in Alexandria, the psychological profile of students rating high on the depression scale indicated that a lack of communication and the presence of parent–child conflicts ranked first (23%), followed by parental conflicts (21%), and 30% had scholastic problems [*15*].

There has been considerable debate on the efficacy and safety of psychopharmacological drugs such as tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI). Some studies have shown empirical limitations compared with placebo concerning improvement of depressive symptoms and disorders among children and adolescents [*16–19*]. Psychological treatments for child and adolescent depression, including cognitive behaviour therapy (CBT), are therefore now often recommended as a first line of treatment [*20*]. Several randomized trials attest to the efficacy and safety of CBT in the treatment of depression in children and adolescents [*21–24*]. Meta-analysis of psychotherapies that have been used in the treatment of child and adolescent depression revealed 63% of those receiving some form of CBT showed significant improvement of symptoms [*25,26*].

The main aim of this study was to assess the prevalence of depressive symptoms among early adolescents, and to determine the clinical effectiveness of CBT in the management of depressive symptoms in school settings.

Methods

Sample

The study was conducted during the academic year 2003–2004 in 2 preparatory schools [one boys' (n = 198) and one girls' school (n = 136)] in a poor socioeconomic district in Alexandria. They were the only such schools in the district. All students enrolled in the first academic year (aged 12–14 years) were eligible for inclusion.

Measures

A questionnaire and psychological tests for depression and self-esteem were administered as baseline screening (pre-test) after

having the consent for participation. We used the Arabic version of the Children Depression Inventory (CDI-Arabic version) [*15*] to measure the severity of depressive symptoms (score range: 0–54, cut-off ≥ 25) and the Coopersmith Self-Esteem Inventory [*27*] to measure the self-esteem (score range: 0–25, cut-off ≤ 13 = low self-esteem).

A sociodemographic questionnaire was completed by the students which included questions on recent stressful life events over the past 6 months, sociodemographic data, and the type of discipline adopted and child interrelations at school and at home. The child's scholastic performance was assessed through school grades and levels of achievement, which were obtained from school records.

Children with the highest scores on the CDI scale ($n = 32$) underwent further clinical assessment to confirm depressive symptoms according to the *Diagnostic and statistical manual of mental disorders* (DSM-IV-TR) diagnostic criteria [*28*].

A more detailed questionnaire was completed by the interviewers for parents and teachers of the 32 children with the highest scores to further assess sociodemographic data, global functioning, academic achievement, peer relationships, communication skills with friends and the reason for frequent absences from school (if applicable).

Exclusion criteria (for participating in CBT)

- Children who had been and still were taking antidepressant treatment or therapy over the past 6 months (1 girl)
- Those who refused to join from the children with high scores (child or parental causes) ($n = 15$; 7 boys and 8 girls).
- Children with suicidal intent and in need of further referral (1 boy).

Treatment intervention

We used the *Cognitive behavioral manual for use with child patients with depressive disorders* [*29*] as a basis for therapy.

The intervention sample was 7 boys and 10 girls ($n = 17$). Nine weekly sessions were conducted at their school during the recreation break; 1 group for the 7 boys and 2 groups for girls with 5 girls each. Each session lasted 60 minutes but some sessions for girls extended to 90 minutes. A set of rules was issued by the children before starting the intervention sessions for control, discipline, respect and confidentiality of the sessions and were approved by their parents.

The main theme for each session was introducing a task or a situation with a role-play approach to solve the different situations. Homework assignments related to the tasks discussed and required them to record at home in writing their own feelings towards the applied activity. Parents attended with their children the discussion and explanation about the intervention as an introduction to what would be applied.

The first session was an ice-breaking session which was followed by 9 therapeutic ones focused on: emotional recognition, self-monitoring, self-reinforcement, activity schedule, communication and interpersonal skills, social problem-solving, cognitive reconstruction I, cognitive reconstruction II, and treatment review plan (final session). The skills were designed to help children learn to get along with peers and adults. We also included parents in some of the sessions where they learned how to encourage healthy behaviour in their children and become better at providing consistent consequences for negative behaviour and praising positive behaviour.

Statistical analysis

Statistical analyses were performed using *SPSS*, version 8.0. The chi-squared test was used for testing the difference in the prevalence between the sexes and the *t*-test for testing clinical effectiveness of treatment with CBT.

Results

The flow of participants through each stage of the study is shown in Figure 1. This shows that those who were the highest scorers on the CDI depression scale and eligible

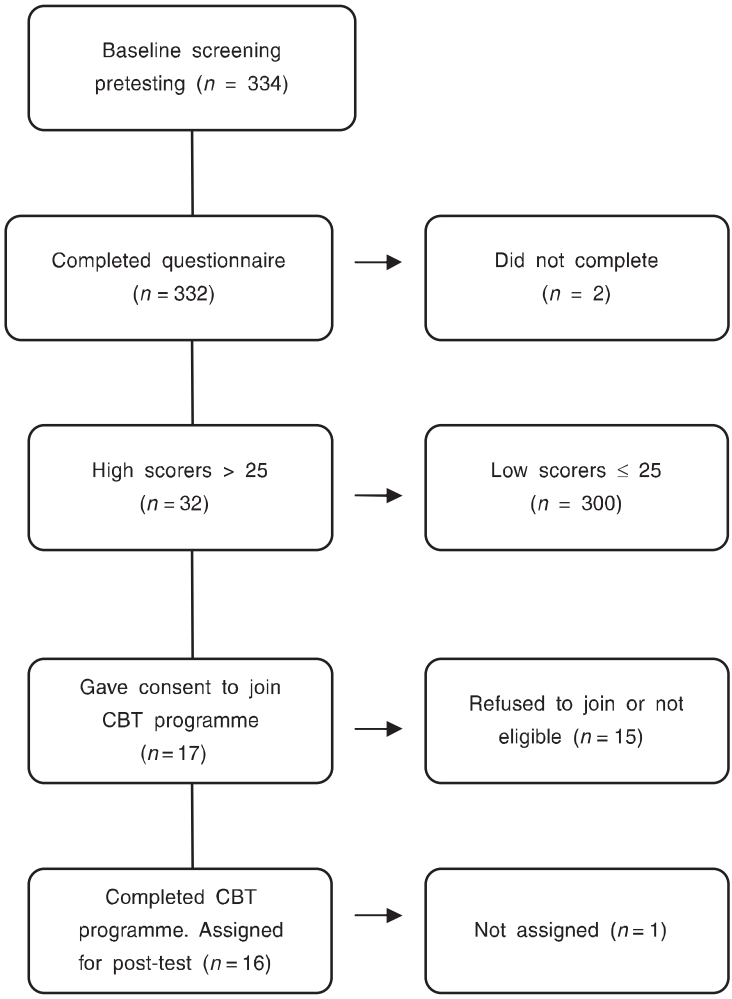

Figure 1 **Flow chart of enrolment of participants in the cognitive behaviour therapy (CBT) programme**

were recruited to CBT programme ($n = 17$) ; 7 boys and 10 girls.

The prevalence of depression was 9.6% among all children; 7.1% in boys and 13.2% in girls, giving a male:female ratio of 1:1.86.

Table 1 shows the sociodemographic characteristics of both the high-scorer group ($n = 32$) and the low-scorer group ($n = 300$). There were no significant differences between the groups except for parental punishment ($\chi^2_2 = 11.4$, $P < 0.0001$) and stressful life events over the past 6 months ($\chi^2_3 = 22.6$, $P < 0.0001$).

Table 2 shows the different mean CDI scores for the 32 highest scorers among all

Table 1 **Characteristics of the students according to depressive symptoms**

Characteristic	Depressive symptoms ($n = 32$)	No depressive symptoms ($n = 300$)	Statistical tests
Age (years)			$t = 1.36$, $P = 0.0622$
Mean (SD)	13.1 (0.7)	13.4 (0.8)	
Range	12–14	12–14	
	No. (%)	**No. (%)**	
Sex			$\chi^2 = 0.496$, P = 0.088
Male	14 (43.8)	182 (60.7)	
Female	18 (56.3)	118 (39.3)	
Parent's marital status			$\chi^2 = 0.274$, $P = 0.7081$
Married	19 (59.4)	200 (66.7)	
Widow	4 (12.5)	30 (10.0)	
Separated	9 (28.1)	70 (23.3)	
Mother's education			$\chi^2 = 0.0228$, $P = 0.2348$
No formal education (illiterate)	5 (15.6)	80 (26.7)	
High school	20 (62.5)	180 (60.0)	
University and higher education	7 (21.9)	40 (13.3)	
Father's education			$\chi^2 = 0.0822$, $P = 0.2011$
No formal education (illiterate)	6 (18.8)	102 (34)	
High school	20 (62.5)	146 (48.7)	
University and higher education	6 (18.8)	52 (17.3)	
Most stressful life events over the past 6 months			$\chi^2 = 22.6$, $P < 0.0001$
Family conflicts and lack of communication	15 (46.9)	17 (5.7)	
Family instability	11 (34.4)	20 (6.7)	
Death of one of the parents	3 (9.4)	15 (5.0)	
No life event of significance	3 (9.4)	248 (82.7)	
Parental punishment			$\chi^2 = 11.4$, $P < 0.0001$
Corporal punishment	18 (56.3)	5 (1.7)	
Verbal punishment	12 (37.5)	45 (15.0)	
No abuse/punishment	2 (6.3)	250 (83.3)	
Coopersmith self-esteem inventory [Mean (SD)]	8.9 (2.0)	23.7 (2.3)	$P = 0.0341$

SD = standard deviation.

Table 2 **Distribution of the highest mean CDI scores according to age and sex**

Age (years)	Boys Mean (SD)	Girls Mean (SD)	*P*-value
12	29.75 (2.6)	28.33 (2.1)	0.6556
13	28.33 (1.4)	32.62 (4.9)	0.0363*
14	30.75 (5.9)	30.00 (4.1)	0.8915

**Significant at* P < *0.05.*
CDI = Child Depression Inventory.
SD = standard deviation.

age groups for both boys and girls. At 13 years, girls had more depressive symptoms than boys ($t_5 = 2.838$, $P < 0.0363$).

Cognitive behaviour therapy intervention programme (pre- and post-intervention differences)

Intervention sessions lasted more than 60 minutes particularly for girls where they felt more suppressed; 8 out of 10 girls reported that the extra household duties and the limitations of outdoor creativity that are available to their boy siblings were the major complaints. In contrast, 5 out of 7 boys mentioned that their deprived families (being the most disadvantaged of the families) made them feel isolated with limited social communication with peers.

The improvement after the end of the intervention programme at the post-test was significantly greater than expected. The changes that occurred were statistically significant both on the depression scale ($t_2 = 9.02$, $P < 0.0001$) and the self-esteem scores ($t_{16} = 18.495$, $P < 0.0001$) (Table 3).

Table 4 shows that there were marked improvements in feelings of worthlessness, interpersonal relations and communication skills with staff and peers, interest in activities and school achievement among girls ($t_2 = 10.9$, $P < 0.0001$) and boys ($t_2 = 12.6$, $P < 0.0001$). As regards overall improvement differences between girls and boys, boys showed greater improvement than girls which was statistically significant ($\chi^2_3 = 46.7$, $P < 0.0001$).

Discussion

In our study, we found the prevalence of depressive symptoms to be 9.6% which is of concern. Life events over the past 6 months (every-day stressors) and parental punish-

Table 3 **Pre- and post-intervention tests scores for depression and self-esteem**

Tool used	Pre-test Mean (SD)	Post-test Mean (SD)	Statistical tests
Child Depression Inventory			$t_2 = 9.02$, $P < 0.0001$
Intervention group (total)	32.5 (4.5)	17.7 (6.9)	
Females	33.5 (4.9)	17.3 (7.6)	
Males	31.1 (3.8)	18.3 (6.1)	
Coopersmith self-esteem inventory			$t_2 = 18.494$, $P < 0.0001$
Intervention group (total)	8.88 (2.00)	15.65 (3.5)	
Females	9.30 (2.11)	16.0 (3.4)	
Males	8.29 (1.80)	15.14 (3.9)	

SD = standard deviation.

Table 4 **Frequency of depressive symptoms pre- and post-intervention by sex**

Depressive symptom	Pre-intervention		Post-intervention	
	Girls (*n* = 10) No. (%)	Boys (n = 7) No. (%)	Girls (*n* = 10) No. (%)	Boys (*n* = 7) No. (%)
Depressed mood	9 (90)	6 (86)	4 (40)	1 (14)
Feelings of worthlessness	9 (90)	5 (71)	4 (40)	2 (29)
No interest in activities	8 (80)	6 (86)	3 (30)	1 (14)
Appetite change	10 (100)	6 (86)	6 (60)	2 (29)
Disturbed sleep patterns	8 (80)	7 (100)	5 (50)	3 (43)
Difficulty in concentrating	7 (70)	6 (86)	4 (40)	3 (43)
Poor school achievement	8 (80)	4 (57)	3 (30)	4 (57)
Poor communication skills with peers and school staff	9 (90)	5 (71)	3 (30)	2 (29)

$t_2 = 10.9$, $P < 0.0001$ *(girls);* $t_2 = 12.6$, $P < 0.0001$ *(boys).*
$\chi^2_3 = 46.7$, $P < 0.0001$ *(girls versus boys).*

ment were significantly associated with such symptoms. Kalb and Raymond [*30*] reported family conflicts and poor inter-family communication and peer problems as stressor factors, while Eliot and Reis [*31*] considered family instability and insecure relationship as stressors.

We found sex differences in the frequency of depression, and early adolescent girls were more likely to be affected than boys with a ratio of approximately 2:1. Several studies have reported that girls are more vulnerable to life transition stressors, conform to social rules and utilize internalizing coping styles more than boys, i.e. they become socially withdrawn [*8,32–34*].

Pomerantz stated that parents using psychological control attempt to regulate their child's psychological and emotional development [*35*]. By constraining verbal expression and invalidating feelings they reinforce the child's depression. With lack of support, the child is less able to communicate effectively and more conflicts in relationships emerge. Our study illustrated the association between the use of violent means of discipline by parents and high depressive symptoms as has been reported in another study in Egypt [*36*]. In addition, maltreated children are significantly more likely to have low cognitive functioning, poorer adaptation to school and academic failure [*37*].

There has been a wave of sentiment against the use of pharmacological intervention as a first-line treatment for child and adolescent depression [*20,38*]. We observed a general concern towards treatment, especially pharmacological drugs, among the parents of our students, either because of fear of drug dependency or social and psychological stigma.

The start of CBT sessions revealed the conflict between children and their parents and suggested poor treatment outcomes. However, over the course of treatment, parents developed positive views of CBT (praising positive behaviour of their children) and children showed rapid response to the treatment as assessed by the pre-

and post-intervention depression scores, which are the main indicators for effective short treatment outcome. Thus, our results confirm those reported by DeCupper and colleagues that CBT can be applied within school and is effective in treating children and adolescents with depressive symptoms [*39*].

Regrettably, because of the limited awareness of the parents of their child's need for the programme, a large proportion of the parents of children showing depressive symptoms refused to enrol their child in the intervention programme. This resulted in only a small sample enrolled in the programme, which is was a limiting factor for the study. Furthermore, the lack of awareness of the school staff on mental health issues related to children hindered different approaches directed towards the group with depressive symptoms.

Depression among 12–14-year-old schoolchildren from deprived areas in Alexandria appears to a problem that needs to be addressed and a school mental health programme should be implemented [*40*]. Follow-up studies with larger sample sizes and adequate control groups will be necessary to evaluate the long-term benefit of CBT. In addition, psychoeducation and parenting skills for parents [*21*] are recommended together with increased training for mental health and school staff on CBT as a simple and effective tool to decrease depressive symptoms among schoolchildren [*41*].

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Neuroleptic-induced tardive dyskinesia among Arab psychotic patients

A. Osman,[1] M. Marghalani,[2] I.Y.A. Turkistani,[3] M. Al-Swaf[4] and B. Bin Sadiq[5]

خلل الحركة الآجل المحدث بفعل الأدوية المضادة للذهان لدى المرضى المصابين به

عبد الكريم عثمان، منال مرغلاني، إبراهيم يعقوب تركستاني، منى الصواف، بكر بن صديق

الخلاصة: أجرى الباحثون دراسة وصفية استعادية لتحديد مدى انتشار خلل الحركة الآجل، وعوامل اختطاره، بين مرضى الذُّهَان الذين يعالجون بأدوية تقليدية مضادة للذهان، في أربعة مراكز بالمملكة العربية السعودية. وقد فُحصت ملفات المرضى الذين تعاطوا دواءً تقليدياً واحداً مضاداً للذهان أو أكثر لمدة ستة أشهر أو أكثر خلال الفترة الواقعة بين كانون الثاني/يناير 1997 وكانون الأول/ديسمبر 2000. وأُدرج 151 من هؤلاء المرضى في التحليل النهائي. وأوضحت الدراسات أن 51 مريضاً فقط أصيبوا بخلل الحركة الآجل، و59 مريضاً آخرين (6.8%) أصيبوا بداء باركنسون المحدث بفعل الأدوية المضادة للذهان. وتبيَّن أن العوامل المتمثِّلة في مدة العلاج (P<0.001)، والجرعات الأعلى من الأدوية المضادة للذهان (P< 0.01)، وكون المريض فوق سن الأربعين (P< 0.01) قد ترابطت مع الإصابة بخلل الحركة الآجل. وتبيَّن أن هناك فرقاً يُعتدُّ به إحصائياً في انتشار هذا الخلل، حيث بلغ المعدل بين المرضى العرب (23.5%)، والعرب الأفارقة (45.5%) (P< 0.01)، في حين بلغ معدل الانتشار العام للإصابة بخلل الحركة الآجل بين مرضى الذهان 5.9%.

ABSTRACT We carried out a retrospective descriptive study to determine prevalence and risk factors for tardive dyskinesia (TD) among psychotic patients treated with conventional neuroleptics in 4 centres in Saudi Arabia. Records of patients who had been taking ≥ 1 conventional neuroleptic for ≥ 6 months from January 1997 to December 2000 were examined; 151 patients were included in the final analysis. Only 51 had TD; another 59 (6.8%) patients had drug-induced Parkinson disease. Duration of treatment ($P < 0.001$), higher doses of neuroleptics ($P < 0.01$) and age over 40 years ($P < 0.01$) were associated with TD. A statistically significant difference in prevalence was found between Arabs (23.5%) and Afro-Arabs (45.5%) ($P < 0.01$). Overall prevalence of TD among psychotic patients was 5.9%.

La dyskinésie tardive post-neuroleptique chez des patients arabes psychotiques

RÉSUMÉ Nous avons mené une étude descriptive rétrospective ayant pour objectif de déterminer la prévalence et les facteurs de risque de la dyskinésie tardive (DT) iatrogène chez des patients psychotiques traités avec des neuroleptiques classiques dans 4 centres d'Arabie saoudite. Les dossiers des patients ayant pris ≥ 1 neuroleptique conventionnel sur une période ≥ 6 mois entre janvier 1997 et décembre 2000 ont été examinés. Ont été inclus dans l'analyse finale 151 patients. Seuls 51 d'entre eux présentaient une DT, 59 autres (6,8 %) étant atteints d'un parkinsonisme iatrogène. La durée du traitement ($p < 0,001$), des doses de neuroleptiques plus élevées ($p < 0,01$) et un âge supérieur à 40 ans ($p < 0,01$) ont été associés à la DT. La prévalence a laissé apparaître une différence statistiquement significative entre les populations arabes (23,5 %) et afro-arabes (45,5 %) ($p < 0,01$). La prévalence globale de la DT chez les patients psychotiques était de 5,9 %.

[1]Psychiatric Department; [5]Department of Family Medicine and Medical Statistics, King Faisal Specialist Hospital and Research Centre, Jeddah, Saudi Arabia (Correspondence to A. Osman: akarimosman@yahoo.co.uk).

[2]Jeddah Psychiatric Hospital, Jeddah, Saudi Arabia.

[3]Department of Psychiatry, Al-Noor Hospital, Mecca, Saudi Arabia.

[4]Department of Psychiatry, King Fahad General Hospital, Jeddah, Saudi Arabia.

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Introduction

Neuroleptic-induced movement disorders consistent with the term tardive dyskinesia (TD), which was coined in 1964 [*1*], were reported in the literature as early as the 1950s. It was described as a movement disorder caused by the prolonged use of neuroleptic drugs. The condition is defined as a disorder characterized by involuntary movements, which may involve oro-facial dyskinesia, coarse tics or choreoathetosis, with abnormal oro-facial movements being the commonest [*2*]. It usually appears while the patient is still on the offending agent or appears for the first time when the drug is discontinued or its dose is reduced.

Reported prevalence rates of TD from across the world have varied widely. Rates from as low as 0.5% to as high as 65% have been reported [*3–11*]. Some of the confounders that have been proposed as contributing to such wide variability include heterogeneity of the populations under investigation, lack of agreement upon definition of what constituted TD and, more importantly, the confounding effect of the type, dosage and duration of the offending agents, and the duration of the illness itself, both prior to and after the commencement of the drug [*4,5,7,9,11–13*].

Tardive dyskinesia remains an enigma without a convincing explanation to its underlying pathophysiology. Two of the most persuasive current hypotheses are the dopamine hypersensitivity hypothesis and the serotonin–dopamine antagonist hypothesis. The dopamine hypersensitivity hypothesis states that neuroleptics may induce a compensatory dopamine hyperfunction owing to the prolonged blocking effect they have on the receptors. The serotonin–dopamine antagonist hypothesis maintains that drugs which have a high affinity for blocking serotonin receptors in the striatum, such as the new atypicals, may lead to increased release of dopamine, which attenuates the blocking effect of neuroleptics to dopamine receptors in the nigrostriatal system due to the inhibitory effect serotonin has on dopamine release in these areas [*14–16*]. Although there are no concrete biological or pathological findings which support these 2 hypotheses, the clinical empirical evidence lend them some good support. Despite the lack of concrete evidence for the underlying pathophysiology of TD, there have been a few consistently reported risk factors which were found to make some patients more vulnerable to developing TD if treated with neuroleptics. These include the prolonged continued use of neuroleptics, especially in large doses; polypharmacy; advancing age of the patient, particularly > 40 years; brain damage; strong negative symptoms or a strong affective component in schizophrenic patients; and the indiscriminate use of anticholinergic agents [*7,8,12,17–22*].

To the best of our knowledge, prevalence rate of TD has not been recorded for patients from Arab countries diagnosed with psychosis and being treated with conventional neuroleptics.

The aim of the study was to determine the prevalence rates of TD among Arab patients with psychosis who had been treated with conventional neuroleptics for a prolonged period. We also looked for any risk factors or protective factors among these patients.

Methods

We carried out a retrospective cross-sectional study to compare patients with neuroleptic-induced TD with those who did not develop it under comparatively similar conditions.

We selected the 4 hospitals which had psychiatric services situated in the western region of Saudi Arabia for this study. The Jeddah Psychiatric Hospital, which is the only general psychiatric hospital in the region and serves the city of Jeddah and the towns around, is a state hospital. It has 150 beds and 3 clinics a day, with 100 to 125 patients attending daily. There are 4 consultants, 8 psychiatric specialists and 3 senior registrars working in the hospital. King Fahad General Hospital is the largest state general teaching hospital in Jeddah, with about 900 beds. It is the main general hospital serving the inner city of Jeddah and the surrounding areas. Two psychiatrists provide the services, which are mainly outpatient clinics and consultation–liaison duties. Al-Noor General Teaching Hospital in Mecca, the second largest city in the area, is a state general hospital. There are 2 consultant psychiatrists and 2 associate specialists, whose main duties include outpatient clinics and liaison services in the hospital. They see about 60–75 patients in their clinics per day. King Faisal Specialist Hospital and Research Centre is in Jeddah; it has 1 full time consultant, 1 part time consultant and 1 specialist psychiatrist. Their main duties are outpatient clinics, liaison–consultation services and a limited number of inpatient cases as the hospital is mostly a tertiary care service hospital.

All patients suffering from a chronic psychosis who were seen between January 1997 and December 2000 in 1 of the 4 participating centres and who had been prescribed neuroleptic drugs for longer than 6 months were selected. Their medical records were examined to identify those patients who were eligible to be included in the study. Taking into consideration all the major drawbacks and pitfalls of a retrospective, multi-centre study, the following inclusion criteria were used:

- age 18–65 years;
- diagnosed as suffering from 1 of the following: schizophrenia, schizoaffective disorder or bipolar affective disorder that had been present for ≥ 3 years;
- well-defined diagnostic criteria, including persistent delusions and/or auditory hallucinations, which must have been documented at least 3 times during follow-up;
- patient had been taking ≥ 1 of the conventional (typical) neuroleptics continuously for ≥ 6 months;
- patient had been taking only conventional (typical) neuroleptics and none of the new atypical antipsychotics had been used at any time prior to the time of inclusion in the study;
- patient had been followed up in the same clinic for at least 3 years.

Results

A total of 866 patients were diagnosed with ≥ 1 of the 3 conditions and had been taking ≥ 1 of the conventional neuroleptics; 783 of them were concurrently taking > 1 anticholinergic drugs. Only 151 patients met all the inclusion criteria and only 51 of these (5.9%) were found to have some movement disorder that was consistent with TD. A further 59 patients (6.8%) were described as having symptoms of drug-induced Parkinson disease.

When only those with complete medical records, including the more frequently and consistently reported risk factors, were identified, the records of only 151 patients [116 (67.8%) males and 35 (23.2%) females] were suitable for inclusion in the final analysis. Among these, 115 were Arabs (27 of whom developed TD) and 22 were Afro-Arabs (10 of whom developed TD) (Table 1). It was not possible to reli-

Table 1 **Association of tardive dyskinesia with diagnosis, duration of illness, and sociodemographic characteristics**

Variable	Total	Tardive dyskinesia[a]		χ^2	df	*P*-value
	No.	No.	%			
Diagnosis						
Schizophrenia	90	30	33.3	0.385	2	0.8
Schizoaffective disorder	23	9	39.1			
Bipolar affective disorder	38	12	31.6			
Duration of illness (years)						
< 5	47	7	14.9	33.48	3	< 0.001
5–9	40	7	17.5			
10–19	43	21	48.8			
> 19	21	16	76.2			
Sex						
Male	118	38	32.2	0.596	1	0.44
Female	33	13	39.4			
Ethnicity						
Arab	115	27	23.5	6.11	1	< 0.01
Afro-Arab	22	10	45.5			

[a]*Mean age (SD) 46.4 (11.4) years for those who had tardive dyskinesia and 36.7 (12.2) years for those who did not (χ^2 = 4.72;* P = *0.01).*

ably determine the ethnicity of the other 14 patients.

Forty-seven patients were > 40 years old, mean 46.4 [standard deviation (SD) 11.4] years and 114 were ≤ 40 years of age, mean 36.7 (SD 12.2) years. From the records, we found 51 patients [38 (74.5%) males and 13 (25.5%) females] had TD; all were described as having oro-facial movement disorder (Table 1). A statistically significant positive association with TD was found only with advancing age of the patients [mean age of those with TD was 46.4 (SD 11.4) years compared with mean age 36.7 (SD 12.2) years for those without TD (χ^2 = 4.72; $P < 0.01$)], longer duration of illness ($P < 0.001$) (Table 1) and longer duration of treatment ($P < 0.001$) (Table 2).

As almost all our patients had been prescribed > 1 drug, we calculated the daily intake in terms of approximate equivalents to chlorpromazine in accordance with the British National Formulary [21]. Only 2 of the drugs used, chlorpromazine ($\chi^2 = 13.70$, $P = 0.001$) and haloperidol ($\chi^2 = 8.70$; $P = 0.012$), had a statistically significant positive association with TD. No association was established between trifluoperazine and TD.

Discussion

We considered very carefully the confounding effects that a retrospective, multi-centre study such as this may have had on our findings and conclusions. We were also cognizant of the drawbacks of this study which included:

- the lack of any inter-rater reliability or validity tests for the diagnostic skills

Table 2 **Association of tardive dyskinesia with type of neuroleptic and duration of treatment**

Variable	Total	Tardive dyskinesia		χ^2	df	*P*-value
	No.	No.	%			
Haloperidol (mg/day)						
5–9	14	1	7.1	8.70	2	0.012
10–19	51	7	13.7			
≥ 20	19	8	42.1			
Total	84	16	19.0			
Trifluoperazine (mg/day)						
5–9	14	3	21.4	0.50	2	0.877
10–19	33	6	18.2			
≥ 20	23	6	26.1			
Total	70	15	21.4			
Chlorpromazine (mg/day)						
50–< 200	75	6	8.0	13.70	2	< 0.001
200–< 400	31	9	29.0			
≥ 400	11	5	45.5			
Total	117	20	17.1			
Duration of treatment (years)						
< 5	59	3	5.1	19.28	3	< 0.001
5–9	44	5	11.4			
10–19	34	10	29.4			
≥ 20	13	26	46.2			
Total	150[a]	24	16.0			

[a]*Data missing for 1 case.*
df = degrees of freedom.

of the psychiatrists who made the diagnoses;

- the diagnostic criteria which were used by the different psychiatrists at the time of diagnosis and the value of their diagnostic significance in reaching that diagnoses;
- what exactly was meant by TD by each of the psychiatrists and how accurate their descriptions and documentations were.

Some of our findings were also related to a relatively small sample size which may, therefore, have made any generalizations or conclusions more difficult to draw up.

The total number included for the final analysis in this study was only 151 patients. Despite this relatively small sample, however, we believe some of our findings merit careful consideration. The lower overall prevalence rate of TD among our patients (5.9%) is not in keeping with most of the reported rates from studies done in Western Europe and North America, where reported rates are 20%–39%, and in the Far East, where reported rates are 29.0%–40.6% [*6,7,10,18,20,22*].

Perhaps more important is the inter-ethnic difference in the prevalence rate of TD between Arabs from the Middle East and the Afro-Arabs, who are of African origin. While TD rate was 23.5% among

the Arabs, it was 45.5% among Afro-Arabs. Although the size of the sample was rather small, this finding, coupled with the relatively high rate of TD (39.7%) reported by Van Harten et al. among the mostly Negroid population in a state public hospital in the Netherlands indicate that some interethnic difference may indeed exist [*19*]. However, the existence of some variability in rates of TD due to ethnocultural factors has not been consistent or agreed upon by all researchers. While some researchers believe that some biological or genetic difference in susceptibility to TD may be found [*16,23*], others believe that susceptibility is most likely related to psychopharmacological factors such as duration of exposure and level of daily intake of neuroleptic drugs rather than to any ethnocultural or biological factors [*8,10,11,22*]. Our findings are more in support of differences related to either ethnocultural or genetic factors. If an interethnic difference in susceptibility between Arabs and Afro-Arabs does indeed exist, it will have important financial implications, particularly as almost all the Afro-Arabs included in this study came from poor African countries. Such a background may emphasize the importance of either early adverse neurodevelopmental factors such as poor prenatal care, infections or birth complications, or a genetic susceptibility which may be operating in these individuals.

We also found that many patients had been prescribed relatively low daily doses of neuroleptics to treat their psychosis. For example, among patients on haloperidol, 65 of them (77.4%) were taking < 20 mg/day with only 8 of those (12.3%) developing TD compared to 8 patients out of 19 patients (42.1%) who were on ≥ 20 mg/day. The same was true among patients taking chlorpromazine: 106 of 117 (90.1%) were taking < 400 mg/day and only 15 of them (14.2%) developed TD compared to 5 out of 11 (45.5%) receiving ≥ 400 mg/day. This finding, coupled with the consistently reported strong positive association of TD with higher daily doses of neuroleptics [*5,7,9,12*] suggests that the lower rates of both TD and Parkinson disease among our patients may be mostly related to the low daily doses of neuroleptics needed to effectively treat their condition. This could have important economic implications for the continuation of the conventional neuroleptics in poorer countries as first choice drugs, especially in countries where the affordability of drugs is the main determining factor in treatment.

One of the risk factors for increased susceptibility to neuroleptic-induced TD is the indiscriminate prescription of anticholinergic agents [*4,7,10,12,18,24*]. In our study, only 51 of the 783 patients taking ≥ 1 anticholinergic drugs developed TD and 59 Parkinson disease, which is not in keeping with what has previously been reported in the literature. We therefore believe that this trend in developing countries for prescribing an anticholinergic drug whenever a neuroleptic drug is given to a psychotic patient, as has been noted among our patients, may prove to have some protective or preventive role in keeping the rate of TD relatively low. This is in contrast to previous findings where anticholinergics have been identified as one of the risk factors. A longitudinal prospective study would be needed to determine if this is so.

In conclusion, in this study we found the overall prevalence rate of TD among Arab patients to be lower than the general rates reported in the literature, as well as the existence of some interethnic difference in rates between Arabs and Afro-Arabs. It is also possible that Arabs who suffer from chronic psychosis might need relatively lower daily doses of neuroleptics to be effective for their illness.

Prevalence of TD and drug-induced Parkinson disease were both relatively low among our patients, and in general, relatively low daily doses of conventional neuroleptics were prescribed. Consequently, we believe that the conventional neuroleptics could still continue to be first choice antipsychotics for the treatment of chronic psychosis rather than the relatively more expensive new atypical drugs which poorer countries may find it difficult to afford.

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Sleep–wake cycle disturbances in protein–energy malnutrition: effect of nutritional rehabilitation

S.Y. Shaaban,[1] H.L. El-Sayed,[1] M.F. Nassar,[1] T. Asaad[2] and S.M. Gomaa[3]

تأثير التأهيل التغذوي على اضطرابات دورة النوم واليقظة لدى الرُّضَّع المصابين بسوء التغذية بالبروتين والطاقة

سناء يوسف شعبان، هدى لطفي السيد، مي فؤاد نصار، طارق أسعد، سعاد محمود جمعة

الخلاصة: تم في هذه الدراسة توزيع استبيان موحَّد حول النوم، وإجراء الاختبار المتعدِّد المعايير polysomnograph لتقييم أنماط النوم لدى 26 من الرضَّع الذين يعانون من سوء التغذية بالبروتين والطاقة. وتم تكرار ذلك بعد حوالي شهرين من تنفيذ برنامج للتأهيل التغذوي وفقاً للدلائل الإرشادية لمنظمة الصحة العالمية. وتمت مقارنة مجموعات الدراسة مع 10 من الرضَّع الأصحاء. كما أُجريت القياسات البشرية مع قياس مستويات سيروتونين المصل. ولوحظ بعد التأهيل التغذوي انخفاض يُعتدُّ به إحصائياً في النسبة المئوية للنوم في مرحلة الحركة غير السريعة للعين، وفي مدة الحركة السريعة الثانية للعين، وفي عدد مرات نوم الكمون والنوم في مرحلة الحركة السريعة للعين. ولوحظ أيضاً ارتفاع يعتدُّ به إحصائياً في النوم في مرحلة الحركة السريعة للعين، وفي مستويات سيروتونين المصل. ويبدو من الدراسة أن سوء التغذية بالبروتين والطاقة يؤثِّر على دورة النوم واليقظة. وقد يكون اضطراب مستويات سيروتونين المصل من بين العوامل المسؤولة عن ذلك.

ABSTRACT A standard sleep questionnaire was given to the parents of 26 infants with protein–energy malnutrition who underwent polysomnographic evaluation. These investigations were repeated approximately 2 months after enrolment in a nutritional rehabilitation programme based on World Health Organization guidelines. Anthropometric values and serum serotonin levels were also measured. After nutritional rehabilitation there was a significantly higher percentage of non-rapid eye movement (REM) sleep; 2nd REM time, and latency times for sleep and REM sleep increased. Percentages of REM sleep and serum serotonin levels decreased significantly. Protein–energy malnutrition seems to affect the sleep–wake cycle; disturbed serotonin levels may be among the factors responsible.

Troubles du cycle veille-sommeil dans la malnutrition protéinocalorique : l'effet de la récupération nutritionnelle

RÉSUMÉ Un questionnaire normalisé sur les habitudes de sommeil de leur enfant a été administré aux parents de 26 nourrissons souffrant de malnutrition protéinocalorique, lesquels ont subi un examen polysomnographique. Ces évaluations ont été répétées 2 mois environ après inclusion des nourrissons dans un programme de récupération nutritionnelle conforme aux directives de l'Organisation mondiale de la Santé. Les paramètres anthropométriques et la sérotoninémie ont également été mesurés. À l'issue de la récupération nutritionnelle, on a pu constater une augmentation significative du pourcentage du sommeil NREM (pour *non-rapid eye movement* – sans mouvements oculaires rapides), ou sommeil lent, ainsi qu'un allongement de la durée de la deuxième phase de sommeil REM (*rapid eye movement* – à mouvements oculaires rapides), ou sommeil paradoxal, de la latence d'endormissement et de la latence du sommeil paradoxal. Il a en outre été noté une diminution significative du pourcentage du sommeil REM et de la sérotoninémie. La malnutrition protéinocalorique semble retentir sur le cycle veille-sommeil; il est probable que l'instabilité de la sérotoninémie figure parmi les facteurs responsables.

[1]Department of Paediatrics; [2]Department of Psychiatry, Faculty of Medicine, Ain Shams University, Cairo, Egypt (Correspondence to M.F. Nassar: maie_nassar@yahoo.co.uk).
[3]Division of Chemistry and Biological Research, National Centre for Social and Criminological Research, Cairo, Egypt.
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Introduction

Nutritional deficiencies are a major health problem in tropical and subtropical regions of the world [*1*]. Malnutrition is still a problem especially in developing countries, where the total number of underweight and stunted children has not changed dramatically since 1980 [*2*]. In Egypt, the incidence of protein–energy malnutrition (PEM) was found to be 16.5% [*3*].

Reduction in the supply of energy and several essential nutrients during the early stages of life has profound effects on the nervous system structural and functional development. Malnutrition impairs brain development, decreasing the number of cell replication cycles, reducing total brain DNA and restricting dendritic arborization, thus reducing the connection between neurons [*4*]. Cintra and colleagues [*5*] stated that prenatal and chronic malnutrition produces important alterations in the homeostatic and circadian process of sleep, thus altering the sleep–wake cycle.

Several neuropeptides affect the sleep–wake cycle [*6*] and a role for gamma-aminobutyric acid (GABA) transmission has been hypothesized [*7*]. Lechin et al. investigated the changes of circulating neurotransmitters (noradrenaline, adrenaline, dopamine, platelet serotonin, plasma serotonin and tryptophan) during the sleep–wake cycle to correlate the profile of circulating neurotransmitters with the well-known central neurocircuitry functioning during the sleep–wake cycle [*8*]. Among many factors associated with PEM, increased levels of the neurotransmitter serotonin were reported to be the cause of sleep disturbances in malnourished rats [*9*].

Since PEM is still a problem in many countries, its effects on children's development and cognition is a concern of many investigators. As far as we know, sleep disturbances in PEM patients have rarely been studied before as most of the data on malnutrition from sleep laboratories is from animal models [*5,9,10,11*] or anorectic adults [*12,13*]. This study was therefore designed to detect disturbances in the sleep–wake cycle of Egyptian infants with PEM, comparing oedematous and non-oedematous cases before and after a nutritional rehabilitation programme, and to correlate the detected abnormalities to the level of the neurotransmitter serotonin.

Methods

Patients

The present study was conducted on 26 infants diagnosed with PEM according to the Wellcome classification [*14*]. They were recruited from the nutritional unit of the Children's Hospital and assessed at the Institute of Psychiatry, Ain Shams University. The patients were further divided into 2 groups according to the 2 clinically distinct disorders of PEM, oedematous and non-oedematous, Heird's preferred terms for kwashiorkor and marasmus respectively [*3*].

Group 1 was 12 infants with the non-oedematous form of PEM (8 males and 4 females), with a mean age of 8.5 months [standard deviation (SD) 3.8 months]. Group 2 comprised 14 infants (8 males and 6 females) with the oedematous form of PEM, with a mean age of 13.7 (SD 7.5) months. Patients of both groups were compared with group 3, 10 clinically healthy age- and sex-matched controls (5 males and 5 females), with a mean age of 12.6 (SD 6.8) months. The controls were recruited from among those presenting for dietetic advice, vaccination or circumcision (in males) at the outpatient clinic in the Children's Hospital.

All the recruited patients and controls were from underprivileged families (having low socioeconomic standard according to Park and Park [*15*]) and had been breastfed for at least 6 months and afterwards weaned while receiving artificial milk products. None of the infants was on any medication or vitamin supplementation at the time of enrolment in the study.

Investigations

An informed written consent was signed by the parents or the legal guardians after obtaining the approval of the ethical committee at the Children's Hospital, Ain Shams University. Each studied infant was then enrolled in the 3-phase study: pre-interventional assessment (phase 1); a nutritional rehabilitation intervention programme according to World Health Organization (WHO) guidelines [*16*] (phase 2); and a post-interventional assessment 2 months (SD 2 weeks) after enrolment (phase 3).

The WHO nutritional rehabilitation programme starts feeding with a diet which is low in protein, fat and sodium and high in carbohydrates (calorie intake 80–100 kcal/kg/day) as almost all severely malnourished infants have infections, impaired liver and intestinal functions and problems related to electrolyte imbalance. At the rehabilitation stage as the infant's appetite returns, the calorie intake is increased to 150–200 kcal/kg/day with an increase in amounts and decrease in frequency. A high protein diet is given and vitamins and minerals (potassium, magnesium and zinc) are continued in increased amounts. Iron is given during this stage to treat the anaemia present. The infant remains in the hospital during the early phase of rehabilitation (at least 3 weeks after admission), and is then followed up in the nutritional rehabilitation outpatient clinic.

Assessment in phases 1 and 2 included detailed dietetic history and clinical examination, with special emphasis on the anthropometric measurements and signs of malnutrition as well as the laboratory workup and recording the sleep data.

Laboratory workup

For the laboratory workup, samples of blood were collected from all subjects and processed as clotted venous blood and EDTA anticoagulated blood. Serum samples were used for the determination of liver and kidney functions (Synchron CX-5 Delta, Beckman Inst. Inc., Scientific Instruments Division, Fullerton, USA). Serum level of serotonin was estimated as well in all studied cases by enzyme-linked immunosorbent assay (ELISA) according to Chauveau et al. [*17*]. The EDTA blood was used for complete blood count (Coulter T660, Miami, USA).

Assessment of sleep

Assessment of sleep was done through a standard sleep questionnaire in simple Arabic language that was answered by the parents [*18*] in addition to polysomnographic evaluation of the study infants and controls who were left to sleep spontaneously without any intervention. The apparatus used was the Neurofax EEG-2110 digital electroencephalograph (Nihon Koden Corporation, Tokyo, Japan), with 3 dedicated respiratory inputs at the headbox and 4 available DC channels. The EEG 2110 can record a variety of biopotential activities necessary for the sleep laboratory. Polysmith TM software provided the immediate staging, scoring and reporting of the polysomnographic recordings.

Hypnographic sleep EEG provided the following variables: sleep continuity (including sleep latency and efficiency and

number of arousals) as well as sleep architecture, including percentage of rapid eye movement (REM) sleep, non-REM (NREM) sleep and slow wave sleep (SWS), as well as REM, NREM and SWS latency periods. The analysis of sleep architecture did not include a differential percentage of each sleep stage (I, II, III, IV), but rather NREM or SWS was considered as a whole.

Statistical analysis

Statistical analysis of the results was done using *SPSS*, version 10 and *Statsoft,* version 5. Non-parametric data were detected by the Shapiro–Wilk test. Student *t*- and paired *t*- tests were used for parametric quantitative data and Mann–Whitney U and Wilcoxon matched pairs tests for non-parametric quantitative data in addition to the correlation studies. The numerical data were represented in mean and standard deviation (SD) and median (interquartile range). The differences were considered significant at $P < 0.05$.

Results

Anthropometric data

The present study revealed significantly lower anthropometric measurements—weight, length and mid arm circumference—in PEM patients compared with those of the controls at the pre-assessment phase (Table 1). These measurements showed significant improvements after nutritional rehabilitation in both oedematous and non-oedematous patients, although the values did not reach control values (Table 2). The same findings were observed regarding haemoglobin and serum albumin levels (Tables 1 and 2). As regards liver and kidney functions, their values were within the normal range for age and sex according to Nicholson and Pesce [*19*] from the start of the study.

Serum serotonin levels were significantly higher in both studied PEM subgroups compared with those of the controls (Table 1) and these decreased significantly after nutritional rehabilitation (Table 2).

The study also revealed significantly lower skull circumference (% of median for age) and serum albumin with significantly higher serum serotonin in the oedematous compared with the non-oedematous patients (Table 1).

Sleep data

Analysis of the sleep questionnaire findings revealed that caregivers reported sleep complaints in 76.9% of cases, mostly disturbed sleep rhythm, in both subgroups of PEM infants.

As regards the sleep data before nutritional rehabilitation, there was no significant difference between both PEM groups before nutritional rehabilitation (Table 3). Comparing both groups of PEM infants with the control infants showed a significantly lower percentage of NREM sleep, REM latency time and 2nd REM time. In addition, the number of minutes of sleep latency was lower in both PEM groups compared with the controls but this result was significant only in non-oedematous patients. On the other hand, the percentage of REM sleep was higher in both PEM groups compared to the controls but this result was significant only in oedematous patients (Table 3). In addition, initial SWS latency time and the percentage of SWS were not significantly different in both subgroups compared with the controls.

Table 4 shows the sleep parameters measured after nutritional rehabilitation. Sleep latency increased in both groups and this was significant in non-oedematous infants. The percentage of NREM sleep and the amount of 2nd REM sleep time increased in both groups, with a statistically significant

Table 1 **Anthropometric measurements and laboratory parameters of infants with non-oedematous and oedematous protein–energy malnutrition before nutritional rehabilitation compared to the controls**

Variable	Mean (SD) [Median (interquartile range)]			Statistics		
	Non-oedematous Group 1 (n = 12)	Oedematous Group 2 (n = 14)	Control Group 3 (n = 10)	Group 1 vs 3 t/Z values	Group 2 vs 3 t/Z values	Group 1 vs 2 t/Z values
Weight (% of median for age)	61.2 (12.5) [58.5 (14.7)]	62.9 (8.9) [66.0 (16.0)]	93.6 (6.7) [94.9 (6.5)]	–3.82[a] (P < 0.001)	–4.10[a] (P < 0.001)	–0.82[a] (P > 0.05)
Length/height (% of median for age)	88.1 (3.7) [88.7 (5.2)]	84.9 (8.8) [87.3 (4.3)]	97.1 (1.1) [97.6 (1.6)]	–3.96[a] (P < 0.001)	–4.10[a] (P < 0.001)	–0.62[a] (P > 0.05)
Skull circumference (% of median for age)	92.3 (1.5) [92.8 (2.5)]	90.6 (4.6) [90.4 (5.0)]	95.6 (1.5) [95.8 (2.0)]	–3.96[a] (P < 0.05)[a]	–4.10[a] (P < 0.05)	–2.16[a] (P < 0.05)
Mid arm circumference (cm)	8.5 (1.0) [8.5 (1.0)]	9.0 (1.6) [9.0 (3.5)]	13.1 (0.8) [13.0 (1.2)]	–3.96[a] (P < 0.001)	–4.10[a] (P < 0.001)	0.93[a] (P > 0.05)
Serum albumin (g/dL)	3.2 (0.5) [3.1 (0.7)]	2.2 (0.2) [2.2 (0.2)]	4.2 (0.5) [4.3 (0.6)]	–3.51[a] (P < 0.001)	–4.12[a] (P < 0.001)	–4.35[a] (P < 0.001)
Haemoglobin (g/dL)	8.9 (1.0) [8.9 (9.0)]	9.7 (1.8) [9.0 (9.7)]	12.1 (1.6) [12.3 (1.5)]	–5.27 (P < 0.001)	–3.23 (P < 0.01)	–1.11 (P > 0.05)
Serum serotonin (ng/mL)	434.7 (270.3) [251.5 (360.4)]	646.5 (238.1) [745.2 (374.8)]	190.5 (34.2) [175.4 (48.2)]	–3.10[a] (P < 0.01)	–4.10[a] (P < 0.001)	–2.57[a] (P < 0.05)

[a]*Non-parametric data were tested by Shapiro–Wilk test. The test of significance was Mann–Whitney test.*
SD = standard deviation.

Table 2 **Comparison between anthropometric measurements and laboratory parameters of infants with non-oedematous and oedematous protein–energy malnutrition before and after nutritional rehabilitation**

Variable	Non-oedematous (n = 10) Mean (SD) [Median (interquartile range)]			Oedematous (n = 10) Mean ± SD [Median (interquartile range)]		
	Before	After	Statistics t/Z values	Before	After	Statistics t/Z values
Weight (% of median for age)	61.2 (12.5) [58.5 (14.7)]	71.2 (9.9) [68.5 (11.1)]	3.18[a] (P < 0.01)	62.9 (8.9) [66.0 (16.0)]	74.1 (10.3) [72.7 (21.1)]	–3.47[a] (P < 0.001)
Length/height (% of median for age)	88.1 (3.7) [88.7 (5.2)]	88.8 (5.3) [87.9 (8.9)]	–0.54 (P > 0.05)	84.9 (8.8) [87.3 (4.3)]	89.0 (6.8) [89.8 (13.2)]	2.41[a] (P < 0.05)
Skull circumference (% of median for age)	92.3 (1.5) [92.8 (2.5)]	93.8 (2.5) [94.0 (1.9)]	2.02[a] (P < 0.05)	90.6 (4.6) [90.4 (5.0)]	93.0 (2.8) [93.8 (4.0)]	–7.15 (P < 0.001)
Mid arm circumference (cm)	8.5 (1.0) [8.5 (1.0)]	9.8 (0.9) [9.8 (1.5)]	–16.58 (P < 0.001)	9.0 (1.6) [9.0 (3.5)]	9.9 (1.8) [9.7 (3.5)]	–8.33 (P < 0.001)
Serum albumin (g/dL)	3.2 (0.5) [3.1 (0.7)]	3.95 (0.3) [3.9 (0.4)]	7.35 (P < 0.001)	2.2 (0.2) [2.2 (0.2)]	3.6 (0.1) [3.5 (0.2)]	25.24 (P < 0.001)
Haemoglobin (g/dL)	8.9 (1.0) [8.9 (9.0)]	9.96 (0.8) [9.5 (9.5)]	–7.98 (P < 0.001)	9.7 (1.8) [9.0 (9.7)]	10.5 (1.2) [10.3 (11.1)]	–4.31 (P < 0.01)
Serum serotonin (ng/mL)	434.7 (270.3) [251.5 (360.4)]	152.1 (63.9) [127.9 (80.9)]	–3.06[a] (P < 0.01)	646.5 (238.1) [745.2 (374.8)]	220.9 (34.2) [238.0 (114.1)]	–3.30[a] (P < 0.01)

[a]*Non-parametric data were tested by Shapiro–Wilk test. The test of significance was Wilcoxon matched pairs test.*
SD = standard deviation.

Table 3 **Sleep data of infants with non-oedematous and oedematous protein–energy malnutrition before nutritional rehabilitation compared with the controls**

Variable	Mean (SD) [Median (interquartile range)]			Statistics		
	Non-oedematous Group 1 (*n* = 15)	Oedematous Group 2 (*n* = 15)	Control Group 3 (*n* = 10)	Group 1 vs 3 *Z* value	Group 2 vs 3 *Z* value	Group 1 vs 2 *Z* value
Sleep latency (min)	2.8 (1.1) [3.1 (1.9)]	4.1 (2.1) [3.2 (3.2)]	5.5 (2.2) [5.1 (3.7)]	–3.03 (*P* < 0.01)	–1.35 (*P* > 0.05)	–1.44 (*P* > 0.05)
Sleep efficiency (%)	95.2 (2.1) [95.3 (4.1)]	93.6 (1.9) [93.2 (2.7)]	94.4 (1.5) [94.4 (2.2)]	–0.86 (*P* > 0.05)	–1.35 (P > 0.05)	–1.65 (*P* > 0.05)
NREM sleep (%)	44.5 (12.0) [44.0 (19.1)]	49.6 (10.3) [50.0 (20.8)]	60.6 (8.9) [63.5 (7.9)]	–2.77 (*P* < 0.01)	–2.58 (*P* < 0.01)	–1.23 (*P* > 0.05)
SWS (%)	20.0 (11.6) [19.4 (14.5)]	18.6 (4.8) [18.5 (2.3)]	13.7 (8.8) [19.0 (14.0)]	–0.92 (*P* > 0.05)	–0.23 (*P* > 0.05)	–0.62 (*P* > 0.05)
REM sleep (%)	41.2 (6.1) [39.0 (11.9)]	43.8 (6.2) [43.0 (12.0)]	36.6 (3.7) [36.5 (7.0)]	–1.85 (*P* > 0.05)	–2.63 (*P* < 0.01)	–1.44 (*P* > 0.05)
SWS latency (min)	17.0 (12.7) [23.5 (26.0)]	19.6 (13.4) [27.0 (31.0)]	13.2 (11.8) [19.0 (20.0)]	–1.12 (*P* > 0.05)	–1.46 (*P* > 0.05)	–1.13 (*P* > 0.05)
REM sleep latency (min)	6.5 (8.3) [2.0 (17.0)]	13.0 (10.1) [13.0 (21.0)]	27.3 (14.3) [31.5 (23.0)]	–2.84 (*P* < 0.01)	–2.34 (*P* < 0.05)	–1.23 (*P* > 0.05)
2nd REM sleep (min)	56.2 (7.3) [56.0 (14.0)]	61.6 (8.4) [59.0 (17.0)]	70.3 (4.4) [70.5 (6.0)]	–3.63 (*P* < 0.001)	–2.52 (*P* < 0.05)	–1.85 (*P* > 0.05)
Arousal index	0.9 (0.35) [0.9 (0.3)]	1.2 (0.5) [1.2 (0.6)]	0.9 (0.5) [1.0 (0.8)]	–0.66 (*P* > 0.05)	–0.88 (*P* > 0.05)	–1.44 (*P* > 0.05)

All data are non-parametric data detected by Shapiro–Wilk test. The test of significance was Mann–Whitney test.
SD = standard deviation; REM = rapid eye movement; NREM = non-rapid eye movement; SWS = slow wave sleep.

Table 4 **Comparison between sleep data of infants with non-oedematous and oedematous protein–energy malnutrition before and after nutritional rehabilitation**

Variable	Non-oedematous (*n* = 10) Mean (SD) [Median (interquartile range)]			Oedematous (*n* = 10) Mean (SD) [Median (interquartile range)]		
	Before	After	Statistics *t*/*Z* values	Before	After	Statistics *t*/*Z* values
Sleep latency (min)	2.8 (1.1) [3.1 (1.9)]	3.9 (0.6) [3.9 (0.5)]	2.02[a] (*P* < 0.05)	4.1 ± 2.1 [3.2 (3.2)]	4.2 ± 3.0 [2.8 (5.9)]	–0.19 (*P* > 0.05)
Sleep efficiency (%)	95.2 (2.1) [95.3 (4.1)]	94.0 (1.1) [94.2 (2.0)]	0.86[a] (*P* > 0.05)	93.6 ± 1.9 [93.2 (2.7)]	94.6 ± 1.8 [94.6 (3.5)]	1.34[a] (*P* > 0.05)
NREM sleep (%)	44.5 (12.0) [44.0 (19.1)]	50.1 (7.5) [52.1 (4.1)]	0.87[a] (*P* > 0.05)	49.6 ± 10.3 [50.0 (20.8)]	58.7 ± 5.9 [60.8 (8.1)]	–5.80 (*P* < 0.001)
SWS (%)	20.0 (11.6) [19.4 (14.5)]	13.1 (8.9) [12.7 (12.4)]	2.46 (*P* < 0.05)	18.6 ± 4.8 [18.5 (2.3)]	13.3 ± 7.5 [19.3 (14.0)]	0.27[a] (*P* > 0.05)
REM sleep (%)	41.2 (6.1) [39.0 (11.9)]	43.0 (3.8) [41.8 (8.4)]	0.87[a] (*P* > 0.05)	43.8 ± 6.2 [43.0 (12.0)]	39.1 ± 3.2 [39.2 (5.2)]	–2.73 (*P* < 0.05)
SWS latency (min)	17.0 (12.7) [23.5 (26.0)]	16.8 (9.8) [18.0 (11.0)]	0.32[a] (*P* > 0.05)	19.6 ± 13.4 [27.0 (31.0)]	17.1 ± 11.8 [23.0 (27.0)]	2.85[a] (*P* < 0.01)
REM sleep latency (min)	6.5 (8.3) [2.0 (17.0)]	6.1 (7.3) [2.8 (14.0)]	0.41[a] (*P* > 0.05)	13.0 ± 10.1 [13.0 (21.0)]	16.1 ± 13.6 [21.0 (20.5)]	0.87[a] (*P* > 0.05)
2nd REM sleep (min)	56.2 (7.3) [56.0 (14.0)]	61.5 (4.8) [61.5 (5.0)]	–0.29[a] (*P* > 0.05)	61.6 ± 8.4 [59.0 (17.0)]	59.7 ± 5.9 [69.0 (10.0)]	3.47[a] (*P* < 0.001)
Arousal index	0.9 (0.4) [0.9 (0.3)]	1.1 (1.0) [0.9 (0.7)]	0.32[a] (*P* > 0.05)	1.2 ± 0.5 [1.2 (0.6)]	0.8 ± 0.7 [0.7 (1.2)]	1.34[a] (*P* > 0.05)

[a]*Non-parametric data were tested by Shapiro–Wilk test. The test of significance was Wilcoxon matched pairs test.*
SD = standard deviation REM = rapid eye movement; NREM = non-rapid eye movement; SWS= slow wave sleep.

difference in the oedematous group only. The percentage of REM sleep decreased significantly in the oedematous group while the non-oedematous one showed a non-significant increase. Moreover, SWS latency time decreased in both subgroups and this was significant only in oedematous patients. As regards percentage of SWS, it decreased significantly in the non-oedematous group, while the oedematous one showed a non-significant increase. However, in spite of the changes occurring after nutritional rehabilitation, most of the sleep EEG parameters of both groups of PEM infants did not reach the control values.

Figure 1 shows the polysomnography of a PEM patient, showing no clear stage differentiation of NREM sleep, while Figure 2 shows the polysomnography of the same patient after nutritional management with greater differentiation of sleep stages.

Anthropometric and sleep data correlations

As regards the correlation studies, the present study revealed significant positive correlation between the rate of change of REM sleep in non-oedematous PEM infants and both of weight and serum albumin (r =

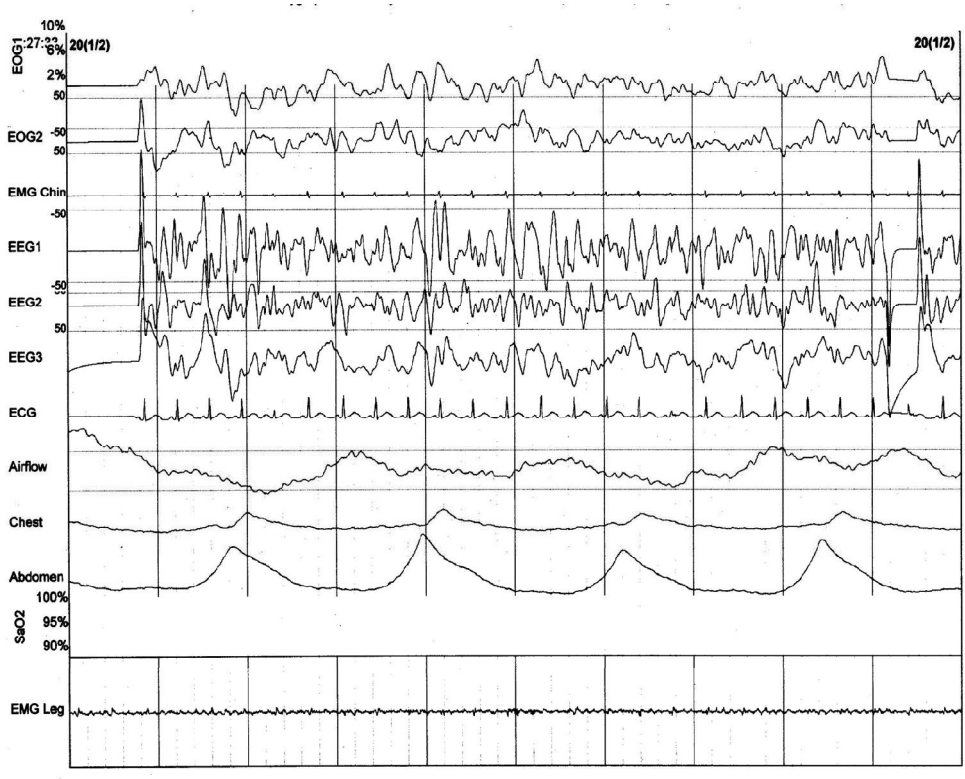

Figure 1 **Polysomnography of protein–energy malnutrition infant showing non-rapid eye movement sleep with no clear stage differentiation before nutrition rehabilitation**

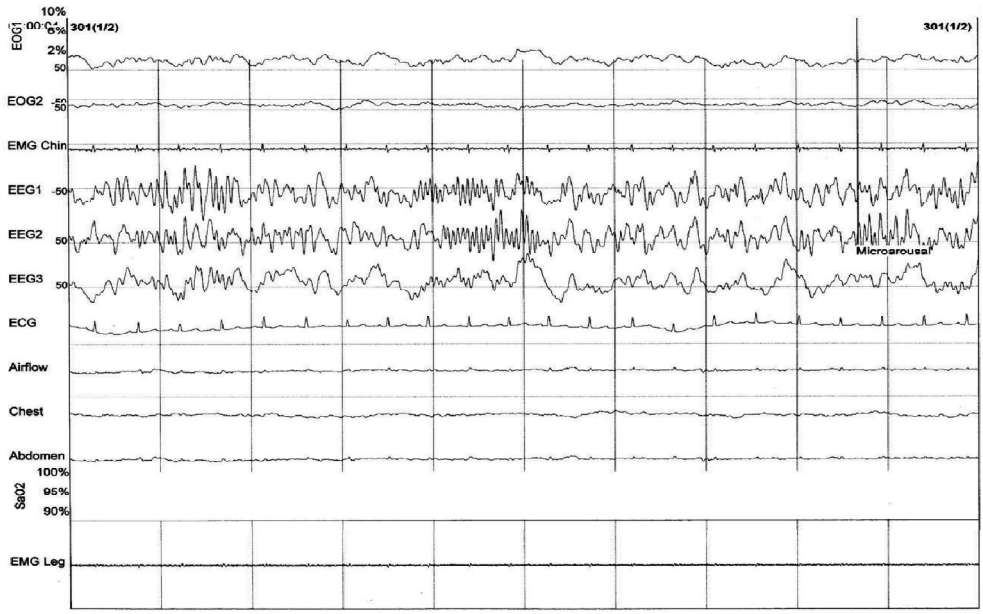

Figure 2 **Polysomnography of a protein–energy malnutrition infant showing greater differentiation of sleep staging after nutritional rehabilitation**

0.88 and 0.80 respectively and $P < 0.05$ for both). In addition the rate of change of REM sleep showed a negative correlation to serum albumin level in oedematous PEM patients but this was not statistically significant ($r = –0.45$). There was also a significant negative correlation between the rate of change of SWS and weight in non-oedematous PEM patients ($r = – 0.72$ and $P < 0.05$).

Discussion

The sleep data of the PEM infants in our study showed that the sleep latency was significantly lower in the non-oedematous malnourished group before nutritional rehabilitation compared with the controls. However, in the oedematous malnourished group sleep latency was lower than in the controls, but not significantly so. After nutritional rehabilitation the sleep latency increased in both subgroups of PEM infants, both non-oedematous and oedematous. This indicates that after nutritional rehabilitation, patients of both PEM types needed more time to fall asleep than in the acute phase of PEM illness which denotes an improvement in their condition, i.e. they are less sleepy or lethargic.

The percentage of NREM sleep was significantly lower in both non-oedematous and oedematous malnourished cases before nutritional rehabilitation compared with the controls. After nutritional rehabilitation, NREM sleep improved in the non-oedematous malnourished group, but was

still significantly lower than the control values. Moreover, the oedematous malnourished group showed improvement after nutritional rehabilitation but the percentage of NREM sleep was still lower than the control values, although not significantly. The failure of complete recovery may be attributed to the short period of nutritional rehabilitation and the immature brain development at this age.

Before nutritional rehabilitation the percentage of SWS was higher in the non-oedematous subgroup of PEM compared to the control values but this was not of statistical significance. This, in addition to the significantly higher serotonin levels detected in the PEM patients, agrees with Datta et al. [*9*]. Their animal study found that the mean percentage of SWS in malnourished rats (73.30%) was significantly higher than in well-nourished ones (61.23%) and they attributed this to increased brain serotonin levels. The same results were stated by Mokler et al. [*20*] who found that malnutrition in rats leads to increased serotonin production in the brain which leads to an increase in the percentage of SWS.

After nutritional rehabilitation, the percentage of SWS in the non-oedematous subgroup of PEM decreased and nearly reached the control levels. This is further supported by the significant negative correlation between the rate of change of SWS and weight in the non-oedematous PEM infants. Similarly Cintra et al. demonstrated that malnourished rats showed a significant reduction in SWS in the nutritional recovery period pre- and postnatally [*5*].

Before nutritional rehabilitation the percentage of REM sleep in the non-oedematous malnourished infants was higher than in the controls, but with no statistical significance. However, in the oedematous malnourished group the percentage of REM sleep was significantly higher than the controls. This may be attributed to immature brain development. After nutritional rehabilitation the percentage of REM sleep in the non-oedematous malnourished group increased but not significantly. This was further demonstrated by the significant positive correlation between the rate of change of REM sleep and that of weight and albumin in the non-oedematous group of PEM patients. On the other hand, the percentage of REM sleep decreased significantly in the oedematous malnourished subgroup, which is the normal expected pattern. This finding is further supported by the negative correlation between the rate of change of REM and that of albumin levels in these patients.

Our results of percentage REM sleep in non-oedematous patients are not consistent with Siegal who suggested that food consumption could produce an increase in REM sleep [*21*]. More recently, Cintra et al. found that there was increase in REM sleep during nutritional rehabilitation in rats with PEM [*5*].

The normalization of REM sleep to near control levels in both subgroups is important, as Shaffery et al. proposed that the primary purpose of the REM phase is to act as an inducer of CNS development in the fetus as well as the neonate [*22*] and we suggest that it might still be of the same importance during infancy.

We hypothesize that the increase in REM sleep in non-oedematous PEM might be related to a transient relative increase in REM following a period of decrease (the so called "REM rebound"), which is supposed to be followed by the stabilization period.

It is worth mentioning here is that in spite of the changes occurring after nutritional rehabilitation, most of the sleep EEG parameters of both groups of PEM infants did not reach the control values. This could be explained by the work of Robinson

et al., who detected electrophysiological abnormalities, persisting despite somatic rehabilitation, of 10 severely malnourished children, and added that this must be associated with the chronic rather than the acute aspects of malnutrition, and can be used to detect any deviation of brain function from normality [*23*].

In conclusion, the ability to maintain normal progression in sleep–wake maturation is an important index of brain development and may serve to assess how environmental factors, including essential nutrient supply, affect central nervous system development. The present study showed that PEM can have an effect on the sleep–wake cycle, which improves after adequate nutritional rehabilitation. The disturbed serotonin levels in PEM could be one of the factors responsible for such changes and this needs further study, together with assessment of the role of other neurotransmitters involved in the central nervous system functional development in PEM.

The changes that we have demonstrated in the sleep pattern in PEM infants should be considered seriously, as they could be detrimental to the development of social, behaviour and cognitive functions. We thus recommend proper and early nutritional rehabilitation for PEM infants not only to improve the physical growth parameters but also to improve their sleep pattern. Follow-up of these patients for longer periods is also recommended to ensure that the residual sleep changes are reversible and that there are no permanent changes. Further studies on PEM patients are advised on a larger scale to support the current results and to measure the specific dietetic elements which could be the causal factors for the sleep disturbances.

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In vivo (rat assay) assessment of nutritional improvement of peas (*Pisum sativum* L.)

S.A. Nagra[1] *and N. Bhatty*[2]

تقييم التحسُّن في القيمة التغذوية للبازلاء في الأحياء (بمقايستها في الجرذان)

سعيد أحمد ناغرة، نكهت بتّي

الخلاصة: استهدفت هذه الدراسة معرفة القيمة التغذوية للبازلاء في شكلها النيِّئ والمطهي، وعند إضافة لحم الدواجن أو الضأن أو البقر إليها. وبيَّنت الدراسة أن البازلاء الغضَّة تحتوي على نسبة 3% من الليزين، وأن هذه النسبة انخفضت إلى 0.6% بعد الطهي. ولوحظ تحسُّن مهم إحصائياً في نسبة الكفاءة البروتينيّة PER في وجبة البازلاء بعد الطهي (P<0.05). كما لوحظ تحسُّن يُعْتَدُّ به إحصائياً في القابلية للهضم، وفي صافي الاستفادة من البروتين NPU (P<0.05). وقد أدَّت إضافة لحم الدجاج أو الضأن أو البقر إلى البازلاء المطهية إلى تحسُّن يُعْتَدُّ به إحصائياً في نسبة الكفاءة البروتينيّة (P<0.05). وبيَّنت الدراسة ارتفاع قيمة كلٍّ من نسبة الكفاءة البروتينيّة، والقابلية للهضم، وصافي الاستفادة من البروتين، في الوجبات المضاف إليها لحم الضأن أو البقر بنسبة 15 – 20%.

ABSTRACT This study was conducted to determine the nutritional value of peas (*Pisum sativum* L.) in raw and cooked form and when supplemented with chicken, mutton or beef. Peas had 3.0% lysine, which decreased to 0.6% on cooking. Protein efficiency ratio (PER) of the raw pea diet improved significantly on cooking ($P < 0.05$). True digestibility (TD) and net protein utilization (NPU) also showed significant improvement ($P < 0.05$). Supplementation of cooked peas with 15% poultry meat, mutton or beef improved PER significantly ($P < 0.05$). Higher PER, TD and NPU values were observed in diets supplemented with 15%–20% mutton or beef.

Évaluation *in vivo* (dosage chez le rat) de l'amélioration nutritionnelle due au petit pois (*Pisum sativum L.*)

RÉSUMÉ Cette étude a été menée afin de déterminer la valeur nutritionnelle du petit pois (*Pisum sativum L.*) cru et cuit et complémenté par de la viande de volaille, de mouton ou de bœuf. Le petit pois contient à l'origine 3,0 % de lysine, teneur qui tombe à 0,6 % à la cuisson. Le coefficient d'efficacité protéique (CEP) du régime alimentaire basé sur la consommation du petit pois cru a montré une amélioration significative après cuisson ($p < 0,05$). La digestibilité vraie (DV) et l'utilisation protéique nette (UPN) ont également mis en évidence une amélioration significative ($p < 0,05$). Une supplémentation en petits pois cuits avec 15 % de viande de volaille, de mouton ou de bœuf a entraîné une amélioration significative du CEP ($p < 0,05$). Des valeurs supérieures de CEP, de DV et d'UPN se sont avérées associées à des régimes alimentaires supplémentés de viande de mouton ou de bœuf à hauteur de 15 à 20 %.

[1]*Biochemistry Section, Institute of Chemistry, University of the Punjab, Lahore, Pakistan (Correspondence to S.A. Nagra: sanagra@gmail.com).*
[2]*Department of Rural Home Economics, University of Agriculture, Faisalabad, Pakistan.*
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Introduction

Peas have been a staple diet of man and livestock since prehistoric times. In certain regions, people have always relied on peas and other pulses to provide protein to complement the cereals in their diet [*1*]. They are now grown in temperate regions all over the world, including higher elevations of the tropics. Cultivation is favoured in dry areas where the weather is cool and moisture is abundant during early growth, but where rainfall is minimal during the later stages of development. Peas are an important part of the crop rotation in many countries of Central America and Europe as well as India, Mayanmar and Pakistan. Green peas have become an important green vegetable in many developed countries. They offer a bulk source of seed protein for man and animals from a relatively short growing season compared with other legumes [*2*]. Pakistan produces about 16 000 tonnes of peas annually and the area under cultivation is about 3.2 thousand hectares [*3*].

This study is a continuation of earlier investigations through which we established the effect of cooking and supplementation with different kinds of meat on the nutritional improvement of mash (*Vigna mung*), mung (*Vigna radiate*), masoor (*Lens esculenta*), lobia (*Phaseolus vulgaris*) and gram (*Cicer arietinum*) [*4–8*]. To assess the extent of improvement in the nutritional quality of peas (*Pisum sativum* L.) by cooking and supplementation with different kinds of meats, biological trials were conducted on albino rats.

Methods

Formulation of diets

Peas (*Pisum sativum* L.) were procured from the local market and dried in a hot air oven at 105 °C for around 4 hours. Flour was obtained by grinding and sieving through a 20 mm mesh sieve. The flour was stored in airtight jars at room temperature until use. Similarly, flour was obtained and stored after cooking the peas by a conventional method as described by Bhatty et al. [*4*]. Briefly, the peas were put in a pot, covered with fresh water to 2.5 cm above the surface and boiled (100 °C) on a natural gas cooker for 40 minutes at high heat, then simmered for 30 minutes. At this stage peas became tender.

Maize starch, corn oil and casein (Merck DGaA, Darmstadt) used for the preparation of the standard diet (protein content 84%) were also purchased from the market.

The experimental diets were prepared using raw and cooked peas. Diets were also prepared by replacing 10%, 15% and 20% of the protein of cooked peas with the same amount of protein derived from lean meat: poultry (chicken), mutton or beef. The composition of the diets is shown in Table 1. The casein diet served as a standard and a nitrogen-free diet was used to determine the endogenous nitrogen. The mineral mixture used in the preparation of the experimental diets was prepared according to the formula of Oser [*9*] and the vitamin mixture according to Miller and Bender [*10*].

Biological assay

Biological evaluation was done by measuring the protein quality of diets containing peas in raw and cooked form with and without supplementation with meat.

Albino rats of the *Sprague–Dawley* strain were used. During gestation and nursing, the mothers were fed a balanced stock diet. Litters born to different mothers within 24 hours were taken to be of same age. Weaning was done at 21 days of age. The rats were then put on stock diet for 7 days prior to the experiment. They were arbitrarily divided into experimental units

Table 1 **Composition of experimental diets**

Diet	Ingredients (%)[a]						
	Maize starch	Casein	Raw peas	Cooked peas	Poultry meat	Mutton	Beef
Standard	56.1	12.5	–	–	–	–	–
Nitrogen free	68.6	–	–	–	–	–	–
Raw peas	22.8	–	45.9	–	–	–	–
Cooked peas	25.1	–	–	43.5	–	–	–
Cooked peas + 10% poultry meat	27.7	–	–	39.1	1.8	–	–
Cooked peas + 15% poultry meat	29.0	–	–	37.0	2.7	–	–
Cooked peas + 20% poultry meat	30.4	–	–	34.7	3.6	–	–
Cooked peas + 10% mutton	27.5	–	–	39.1	–	2.0	–
Cooked peas + 15% mutton	28.7	–	–	37.0	–	2.9	–
Cooked peas + 20% mutton	29.9	–	–	34.8	–	3.9	–
Cooked peas + 10% beef	27.7	–	–	39.3	–	–	1.8
Cooked peas + 15% beef	28.9	–	–	37.0	–	–	2.7
Cooked peas + 20% beef	30.3	–	–	34.8	–	–	3.6

[a]*In addition, each diet contained glucose 15.0%, corn oil 5.0%, vitamin mixture 3.5%, mineral mixture 3.1%, dicalcium phosphate 2.5%, calcium carbonate 2.0%, choline chloride 0.15% and inositol 0.1%.*

of 2 rats each in such a way that the initial weight of the rats in each cage was 90 g; 3 experimental units were randomly allotted to each diet. The rats were fed the allotted diet *ad libitum* for a period of 10 days. During this period fresh, clean water was made available at all times and room temperature was maintained at 24–27 °C. The weight of each replicate was recorded daily. The faecal matter from each cage was collected daily, dried to a constant weight and stored in glass bottles for nitrogen determination. At the end of 10 days trial, all the rats were killed with an overdose of chloroform and their cranial and abdominal cavities were opened. The carcasses of each group, inclusive of intestinal contents, were weighed before and after drying at 105 °C to constant weight. The dried carcasses were run twice through a domestic mincer and stored in airtight bottles for estimation of body nitrogen. The nitrogen content of the diet, faeces and carcasses of each group was determined by Khjeldahl's method [*11*]. Data obtained was used to determine the protein efficiency ratio (PER), true digestibility (TD) and net protein utilization (NPU) [*10*].

Table 2 **Proximate composition of peas**

Proximate principals	Raw peas %	Cooked peas %
Moisture	8.0	8.0
Crude protein	23.7	23.2
Ether extract	2.3	2.5
Crude fibre	6.8	6.5
Nitrogen-free extract	62.4	64.6
Ash	4.8	3.2

Samples of peas were analysed for proximate composition (moisture, crude protein, ether extract, crude fibre, total ash and nitrogen free extract, according to standard methods [*11*]. Samples of the

3 kinds of meat were analysed for protein content only.

Amino acid analysis

The amino acid analysis of peas was carried out by the method of Spackman, Steir and Morre using a Beckman Model 120C amino acid analyser (Beckman, Fullerton, California) [*12*].

Statistical analysis

The data obtained for PER, TD and NPU were used for analysis of variance using a completely randomized design. The analysis was computed using *SPSS-400*. Multiple comparisons of means were made using Fisher protected least significant difference (PLSD) test [*13*].

Results

The change in the proximate principals of raw and cooked peas is given in Table 2. Cooking resulted in a slight reduction in crude protein, crude fibre and ash. The lysine content of raw peas was 3.0%, which decreased to 0.6% after cooking.

Comparison of experimental diets containing peas only with standard casein diet (Table 3) indicated that the PER of cooked peas was very close to that of the standard casein diet whereas the diet containing raw peas had a PER value almost half of the cooked pea diet. Other biological parameters, TD and NPU, also showed improvement when peas were cooked.

Biological evaluation of experimental diets is given in Table 4. On average, inclusion of 15% protein from poultry meat yielded comparatively better results in terms of PER, TD and NPU as it is cheaper than the other 2 meats.

Discussion

Chemical composition

Proximate composition of raw peas in our study was 8.0% moisture and 23.7% protein. Augustin and Klein [*14*] reported similar amounts of moisture and protein in raw peas. Ali-Khan and Youngs [*15*] showed the protein content to be 22%–23% in field peas. The variation in crude protein content is a reflection of varietal differences and may be attributed to genetic and environmental factors.

In this study, ether extract was 2.3% in raw peas. Augustin and Klein reported a lower value [*14*] and other reports of fat content range from 1.0% to 3.1% [*2*]. These variations could be due to variety differences. Raw peas had 6.8% crude fibre. Augustin and Klein [*14*] reported a much higher fibre content.

Table 3 **Comparison of experimental diets containing peas only and standard casein diet**

Parameter	Diet					
	Standard		Raw peas		Cooked peas	
	Mean	SD	Mean	SD	Mean	SD
Protein efficiency ratio	2.1[a]	0.05	01.4[b]	0.08	2.0[a]	0.04
True digestibility %	89.5[a]	0.4	74.7[b]	0.6	79.8[c]	0.7
Net protein utilization %	55.8[a]	0.4	41.6[b]	0.3	46.3[c]	0.7

[a,b,c]Means with different superscripts in a row are significantly different at $P < 0.05$. *SD = standard deviation.*

Table 4 **Biological evaluation of experimental diets containing cooked peas and different supplementary levels of poultry meat, mutton and beef**

Parameters	Level of supplementation (%)					
	10		15		20	
	Mean	SD	Mean	SD	Mean	SD
Protein efficiency ratio						
Poultry meat	2.1[a]	0.02	2.2[a]	0.05	2.2[a]	0.03
Mutton	2.2[a]	0.02	2.2[a]	0.03	2.2[a]	0.03
Beef	2.1[a]	0.04	2.2[a]	0.02	2.2[a]	0.03
True digestibility %						
Poultry meat	81.7[a]	0.4	84.1[b]	0.6	85.8[b]	0.59
Mutton	81.8[a]	0.4	86.5[b]	0.7	87.6[b]	0.3
Beef	77.9[a]	0.4	81.4[b]	0.6	84.4c	0.8
Net protein utilization %						
Poultry meat	46.4[a]	0.7	53.2[b]	0.7	54.2[b]	0.8
Mutton	43.6	0.3	49.7[b]	0.6	52.1[b]	0.6
Beef	45.9[a]	0.4	48.5[b]	0.6	50.5[b]	0.4

[a,b,c]*Means with different superscripts in a row are significantly different at* P < *0.05*
SD = standard deviation.

Nitrogen free extract in raw peas was 62.4% [*14*]. Savage and Deo reported nitrogen free extract in the range 60.0%–71.7% [*2*]. Pea seeds had 4.8% ash; other researchers have reported ash contents of 2.4%–4.1% [*16*] and 1.0%–3.4% [*2*].

Raw peas contained 3.0% lysine, providing well above the recommended requirement (12 mg/kg body weight per day) [*17*], making peas an ideal supplement to a cereal based diet. Legumes are considered a good source of lysine and as such provide this essential amino acid to enhance the nutritive value of the protein in mixed diets [*18*]. Savage and Deo reported lysine content at 6.22%–12.3% in peas [*2*]. El-Refai, Gouda and Ammar showed that in general the amino acid content changed only slightly during storage except for small decreases in lysine, cystine, methionine and tryptophan [*19*]. Sarwar, Sosulski and Bell concluded that field peas were superior to soybean when blended with wheat flour or supplemented with additional amino acids [*20*].

A slight lowering was observed in proximate crude protein content of peas after cooking. Other studies have found similar changes [*19,21*].

James and Hove reported that improvement in nutritive value on cooking was a result of the destruction of anti-nutritive factors [*22*]. Manan et al. observed that cooking peas resulted in considerable reduction in the phytic acid content of Pakistani varieties, without any loss of total phosphorus [*23*]. The nutritive value of peas considerably improved on cooking, suggesting that other water soluble and or heat labile anti-nutritive factors might be more important than phytic acid in affecting the overall nutritive quality of seeds. It was observed that cooking affected the amino acid profile. All amino acids showed losses during cooking of peas.

Biological evaluation

Protein efficiency ratio (PER)

Raw peas had PER 1.4, which increased significantly on cooking to 2.0. James and Hove showed a similar increase, 1.87 to 2.21 [*22*]. The improvement in nutritive value on cooking could be due to destruction of anti-nutritive factors. Shah also reported a significant increase in the body weight gain of rats due to cooking of the whole seed [*24*]. Supplementation of a diet based on cooked peas with different types of meat also showed significant improvement over a diet containing raw peas, irrespective of the kind of meat. However, supplementation with different types of meat did not improve the PER significantly over that of the diet containing only cooked peas.

True digestibility (TD)

The TD of protein of peas increased significantly on cooking from 74.7% to 79.8%. It has been reported that protein TD of autoclaved peas increased from 85% to 88% [*20*]. Goodlad and Mather, however, claimed that there were only minor effects of cooking on the digestibility of non-starch polysaccharides and their constituent sugars [*25*]. Fleming and Vose showed that the *in vivo* digestibility of raw and cooked starch from peas was high in rat experiments [*26*]. The increase in digestibility on cooking may be due to the elimination of trypsin and chymotrypsin inhibitors.

In our study, TD also increased significantly when the pea-based diet was supplemented with meat, and increased with increasing level of supplementation. The TD of the diet containing peas supplemented with 20% mutton was significantly higher than the digestibility of other diets.

Net protein utilization (NPU)

The NPU of the diet containing raw peas was 41.6% and on cooking it significantly increased to 46.3%. Shah showed NPU values of 42.4%–46.8% in raw peas and 49.0%–52.0% in cooked peas [*24*]. The NPU values were significantly higher when were supplemented with 20% poultry meat. The NPU also increased with the increase in the levels of supplemental mutton and beef beyond the 10% level. Bell and Youngs reported that biological value of pea protein concentrate alone was low but was considerably improved by the addition of methionine [*27*]. Shah reported a non-significant increase in biological value on cooking; reduction in biological value was suggested as being due to the destruction or leaching of essential amino acids during the cooking process [*24*].

Conclusion

Overall, supplementation of peas with 15% poultry meat optimally enhances the protein quality. Cooking alone can also be used for the improvement of protein quality of peas.

Although this study was conducted on laboratory rats, it provides a rationale for the supplementation of peas with small quantities of poultry meat for the nutritional rehabilitation of poorly-fed communities.

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Technical consultation to review the regional food-based dietary guidelines

The World Health Organization Regional Office for the Eastern Mediterranean organized the above-mentioned technical consultation in Cairo, Egypt, from 2 to 4 April 2007.

The objectives of the consultation were:

- to review the draft regional food-based dietary guidelines under preparation;
- to incorporate additional relevant food and dietary information from Member States; and to
- finalize the content and format of the regional food-based dietary guidelines.

Experts from Egypt, Islamic Republic of Iran, Lebanon, Pakistan, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates, United Kingdom, as well as WHO concerned staff, participated in this consultation.

Epidemiology and cost of haemodialysis in Jordan

A. Batieha,[1] S. Abdallah,[2] M. Maghaireh,[3] Z. Awad,[4] N. Al-Akash,[5] A. Batieneh[6] and K.A. Ajlouni[4]

وبائيات وتكاليف الدّيال الدموي (الغسيل الكلوي) في الأردن

أنور بطيحة، سلطان عبد الله، مأمون مغايرة، زياد عواد، نبيل العكش، أحنف بطاينة، كامل العجلوني

الخلاصة: أُجري، خلال شهرَيْ أيلول/سبتمبر وتشرين الأول/أكتوبر 2003، مسحٌ شمل جميع المرضى الذين يتلقّون ديالاً دموياً (غسيلاً كلوياً) في الأردن (1711 مريضاً)، لتقييم وبائيات الفشل الكلوي والعبء الناجم عن عمليات غسل الكلى. وبلغ متوسط العمر لدى هؤلاء المرضى 48.9 عاماً، وكانت نسبة الذكور بينهم 56%. وكان 86.8% منهم عاطلين عن العمل و92% يعانون من الفقر. وبلغ متوسط المسافة للوصول إلى مركز الغسيل الكلوي 13.6 كيلومتر. وكانت نسبة انقلاب تفاعلية المصل بالنسبة إلى التهاب الكبد "بي" و"سي": 0.34% و2.6% على التوالي، في المرضى الذين كانوا سلبيِّي المصل قبل خضوعهم للغسيل الكلوي. وبلغ معدل انتشار الغسيل الكلوي 312 لكل مليون من السكان، بعد أن كان 111 لكل مليون في عام 2002. كما بلغ معدل الإماتة 20% بعد مرور سنة واحدة. ومثّل السكّري السبب الرئيسي وراء الاحتياج للغسيل الكلوي لدى 29.2% من الحالات، وقُدِّر إجمالي تكلفة الغسيل الكلوي في عام 2003 بـ 29.7 مليون دولار أمريكي.

ABSTRACT To assess the epidemiology and burden of haemodialysis in Jordan, all patients on haemodialysis (1711 patients) were surveyed during September/October 2003. Mean age was 48.9 years, 56% were male, 86.8% were unemployed and 92% were poor. Mean distance to the haemodialysis service was 13.6 km. Annual hepatitis B and C seroconversion for patients negative before dialysis was 0.34% and 2.6% respectively. Prevalence of haemodialysis was 312 per million population; the incidence in 2002 was 111 per million population. Fatality rate at 1 year was 20%. Diabetes mellitus was the leading cause of haemodialysis, 29.2% of cases. Total estimated cost of haemodialysis in 2003 was US$ 29.7 million.

Épidémiologie et coût de l'hémodialyse en Jordanie

RÉSUMÉ Afin d'évaluer l'épidémiologie et le coût financier de l'hémodialyse en Jordanie, tous les patients hémodialysés, à savoir 1711 sujets, ont fait l'objet d'une enquête conduite au cours des mois de septembre et octobre 2003. L'âge moyen de la population enquêtée était de 48,9 ans, celle-ci étant composée à 56,0 % d'individus de sexe masculin, à 86,8 % de chômeurs et les économiquement faibles représentant 92,0 %. L'unité d'hémodialyse la plus proche se situait à une distance moyenne de 13,6 km. Les taux annuels de séroconversion pour les hépatites B et C de patients séronégatifs avant dialyse étaient respectivement de 0,34 % et de 2,6 %. La prévalence de l'hémodialyse se chiffrait à 312 cas par million d'habitants, son incidence en 2002 étant de 111 cas par million d'habitants. La mortalité à 1 an était de 20,0 %. Le diabète sucré était la principale indication de l'hémodialyse, soit 29,2 % des cas. Pour l'année 2003, le coût total estimé de l'hémodialyse atteignait USD 29,7 millions.

[1]Department of Epidemiology and Public Health; [6]Nephrology and Internal Medicine, Jordan University of Science and Technology, Irbid, Jordan.
[2]Ministry of Health, Amman, Jordan.
[3]General Directorate of Health Insurance, Amman, Jordan.
[4]University of Jordan, Amman, Jordan (Correspondence to K.M. Ajlouni: ajlouni@ju.edu.jo).
[5]Royal Medical Services, Amman, Jordan.
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Introduction

End-stage renal disease (ESRD) is a growing problem worldwide and renal replacement therapy is increasingly exerting pressure on health systems [*1*]. The situation is particularly serious in developing countries where health resources are limited.

The adjusted incidence of renal replacement therapy in 9 European countries has increased from 79.4 per million population (pmp) in 1990–91 to 117.1 pmp in 1998–99, i.e. an average annual increase of 4.8% [*1*]. This increase occurred largely among older age groups. The incidence of ESRD due to diabetes, hypertension and renal vascular disease almost doubled over the same period. Similar trends were observed in Japan [*2*], Australia and New Zealand [*3*] and the United States of America (USA) [*4*].

The distribution of patients on haemodialysis in the world is strongly influenced by economic factors [*5*]. In Jordan, the number of patients on haemodialysis has doubled over the past 5 years presenting a real challenge for the scarce health resources.

The objective of the study was to report on the epidemiology of haemodialysis in Jordan and to provide current estimates of the associated costs.

Methods

We conducted a survey in all haemodialysis units in Jordan (56 units) between 1 September and 31 October 2003. Each patient was personally interviewed in the haemodialysis unit by the attending nurse, using a structured questionnaire specifically designed for the purpose of this study. Additional data such as hepatitis B and C positivity were collected from the patient's medical record. The cause of ESRD was provided by the attending physician. We also collected relevant data on each haemodialysis unit. This included: number of patients on haemodialysis in the unit at the time of the survey (July 2003), number of patients who died in the unit in 2002, and the number of patients who started haemodialysis in the unit in 2002 and their status in July 2003.

Epi-Info, version 6 software was used for data entry and analysis. The distribution of the patients by relevant sociodemographic and clinical characteristics was obtained. The prevalence of haemodialysis by certain variables was obtained using population estimates of Jordan from the Department of Statistics as the denominator for these rates. Incidence of haemodialysis in the year 2002 was obtained by dividing the total number of patients who started haemodialysis in all units in 2002 (irrespective of whether they were still living at the time of the survey) by the population of Jordan in 2002. The case fatality rate in the first year after initiating haemodialysis was obtained by dividing the number of deaths that occurred among all patients who started haemodialysis in 2002 followed through June 30, 2003 by the total starting haemodialysis. The cost of haemodialysis in Jordan for the year 2003 was calculated by adding the cost of the haemodialysis session (US$ 105 in the private sector and US$ 85 in the public sector), the cost of medications and investigations, the cost of admissions, and the cost of the arterial access (arterio-venous fistula in over 95% of patients).

Results

A total of 1711 patients were on haemodialysis at the time of the survey in Jordan.

Sociodemographic characteristics of the patients

Table 1 shows the sociodemographic characteristics of the patients on haemodialysis. The age of patients ranged from 5 years to

Table 1 **Sociodemographic characteristics of patients on haemodialysis in Jordan, 2003**

Characteristic	No. (*n* = 1711)	%
Age[a] (years)		
< 20	82	4.8
20–39	440	25.7
40–59	620	36.2
≥ 60	569	33.2
Sex		
Male	957	55.9
Female	754	44.1
Education (years of schooling completed)		
Illiterate	476	27.8
1–6	353	20.7
7–12	648	37.8
> 12	234	13.7
Smoking status		
Current smoker	294	17.2
Past smoker	209	12.2
Never smoked	1208	70.6
Employment status		
Employed	225	13.2
Retired	227	13.3
Unemployed	1259	73.5
Family income/month (US$)		
< 140 (very poor)	609	35.6
140–420 (poor)	962	56.2
≥ 421 (comfortably off)	140	8.2

[a]*Mean (standard deviation) = 48.9 (16.7) years.*

88 years with a mean age (standard deviation) of 48.9 (16.7) years. About one-third of the patients were 60 years of age or more. Of the 1711 patients, 957 (55.9%) were male. About 28% of the patients were illiterate and 17% current smokers. Only 13.2% were employed and the vast majority was poor (92%) (family income < US$ 420/month).

Service-related characteristics

Although the average distance to the haemodialysis unit was 13.6 km, a good proportion of patients (11.5%) had to travel 30 km or more. The major service provider was the private sector (43.4%) followed by the Ministry of Health (27.4%). The duration on haemodialysis ranged from 1 month to 27 years resulting in a skewed distribution (mean = 42.7 months, median = 28 months). Over 54% of patients were maintained on 3 haemodialysis sessions per week, 45% on 2 sessions per week, and only 9 patients on 1 session per week (Table 2). The proportion of patients on 3 sessions per week was much higher in the private sector (89%) than in

Table 2 **Service-related characteristics of patients on haemodialysis in Jordan, 2003**

Characteristic	No. (*n* = 1711)	%
Distance to haemodialysis unit[a] (km)		
< 10	832	48.6
10–19	494	28.9
20–29	189	11.0
30+	196	11.5
Haemodialysis service provider		
Ministry of Health	468	27.4
Royal Medical Services	385	22.5
University hospitals	115	6.7
Private sector	743	43.4
Duration on haemodialysis[b] (years)		
< 1	444	25.9
1–2	545	31.9
3–5	306	17.9
> 5	416	24.3
No. of haemodialysis sessions/ week		
1	9	0.6
2	774	45.2
3	928	54.2

[a]*Mean (standard deviation) = 13.6 (16.2) km.*
[b]*Mean (standard deviation) = 42.7 (44.8) months, median = 28 months.*

the Ministry of Health (32.7%) or the Royal Medical Services (20%). These proportions were inversely correlated with the ratio of patients per haemodialysis machine in the different sectors: 3.1, 4.4 and 5.7 respectively.

Sexual activity

Because of the considerable impact on the quality of life of patients on dialysis, we asked about patients' sexual activity. For cultural reasons, the frequency of sexual intercourse was assessed only in married males. Out of the 744 patients, 689 (93%) responded to the question. Table 3 demonstrates the frequency of intercourse by age. Overall about 48% were not sexually active at all. As expected, lack of sexual activity increased markedly with age from 6.4% in patients < 40 years to 36.4% in patients 40–59 years to reach 79.2% at age ≥ 60 years.

Hepatitis B and C status

The hepatitis B and C status of the patients before dialysis was unknown in 12% and 24% of the patients respectively. Seroconversion rates were calculated only for patients with known hepatitis B and C status prior to haemodialysis.

The overall positivity rate for hepatitis B virus (HBV) among our patients was 4% (Table 4). Of the 68 positive patients, 17 (25%) seroconverted after starting haemodialysis. The percentage of HBV-negative patients who seroconverted after initiation of haemodialysis was 1.2%. Given an average duration of haemodialysis of 3.5 years, the annual seroconversion rate was 0.34%

With respect to hepatitis C virus (HCV), the overall positivity rate was 21%. About one-third (32.2%) of HCV-positive patients were negative before starting haemodialysis. The percentage of HCV-negative patients who became positive after initiation of haemodialysis was 9.2% yielding an annual seroconversion rate of 2.6%. The HCV status before starting haemodialysis was unknown for 24% of this population.

Table 3 **Sexual activity of patients on haemodialysis in Jordan by age, 2003**

Frequency of intercourse	Age (years) < 40 %	40–59 %	≥ 60 %
Twice/week or more	32.7	15.7	2.4
Once/week	47.3	24.7	5.1
Twice/month	13.6	21.3	12.9
Once/month or less	0	1.9	0.4
None	6.4	36.4	79.2

Table 4 **Hepatitis B and C positivity of the 1711 patients on haemodialysis in Jordan, 2003**

Hepatitis	Positive No.	%	Negative No.	%	Unknown No.	%
B	68	4	1643	96	0	0
C	351	21	1341	78	19	1

Table 5 **Prevalence of haemodialysis in Jordan by age and sex, 2003**

Variable	Population	Patients	Prevalence (per million population)
Age group (years)			
< 20	2 745 480	82	30
20–39	1 723 460	440	255
40–59	598 700	620	1036
≥ 60	312 360	569	1822
Sex			
Male	2 866 200	957	334
Female	2 613 800	754	288
Total	5 480 000	1711	312

Prevalence and incidence of haemodialysis

The overall prevalence of haemodialysis in Jordan was 312 pmp. Table 5 shows the prevalence by age and sex. The prevalence increased from 30 pmp below age 20 years to 1822 pmp among the elderly (≥ 60 years). The prevalence was also higher among males (329 pmp) as compared to females (288 pmp).

The total number of patients who started haemodialysis in 2002 in all units, irrespective of whether they were still on haemodialysis at the time of the survey, was 578 accounting for an incidence of 111 pmp in 2002 (the total population of Jordan in 2002 was 5.2 million).

Mortality

The total number of deaths among patients on haemodialysis in Jordan during the 1-year period preceding the survey was 292. Of the 578 who started haemodialysis in 2002, 116 had died by 1 July 2003 giving a case fatality of 20% during the first year. Kidney transplantation was carried out for only 5% of those patients.

Cause of ESRD leading to haemodialysis

Table 6 presents the causes of ESRD among patients on haemodialysis at the time of the survey. The commonest cause was diabetes mellitus (29.2%) followed by hypertension (18.4%) and glomerulonephritis (12.3%). The category of other causes in Table 6 included, for example, systemic lupus erythematosus, analgesic nephropathy, Alport syndrome, and familial Mediterranean fever. For over one-fifth of the patients, the cause was classified as unknown as the attending physician was unable to provide the cause which led to ESRD after full investigation, including renal biopsy. In fact, these cases may be considered as having primary kidney disease although they are categorized separately in Table 6.

For patients who started haemodialysis during 2002 and 2003, diabetes mellitus was the cause in 33.4% and 44.0% respectively.

Cost of haemodialysis in Jordan

The estimated total annual cost of haemodialysis in Jordan was US$ 29 715 553 (Table 7). Haemodialysis sessions accounted for about three-quarters of the total cost while medications and investigations accounted for an additional 20%. Erythropoietin was

Table 6 **Cause of end-stage renal disease among patients on haemodialysis in Jordan, 2003**

Cause	No. (*n* = 1711)	%
Diabetes mellitus	499	29.2
Hypertension	315	18.4
Glomerulonephritis	210	12.3
Obstructive uropathy	70	4.1
Reflux uropathy	70	4.1
Primary kidney disease	40	2.3
Other causes	141	8.2
Unknown	366	21.4

Table 7 **Estimated annual cost of haemodialysis in Jordan, 2003**

Item	Cost (US$)
Haemodialysis sessions	22 555 573
Medications and investigations	5 781 000
Admissions	1 205 550
Arterial access	173 430
Total	29 715 553

regularly supplied to 92% of patients on haemodialysis, calcium to 98%, vitamin D to 91% and iron to 88%. Erythropoietin was given twice weekly on average with the objective of raising the haemoglobin level to 10–12 g/dL.

Discussion

Data on haemodialysis in Jordan are very scarce. The present study has shown an incidence of haemodialysis in Jordan of 111 pmp in 2002, a figure slightly lower than reported from Europe in 1998–1999 (117 pmp) [*1*] but much higher than the incidence in Baltic countries [*6*]. In the United States, the incidence of ESRD in the year 2000 was 291 pmp [*7*]. In Egypt the reported incidence of ESRD in the year 1992 was 200 pmp, of whom 80 pmp were accepted on the dialysis programme [*8*]. Variation in the incidence of haemodialysis largely reflects differentials in acceptance of patients onto the haemodialysis service, as well as the reference year for the reported incidence, since an increasing trend has been observed almost everywhere. The prevalence of haemodialysis in Jordan seems to be increasing at a high pace from 114 pmp in 1992 [*9*] to 181 pmp in 1998 [*10*] reaching 312 pmp in the year 2003 (average annual increase of 8.5%). Such an increase may largely reflect the increasing availability of haemodialysis in Jordan.

Consistent with data from other countries [*1,4,7*], diabetes mellitus was the commonest underlying cause for haemodialysis among our patients (29.2%) followed by hypertension (18.4%) and glomerulonephritis (12.3%). However, considering patients who started haemodialysis in 2003 alone, diabetes accounted for 44% of the cases. Several explanations can be offered, such as more elderly persons accepted on haemodialysis, shorter survival of diabetics on haemodialysis, or an actual increase in the contribution of diabetes to ESRD. Diabetes mellitus is a highly prevalent disease in Jordan affecting 13.4% of Jordanians $\geq$ 25 years of age [*11*]. The mean age of patients on haemodialysis in Jordan has increased from 44.6 years in 1998 [*10*] to 48.9 years in 2003 and the percentage of patients aged $\geq$ 60 years has increased from 21% in 1998 [*10*] to 33% in 2003.

In agreement with data from other countries [*1*], more males (55.9%) than females were being maintained on haemodialysis and the prevalence of haemodialysis was 334 pmp in males compared to 288 pmp in females.

HBV positivity was relatively low (4%), and annual seroconversion occurred in 0.34% of our patients after starting haemodialysis. HCV positivity among our patients was 21% with an annual seroconversion of 2.6%. These figures are assuring even when compared with data from a number of European countries, Japan and the United States [*12*]. The DOPPS study showed the prevalence and seroconversion of HBV among haemodialysis patients in 5 European countries, Japan and the United States [*12*]. The overall prevalence and seroconversion was 3.3% and 0.78 per 100 patient-years respectively. Recent data on HBV in the general population are lacking in Jordan but the prevalence is generally low in selected groups such as healthy blood donors (1.8%–3.9%) [*13*] and multi-transfused patients for hereditary haemolytic anaemia (3.5%) [*14*]. With respect to HCV, the prevalence among haemodialysis patients in Jordan was much lower than in many countries in our region such as Saudi Arabia (72.3%) [*15*], Kuwait (40%) [*16*] and Pakistan (68%) [*17*], but higher than that in developed countries such as Germany (7%) [*18*]. In Jordan, the prevalence of HCV in the general population is not known, but it

is available for subgroups of the population such as healthy blood donors (0.65–2.1%) [*13*] and multi-transfused patients (40.5%) [*14*]. A previous study in 6 Ministry of Health haemodialysis units in Jordan reported an HCV prevalence of 34.6% [*19*]. In the present study, HCV prevalence in Ministry of Health haemodialysis units was very similar (33%) compared to 7.3% in the private sector. The most likely explanation for the observed lower rate in the private sector is a reluctance to accept HCV positive patients since neither the private nor the public sector have HCV infection control protocols which could account for such a discrepancy. In contrast, a standard HBV prevention protocol exists in all haemodialysis units in Jordan. It should be noted that strict infection control measures in haemodialysis units and isolation policy for HCV-positive patients have been shown to limit HCV transmission as it has done in reducing HBV transmission [*12,20*–22]. Patient-to-patient transmission of HCV also occurs in haemodialysis units highlighting the importance of the strict enforcement of standard infection prevention measures [*23*]. Nurse understaffing of haemodialysis units was shown to have a negative effect on HCV transmission [*24*] probably because of difficulty in ensuring adherence to infection control measures in such a situation.

Among the interesting issues in our study was the assessment of sexuality. Total sexual inactivity affected the great majority of patients ≥ 60 years of age and over one-third of those aged 40–59 years. Complete lack of sexual intercourse was a problem even at a younger age for over 6% of the patients. These findings may add to our understanding of the suffering of haemodialysis patients and their quality of life. Attending physicians should be aware of this problem and be ready to assist their patients in this regard. Sexual dysfunction of patients on haemodialysis has been reported by other studies [*25,26*].

The fatality rate observed in our study (20%) is similar to rates in the United States where the 1-year fatality rate was approximately 22% in 2002 [*27*]. However, patients accepted for haemodialysis in Jordan tend to be younger than United States patients, and this may explain the favourable outcome in Jordan.

Expansion of haemodialysis services in Jordan has a high cost. Jordan is a developing country with an annual per capita income of approximately US$ 1800. The overall expenditure on haemodialysis in 2003 was about US$ 30 million, i.e. about 4% of the total health expenditure in Jordan. In Turkey, the annual cost of haemodialysis was US$ 22 759 per patient, while the cost of transplantation was US$ 23 393 and US$ 10 028 per patient respectively for the first and second year [*28*]. In industrialized countries, the annual costs of haemodialysis are much higher, being highest in France (US$ 78 947 per patient) [*29*] compared to Japan [*30*] and the United States [*31*] (US$ 46 000 per patient).

Expenditure in Jordan is likely to increase rapidly in the near future as more and more of the elderly are accepted into the service. The government of Jordan bears almost all the costs of haemodialysis. Although the cost of haemodialysis in Jordan is relatively low (US$ 17 385/patient/year), the burden is huge in a country with limited resources like Jordan, and the efficiency of the allocated resources for haemodialysis should be an issue for consideration.

The cost of kidney transplantation in Jordan is not accurately known but has been shown in other countries to be a less costly alternative [*28,31*]. Rough estimates of the cost of transplantation in Jordan, based on

personal communication, range from US$ 20 000–22 000 in the first year, dropping to US$ 10 000–12 000 in the second year, to reach US$ 8000–10 000 later on. Unfortunately, kidney transplant is used by only a small minority (5%) of patients with ESRD in Jordan. The reasons behind this are not clear but restrictions on transplants from non-relative donors exist by law to prevent the sale of human organs and may contribute significantly to this underuse. While permitted in Jordan, cadaveric transplants are not widely available, probably because of a lack of efforts to raise the awareness of people of the importance of organ donation after death. Appropriate strategies to promote kidney transplantation are needed and may succeed in containing the escalating costs. However, in the long run, prevention of ESRD is particularly important and can be achieved by early detection and prompt treatment of the major diseases leading to ESRD, namely diabetes, hypertension and glomerulonephritis. Restriction of haemodialysis to patients who are likely to benefit from the intervention and excluding patients with advanced multi-organ disease have been suggested [*28*] as a way to contain cost, but may be unacceptable on ethical grounds.

In the present study, we did not collect data on peritoneal dialysis which is rarely used in Jordan. In fact, no programme for peritoneal dialysis exists in Jordan. There is no system to reimburse private physicians for caring for patients on peritoneal dialysis and therefore they direct their patients to haemodialysis. Moreover, as peritoneal dialysis is usually carried out at home, it is more likely to be successful in educated patients.

In conclusion, our study has provided a profile of patients on haemodialysis in Jordan. Diabetes is the leading cause of haemodialysis and its role seems to be increasing. Haemodialysis is expanding rapidly and the burden is high given the limited resources in Jordan. HBV and HCV prevalence and seroconversion are relatively low suggesting that the current infection control measures are working and, therefore, should be intensified. Promotion of less expensive interventions such as kidney transplantation and prevention of the main causes leading to ESRD may be needed to curb the escalating costs. Research is needed on the quality of life of patients on haemodialysis and their families.

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Efficacy of DOTS strategy in treatment of respiratory tuberculosis in Gorgan, Islamic Republic of Iran

A. Abassi[1] and A.R Mansourian[2]

نجاعة استراتيجية المعالجة القصيرة الأمد تحت الإشراف المباشر في معالجة السل التنفسي في مدينة غورغان الإيرانية

عبد الله عباسي، آزاد رضا منصوريان

الخلاصة: أُجريت دراسة على مدى عامَيْن، لمتابعة 260 من المرضى الأتراب الإيجابيِّي اللطاخة (178 منهم يتلقّون المعالجة بحسب استراتيجية المعالجة القصيرة الأمد تحت الإشراف المباشر؛ و82 منهم لا يتلقّون المعالجة بهذه الاستراتيجية)، وذلك لتقييم فعَّالية هذه الاستراتيجية في معالجة السل. وكان جميع المرضى قد عانوا من السعال لمدة تزيد على 3 أسابيع قبل بدء الدراسة؛ وكانت نسبة 91.9% مصابين بالحمى، و60.8% منهم يعانون من البلغم؛ وكان لدى 27.7% منهم سوابق عائلية إيجابية للإصابة بالمرض. وبلغت نسبة إخفاق المعالجة بالاستراتيجية المنفَّذة 9% في نهاية الشهر الثاني، و1.7% في بداية الشهر الخامس. أما المجموعة الشاهدة، فقد بلغت نسبة إخفاق المعالجة فيها 18.3% في نهاية الشهر الثاني، و7.3% في بداية الشهر الخامس. وخلصت الدراسة إلى أن استراتيجية المعالجة القصيرة الأمد للسل تحت الإشراف المباشر تعزِّز نسبة النجاح في معالجة السل بشكل كبير ($P<0.05$).

ABSTRACT We carried out a follow-up cohort study of 260 smear-positive patients [178 on directly observed treatment, short-course (DOTS); 82 on non-DOTS] over a 2-year period to evaluate the efficacy of the DOTS strategy in treatment of tuberculosis (TB). All the patients had had cough for > 3 weeks; 91.9% had fever, 60.8% of them with sputum; and 27.7% had a positive family history. The rate of treatment failure with DOTS was 9.0% at the end of the 2nd month and 1.7% at the beginning of the 5th month. In the control group these rates were 18.3% and 7.3% respectively. The DOTS strategy significantly increased the success rate of TB treatment ($P < 0.05$).

Efficacité de la stratégie DOTS dans le traitement de la tuberculose pulmonaire à Gorgan en République islamique d'Iran

RÉSUMÉ Nous avons conduit une étude de cohorte portant sur 260 patients à frottis positif (178 sous traitement de brève durée sous surveillance directe [DOTS, pour *Directly Observed Treatment, Short-course*] et 82 sous traitement non-DOTS) sur une période de 2 ans afin d'évaluer l'efficacité de la stratégie DOTS dans le traitement de la tuberculose. Tous les patients toussaient depuis plus de 3 semaines, 91,9 % d'entre eux étaient fébriles, 60,8 % présentaient des expectorations et 27,7 % une histoire familiale positive. Le taux d'échec thérapeutique sous DOTS était de 9,0 % à la fin du 2e mois de traitement et de 1,7 % au début du 5e mois. Dans le groupe témoin, ces taux étaient respectivement de 18,3 % et de 7,3 %. La stratégie DOTS a entraîné une augmentation significative du taux de succès thérapeutique du traitement antituberculeux ($p < 0,05$).

[1]Department of Infectious Diseases; [2]Department of Biochemistry, Gorgan University of Medical Sciences, Gorgan, Islamic Republic of Iran (Correspondence to A. Abassi: abdolbas@yahoo.com).
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Introduction

Tuberculosis (TB) is the most common infectious disease worldwide, and causes the death of about 2–3 million people each year [*1*].

Incidence of TB has increased dramatically recently and a high prevalence of respiratory disease has been reported during recent years [*2*]. These reports most commonly come from developing countries. Factors involved in the increased number of TB cases include poverty, immigration, poor health facilities and drug abuse [*3*]. In addition, irregular use of antituberculosis drugs, incorrect dosage, poor knowledge among general physicians, improper attention of doctors, and drug resistance of *Mycobacterium tuberculosis* can be factors in treatment failure [*4*]. Studies done throughout the world show that by using the directly observed treatment, short-course (DOTS) strategy, the success rate of treatment is about 90%–95%, or even greater [*5*]. According to the same studies, even in industrialized countries and among knowledgeable and educated individuals at least 30% of patients, owing to a perception of improvement, do not take their medication properly and discontinue treatment after a while. In the DOTS strategy, in addition to direct observation of drug consumption, having a standard regimen for treatment and follow-up of patients improves the success rate. Conversely, for the reasons outlined above, treatment regimens other than DOTS have a low success rate, and may lead to TB transmission in the community and mycobacterial drug resistance [*5*].

Prevalence of TB in the Islamic Republic of Iran is about 39 per 100 000 [*6*]. Prevalence in Golestan province, where this study was carried out, is quite high, the second highest in the country [*7*].

The aim of this study was to evaluate the efficacy of the DOTS strategy in reducing the failure rate of TB treatment in comparison with the conventional strategy. The clinical and epidemiological features of 260 smear-positive respiratory TB patients in Gorgan were studied for a period of 2 years.

Methods

We carried out a follow-up cohort study to investigate the epidemiologic and clinical efficacy of DOTS strategy in treatment of TB patients in residential areas of Gorgan: a few areas classified as rural and one area classified as urban. All new patients (having had no prior treatment for TB) presenting to the health services during the period 1998–2000 whose respiratory specimens were smear-positive were included in the study. It should be noted that the rural area in this study was immediately adjacent to the urban area, therefore, the DOTS and the non-DOTS groups were comparable.

All the new cases of TB in the patients we studied had been diagnosed with sputum smear-positive tests using the Ziehl–Nielsen technique. The 178 patients in the rural areas were kept on the DOTS regimen (i.e. the drugs were dispensed in the health centre by a health worker, who observed the drugs being taken) in accordance with the national protocol (DOTS is obligatory in rural areas but optional in urban areas). The 82 patients in the urban areas (control group) were treated using a non-DOTS strategy, i.e. the same drug regimen was used and the drugs were dispended in the health centres but patients consumed them at home; there was no observation of their taking the medication.

All of the new TB cases underwent a 6-month treatment regimen according to

the World Health Organization protocol: 2 months with 4 drugs (isoniazid, rifampin, pyrazinamide, ethambutol) and 4 months with 2 drugs (isoniazid, rifampin) [*8*]. In the DOTS group, these drugs were given to fasting patients by trained health workers in 15 health centres every morning. In the non-DOTS group, the drugs were taken by the patients themselves without any observation of consumption.

During the treatment period, sputum samples were taken at the end of the 2nd month and the beginning of the 5th month. Patients who were smear-positive after the 2nd month had an extra month on the 4-drug regimen. Those smear-positive at the beginning of the 5th month were considered treatment failures. In these cases, drug resistance was suspected and samples were sent to the Tuberculosis and Respiratory Disease Research Centre in Masih Daneshvari Hospital, Tehran for further investigation.

Results were entered into *SPSS*, version 11, statistical software and analysed using χ^2 and Fisher's exact tests, with $P < 0.05$ considered statistically significant. Age, sex, clinical manifestation, TB in the family and also the treatment results (sputum smear status after 2 months and at the beginning of the 5th month) were recorded.

Results

A total of 260 smear-positive patients were diagnosed during the study period. The clinical manifestations of TB are presented in Table 1. There were more females (51.5%) than males. The largest age group was females aged 15–24 years. There were no significant differences between the 2 groups with regard to age, sex, socioeconomic status or nationality.

Of the 178 patients who were under treatment using the DOTS strategy, 3 (1.7%) were still smear-positive at the beginning of the 5th month. Of the 82 patients who were on the non-DOTS regimen, 6 (7.3%) were still smear-positive at the beginning of the 5th month (Table 2).

Table 1 **Observed clinical manifestation of tuberculosis in patients in Gorgan (1998–2000)**

Clinical manifestation	No. (*n* = 260)	%
Cough	260	100.0
Fever	239	91.9
Sputum	158	60.8
Family history	72	27.7
Haemoptysis	44	16.9

In the DOTS group, 91.0% were smear-negative at the end of the 2nd month and 98.3% at the beginning of the 5th month. In the non-DOTS (control) patients without direct observation, the corresponding values were 81.7% and 92.6% ($P < 0.05$).

Discussion

Through numerous studies and experience in various situations, it is now widely accepted that the most important cause of failure in TB treatment programmes is irregular drug-taking by patients, which is a direct consequence of poor motivation [*5*]. A successful, cost-effective, community-based programme of directly observed therapy, using volunteers, clinic staff and community health workers or trained personnel can help ensure adherence to therapy [*9*].

This is the first report about the efficacy of DOTS strategy in Golestan province in the Islamic Republic of Iran. The rate of negative smears at the beginning of the 5th month is an excellent index for evaluating the efficacy of TB treatment. Treatment

Table 2 **Comparison of treatment failure rate in patients on the DOTS and the non-DOTS regimens**

Treatment regimen	End of 2nd month				Beginning of 5th month[a]				Total
	Treatment failure		Conversion rate		Treatment failure		Conversion rate		
	No.	%	No.	%	No.	%	No.	%	
DOTS	16	9.0	162	91.6	3	1.7	175	98.3	178
Non-DOTS	15	18.3	67	81.7	6	7.3	76	92.7	82

[a]P < *0.05, Fisher exact test.*

failure in patients on the DOTS strategy was much lower than in the non-DOTS group. This correlates well with the results of studies done in other Asian countries [*10–15*].

In a study in China with a large sample population the treatment failure rate in patients under the DOTS strategy was 6.2% [*12*]; in our study we had better results with patients on the DOTS strategy.

In Iraq treatment failure in patients under the DOTS strategy was 2.0% and in the control group it was 5.8%, which is agreement with our findings, and emphasizes the importance of the DOTS strategy [*14*]. Murali and Udaya also reported a lower treatment failure rate among DOTS patients, 9% compared to 47% in the non-DOTS group, although the failure rate in our study was lower than theirs [*15*].

Although these differences were not statistically significant, there is a basis for further investigation. In our study, the highest rate of infection was among the younger age group, 15–24 years; in a study done in Canada, the highest rate of infection was in those > 65 years [*16*]. Given that in industrialized countries TB is mostly the reactivated form of primary infection [*17*], the high prevalence in older age groups may be a result of weaker immunity in those patients. All the patients in our study were, however, new TB cases.

The clinical syndrome in this study (sputum, cough, fever, haemoptysis) had a good correlation with a previous study [*18*]. The most common clinical manifestation was cough, which was also found in other studies [*13,15,16*].

In accord with those of other investigations, the findings of this study demonstrate the effectiveness of the DOTS strategy in treatment of TB patients. Considering conversion rates, our study showed a better efficacy in the DOTS group compared to some studies from other countries, such as a study in India which showed a 90% success rate with the DOTS strategy compared to 81% for the control patients [*11*]; in a study done in Iraq, the treatment success rate with the DOTS strategy was 96.2% but 76.2% in the control group [*13*].

In 27.7% of cases there was a positive family history of TB. This agrees with the findings of a study from Masih Daneshvari teaching hospital in Tehran (26.9%) [*18*]. Therefore, family members of infected patients also need to be checked. In a study in Pakistan it was reported that only 8.5% of family members of TB patients had the disease itself. It is nevertheless an important point to be taken into consideration when managing TB patients [*19*].

Recommendations

The DOTS strategy is an excellent way to reduce treatment failure, therefore, the

health system authorities in our country should make every effort to get the cooperation of all the relevant organizations (both private and public sector) to implement the DOTS strategy suggested by the World Health Organization. It is also a safe and effective way of controlling and preventing multidrug resistance in *Mycobacterium tuberculosis*.

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Tuberculosis of the breast: report of 4 clinical cases and literature review

S.M. Mirsaeidi,[1] M.R. Masjedi,[2] S.D. Mansouri[2] and A.A. Velayati[2]

سل الثدي: تقرير عن أربع حالات سريرية واستعراض للأدبيات المنشورة

سيِّد مهدي مير سعيدي، محمد رضا مسجدي، سيد داوود منصوري، علي أكبر ولايتي

الخلاصة: هناك حوالي 18% من حالات السل لا تحدث مظاهرها إلا خارج الرئة. ويُعدُّ سل الصدر أحد أنواع السل التي يندر حدوثها خارج الرئة. وتقدِّم هذه الدراسة تقريراً عن أربع حالات لسل الثدي مع تأكيد إصابتها بالسل الباثولوجي، أو المتفطِّري، أو كلَيْهما. وأوضحت هذه التقارير أنه يتعيَّن دائماً أخذ إمكانية الإصابة بالسل، بعَيْن الاعتبار أولاً، لدى إجراء التشخيص التفريقي في حالات التهاب الثدي الورمي الحبيبي، في المناطق الموطونة بالسل. واشتملت المعالجة على الأدوية المضادة للسل لمدة ستة أشهر على الأقل، والجراحة في الحالات التي استدعت ذلك.

ABSTRACT Nearly 18% of tuberculosis (TB) cases have only extrapulmonary manifestations. Breast tuberculosis is a rare type of extrapulmonary TB. This paper reports 4 cases of breast TB confirmed either pathologically or mycobacteriologically or both. These reports showed that TB should always be considered first in the differential diagnosis of granulomatous mastitis in TB-endemic areas. Therapy included at least 6 months of anti-TB medication and surgery when indicated.

Tuberculose mammaire : étude de 4 cas cliniques et synthèse de la littérature

RÉSUMÉ Près de 18 % des cas de tuberculose ne s'accompagnent que de manifestations extrapulmonaires. La tuberculose mammaire est une localisation rare de la tuberculose extrapulmonaire. Le présent article rapporte 4 cas de tuberculose mammaire, confirmée par l'anatomopathologie ou l'examen mycobactériologique ou les deux ensemble. Ces observations montrent que la tuberculose doit toujours être envisagée d'emblée dans le diagnostic différentiel de la mastite granulomateuse dans les zones d'endémie tuberculeuse. Le traitement a consisté en l'administration d'antituberculeux pendant un minimum de 6 mois et la chirurgie si indication.

[1]Kosair Children's Hospital Research Institute, Louisville, Kentucky, United States of America (Correspondence to S.M. Mirsaeidi: m0mirs01@gwise.louisville.edu).
[2]National Research Institute of Tuberculosis and Lung Disease, Shaheed Beheshti Medical Science University, Islamic Republic of Iran.
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Introduction

Tuberculosis (TB) has traditionally been regarded as a pulmonary disorder. However, nearly 17.9% of TB cases have only extrapulmonary manifestations [*1*]. Breast and skin are considered to be rare sites of extrapulmonary mycobacterial infection, comprising 0.1% to 0.5% of all TB cases, respectively [*2*]. Tuberculous mastitis is an uncommon lesion [*1*] even in countries where the incidence of pulmonary and extrapulmonary TB is still very high [*3*]. The clinician may confuse TB of the breast with either breast carcinoma or abscess [*4–6*]. Although the usual form of the disease is unilateral, it occasionally presents bilaterally [*7*].

We summarize here 4 cases of tuberculous mastitis presenting to the National Research Institute of Tuberculosis and Lung Disease over a 5-year period at Shaheed Beheshti Medical Science University.

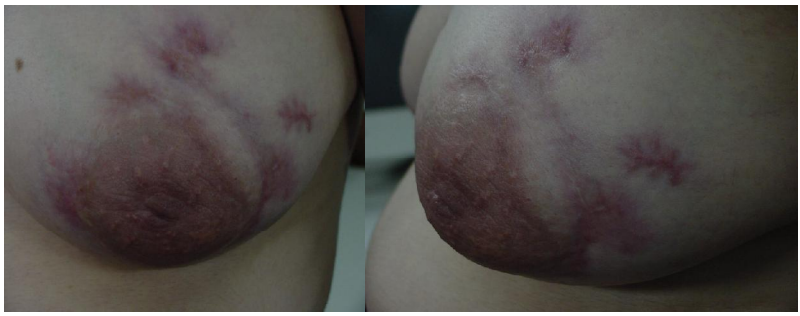
Case presentations

Case 1

A 37-year-old female was referred to this centre for management of left breast pain. There was no history of recent pregnancy or lactation or a history of breast trauma. She first noticed a painful mass in her left breast 1.5 years ago, 20 days later she noticed a visible lesion on the breast skin with purulent discharge. Subsequently, sinus tracts with purulent discharges appeared in a total of 6 locations. She received at least 8 courses of antibiotic therapy with no therapeutic effect before she was referred to our centre.

On physical examination, a painful nodular mass was detected in the medial half of the breast. A surgical scar, more than 6 healed sinus tracts, and a region containing exudate were detected (Figures 1 and 2). Sonography showed a well-defined 20 × 12 × 14 mm mass in the medial portion of the left breast.

Based on the sonography and mammography results, the patient underwent biopsy with a suspicion of malignancy. Diagnosis of granulomatous mastitis was established from biopsy. A second biopsy of the new sinus tract also confirmed a granulomatous lesion and there was no sign of malignancy. The fine-needle aspiration (FNA) smear was negative for acid-fast bacilli (AFB). FNA was negative on polymerase chain reaction testing for mycobacterium TB and culture-negative for actinomycetes and fungi. The angiotension converting enzyme



Figures 1 and 2 **Multiple breast sinus tract and erythematous skin lesions**

level was in the normal range. Complete blood counts and liver function tests were all normal. The patient's purified protein derivative (PPD)/Mantoux skin test was 16 mm in diameter. Chest radiography was intact and there were no changes compatible with TB or sarcoidosis. High resolution computerized tomography of the lung was normal.

Although we found no laboratory evidence for TB mastitis, due to the Mantoux skin test and strong clinical suspicion, the patient was put on standard anti-TB regimen of isoniazid, rifampin, pyrazinamide and ethambutol. In the subsequent 6-month period no other sinus tracts appeared and the breast mass showed an apparent remission on multiple sonography.

Case 2

A 41-year-old woman presented with pain and swelling of the left breast. She was a known case of TB from 18 years before and had received a complete 6-month period of anti-TB treatment. The patient's symptoms had started one year after discontinuation of breast feeding with pain and a mass in the superolateral portion of the left breast. The symptoms progressed over a few months and no associated constitutional symptoms were found.

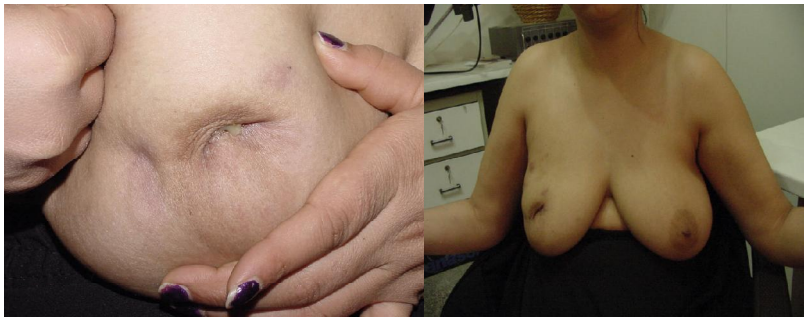
After ultrasound examination, a biopsy was taken with the suspicion of breast carcinoma. The result was reported as granulomatous mastitis and after ruling out other diagnoses, the patient underwent anti-TB treatment with an excellent response; however, she discontinued medication after 3 months. Two weeks later, the left breast mass reappeared, associated with multiple lymph nodes in the left axillary pit. Sonography supported the prior diagnosis of granulomatous mastitis. This time, a 6-month course of anti-TB therapy was started with a standard regimen and no mass or abscess was reported on ultrasound examination during the course of treatment. After 6 months of follow-up, starting from the end of treatment, no mass or lymphadenopathy appeared and the patient complained only of minor pain.

Case 3

A 19-year-old female was referred to this centre with a complaint of breast pain and retraction of the right nipple with yellowish discharge. She was nulliparous with no history of breast trauma. Her symptoms began 1 year before referral and gradually progressed. She took various different kinds of antibiotics during this period. On physical examination, painful masses were palpated in the centre and superolateral quadrant of the right breast. An enlarged lymph node in the right axilla, dimension 20 × 20 mm, was also palpable on physical examination. Full nipple retraction and purulent yellowish discharge from the same nipple was detected (Figures 3 and 4). At least 4 openings of sinus tracts were visible with no purulent discharge at the time.

On sonography, there was thickening of the breast skin in the superolateral and supercentral portion. This abnormality along with several hypoechoic lesions suggested abscess formation. There was evidence of left pleural effusion on chest radiography. The PPD/Mantoux skin test was 11 mm. Complete blood count and liver function tests were all normal. Sputum smears were negative; however, direct smear of breast discharge was 1+ positive for AFB, compatible with World Health Organization criteria. Aspiration of pleural fluid was not performed because of the patient's dissent.

Considering AFB secretions and concomitant pulmonary and pleural involvement, a diagnosis of TB was suggested and a standard anti-TB drug regimen of isoniazid,



Figures 3 and 4 **Full nipple retraction and purulent yellowish discharge from the same nipple was detected**

rifampin, pyrazinamide and ethambutol was prescribed.

After beginning anti-TB medication, the breast discharge and pain decreased significantly after 2 months. Direct smear of breast discharge became negative after 2 months although discharges continued. After 6 months of chemotherapy, a decision for surgical intervention was made to alleviate persistent discharges; however, the patient left the country and the treatment remained interrupted.

Case 4

A 49-year-old woman presented with suppurative secretions from her left breast. She had suffered from pain and a mass in the left breast for 4 years. An ultrasound-based diagnosis of suppurative abscess had been suggested and she underwent antibiotic therapy plus aspiration. Due to recurrence, repeated courses of antibiotic therapy were given. A sinus tract appeared in the left breast, superior to the nipple with suppurative secretions 8 months previously. Bacteriologic studies at different periods from abscess and sinus tract secretions gave negative results. Mycologic studies led to negative results. The PPD/Mantoux skin test was also negative. Liver function tests and other tests were normal and lung computerized tomography scan gave no abnormal findings. Smear and culture from sinus tract secretions were sent for bacteriological evaluation which showed negative-smear results. However, AFB colony growth in the culture was confirmed and using differential tests, *Mycobacterium tuberculosis* was eventually identified.

Discussion

The first case had a granulomatous lesion in her breast. Granulomatous mastitis is a descriptive and non-specific term which encompasses many specific lesions such as TB, fungal infections, sarcoidosis and granulomatous reactions in carcinoma [*8*]. Several diagnoses must be ruled out to establish TB mastitis.

Idiopathic granulomatous mastitis was first described in 1972 [*9*], for which TB mastitis should always be considered as a differential diagnosis in women with a positive history of exposure to TB patients [*10*]. This kind of exposure occurs very frequently in endemic countries. A similar granulomatous reaction has also been described in actinomycosis of the breast which

was ruled out by culture of the patient's discharge obtained by FNA in our patients [*11*].

The best description of TB mastitis is by Shinde et al. in India [*12*]. They showed that a lump in the breast with or without ulceration was the commonest presentation in TB of the breast, the other less common forms being diffuse nodularity and multiple sinuses. Concomitant axillary lymph nodes were found in one-third of the patients. Our second case had similar symptoms. This suggests that a young, multiparous, lactating woman with a similar lesion should always raise the suspicion of TB mastitis, although pre-therapeutic pathologic confirmation of benign conditions is mandatory. Similar results were reported by Al-Marri et al. from 13 multiparous women with TB of the breast from Qatar [*13*]. All of them presented with a lump, 2 had nipple discharge and 1 had a palpable axillary node on the same side. In that study all diagnoses were confirmed histologically.

In both these previous studies the type of breast lesion was similar to what we found in our cases; in our second case, the breast lesion emerged as an abscess, corresponding to Daali's report [*14*].

According to different studies, the age of patients with breast TB ranges between 20 and 40 years, which corresponds to the age of our patients. However, many other investigators have also reported breast TB in post-menopausal ages [*4,6,15–17*].

With regard to pathogenesis, the route of entry of mycobacterial TB to the breast varies. Spreading of infection from other TB foci via haematogenic path during primary infection is a common route [*18*].

TB mastitis should also be considered in immunodeficiency states in which pathogenesis is also via the haematogenic route [*19,20*]. There is also much controversy about the diagnostic criteria for TB mastitis and different surgical biopsies and FNA have been recommended [*13*]. However, in several studies it has been shown that the overall rate of positivity of AFB in nipple discharge, FNA and tissue samples was 12.0%–22.7%. [*12,16,21*]. Although we obtained samples for smear and direct visualization from breast discharge samples and FNA for all our patients, only patient 3 was AFB-positive.

The differential diagnoses include duct ectasia, foreign-body giant-cell reaction with fat necrosis, foreign material or an abscess, idiopathic granulomatous mastitis, sarcoidosis, syphilitic gumma and Wegener's granulomatosis [*16,22*], all of which must be ruled out using proper diagnostic tests.

Various modes of therapy ranging from chemotherapy alone to mastectomy have been suggested for tuberculous mastitis [*12*]. In a study by Shinde et al., 14% of patients required simple mastectomy due to either lack of response to chemotherapy (10%) or large painful, ulcerative lesions involving the entire breast (4%). Axillary dissection was performed in only 8% of patients with large ulcerated axillary nodes. Al-Marri recommends that incisional or excisional biopsy together with anti-TB drugs is the most successful treatment [*13*]. Daali et al. recommend anti-TB chemotherapy for 9 months [*14*]. The clinical course was favourable at 6 months. They recommend that anti-TB antibiotic therapy might be accompanied by surgery in case of extension, therefore several authors suggest that anti-TB antibiotic therapy in combination with aspiration or surgical drainage are usually associated with an excellent outcome [*4,6,7,23,24*]. We recommend at least 9 months of anti-TB therapy and surgery in cases with unsatisfactory treatment results.

Although TB of the breast is a rare entity, it should always be considered in the

differential diagnoses of granulomatous mastitis in endemic areas. It seems that empirical therapy might be effective when primary evaluations for other causes lead to no definite conclusion. Diagnosis is based on histopathology and it is less probable that a microbiological diagnosis be made. Therapy includes at least 6 months of anti-TB medication, and surgery when indicated.

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Epidemiology and risk factors of brucellosis in Alexandria governorate

F.A. Meky,[1] E.A. Hassan,[2] A.M. Abd Elhafez,[1] A.M. Aboul Fetouh[1] and S.M.S. El-Ghazali[1]

وبائيات داء البروسيلات وعوامل اختطاره في محافظة الإسكندرية

فاطمة عبد السلام محمد مكي، إيمان عبد الكريم حسن، أماني مختار عبد الحافظ، عائشة محمد أبو الفتوح، سوسن محمد شوقي الغزالي

الخلاصة: تـَمثَّل الغـرض مـن هـذه الدراسـة في بيـان الاتجـاه وتحديـد عوامـل الاختطـار المحتملـة للإصـابة بـداء البروسيلات، في محافظة الإسكندرية، شماليَّ مصر. وقام الباحثون في هذه الدراسـة بـإدراج 72 مريـضاً ممـن لـديهم إصابة مؤكَّدة بداء البروسيلات، و144 من الشواهد من نفس الفئة العمرية. وأُجريت مقـابلات مـع المـشاركين في الدراسة تمت في منازلهم، باستخدام الاستبيان الـمُعَدُّ لهذا الغرض. وكانت العوامـل المتمثِّلـة في مخالطـة الحيوانـات، وتربية الماعز، وتناول المثلجات المشتـراة من الباعة الجائلين، مرتبطة ارتباطاً يُعْتَدُّ بـه إحـصائياً (P<0.05) بالإصـابة بداء البروسيلات، وذلك من واقع التحليل الوحيد المتغيِّـر والعديـد المتغيِّـرات. ومثَّلـت مخالطـة الحيوانـات المـصابة ومنتجاتها أهم الوسائل في انتقال هذا المرض.

ABSTRACT This study aimed to describe the trend and to identify possible risk factors for brucellosis in Alexandria in northern Egypt. We enrolled 72 confirmed cases of brucellosis and 144 age-matched controls in this study. Participants were interviewed at home using a structured questionnaire. Working with animals, breeding goats and eating ice cream bought from street vendors were significantly associated ($P < 0.05$) with brucellosis by univariate and multivariate analysis. Contact with infected animals and their products was the most important method of transmission.

Épidémiologie et facteurs de risque de la brucellose dans le gouvernorat d'Alexandrie

RÉSUMÉ Cette étude avait pour objectifs de décrire l'évolution de la brucellose à Alexandrie, ville située au nord de l'Égypte, et d'identifier les éventuels facteurs de risque de cette maladie. Ont été enrôlés dans cette étude 72 cas confirmés de brucellose et 144 témoins appariés selon l'âge. Les participants ont été interrogés à leur domicile à l'aide d'un questionnaire structuré. Les analyses uni- et multi-variées ont mis en évidence l'existence d'une association significative ($p < 0,05$) entre le travail avec les animaux, l'élevage de chèvres et la consommation de glaces achetées à des vendeurs ambulants et la brucellose. Le contage avec des animaux infectés et leurs produits s'avère être le mode de transmission prédominant.

[1]Department of Community, Environment and Occupational Medicine, Ain Shams University, Cairo, Egypt (Correspondence to F.A. Meky: fammeky@yahoo.co.uk).
[2]Ministry of Health and Population, Cairo, Egypt.
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Introduction

Brucellosis is a zoonotic infection caused by bacteria of the genus *Brucella*; species considered important agents of human disease are *B. melitensis*, *B. abortus* and *B. suis* [*1*]. Brucellosis has worldwide distribution; but nowadays the disease is rare in the United States of America and in many other industrialized nations because of routine screening of domestic livestock and animal vaccination programmes [*2–4*]. This disease is, however, still a leading zoonosis in the countries of the Eastern Mediterranean Region and a disease of economic importance [*5*]. Additional losses result from human infection (undulant fever) with its prolonged misery, debility and generalized aching, which may last for months or years [*5,6*]. Sheep and goats and their products are the main sources of infection. Consequently, brucellosis has been an occupational risk for farmers, veterinary surgeons and employees in the meatpacking business [*1*]. Non-occupational sources of infection include consumption of fresh, unpasteurized goat cheese and raw fresh (untreated) milk [*7*].

In Egypt, the infection is mostly caused by *B. melitensis* and *B. abortus* [*2*]. The Epidemiology and Surveillance Unit of the Egyptian Ministry of Health and Population has recorded a substantial increase in the number of patients with brucellosis in the recent past, from 24 cases in 1988 to 1429 in 1998 [*8*]. An earlier report (1992) described the distribution pattern of human cases of brucellosis during the period 1982–91: the infection rate was generally low except in 1987 and 1991, when there were marked increases in numbers of cases. This was clearly observed in Alexandria and Menofiya, and also in Giza and Domiyat [*9*].

A full description of the epidemiology of the disease is needed for planning of any intervention for its control. Therefore, the objectives of this study were to define the trend of brucellosis in Alexandria governorate over a 16-year period and to determine the risk factors.

Methods

The study was conducted at the Alexandria Fever Hospital. This hospital was selected because it has well-trained staff and well-equipped laboratories and because of its accessibility. Although the hospital is located in an urban area, its catchment area includes not only districts from Alexandria city, but also from nearby rural areas such as El-Amriya and Abis. Although these areas are administratively related to El-Beheira governorate, they are near enough to Alexandria that, for any case of fever, it is easier to go to Alexandria Fever Hospital than Damanhour Fever Hospital in El-Beheira [*8*].

The logbooks of the health directorate over the 16 years 1988–2003 were reviewed to detect the annual number of brucellosis cases. The reliability of data from the logbooks was checked by comparing with the same data collected by the Department of Communicable Diseases in the Ministry of Health and Population.

A case–control study was also conducted in 2001 to determine the epidemiologic risk factors of brucellosis. Cases of brucellosis were identified from the admission logbooks of the Alexandria Fever Hospital. Basic demographic data such as name, age, sex and address were collected from the logbooks.

For this study, a case of brucellosis was defined as any case hospitalized with a physician's diagnosis of brucellosis between January 1999 and October 2000. Diagnosis depended on the presence of clinical symptoms such as recurrent fever, profuse sweat-

ing, headache and generalized bone pain, with rising titre of brucella IgG antibody > 1/160 using a serum agglutination test (tube and slide). Diagnosis was confirmed by performing a blood culture.

The total number of confirmed cases was 120, but only 72 were included in the study (all districts). Of the 48 patients not enrolled in the study, 20 lived in another governorate, 10 were abroad, the address was unclear for 12 and 6 refused to participate.

For each case, 2 age-matched (± 2 years) controls were selected from households within the same neighbourhood.

Informed consent was obtained from all participants following explanation of the aims and importance of the study.

Cases and controls were interviewed in their homes by one of the authors using a standardized questionnaire, which covered demographic data (marital status, occupation, educational level and family size), date of onset of symptoms, infection of other members of the family and the main risk factors. These included contact with animals (goats, cattle, sheep, camels, pigs and dogs), mode of contact (cleaning farms, delivery or handling of abortus and slaughtering animals), consumption of unboiled milk and milk products (cottage cheese and ice cream) and knowledge about brucellosis.

Data were analysed using *Epi-Info*, version 6. Odds ratio, chi squared, and Student *t*-test were used in analysis of data. Test results were considered significant if *P*-value was ≤ 0.05. Factors found to be significant in the univariate analysis were included in the multivariate analysis.

Results

The number of reported cases is shown in Figure 1. A mean of 61 cases has been reported annually during the period 1988–

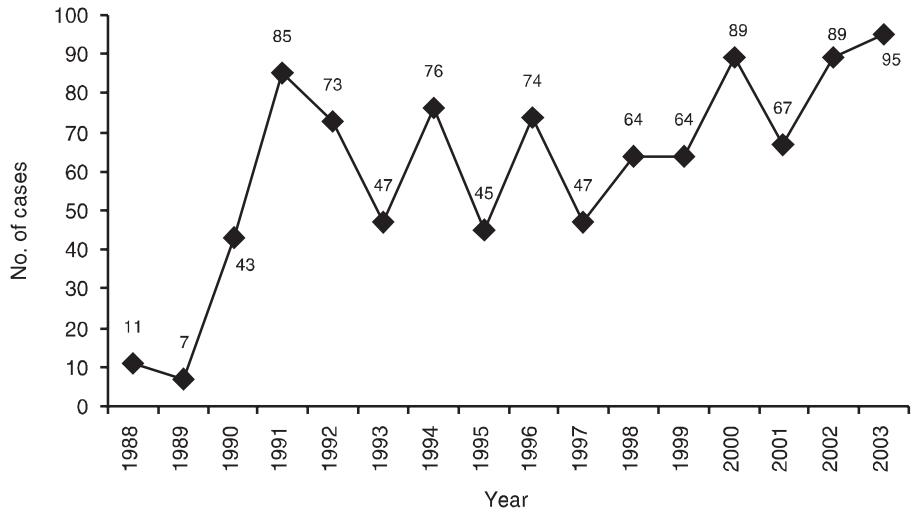

Figure 1 **Reported cases of brucellosis in Alexandria governorate, 1988–2003**

2003, with an increase in the number of reported cases, particularly in 1991, 2000 and 2003.

Sociodemographic characteristics of the 2 groups are described in Table 1. Age range was 8–69 years for cases [mean 37.1 years, standard deviation (SD) 15.4] and 9–67 years for controls (mean 36.7 years, SD 15.1) ($P = 0.8$). Those with brucellosis ($n = 72$) were distributed by age as follows: ≤ 10 years 2.7%, 11–20 years 15.2%, 21–30 years 19.4%, 31–40 years 19.4%, 41–50 years 26.3%, 51–60 years 8.3% and > 60 years 8.3%. Male to female ratio was 2:1.

The most frequent symptoms were recurrent attacks of fever (100%), profuse sweating at night with no prior antipyretic (82%) and headache (75%). The overall case fatality rate was 0.0%. Recurrence of symptoms was experienced by 36% of patients (16 males and 10 females; 4 under the age of 15 years) during the first 6 months of illness. Onset of illness was greatest in spring, 44% of cases, followed by summer, 29%.

The association between brucellosis and some risk factors is shown in Table 2. Occupation was an important risk factor for

Table 1 **Demographic characteristics**

Characteristic	Cases ($n = 72$)		Controls ($n = 144$)		P[a]
	No.	%	No.	%	
Education					
Illiterate	29	40.8	59	41.0	0.82
Read and write or primary school	21	29.6	34	23.6	
Preparatory school	14	19.7	33	22.9	
Secondary school or university	8	9.9	18	12.5	
Marital status					
Single	15	20.8	49	34.0	0.096
Married	47	65.3	86	59.7	
Widowed	6	8.3	6	4.2	
Divorced	4	5.6	3	2.1	
Occupation					
Farmer	17	22.5	19	13.6	0.011
Housewife	17	22.5	56	40.0	
Skilled worker	13	18.3	31	22.1	
Student	7	9.9	20	14.3	
Clerical worker	2	2.8	4	2.9	
Butcher	4	5.6	2	1.4	
Meat transport and vehicle driver	2	2.7	0	–	
Other[b]	10	13.8	8	5.7	

[a] *P value based on χ^2 test for categorical variables and Student t-test for continuous variables.*

[b] *Includes professional, veterinary surgeon, nurse, fisherman, street vendor (milk and milk products), retired and unemployed.*

Table 2 **Univariate analysis of some risk factors for brucellosis**

Variable	Cases (%)	Controls (%)	OR (95% CI)	*P*-value
Illiterate	40.3	41.0	1.0 (0.5–1.9)	0.9
Occupation dealing with animals[a]	29.6	14.7	2.4 (1.2–5.2)	0.009
Breeding animals	40.3	22.9	2.3 (1.2–4.3)	0.006
Eating ice cream from street vendor	42.3	28.6	1.8 (1.1–3.3)	0.04
Drinking raw milk	6.9	6.0	0.9 (0.2–3.8)	0.9
Eating cottage cheese (unprocessed)	85.9	82.5	1.3 (0.5–2.9)	0.5
Eating butter	58.3	63.2	0.8 (0.4–1.5)	0.4
Dealing with unvaccinated animals	73.6	65.5	0.6 (0.3–1.4)	0.2
Knowledge about the disease	29.2	29.9	0.9 (0.5–1.9)	0.9
Slaughtering animals 4 weeks before onset of illness	19.6	10.4	1.8 (0.7–4.2)	0.1

[a]*Includes farmer, slaughterhouse worker, butcher and veterinary surgeon. Occupations not dealing with animals include housewife, skilled worker, clerical worker, student and other.*
OR = odds ratio; CI = confidence interval.

brucellosis. Workers in occupations dealing with animals (including farmers, slaughterhouse workers, butchers and veterinary surgeons) had a 2.4-fold higher risk of brucellosis than those in occupation not dealing with animals ($P = 0.009$). Breeding animals was a significant risk factor, but when the type of animal was considered, the odds for presenting with brucellosis was significantly higher only for goats ($P = 0.006$). Other animals (cattle, sheep, camels, pigs and dogs) were not associated with the risk of disease. Eating ice cream from street vendors was also significantly associated with brucellosis: the odds were 1.8 times higher among those who ate ice cream from street vendors than those who did not ($P = 0.04$).

All significant variables from the univariate analysis were included in multivariate analysis using a conditional logistic regression model. Most were not significantly associated with disease in the multivariate model, with the exception of male sex, jobs dealing with animals, breeding goats and eating ice cream bought from street vendors (unknown source) (Table 3).

Discussion

Brucellosis has been recognized as one of the most common zoonoses in the Eastern Mediterranean Region, with more than 45 000 cases reported annually. The epidemiological data on the disease is frequently incomplete. This is partly explained by the lack of proper laboratory facilities in some remote areas as well as by poor cooperation and exchange of information between veterinary and health services [*10*].

In this study, a rise in the number of brucellosis cases was noticed in 1991 and this was in agreement with Wassif et al., who described the distribution of brucellosis cases in a number of Egyptian governorates: the highest number of brucellosis cases was in Alexandria governorate in 1991 [*9*]. A similar rise was reported in a neighbouring country, the Palestinian Territories, during the late 1980s (W. Tarazi, unpublished report, 1990). The increase in number of brucellosis cases in 1991 may be a true epidemic of brucellosis or a

Table 3 **Multivariate analysis of some risk factors for brucellosis**

Variable	OR (95% CI)
Male sex	2.2 (1.0–5.0)*
Age	1.0 (1.0–1.0)
Education	0.8 (0.4–1.5)
Occupation dealing with animals[a]	2.4 (1.2–4.9)*
Breeding goats	3.2 (1.2–8.7)*
Breeding cattle	0.8 (0.3–2.2)
Breeding sheep	0.6 (0.2–1.6)
Breeding dogs	0.4 (0.2–1.2)
Knowledge about the disease	0.6 (0.3–1.3)
Dealing with vaccinated animals	2.1 (0.8–5.4)
Drinking unboiled milk	1.5 (0.5–4.5)
Eating cottage cheese	1.0 (0.4–2.4)
Eating ice cream from street vendor	2.4 (1.2–4.6)*
Slaughtering animals 4 weeks before onset of illness	2.0 (0.8–5.4)

**Significantly associated with brucellosis (P < 0.05).*
[a]Includes farmer, slaughterhouse worker, butcher and veterinary surgeon. Occupations not dealing with animals include housewife, skilled worker, clerical worker, student and other.
OR = odds ratio; CI = confidence interval.

false increase because of the use of better diagnostic measures and more meticulous notification [*9*]. In fact, the number reported was probably much lower than the actuality as under-diagnosis and under-reporting of cases is a recognized problem in many developing countries [*10*]. It has been estimated that for each reported case, there are at least 2 additional cases that are not reported or not diagnosed [*11*]. Therefore, the actual number of cases may be up to 3 times as many as the reported number.

We also noted another increase in number of cases between 2000 and 2003. This could be related to improvement in the regulated surveillance system for notifying brucellosis cases accomplished by the Ministry of Health and Population in 2001 [*8*].

The age group 15–50 years was the most commonly affected with brucellosis in this study. Comparable findings have been reported from Kuwait (mean age 34.4, SD 11.5, years), Saudi Arabia (mean age 33.8, SD 13.9, years) and Djibouti (mean age 31.6 years) [*12–14*]. Brucellosis is predominately an occupational disease [*1*], so it would be expected that this age group would be the most affected, having been exposed longer to risk factors related to their occupation.

More males were affected than females (2:1) in our study and this is in accord with studies conducted in Sharkia governorate (Egypt), Kuwait, Saudi Arabia and India [*9,12,13,15*]. This sex distribution in the incidence of brucellosis infection may be because males are more concerned in activities such as slaughter and handling of carcases, and as a consequence they are at greater risk of exposure to infection. In both children (0–14 years) and adults, the disease was more prevalent among males. Abdou reported similar conclusions in a 1995 report [*16*]. Male children in the areas studied may be exposed to the same risk factors as male adults.

Other studies have, however, observed that the incidence of infection was greater in females than males (or roughly equal) [*17,18*]; in the study areas, those milking the cows, and thus having a higher chance of contact and acquiring infection, were mainly females.

Recurrent attacks of fever with profuse sweating at night with no prior antipyretic were the most prevalent symptoms in our study and in other studies carried out in south Jordan, Yemen and Greece [*18–20*]. The case fatality rate in our study was 0%; the same rate was reported in a 1998 study from Palestine [*11*]. The disease is insidious

in onset with long-standing fever, so there is more likelihood of diagnosis. In addition, the availability of well-known and effective therapy enhances the outcome of the disease. Recurrence of symptoms during the first 6 months of illness among cases we studied was 3 times higher than that reported by Awad and 11 times higher than reported by Shehata [*11,12*].

The onset of symptoms showed a seasonal pattern with high incidence in spring followed by summer. Several other studies have shown a similar seasonal pattern [*9,11,12*]. The increase is believed to be linked to the delivery (parturition) season of sheep and goats where there is a greater possibility for direct contact with vaginal discharge, foetuses and placentas, which may play a major role in increasing risk of exposure to infection.

People in occupations dealing with animals were at greater risk of developing brucellosis. A study conducted in several regions in Lebanon on 597 persons in high-risk occupations found overall prevalence of IgG and IgM antibodies for brucella was around 60%. Exposure to brucellosis was high among persons in high-risk occupations from all surveyed regions in Lebanon [*21*]. Similarly in a case–control study conducted in Yemen, occupation dealing with animals was a significant risk factor for infection; socioeconomic and educational factors were independent risk factors [*22*]. The majority of the participants in our study had not been educated beyond preparatory school level and were mostly of a low socioeconomic standard so we could not confirm these issues as independent risk factors.

Contact with goats was an important risk factor in the group we studied. In a Saudi Arabian case–control study, greater risk for brucellosis was associated with products derived from sheep and goats as opposed to camels and cattle [*23*]. Direct contact with domestic animals and consumption of raw products of animal origin have also been identified as major risk factors [*24*]. In a study done in Eritrea, the highest prevalence was among dairy farm workers and owners in randomly selected dairy-cattle farms, followed by veterinary personnel [*25*]. A higher risk was associated with the presence of sheep on the farm.

Eating ice cream from street vendors (i.e. unknown source, possibly made from the milk of infected animals) was an important source of infection in our study. Kolar also noted that there had been reports of transmission of the disease from eating ice-cream [*26*].

Consumption of unboiled milk appeared to have no association with brucellosis. In a study from Spain, no statistically significant relationship was demonstrated between consumption of dairy products and being seropositive for brucella antibodies [*27*]. This may be due to the fact that drinking fresh milk without boiling it is an uncommon practice in the study areas owing to fear of contracting other infections such as tuberculosis. Other studies have, however, found that milk and dairy products appeared to be associated with brucellosis [*19,28*]. In a study on 5726 blood specimens from children aged $\leq$ 14 years for serological evidence of brucellosis, > 60% had a history of both consumption of fresh goat's milk and close contact with animals [*15*].

Eating soft cheese and butter were not significantly related to brucellosis in our study; our cases were from urban areas, however, and cheese and butter were bought from sources which used pasteurized milk in manufacturing. Raw milk and milk products from infected sheep, goats and cattle have been cited as important sources of infection with brucellosis; soft cheeses made using traditional methods which do not ensure

killing of organism have also been implicated [*11,13*].

Occupation dealing with animals, breeding goats, male sex and eating ice cream bought from street vondors were the only significant risk factors in the logistic regression model in our study. Similarly, Bikas et al., using multivariate stepwise analysis, found that that occupation dealing with animals, place of residence, absence of stables and trauma during animal delivery were the most important risk factors remaining in the model [*29*].

Conclusion

Our findings emphasize the importance of contact infections, i.e. contact with infected animals and their products, as method of transmission of brucellosis rather than ingestion of contaminated animal products. This means that prevention of brucellosis in man ultimately depends upon its control in the principal animal hosts. Therefore, information is needed concerning the present incidence of brucellosis in livestock (sheep, goats and cattle).

A control programme for human brucellosis would depend to a large extent on public health education about the disease and its risk factors, good administrative arrangement and ensuring the maximum cooperation of the community (particularly between health and veterinary authorities). Active cooperation between health services and veterinary services should be promoted.

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Vectors and reservoirs of cutaneous leishmaniasis in Marvdasht district, southern Islamic Republic of Iran

Y. Rassi,[1] M.M. Gassemi,[1] E. Javadian,[1] S. Rafizadeh,[2] H. Motazedian[1] and H. Vatandoost[1]

نواقل ومستودعات داء الليشمانيات الجلدي في منطقة مارفداشت، جنوب جمهورية إيران الإسلامية

ياور رائي، محمد مسعود قاسمي، عزت الدين جواديان، سينا رفيع زاده، حسين معتضديان، حسن وطن دوست

الخلاصة: أُجريت دراسة وبائية حول نواقل ومستودعات داء الليشمانيات الجلدي في المناطق الريفية في مارفداشت، بإقليم فارس، جنوب جمهورية إيران الإسلامية، خلال الفترة الواقعة بين عامَيْ 2003 و2004. وتم، باستخدام المصائد، جمع 126 من القوارض، 75.4% منها من الجرذان الليبية، و14.3% من القداد *Cricetulus*، و10.3% من الكعبر *Meriones*. وتبيَّن أن ثمانية من الجرذان الليبية الـ 95 (8.4%) مصابة بالليشمانية الكبيرة، أمكن تحديدها عن طريق اختبار التفاعل السلسلي للبلمرة المتشابك. ولم تأت نتائج الاختبار إيجابية لأي من القوارض الأخرى. وجمعت إناث الفواصد من مواقع داخل البيوت: 75% منها من نوع الفاصدة الباباستية، ووجد أن 2.7% منها فقط مصابة طبيعياً بالليشمانية الكبيرة. ويُعَدُّ هذا أول تقرير يدلّ على نحو مُثْبَت، أن الفاصدة الباباستية هي من نواقل داء الليشمانيات الجلدي الحيواني المصدر في هذه المنطقة.

ABSTRACT An epidemiological study was made of vectors and reservoirs of cutaneous leishmaniasis in rural regions of Marvdasht, Fars province, southern Islamic Republic of Iran during 2003–04. Using live traps, 126 rodents were collected: 75.4% were *Meriones libycus*, 14.3% *Cricetulus migratorius* and 10.3% *Microtus arvalis*. Eight out of 95 *Meriones libycus* (8.4%) were found to be infected with *Leishmania major*, identified by nested-PCR; none of the other rodents were positive. Female sandflies were collected from indoor locations: 75% were *Phlebotomus papatasi* and only 2.7% were found naturally infected with *L. major*. This is the first report of *P. papatasi* as a proven vector of zoonotic cutaneous leishmaniasis in this area.

Vecteurs et réservoirs de la leishmaniose cutanée dans le district de Marvdasht au sud de la République islamique d'Iran

RÉSUMÉ Au cours des années 2003 et 2004, une enquête épidémiologique a été menée sur les vecteurs et réservoirs de la leishmaniose cutanée dans les zones rurales de Marvdasht, province de Fars, au sud de la République islamique d'Iran. À l'aide de pièges permettant de capturer l'animal vivant, 126 rongeurs ont été collectés dont 75,4 % de l'espèce *Meriones libycus* (Mérion de Libye), 14,3 % de l'espèce *Cricetulus migratorius* (Hamster migrateur) et 10,3 % de l'espèce *Microtus arvalis* (Campagnol des champs). Huit des 95 Mérions de Libye (8,4 %) se sont avérés infectés par *Leishmania major*, identifié par PCR (réaction de polymérisation en chaîne) nichée, aucun des autres rongeurs n'étant positif pour ce protozoaire. Des phlébotomes femelles ont été capturées en intérieur : 75 % appartenaient au genre *Phlebotomus papatasi* et seules 2,7 % étaient naturellement infectées par *L. major*. Il s'agit ici du premier rapport confirmant le rôle de *P. papatasi* comme vecteur de la leishmaniose cutanée zoonosique dans cette région.

[1]*School of Public Health and Institute of Health Research, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran (Correspondence to Y. Rassi: rasiyava@sina.tums.ac.ir).*
[2]*Genetics Office, Centre of Disease Control, Ministry of Health and Medical Education, Tehran, Islamic Republic of Iran.*
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Introduction

Cutaneous leishmaniasis (CL) is still endemic and an important health problem in many countries of the Eastern Mediterranean Region [*1–4*]. Three species of *Leishmania* parasites cause CL in the old world: *L. major, L .tropica* and *L. aethiopica* [*5*].

Zoonotic cutaneous leishmaniasis (ZCL) is endemic in half of the 28 provinces of the Islamic Republic of Iran. The most important hyperendemic focus of ZCL has been located in Isfahan province, in the central part of the country, where the great gerbil, *Rhombomys opimus*, is the principle reservoir host of the disease [*6*]. In the other high risk parts of the country (the west and south-west regions), *Tatera indica* is the primary reservoir host [*7*]. In both the above-mentioned areas, *Meriones libycus* plays a secondary role as a source for transmitting of *L. major* by sandfly vectors [*6,7*]. In the central parts of the Islamic Republic of Iran (Isfahan province) as well as southeast of the country, female sandflies of *Phlebotomus papatasi* have been reported as the main vector of CL responsible for *L. major* infection [*8,9*].

In southern Islamic Republic of Iran, there is concern that the annual incidence of CL has gradually risen over the past decade, increasing from 1560 cases in 1991 to 3861 in 2001 (unpublished data). The most likely reason for this trend is an increase in human–sandfly contact. This is attributed to the development of villages and the spread of the human population into the habitats of the local vectors, *P. papatasi*, as well as rodents which act as reservoir hosts. It should be emphasized that most Iranian cases of CL are zoonotic. Our recent studies in some foci of ZCL in southern Islamic Republic of Iran showed that *Mer. libycus* was the main reservoir host, and *R. opimus* and *T. indica* were absent [*10,11*]. Although there are several studies on different aspects of disease in the region, there has been no comprehensive study on vectors of ZCL in the southern part of the Islamic Republic of Iran.

The aim of this study was to determine the species composition of reservoirs and vectors from the field in the Marvdasht focus of ZCL, southern Islamic Republic of Iran. In addition, we evaluated a new molecular technique, nested polymerase chain reaction (PCR), for species determination.

Methods

Study area

The study was carried out in 3 villages (Raja-Abad, Ghorbanlak and Soltan-Velayat) in the Mohammad Abad district (52° 56′ E, 29° 54′ N) at an altitude 1595 m above sea level and 9–11 km from Marvdasht city. The weather is very hot in the summer and cold and snowy in the winter. The major activities of the population are agriculture and animal farming.

Collection of rodents and preparation of smears

Rodents were captured monthly by Sherman live traps during October to December 2003 and April to October 2004. Traps were baited with roasted walnuts and placed in the active burrows. The traps were set in the early morning and evening once a month. Around 20–25 traps were used for each collection. Collected animals were transferred to the laboratory for preparation of smears from the ears or any suspected skin lesion of the animals. The prepared smears were stained with Giemsa and checked under light microscope for the presence of *Leishmania* parasites. Similar smears were prepared from the hand of 2 local cases of CL (a 5-year-old girl from Ghorban-Lak village

and a 15-year-old boy from Raja-Abad village). Identification was made using the standard reference for rodents in the Islamic Republic of Iran [*12*].

Extraction of DNA from positive smears of rodents

Total DNA was extracted from positive smears by digestion in lysis buffer. The dry smear was scraped with a sterile scalpel and dissolved in 200 µL buffer [50 mM Tris-HCL (pH 7.6), 1 mmol/L EDTA, 1% Tween 20] containing 8.5 µL proteinase K solution (19 µg/µL), in a 1.5 mL tube. The tube was incubated for 2 hours at 56 °C before adding 200 µL phenol–chloroform: isoamyl alcohol (25:24:1 by volume). After being shaken vigorously, the tube was centrifuged at 6000 × g for 10 minutes and then DNA was precipitated with 400 µL pure ethanol, re-suspended in 100 µL double-distilled water and stored at –20 °C before being used in PCR.

Nested PCR of minicircle kinetoplast (k) DNA for identifying *L. major*

The variable segment on minicircles of kinetoplast DNA from any *Leishmania* parasites present in the smear scraping was amplified using 2 rounds of nested PCR [*13*].

The primers were CSB1XR (CGA GTA GCAGAA ACT CCC GTT GA) and CSB2XF (ATT TTT CGC GAT TTT CGC AGA ACG) for the first round and LiR (TCG CAG AAC GCC CCT) and 13Z (ACT GGG GGT TGG TGT AAA ATA G) for the second round. Reference strains of *L. major* MHOM/IR/XX/LV114) and *L. tropica* (MHOM/IR/89/ARD22) from Tehran University of Medical Sciences were used as standards.

The first round reaction mixture contained 250 µmol/L deoxynucleoside-triphosphate (dNTP), 1.5 µmol/L $MgCl_2$, 1.0 U Taq polymerase, 50 mmol/L Tris-HCl (pH 7.6), 1% Tween 20, and 40 ng each of primers CSB1XR and CSB2XF, in a final volume of 25 µL. The DNA was amplified for 25 cycles in a Progen thermocycler (Thecne, Cambridge, UK) set to run at 94 °C for 1 min, 54 °C for 1 min, and then 72 °C for 1 min in each cycle.

The first round product (1.0 µL of a 9:1 dilution in distilled water) was used as template for the second round, in a total volume of 25 µL and under similar conditions to those for the first round except using LiR and 13Z as the primers.

Collection and dissection of sandflies

Sandflies were collected bi-weekly by an aspirator from indoor areas (guest rooms, sleeping rooms, latrines) and livestock stables, 2 hours after sunset during August and September 2004 (the main activity season of sandflies). Temperature and humidity were also recorded.

The collected sandflies were transferred to the laboratory and dissected in a drop of normal saline. For each female, the head with the 3 last segments of abdomen was cut and mounted in a slide with a drop of Puri medium for species identification. The remaining body parts of each specimen were transferred to a microtube filled with methanol 95% for DNA extraction and PCR examination.

Extraction of DNA and PCR of sandflies

DNA was extracted as described by Motazedian et al. [*14*]. Briefly, individual female, unfed and parous sandfly bodies were homogenized with a sealed pasture pipette in 1.5 mL tubes. Then 200 µL lysis buffer [50 µmol/L Tris-HCl (pH, 7.6); 1 µmol/L EDTA; 1% Tween 20] and 12 µL proteinase K (19 µg/mL) were added and incubated in 37 °C overnight before 300 µL

phenol–chloroform–isoamylalcohol (25:24:1 by volume) were added. After being shaken vigorously, the tube was centrifuged at 10 000 rpm for 10 min and then the DNA in the supernatant solution was precipitated with 400 µL cold, pure ethanol, re-suspended in 50 µL double-distilled water and stored at –20 °C before being used in PCR. Nested-PCR was employed for detection of *L. major* in sandfly specimens [*13*].

Results

Rodent and human cases

During this study 126 rodents were captured and identified as *Mer. libycus* (75.4%), *Microtus arvalis* (10.3 %) and *Cricetulus migratorius* (14.3%) (Table 1). Although all collected animals were examined for parasite infection under light microscope, amastigotes were only found in smears of 8 (8.4%) from 95 *Mer. libycus* (Table 2). Each infected *Mer. libycus* had at least 1 lesion either on an ear or at the base of its tail. Amastigotes from infected *Mer. libycus* were similar, with a mean diameter of 4 µm (Figure 1).

Parasite infection was observed among males and females animals from 2 of 3 study villages. In our study area, *Mer. libycus* had diurnal activity and each *Meriones* colony was around 2 m deep, with several burrow entrances.

All 30 smears from host and reservoir were amastigote-positive using microscopy. Out of 30 smears tested, 24 were from *Mer. libycus* and 6 from 2 local cases of ZCL, which were also shown positive for *Leishmania* DNA by PCR. For each PCR-positive sample, the second-round products of the nested PCR were identical to those of the *L. major* reference strain with a main band of 650 bp and distinct from those of the *L. tropica* standard with its main band of 750 bp (Figures 2 and 3).

Sandflies

A total of 200 parous, unfed female sandflies were checked by PCR for the presence of *Leishmania* parasite. They were *P. papatasi* (75%), *P. segenti* (15%) and *P. caucasicus* (10%). Among the examined sandflies, only 4 out of 150 *P. papatasi* (2.7%) were found naturally infected with *L. major* (Figure 3).

Discussion

Control of leishmaniasis in areas of endemicity requires a thorough knowledge of *Leishmania* ecology and epidemiology. There is a major problem for epidemiolo-

Table 1 **Density of collected rodents in Marvdasht rural district, Fars province, southern Islamic Republic of Iran, 2003–04**

Rodent species	Village			Total No.	%
	Raja-Abad No.	Ghorbanlak No.	Soltan-Velayat No.		
Meriones libycus	49	27	19	95	75.4
Cricetulus migratorius	9	5	4	18	14.3
Microtus arvalis	6	2	5	13	10.3
Total	64	34	28	126	100.0

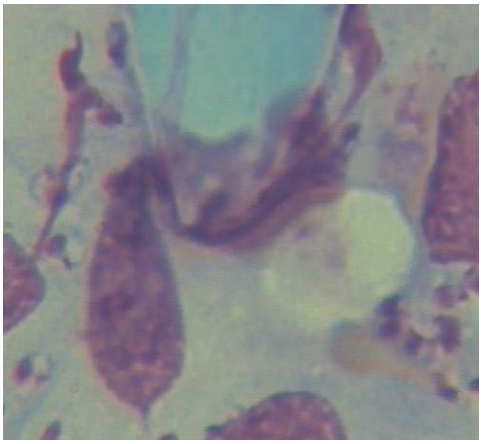

Figure 1 ***Leishmania major*** **amastigotes from smear of ear tissue in** ***Meriones libycus*** **stained by Giemsa**

gists both in the identification of reservoir hosts and in the detection of vectors.

The suggested criteria for incrimination of a vector are anthropophily and common infection with the same *Leishmania* parasite as that found in man in the same places [*15*]. Dissection of sandflies for detection of *Leishmania* parasite is difficult, and accurate estimates of infection are not possible [*16*]. Isoenzymes provide the gold standard for species identification and reference strains of *Leishmania* [*3*]. This method was used by Yaghoobi-Ershadi et al. [*8,17*] who identified single infections of the strain (zymodeme MON26) of *L. major* in *P. papatasi* and *P. caucasicus* in Isfahan province, central Islamic Republic of Iran [*8,17*]. However, this method has the disadvantage of requiring the culture of a large number of parasites, and primary isolates can easily become contaminated, or in mixed infection yield only the strain that grows fastest in laboratory conditions [*9*].

At the present time the applicability of molecular techniques (PCR) including kinetoplast DNA for detection and identification of *Leishmania* within sandflies by DNA hybridization has been demonstrated [*18–20*]. The highly sensitive technique of PCR has been used before for detecting *Leishmania* in sandflies of the new world [*21*], Islamic Republic of Iran [*9*] and India [*22*]. This is the first report of *P. papatasi* (collected from indoors) as a main and primary vector of *L. major* in the southern part of the Islamic Republic of Iran. The results of our study showed that nested-PCR is faster and more reliable for directly detecting *L. major* in wild populations of *P. papatasi* in comparison with other methods, i.e. dissection and isoenzyme techniques [*9,16*]. This species has been reported as a principle vector of ZCL transmitted to humans in other parts of the Islamic Republic of Iran [*8,9*].

Table 2 **Prevalence of leishmaniasis in captured rodents in Marvdasht rural district, Fars province, southern Islamic Republic of Iran, 2003–04**

Species of rodents	No. examined	No. positive	% positive
Meriones libycus	95	8	8.4
Cricetulus migratorius	18	0	0
Microtus arvalis	13	0	0
Total	126	8	6.4

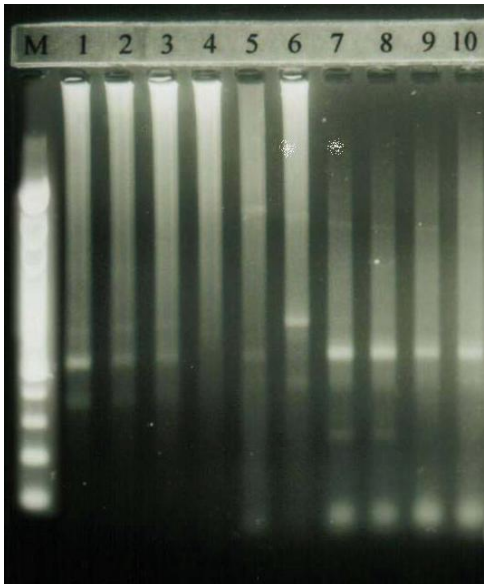

Figure 2 **Nested-PCR based amplification of DNA extracted from Giemsa-stained smears. The bands shown correspond to reference strains of** *Leishmania major* **(lane 1) and** *L. tropica* **(lane 6), molecular-weight markers (M) and smear samples of DNA from human skin lesions caused by** *L. major* **(lanes 2, 3 and 5); a human skin lesion caused by agents other than** *L. major* **(lane 4), and** *Meriones libycus* **skin lesions caused by** *L. major* **(lanes 7,8,9 and 10).**

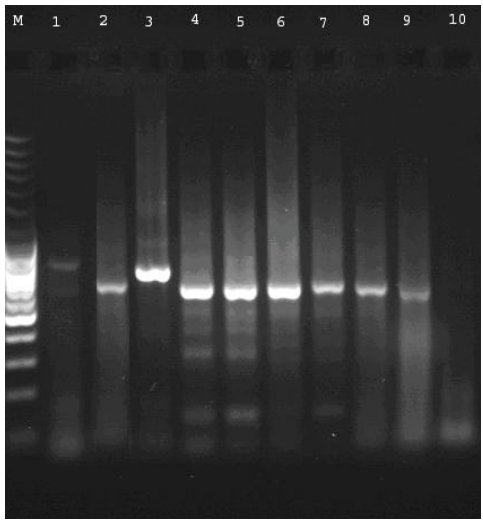

Figure 3 **Nested-PCR based amplification of DNA extracted from** *Phlebotomus papatasi* **and from Giemsa-stained smears. The bands, correspond to reference strains of** *Leishmania tropica* **(lane 1) and** *L. major* **(lane 2), molecular-weight markers (M)** *L. infantum* **(lane 3); a sample from infected** *P. papatasi* **(lane 4); a sample from uninfected** *P. papatasi* **(lane 10); a sample from infected** *Meriones libycus* **(lane 5); a sample from infected human (lane 6); two sample of infected** *Mer. libycus* **(lanes 7,8); and a sample from other infected human (lane 9).**

Another important finding of this survey was confirmation of *Mer. libycus* as a principal reservoir of ZCL in rural regions of Marvdasht focus. This rodent has been reported as a main reservoir in the foci of Arsanjan and Neiriz, adjacent to our study areas [*10,11*]. In the central and west of the Islamic Republic of Iran, *Mer. libycus* is a secondary reservoir host, where *R. opimus* and *T. indica* are present [*1,7*].

L. major has also been isolated from *Mer. libycus* in ZCL foci of Saudi Arabia [*23*] and Uzbekistan [*24*]. This animal is common and widespread in central and southern Islamic Republic of Iran. It seems that agriculture and rural development in many parts of this region will lead to more human contact with the rodent–sandfly–rodent cycle of *Leishmania* transmission.

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Dedication

This study is dedicated to our colleague and friend M.M. Gassemi who passed away in a car accident during this study.

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معالجة النفايات الطبية في مراكز الرعاية الصحية بالأراضي الفلسطينية المحتلة

عصام أحمد الخطيب

الخلاصة: تم تقييم معالجة النفايات الطبية في مراكز الرعاية الصحية الأولية، والثانوية بالأراضي الفلسطينية المحتلة. وقدر إجمالي كمية النفايات الطبية التي تخرج شهرياً من مراكز الرعاية الصحية بحوالي 512.6 طناً، وقد بينت النتائج أن 10.8% فقط من مراكز الرعاية الصحية تقوم بالفصل بين كافة أنواع النفايات الصلبة، بينما يقوم 15.7% مركز صحي بمعالجة النفايات الصلبة الطبية، وكان الحرق المفتوح لهذه الفضلات هو الوسيلة الرئيسية للمعالجة. وتبين نتائج هذه الدراسة تعرض الفلسطينيين إلى مخاطر صحية وبيئية من جراء الأسلوب غير السليم للتخلص من النفايات الطبية ، ولذا كان هناك حاجة لاتخاذ خطوات تعمل على تحسين الوضع من خلال سن القوانين وتنفيذها، وتوفير البنية التحتية الضرورية للمعالجة السليمة للنفايات مع تدريب العاملين ومن يتولون مهام النظافة في مجال الرعاية الصحية.

Medical waste management in healthcare centres in the occupied Palestinian territory

ABSTRACT Medical waste management in primary and secondary healthcare centres in the occupied Palestinian territory was assessed. The overall monthly quantity of solid healthcare waste was estimated to be 512.6 tons. Only 10.8% of the centres completely segregated the different kinds of healthcare waste and only 15.7% treated their medical waste. In the centres that treated waste, open burning was the main method of treatment. The results indicate that Palestinians are exposed to health and environmental risks because of improper disposal of medical waste and steps are needed to improve the situation through the establishment and enforcement of laws, provision of the necessary infrastructure for proper waste management and training of healthcare workers and cleaners.

Gestion des déchets médicaux dans les centres de soins de santé du territoire palestinien occupé

RÉSUMÉ La gestion des déchets médicaux dans les centres de soins de santé primaires et secondaires dans le territoire palestinien occupé a été évaluée. La quantité mensuelle globale de déchets solides d'activités de soins a été estimée à 512,6 tonnes. Seuls 10,8 % des centres procèdent au tri sélectif complet des déchets d'activités de soins, le traitement des déchets médicaux n'étant effectif que dans 15,7 % des centres. Dans les centres pratiquant le traitement de leurs déchets, le brûlage à ciel ouvert constitue la technique de prédilection. Les résultats révèlent que l'inadéquation des méthodes d'élimination des déchets médicaux expose les Palestiniens à des risques tant sanitaires qu'environnementaux. À l'évidence, des mesures doivent être prises pour améliorer la situation, à savoir instituer une législation spécifique et veiller à son application, créer les infrastructures nécessaires à une bonne gestion des déchets et former les personnels de santé et d'entretien.

معهد الصحة العامة والمجتمعية وكلية الهندسة، جامعة بيرزيت، فلسطين
البريد الإلكتـــروني: ikhatib@birzeit.edu
الاستلام: 14/05/06، القبول: 27/09/06

Issam A. Al-Khatib, Environmental Health Unit, Institute of Community and Public Health and Faculty of Engineering, Birzeit University, West Bank, Palestine.

المقدمة

تعتبر النفايات الطبية الناتجة عن الرعاية الصحية بالمرضى في مراكز الرعاية الصحية، أو المخلفات الطبية الناتجة عن عمليات التشخيص أو التحاليل الطبية والمختبرات الطبية وغيرها، جزءًا من النفايات الخطرة إن لم تعالج بصورة سليمة، وذلك بسبب ما تسببه من آثار سلبية على العاملين في المؤسسات الصحية، وفي المجتمع، وفي مجالات الصحة العمومية. فهذه النفايات تحتوي فيما تحويه على مواد معدية من ميكروبات وفيروسات سريعة الانتشار، وأدوات حادة ملوثة بسوائل المرضى، إضافةً إلى احتوائها على مواد كيماوية خطرة على الإنسان، مما قد يتسبب في حدوث طفرات وتشوهات للأحياء الموجودين بالبيئة المحيطة [1-3].

هنالك العديد من الأمراض التي يمكن أن تنتقل عن طريق النفايات الطبية مثل التهاب الكبد الفيروسي بي والتهاب الكبد الفيروسي سي والإيدز وغيرها من الأمراض، وذلك من خلال التعرض للإصابة بالجروح من الأدوات الحادة الموجودة في المخلفات الطبية، مثل الإبر الملوثة بدماء المرضى الحاملين لمثل هذه الجراثيم. ويجب أن تؤخذ هذه المخاطر بعين الاعتبار في نظام معالجة النفايات، الذي يتعين تطبيقه في مراكز الرعاية الصحية المختلفة، كما يجب العمل على الحد من هذه المخاطر. [5,4]. ولا يخفى أن الدول المتقدمة تنتج كميات من النفايات الطبية أكبر من تلك التي تنتجها الدول النامية، بسبب التكنولوجيا المستخدمة في المراكز الصحية المختلفة، مما يجعل النفايات الطبية مشكلة حرجة تحتاج إلى مزيد من الاهتمام. [6].

وأكثرُ من يتعرض بصورة مباشرة إلى هذه المخاطر هم العاملون في مراكز الرعاية الصحية، وعلى وجه الخصوص كل مَنْ يعمل في مجال التمريض، ثم يأتي بعد ذلك العاملون في مراكز الرعاية الصحية، وكذلك طاقم النظافة خارج المستشفى، بالإضافة إلى الزائرين لمراكز الرعاية الصحية والسكان المجاورين لأماكن التخلص النهائي من النفايات الطبية مثل المكبَّات، وأماكن معالجتها مثل المحارق [7-10]. وهناك مخاطر على الصحة العمومية وعلى البيئة تنشأ من خلال أساليب نقل النفايات الخطرة والمعدية، بالإضافة إلى ما ينجم عن ذلك من تلوث الهواء والماء والتربة.

وتوجد أشكال عديدة للنفايات الطبية فمنها نفايات صلبة وأخرى سائلة، ونفايات غازية وأخرى إشعاعية، إضافة إلى تنوع مصادرها. وتنتج هذه النفايات عادة من خلال أساليب وطرق المعالجة، والوقاية، والتشخيص، أو ما يجرى من بحوث في مجال الأمراض الخاصة بالإنسان أو الحيوان. وتنتج سنوياً كميات تقدر بملايين الأطنان من هذه النفايات الطبية، تخرج من مراكز الرعاية الصحية في العالم [11].

مصادر النفايات الطبية

تنتج النفايات الطبية بشكل عام من مصادر مختلفة، رئيسية كانت أم ثانوية، وذلك حسب الكمية المنتجة. ومن المصادر الرئيسية لهذه النفايات: المستشفيات بكافة أنواعها، كالمستشفيات الجامعية والمركزية وغيرها؛ والمراكز والعيادات التخصصية، مثل مراكز علاج العقم ومراكز علاج السل وغيرها؛ وخدمات حالات الطوارئ والإسعاف؛ والعيادات التخصصية المختلفة مثل عيادات الولادة وأمراض النساء، وعيادات الكشف الخارجية؛ ومراكز غسيل الكلى، وبنوك الدم، والمختبرات الطبية؛ ومراكز البحوث المتعلقة بالتقنيات الحيوية؛ وعيادات الأسنان، ومصانع الأدوية؛ والعيادات الخارجية؛ والعيادات البيطرية؛ والمعالجة داخل المنزل؛ والصيدليات؛ وغيرها.

تصنيف النفايات الطبية

يوجد العديد من النُظُم المستخدمة لتصنيف النفايات الطبية، وتمييز مكوناتها المختلفة، وهي نُظُم تختلف من بلد لآخر أو من مؤسسة لأخرى. وقد وضعت منظمة الصحة العالمية تصنيفاً خاصاً بالبلدان وذلك لأغراض عملية، يمكن تلخيصه في ما يلي [*12*]:

أ- نفايات طبية غير خطرة (نفايات عامة)

ب- أدوات حادة

ت- نفايات مسببة للعدوى (باستثناء الأدوات الحادة المعدية)

ث- نفايات كيميائية وطبية

ج- سائر النفايات الطبية الخطرة

هذا التصنيف الخاص بالبلدان النامية تم تقسيمه إلى خمسة أقسام حتى يسهل فصل النفايات الطبية، ثم تجميع كل شكل منها وتخزينها ونقلها في المؤسسة الطبية وخارجها. إذ إنه كلما ازدادت أشكال هذه النفايات ازدادت صعوبة فصلها وجمعها وتخزينها ونقلها. وهذا التصنيف يمكن اعتماده في المستشفيات الكبيرة. أما المراكز الصحية الصغيرة فيمكن تقسيم هذا التصنيف إلى قسمين فقط: نفايات طبية ونفايات غير طبية.

عناصر معالجة النفايات الطبية

تشمل معالجة النفايات الطبية بشكل أساسي سبعة عناصر هي: التمييز المناسب لأنواع النفايات الطبية وتوفير البنية التحتية لها، وفصل النفايات الطبية إلى مكوناتها الأساسية، وعادة يتم فصل النفايات الطبية عن النفايات العامة، والمعاملة (تشمل الجمع، والقياس، والتخزين، والنقل)، والمعالجة، والتخلص النهائي من النفايات الطبية بعد المعالجة، وتدوين المعلومات الخاصة بمعالجة النفايات الطبية، والتدريب.

ونظراً لتنوع أصناف النفايات الطبية الصلبة، فلا توجد طريقة واحدة مثالية لمعالجة كل النفايات الطبية، حيث يوجد هنالك العديد من البدائل والخيارات لإجراء هذه المعالجة، لكل منها مميزاته التي يتعين دراستها بالتفصيل قبل اختيار إحداها. فالاختيار يشمل النظر إلى تكلفة طريقة المعالجة ونفقات الصيانة والخدمات ، وفعالية المعالجة، والقدرة على إعدام النفايات، ومدى خطورة النفايات بعد معالجتها، وكمّ التلوث البيئي الناجم عنها [*13-18*]. وأهم الطرق المستخدمة في معالجة النفايات الطبية هي [*11*]: الحرق الآلي أو الترميد Incineration، والتطهير بالمُوْصَدَة Autoclaving، والتطهير الإشعاعي بالموجات الصغرية Microwave irradiation disinfection، والتطهير الكيميائي Chemical disinfection.

وتهدف هذه الورقة إلى إلقاء الضوء على واقع معالجة النفايات الطبية في الأراضي الفلسطينية المحتلة، من حيث كمية هذه النفايات ، وكيفية التعامل معها في المراحل المختلفة لمعالجتها من حيث طريقة الجمع، ووسائل النقل، والتخزين، والمعالجة، وكيفية التخلص النهائي منها.

المنهجية

تعتمد نتائج هذه الدراسة بشكل أساسي ما قام به الجهاز المركزي للإحصاء الفلسطيني من مسح بيئي لمراكز الرعاية الصحية [*19*]، وقد كان الهدف الأساسي من الاستفادة بهذه النتائج هو إمداد الباحثين بالإحصاءات. ولقد تم تحليل نتائج هذا المسح البيئي وخضع للعديد من المناقشات للخروج بوصف للوضع الواقعي لمعالجة النفايات الطبية في فلسطين.

ويشكل المجتمع الذي شملته الدراسة، جميع المؤسسات الحكومية التي تقدم خدمات الرعاية الصحية، والمؤسسات التابعة لمنظمات غير حكومية، والمراكز الطبية الخاصة التي تقدِّم هذه الخدمات. وقد بلغ حجم العينة 210 مركزاً من مراكز الرعاية الصحية التابعة للقطاع الخاص، و525 مركزاً من مراكز الرعاية الصحية التابعة للقطاعات الأهلية والحكومية والمنظمات غير الحكومية. أما إطار المعاينة للبيانات فقد جاء من مصدرين بحسب نوع مراكز الرعاية الصحية: (أ) الإطار الأول مراكز الرعاية الصحية الخاصة: وهي منشآت تم حصرها في التعداد العام في 1997، ثم بعد ذلك من خلال إجراء مسح في عام 2002، (ب) مراكز الرعاية الصحية الحكومية ومراكز الرعاية الصحية التابعة لمنظمات غير حكومية: ويشمل إطار المعاينة الثاني جميع المراكز العاملة في مجال الرعاية الصحية والتابعة للقطاع الحكومي أو لقطاع المنظمات غير الحكومية والذي يتم تحديثه بشكل سنوي من خلال السجلات الإدارية في الجهاز.

أما العينة فكانت عينات عشوائية طبقية ذات مرحلة واحدة، وقد تم تقسيم المؤسسات إلى نوعين: النوع الأول هو المؤسسات التي تم حصرها حصرًا شاملا (أي باحتمال 1)، وهي المؤسسات التي تقل عن 30 منشأة في الطبقة الواحدة، والمؤسسات الكبيرة من حيث عدد العمال (أي التي يزيد عدد العمال فيها على عشرين عاملاً). أما النوع الثاني فيتمثَّل في مؤسسات تم اختيارها بطريقة عشوائية منتظمة.

ولقد اشتملت استمارة المسح على بيانات مختلفة حول كمية المياه المستخدمة في مراكز الرعاية الصحية، ومعلومات حول المياه العادمة فيها، ومعلومات حول النفايات الطبية من حيث كميتها، وفصلها، ودورية جمعها، ونقلها، ومعالجتها. ولم يتم التطرق إلى المياه العادمة والمياه في هذه الورقة البحثية، وإنما كان التركيز على النفايات الطبية الصلبة فقط.

ولقد تم جمع البيانات من قبل فريق من الباحثين الميدانيين، تم اختيارهم من العناصر المؤهلة من العاملين في مجال العمل الإحصائي، ثم جرى تدريبهم على العمليات الميدانية المختلفة قبل البدء بتنفيذ المسح. ولقد تم تدقيق البيانات قبل إدخالها، ثم تم إدخالها، وتحليلها من خلال منظومة إحصائية تحليلية *(SPSS)*.

النتائج

كمية النفايات الطبية

تقدر كمية النفايات الصلبة الكلية الناتجة عن مراكز الرعاية الصحية في الشهر الواحد، بحوالي 512.6 طناً، منها 309 أطنان في الضفة الغربية، و203 أطنان في قطاع غزة. كما تقدَّر كمية النفايات الناتجة عن مراكز الرعاية الثانوية بـ 384.7 طناً؛ منها 184 طناً في الضفة الغربية، و164 طناً في قطاع غزة.

فصل النفايات الطبية

تبيَّن من النتائج أن 43.6% من مراكز الرعاية الصحية في الضفة الغربية وقطاع غزة، تقوم بعملية فصل لمكونات النفايات الصلبة الناتجة عن مراكز الرعاية الصحية؛ إذْ تقوم 75.3% من هذه المراكز بفصل بعض أنواع النفايات فحسب، في حين تقوم 24.7% منها بفصل كافة الأنواع. وبينت النتائج أن النفايات من الأدوات الحادة هي أكثر أنواع النفايات المفصولة في مراكز الرعاية الصحية التابعة للقطاع الحكومي أو التابعة للمنظمات غير الحكومية، حيث إن 40.2% منها يقوم بفصل هذا النوع من النفايات. والجدول رقم 1 يوضح التوزيع النسبي لمراكز الرعاية الصحية في الضفة الغربية وقطاع غزة.

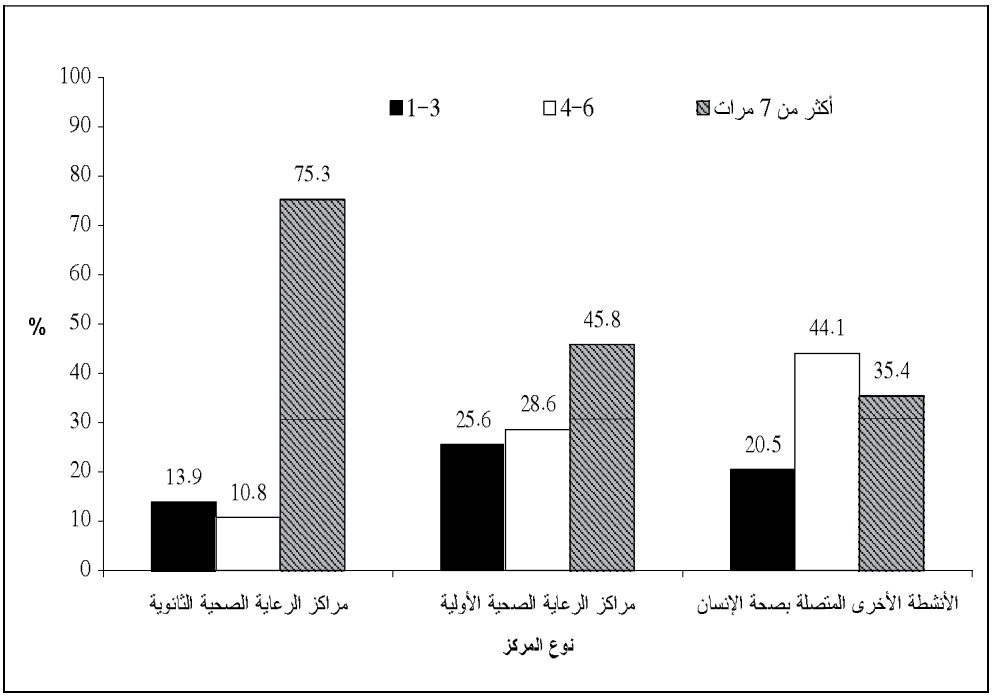
الجدول 1 **التوزيع النسبي لمراكز الرعاية الصحية في الضفة الغربية وقطاع غزة حسب توافر إمكانية لفصل النفايات الناتجة ونوعيتها قبل التخلص منها، والمنطقة، ونوع مركز الرعاية الصحية**

المنطقة ونوع مركز الرعاية الصحية	وجود فصل	نوع الفصل	
		كلي	جزئي
الضفة الغربية وقطاع غزة	**43.6**	**24.7**	**75.3**
مراكز الرعاية الصحية الثانوية	82.4	18.4	81.6
مراكز الرعاية الصحية الأولية	41.1	25.7	74.3
الأنشطة الأخرى المتصلة بصحة الإنسان	51.0	22.2	77.8
الضفة الغربية	**43.8**	**16.8**	**83.2**
مراكز الرعاية الصحية الثانوية	82.7	20.8	79.2
مراكز الرعاية الصحية الأولية	41.9	14.8	85.2
الأنشطة الأخرى المتعلقة بصحة الإنسان	47.6	26.9	73.1
قطاع غزة	**42.9**	**52.3**	**47.7**
مراكز الرعاية الصحية الثانوية	81.2	10.7	89.3
مراكز الرعاية الصحية الأولية	38.1	68.2	31.8
الأنشطة الأخرى المتعلقة بصحة الإنسان	59.9	12.1	87.9

معاملة النفايات الطبية داخل مراكز الرعاية الصحية

بالنسبة لدورية جمع النفايات التي يتم فصلها داخل المراكز، فقد بينت النتائج أن 46.8% من مراكز الرعاية الصحية التي تقوم بفصل النفايات الصلبة الناتجة عنها، تقوم بجمعها أكثر من 7 مرات أسبوعياً، و29.1% منها تقوم بجمعها من 4-6 مرات أسبوعياً، ويوضح الشكل (1) التوزيع النسبي لمراكز الرعاية الصحية، حسب دورية جمع النفايات التي يتم فصلها أسبوعياً، ونوع المركز.

أما من حيث كيفية نقل النفايات الطبية من مراكز الرعاية الصحية إلى مكان التخزين المؤقت خارج هذه المراكز، فقد تبيَّن أن معظمها تُنقل بشكل يدوي، إذ إن 95.9% من المراكز التي تقوم بفصل النفايات الطبية و96.2% من المراكز التي لا تقوم بهذا الفصل يتم فيها نقل النفايات بشكل يدوي، أما بقية المراكز فيتم فيها نقل النفايات الصلبة بواسطة عربات خاصة.



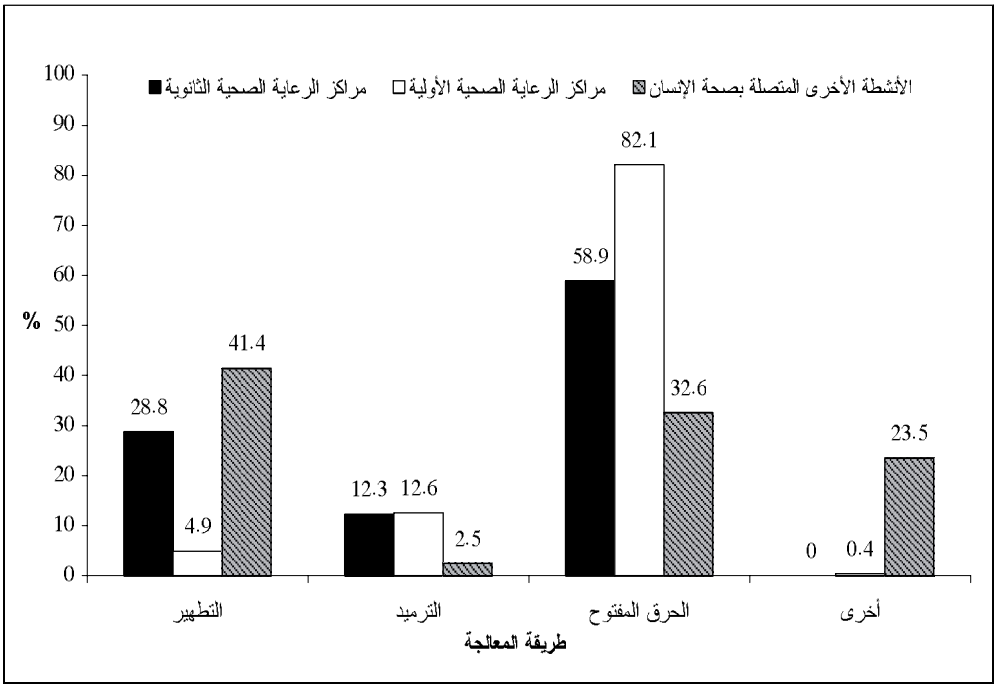
الشكل 1 **التوزيع النسبي لمراكز الرعاية الصحية، حسب دورية جمع النفايات المفصولة أسبوعياً، ونوع المركز**

معالجة النفايات الطبية

بلغت نسبة مراكز الرعاية الصحية التي تقوم بمعالجة النفايات الصلبة الناتجة عنها 15.7%، كما هو موضح في الجدول (2) والشكل (2)، وذلك بواقع 27.3% من مراكز الرعاية الثانوية، و13.9% في مراكز الرعاية الصحية الثانوية، و24.4% في المراكز الأخرى التي تمارس أنشطة أخرى متصلة بصحة الإنسان. أما بالنسبة لطرق معالجة النفايات ، فتبين أن طريقة الحرق تستخدم لمعالجة النفايات في 70.6% من مراكز الرعاية الصحية في الضفة الغربية وقطاع غزة، مقابل 13.8% تستخدم طريقة التطهير، و10.5% منها تستخدم طريقة الترميد للمعالجة. ويوضح الشكل (2) التوزيع النسبي لمراكز الرعاية الصحية حسب طريقة معالجة النفايات الصلبة الناتجة عنها ونوع المركز.

كذلك يوضح الجدول (3) الجهة التي تقوم بمعالجة النفايات الصلبة الطبية، حيث يلاحظ أن 77.3% من مراكز الرعاية الصحية التي تعالج النفايات الطبية، في الضفة الغربية وقطاع غزة، تقوم بعملية المعالجة بنفسها.

بعد تجميع النفايات الصلبة في سلال وحاويات داخل مراكز الرعاية الصحية، يتم تجميعها وتخزينها في مكان مؤقت، ومن ثم يتم نقلها إلى مكان التخلص النهائي منها، حيث تقوم 57.5% من مراكز الرعاية الصحية بتجميع النفايات الناتجة عنها في حاويات مكشوفة خاصة بالبلدية، و7.9% من المراكز تستخدم حاويات مغلقة خاصة بالبلدية، و3.4% من المراكز تستخدم حاويات مكشوفة خاصة بها، و3.2% من المراكز تستخدم حاويات مغلقة خاصة بها، و28.0% من المراكز لا تستخدم الحاويات في تجميع النفايات.



الشكل 2 **التوزيع النسبي لمراكز الرعاية الصحية، حسب طريقة معالجة النفايات الصلبة الناتجة عنها، ونوع المركز**

التخلص من النفايات الطبية

تقوم السلطة المحلية بنقل النفايات إلى مكان التخلص النهائي في 77.6% من مراكز الرعاية الصحية، في حين أن 18.9% من مراكز الرعاية الصحية تقوم بنفسها بنقل النفايات الناتجة عنها. كما أن مكان التخلص النهائي للنفايات بالنسبة إلى 93.0% من مراكز الرعاية الصحية هو مَكَبُّ السلطة المحلية، وهو مَكَبٌّ عشوائي في معظم الأحيان.

المناقشة

تنتشر مراكز الرعاية الصحية بين العديد من التجمعات السكانية في الضفة الغربية وقطاع غزة، وينتج عنها كميات كبيرة من النفايات الطبية الصلبة. ولكن النتائج تدل على ضعف واضح في أسلوب معالجة النفايات الطبية. إذ يلاحظ عدم وجود سياسة واضحة المعالم لفصل النفايات الصلبة للمراكز الطبية، حيث إن 10.8% فقط من هذه المراكز لا تقوم بعملية الفصل الكامل للنفايات الطبية، وبصفة عامة فإن سياسة الفصل تعبر عن مدى تقدم معالجة النفايات الطبية، ولها التأثير الرئيسي في خيارات المعالجة والتخلص من النفايات [*1، 18*]. وفي الأماكن التي تستخدم نظام فصل النفايات الطبية، تكون الكمية التي تفصل لأغراض الحرق كمية منخفضة، ومن ثم فإن التكلفة الإجمالية لمعالجة النفايات تجنح للانخفاض، وهذا يتناقض مع الواقع. ويلاحظ أن نسبة الفصل الكلي للنفايات الطبية في مراكز الرعاية أكبر في قطاع غزة منها في الضفة الغربية، إذ بلغت نسبة الفصل الكلي للنفايات الصلبة في المراكز التي تتبع هذا النظام في قطاع غزة وفي الضفة الغربية 52.3% و18.6% على التوالي.

الجدول 2 **التوزيع النسبي لمراكز الرعاية الصحية في الضفة الغربية وقطاع غزة حسب توافر إمكانية لمعالجة النفايات الصلبة، ونوعها، والمنطقة، ونوع مركز الرعاية الصحية**

المنطقة ونوع مركز الرعاية الصحية	وجود معالجة للنفايات الصلبة	نوع المعالجة							
		التطهير الكيماوي	التطهير الحراري	التطهير بالأشعة	الترميد	الحرق المفتوح	عزل إشعاعي	المعالجة الميكانيكية	أخرى
الضفة الغربية وقطاع غزة	**15.7**	**8.1**	**2.5**	**3.2**	**10.5**	**70.6**	**0.3**	**1.9**	**2.9**
مراكز الرعاية الصحية الثانوية	27.3	19.3	3.8	5.7	12.3	58.9	0.0	0.0	0.0
مراكز الرعاية الصحية الأولية	13.9	1.9	3.0	0.0	12.7	82.1	0.0	0.3	0.0
الأنشطة الأخرى المتعلقة بصحة الإنسان	24.4	27.3	0.0	14.1	2.5	32.6	1.3	8.1	14.1
الضفة الغربية	**17.1**	**8.8**	**2.7**	**3.8**	**11.2**	**69.5**	**0.3**	**0.3**	**3.4**
مراكز الرعاية الصحية الثانوية	17.9	11.3	0.0	11.3	0.0	77.4	0.0	0.0	0.0
مراكز الرعاية الصحية الأولية	15.4	2.2	3.5	0.0	13.8	80.1	0.0	0.4	0.0
الأنشطة الأخرى المتعلقة بصحة الإنسان	28.1	32.6	0.0	16.8	3.0	29.2	1.6	0.0	16.8
قطاع غزة	**11.0**	**4.4**	**1.2**	**0.0**	**7.1**	**76.8**	**0.0**	**10.5**	**0.0**
مراكز الرعاية الصحية الثانوية	57.2	27.2	7.6	0.0	24.7	40.5	0.0	0.0	0.0
مراكز الرعاية الصحية الأولية	8.6	0.0	0.0	0.0	5.0	95.0	0.0	0.0	0.0
الأنشطة الأخرى المتصلة بصحة الإنسان	14.5	0.0	0.0	0.0	0.0	50.0	0.0	50.0	0.0

ويلاحظ أن هناك نسبة لا بأس بها من مراكز الرعاية الصحية التي لا يتم فيها جمع النفايات بشكل يومي، مما يفاقم من مخاطر النفايات الطبية، لاسيَّما وأن معظم سِلال الجمع تكون مفتوحة، مما يؤدي إلى تواجد حشرات عليها قد تتسبب في انتقال ميكروبات بعض الأمراض إلى الأصحاء.

أما كيفية نقل النفايات الطبية من مراكز الرعاية الصحية إلى مكان التخزين المؤقت خارجها، فقد تبيَّن أن معظمها يتم بشكل يدوي، وهذا يتناقض مع السلامة المهنية لعمال النظافة الذين يقومون بنقل هذه النفايات، فالأصل أن يتم نقلها بواسطة عربات خاصة، حتى تبقى النفايات الطبية بعيدة عن أجسام عمال النظافة أثناء نقلها لتفادي تعرضهم لأي أذى. ففي إحدى الدراسات التي تمت في محافظة رام الله والبيرة من فلسطين، تبين أن 40.5% من عمال النظافة في المستشفيات قد تعرضوا للوخز بالإبر أثناء تعاملهم مع النفايات الطبية في المستشفيات، ويعود السبب الرئيسي في ذلك إلى عدم فصل النفايات الطبية من جهة، والنقل اليدوي لها من جهة أخرى [*20*].

الجدول 3 **التوزيع النسبي لمراكز الرعاية الصحية في الضفة الغربية وقطاع غزة حسب توافر إمكانية لمعالجة النفايات الناتجة، والجهة التي تقوم بالمعالجة، والمنطقة، ونوع مركز الرعاية الصحية**

المنطقة ونوع مركز الرعاية الصحية	وجود معالجة للنفايات الصلبة	الجهة التي تقوم بالمعالجة	
		المراكز نفسها	مؤسسات أخرى
الضفة الغربية وقطاع غزة	**15.7**	**77.3**	**22.7**
مراكز الرعاية الصحية الثانوية	27.3	72.7	27.3
مراكز الرعاية الصحية الأولية	13.9	75.6	24.4
الأنشطة الأخرى المتعلقة بصحة الإنسان	24.4	84.6	15.4
الضفة الغربية	**17.1**	**75.1**	**24.9**
مراكز الرعاية الصحية الثانوية	17.9	89.6	10.4
مراكز الرعاية الصحية الأولية	15.4	72.8	27.2
الأنشطة الأخرى المتعلقة بصحة الإنسان	28.1	81.6	18.4
قطاع غزة	**11.0**	**88.8**	**11.2**
مراكز الرعاية الصحية الثانوية	57.2	57.6	42.4
مراكز الرعاية الصحية الأولية	8.6	93.0	7.0
الأنشطة الأخرى المتعلقة بصحة الإنسان	14.5	100.0	0.0

ويلاحظ أن نسبة مراكز الرعاية الصحية التي تقوم بمعالجة النفايات الطبية الصلبة، هي نسبة منخفضة لا تزيد على 15.7%، وإن كانت نسبة المعالجة في مراكز الرعاية الصحية الثانوية أكبر منها في مراكز الرعاية الأولية، إلا أن هذه النسب تبقى متدنِّية جداً، لاسيَّما وأن النفايات الطبية غير المعالجة تحمل العديد من المخاطر لجميع من يتعاملون معها ولجميع العاملين داخل مراكز الرعاية الصحية، بالإضافة إلى الذين يقطنون بجوارها [*21*، *22*]، وكذلك فئات كثيرة من أفراد الشعب الفلسطيني.

وهناك مشكلة كبيرة في طرق معالجة النفايات الطبية المستخدمة، لاسيَّما وأن طريقة الحرق المفتوح هي الطريقة الرئيسية التي تستخدم لمعالجة النفايات، في 70.6% من مراكز الرعاية الصحية في الضفة الغربية وقطاع غزة. وهذه الطريقة غير سليمة ولها العديد من المخاطر، أهمها انبعاث الغازات السامة كالفرينز والديوكسين. والأصل هو استخدام أحد أشكال التكنولوجيا المناسبة لهذا الغرض، خاصةً وأن النفايات الطبية الصلبة توجد بأصناف مختلفة، وأنه لا يوجد طريقة واحدة مثالية لمعالجة كل النفايات الطبية [22]، حيث يوجد العديد من البدائل لمعالجة النفايات الطبية الصلبة، كل منها له مميزاته التي ينبغي أن تدرس بالتفصيل قبل الاختبار.

وبالرغم من استخدام ما نسبته 10.5% من المراكز التي تعالج النفايات الطبية لطريقة الترميد للمعالجة، وهي حرقٌ آلي منظم لمواد النفايات الصلبة في درجة حرارة مرتفعة، إلا أن هذه الطريقة ينتج عنها تلويث مباشر للهواء، خاصة وأنه لا يتوافر لها مَرَاشح (فلاتر) لتنقية الغازات الناتجة عنها [*18*]. وكل ذلك يؤدي إلى مخاطر صحية على المواطنين الذين يقطنون بالقرب منها.

أما بقية مراكز الرعاية الصحية التي تعالج النفايات الصلبة ونسبتها 13.8% ، فهي تستخدم طريقة التطهير، وهي قتل فعال عن طريق عمليات كيميائية طبيعية، لكل الكائنات الحية القادرة على التسبب في الأمراض المعدية [*22*]. وتعتبر هذه الطريقة مكلفة، وغير مناسبة لجميع أنواع النفايات الصلبة، إلا أنها سريعة المعالجة . ونظرًا لعدم وجود سياسة واضحة لمعالجة النفايات الطبية الصلبة ، فإن 77.3% من مراكز الرعاية الصحية تقوم بنفسها بمعالجة النفايات الصلبة الناتجة عنها، مما يزيد من نسبة تكاليف المعالجة.

إن عملية تجميع النفايات في الحاويات الخاصة بالبلدية والتي تتواجد عادة على الشارع العام أمر مخالف لشروط التخزين المؤقت، ويهدد الصحة العامة، والأصل أن تكون الحاويات مغلقة بشكل محكم كل الوقت باستثناء أوقات التعبئة أو التفريغ، وأن تكون في مكان مخصَّص لذلك، وأن لا يسمح لأحد بالدخول لمنطقة وجودها باستثناء المخولين للدخول. والأصل هو عدم تعرض الحاويات المخصصة للنفايات الطبية لمياه الأمطار، وأن تخضع المنطقة للرقابة والحراسة قدر الإمكان [*18*]. وكل ما ذُكر يتنافى مع وجود الحاويات مفتوحة على الشارع العام. وتزداد المشكلة حدّةً عندما يتم التخلص من النفايات مباشرة على الشارع العام دون وضعها نهائياً في حاويات، مما يسهل عملية العبث بها من قبل الأطفال، وغيرهم من العابثين، وكذلك الحيوانات. وكل ذلك يسهم إسهاماً كبيراً في انتشار الأمراض المعدية، وزيادة مخاطر النفايات الطبية على الصحة العامة والبيئة.

ونظراً لأن عملية تجميع معظم النفايات الطبية تكون في حاويات خاصة بالسلطات المحلية، فإن عمل نقل النفايات إلى مكان التخلص النهائي، تقوم بها السلطات المحلية. أما بالنسبة لمكان التخلص النهائي فهو مكبَّات عشوائية غير صحية، ومعظمها لا حماية له، مما يزيد من مخاطر النفايات الطبية، لاسيَّما وأن هناك العديد ممن يرتادون مكبات النفايات الصلبة للبحث عن أشياء ذات قيمة بالنسبة لهم كالنحاس والألمنيوم وغيرها. كذلك يرتاد مكبَّات النفايات العشوائية العديد من الحيوانات الأليفة، والحيوانات الضالة كالكلاب. وكل هذه الحلول غير مقبولة كلياً. فالطمر بدون اللجوء لمعالجة أولية خطر جداً، لأن احتمال تلوث التربة وتسرب السائل السام الصادر عن الطمر إلى خزانات المياه الجوفية كبير. ومن الجدير بالذكر أنه لا يوجد في الضفة الغربية وقطاع غزة أي مؤسسات متخصصة لديها تسهيلات أو وسائل ملائمة لمعالجة النفايات الطبية والتخلص منها.

ومن الجدير بالذكر أيضًا، أن تدوين المعلومات الخاصة بمعالجة النفايات الطبية غير وارد في المرحلة الحالية، في جميع مراكز الرعاية الصحية في الضفة الغربية وقطاع غزة، كما أن التدريب حول معالجة النفايات الطبية قليل جداً، ويكاد يقتصر على بعض المستشفيات.

الخلاصة والتوصيات

ويمكن الأخذ بالتوصيات التالية لتحسين هذا الوضع :

- ينبغي إعادة تقييم الوضع، والعمل على تعديله. ولا بد من إيجاد حل شامل ومتكامل لإدارة مشكلة النفايات الطبية، بمشاركة جميع الأطراف المعنية، وعلى وجه الخصوص وزارة الصحة، والسلطات المعنية بالبيئة، ووزارة الحكم المحلي، ووزارة التخطيط، وذلك بمشاركة مؤسسات المجتمع المدني وذوي العلاقة من أصحاب مراكز الرعاية الصحية الخاصة.
- ينبغي العمل على إيجاد سياسات، وتشريعات، وإرشادات، وربطها بالضرورات الفورية لفرز النفايات الطبية، ومعالجتها من المصدر. وينبغي أن يشتمل هذا الربط على تكنولوجيات ملائمة لتأمين الحماية المضمونة الاستمرار للبيئة، والصحة العامة.
- ينبغي وضع خطة شاملة ترتكز على حملات توعية شعبية، وحوافز مالية وتقنية، وفرز تطوعي، وتعزيز قانوني لمسؤولية المنتج.
- ضرورة التأكيد على عملية الفصل الفعالة في الضفة الغربية وقطاع غزة في أول مرحلة تنتج فيها النفايات؛ لأن ذلك أفضل طريقة لتخفيض كمية النفايات إلى الحد الأدنى، حيث يتم فصل المواد المختلفة عند مصدرها، وبذلك نمنع تلويث النفايات العادية بالنفايات الطبية.
- ضرورة التأكيد على أهمية جمع النفايات بشكل يومي، أو أكثر من مرة في اليوم، ولاسيَّما في فصل الصيف، وتحديدًا في مراكز الرعاية الصحية الثانوية التي تنتج عنها كميات كبيرة من النفايات الطبية.
- يفضل وجود معالجة مركزية يشرف عليها أشخاص مختصون، مما يسهل عملية المعالجة، ويزيد من فعاليتها، ويقلل من تكاليفها.
- ضرورة الابتعاد عن الحرق في الهواء الطلق، لأنه لا يمثل الحل الأمثل لمشكلة النفايات الطبية، ولأنه صورة بسيطة من صور انتقال الملوثات من النفايات نفسها عن طريق انبعاث الدخان والرماد.
- ضرورة البحث عن تقنيات بديلة سليمة بيئياً واقتصادياً، تفوق المحارق والحرق في الهواء الطلق، مثل استخدام التعقيم بالموصَدَة، مع وجود آلة لتقطيع النفايات الطبية، لإخفاء معالمها، ويمكن الاستفادة منها كذلك في معالجة العديد من المعدَّات الملوثة لإعادة استعمالها.

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Review

Khat (*Catha edulis*): health aspects of khat chewing

N.A.G.M. Hassan,[1] A.A. Gunaid[2] and I.M. Murray-Lyon[3]

الآثار الصحية لمضغ أوراق القات

نجيب عبد الجليل محمد حسن، عبد الله أحمد جنيد، إيان موري لايون

الخلاصة: هناك نسبة مرتفعة من السكان البالغين في اليمن ممن يمضغون أوراق نبات القات بصورة يومية، بالنظر إلى تأثيره المنبِّه الخفيف. ويُعتقدُ أن الكاثينون هي المادة الفعَّالة الأساسية الموجودة في أوراق القات الطازجة، وهي مشابهة، من حيث التركيب البنيوي والتأثير الدوائي للأمفيتامين. وتنتشر عادةُ مضغ أوراق القات انتشاراً واسعاً في اليمن، حيث تُعَدُّ من الموروثات الاجتماعية والثقافية المتأصِّلة، مما يجعلها تمثِّل مشكلة صحية عمومية. ويتمثَّل الغرض من هذا الاستعراض للمواد المنشورة في هذا المجال، في تفحُّص الدراسات التي أُجريت عن القات، ولاسيَّما الدراسات التي أُجريت على البشر، مع الإشارة بوجه خاص إلى تأثير ذلك على الجهاز العصبي المركزي، والجهاز القلبي الوعائي، والجهاز الهضمي، والجهاز التناسلي والبولي، وأنسجة الفم والأسنان، وأمراض السكَّري والسرطان.

ABSTRACT *Catha edulis* Forsk leaves (khat) are chewed daily by a high proportion of the adult population in Yemen for the mild stimulant effect. Cathinone is believed to be the main active ingredient in fresh khat leaves and is structurally related and pharmacologically similar to amphetamine. The habit of khat chewing is widespread with a deep-rooted sociocultural tradition in Yemen and as such poses a public health problem. The objective of this literature review was to examine studies on khat, particularly human studies, with special reference to its effect on the central nervous system, cardiovascular, digestive and genitourinary systems, oral–dental tissues, diabetes mellitus and cancer.

Le khat (*Catha edulis*) : effets de la mastication du khat sur la santé

RÉSUMÉ Les feuilles de *Catha edulis* Forskal, ou khat, sont mastiquées quotidiennement par une forte proportion de la population yéménite pour leur effet légèrement stimulant. La cathinone, structurellement apparentée à l'amphétamine et possédant des propriétés pharmacologiques comparables, semble être la principale substance active contenue dans les feuilles de khat fraîches. La pratique masticatoire du khat est très répandue au Yémen, où elle constitue une tradition socioculturelle profondément enracinée et, en tant que telle, soulève un problème de santé publique. La présente synthèse de la littérature a pour objectif l'analyse des études consacrées au khat, notamment à sa consommation humaine, avec une attention toute particulière sur son action sur le système nerveux central, les appareils cardiovasculaire, digestif et urogénital, les tissus bucco-dentaires, le diabète sucré et le cancer.

[1]Department of Clinical Pharmacology and Therapeutics; [2]Department of Internal Medicine, Al-Thawra Teaching Hospital, Faculty of Medicine and Health Sciences, University of Sana'a, Sana'a, Yemen (Correspondence to A.A. Gunaid: abdullahg@y.net.ye).
[3]Chelsea and Westminster Hospital, London, United Kingdom.
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Introduction

The khat plant *(Catha edulis* Forsk*)* is a tree of the family Celastraceae that is frequently cultivated in certain areas of East Africa and the Arabian Peninsula. The leaves of the khat plant contain alkaloids structurally related to amphetamine. They are chewed daily by a high proportion of the adult population in Yemen for the pleasant mild stimulant effect.

Khat appears to have been used first as a drink prepared from dry leaves, but its effect is weak compared with coffee [*1*]. It was found later that drying the leaves results in loss of some active constituents [*2*] and therefore the habit of chewing the green leaves was adopted. For many hundreds of years the custom of chewing khat leaves has been practised for the resulting central stimulant effects [*3*]. In Yemen, the habit is widespread with a deep-rooted sociocultural tradition. The pleasurable central stimulant properties of khat are commonly believed to improve work capacity, and are used on journeys and by students preparing for examinations and to counteract fatigue. In recent years, because of improved air transport, the consumption of fresh khat leaves has expanded considerably, even to communities in Europe.

Early clinical observation suggested that khat had amphetamine-like properties [*4*]. Subsequent chemical analysis confirmed that the fresh leaves contain a number of compounds, including phenylalkylamine compounds (alkaloids) such as norpseudoephedrine (cathine) and alpha aminopropiophenone (cathinone), the latter being structurally related [*5*] and pharmacologically similar to amphetamine [*6,7*]. Khat leaves also contain considerable amounts of tannins (7%–14% in dried material), vitamins, minerals and flavonoids [*4,8*]. Cathinone is currently believed to be the main active ingredient in fresh khat leaves [*7*].

Supporters of khat chewing claim that it is useful in diabetic patients because it lowers blood glucose, it acts as a remedy for asthma, it eases symptoms of intestinal tract disorders [*9*] and maintains social contact as a socializing herb [*10*]. Opponents claim that khat damages health and affects many aspects of life with its adverse social, economic and medical consequences. In Yemen, because of its widespread use, it has become a problem of grave national concern.

The objective of this review of the literature was to examine studies on khat, particularly human studies, with special reference to its effects on the body systems and its relationship with common diseases.

Khat and the central nervous system

The effect that accounts for the popularity of khat is its central nervous system stimulation, believed to be induced by cathinone, an active ingredient of khat leaves [*7*]. Cathinone has a more rapid and intense action compared with cathine due to its higher lipid solubility which facilitates access into the central nervous system.

Several studies have shown that the psychostimulant effects induced by chewing khat leaves include a moderate degree of euphoria and mild excitement resulting in promotion of social interaction and loquacity [*8,11,12*]. While attaining a state of subjective well-being, the chewers feel an increased alertness and energy together with enhanced depth of perception [*7,13*]. These effects were found to be maximum between 1.5–3.5 hours after starting to chew [*14*] and they were progressively replaced by mild dysphoria [*14*], anxiety, reactive

depression [*15*], insomnia [*4,16,17*] and anorexia [*17,18*].

These psychic effects of khat chewing recall those of amphetamine [*19*], but a major role of environmental factors in the expression of khat effects has also been suggested [*14*]. It has been proposed that the differences in the effect of khat and amphetamine are quantitative rather than qualitative [*20,21*]. It has been also reported that the khat-induced behavioural syndrome can resemble hypomania, as it may include hyperactivity and logorrhoea [*4*].

In recent years khat-induced psychosis has become more common in Europe [*22*]. Khat may cause a functional psychosis following consumption of exceptionally potent material, when taken in excess or in a predisposed individual [*4,23,24*]. In the literature reviewed, a number of reports on psychiatric disorders secondary to khat chewing with features of mania-like psychosis [*25*], schizophreniform psychosis [*26*], paranoid psychosis [*27*] or symptoms of acute schizophrenia-like psychosis have been documented [*11,26*]. Moreover, a number of chronic khat chewers experienced persistent hypnagogic hallucinations [*13*]. In one case report from the United Kingdom, khat appeared to induce full-blown paranoid psychosis with the added complication of a suicide attempt [*24*]. In Kenya, grossly excessive chewing led to psychotic states, which were paranoid in type and transitory in nature [*28*]. However, when khat is chewed in moderate quantities, there was no increase in psychiatric morbidity [*28*].

Preliminary data on 65 psychotic male patients admitted for psychiatric care in Sana'a because of symptoms uncontrolled by treatment were analysed [*29*]. They indicated that khat chewing in psychotic patients was likely to be associated with disturbance of mood and behaviour, aggravation of delusional symptoms and diminished response to antipsychotic therapy. Previous similar studies have shown that failure to abstain from khat use might prolong a psychotic episode, even during treatment with psychiatric medication [*11,24–28,30*].

Recently, Alem and Shibre considered khat as a substance of abuse and noted that chewing had the potential to complicate psychiatric conditions and forensic events [*30*].

In comparison with amphetamine, khat is much less likely to cause tolerance [*31*]. In particular, the stimulant central nervous system effects of khat do not seem subject to the development of tolerance [*4*], but some degree of tolerance to insomnia [*3*] and anorexia [*32*] has been observed in most chronic khat chewers.

The issue of dependence on khat has been reviewed by a World Health Organization (WHO) Expert Group on drug dependence, which concluded that khat consumption may induce a persistent psychic dependence rather than physical dependence [*22*] although a certain degree of psychological dependence can occur [*33*]. However, the psychological withdrawal symptoms after prolonged khat use seem to be limited to lethargy, mild depression, slight trembling and recurrent bad dreams [*4,31*]. The lack of physical symptoms of withdrawal suggest that only rebound phenomena rather than a specific abstinence syndrome occurs [*3,34*]. However, the WHO Expert Committee on Drug Dependence recently subjected khat to the preliminary review of psychoactive substances. The Committee reported that khat is believed to be dependence-producing and recommended that there was sufficient information on it to justify a critical review (a fully documented review) at a future meeting [*35*].

Khat use is often accompanied by the use of other substances. Simultaneous ciga-

rette smoking is a common habit that might influence khat-induced symptoms [*4*]. Khat-induced insomnia is frequent and khat users try to overcome this with sedatives or alcohol [*12*]. A report from Ethiopia confirmed the simultaneous use of cigarettes, alcohol, gasoline inhalation and glue sniffing with khat among university students, a pattern similar to that reported for substance abuse in other countries [*36*].

Khat and the cardiovascular system

Recent work on healthy Yemeni adult volunteers provided evidence that khat chewing induced a significant rise of arterial systolic and diastolic blood pressure and pulse rate in comparison with the baseline values [*37*]. The peak effect on the arterial blood pressure and pulse rate was reached 3 hours after starting to chew, followed by a decline 1 hour after spitting the leaves out. These changes run parallel with changes in plasma cathinone levels during and after khat chewing [*38*]. Similar blood pressure changes have also been observed in smaller numbers of subjects when pure cathinone in gelatine capsules was taken orally [*39*] or when khat leaves were chewed [*40*]. These observations support the suggestion that cathinone is the constituent that is mainly responsible for the increase in arterial blood pressure and pulse rate during khat chewing. A possible mechanism is the release of catecholamines from presynaptic storage sites.

To gain further insight into the pharmacological effects of khat chewing, a randomized controlled clinical trial of α_1 and selective β_1 adrenoceptor blockade was conducted on adult Yemeni volunteers [*41*]. The results indicate that selective β_1 adrenoceptor blockade with atenolol prevented the elevation of systolic blood pressure and increase in pulse rate suggesting these effects are mediated by the stimulant effect of cathinone in khat on β_1 adrenoceptors in the heart. By contrast the intake of indoramin, an α_1 adrenoceptor blocker, or placebo premedication failed to antagonize the effects of khat on arterial blood pressure or pulse rate.

It can be concluded from the previous studies that khat-induced blood pressure elevation is probably mediated at least in part through its cardiac action. Therefore, khat chewing carries a potential cardiovascular risk in patients with hypertension and heart disease [*41*], and may precipitate the occurrence of cerebrovascular accidents and myocardial infarction in susceptible individuals [*42*].

The effect of khat chewing on blood pressure and cardiac rhythm among Yemeni patients with hypertension and ischaemic heart disease was also explored using a 24-hour ECG Holter monitor and ambulatory blood pressure monitor [*43*]. The study showed a progressive increase in blood pressure and heart rate that occurred rapidly in the 1st hour of khat chewing; the peak effect was reached at the 2nd and 3rd hours and the blood pressure and heart rate values returned to their baseline values by the 4th or 5th hours after stopping chewing. The normal circadian rhythm and the nocturnal blood pressure drop were well preserved in khat-chewing hypertensive patients. The 24-hour Holter monitor revealed ischaemic changes (ST-segment depression) in 20% of patients with ischaemic heart disease and it was associated with sinus tachycardia and extrasystoles during khat chewing. β1 blockade with atenolol reduced the effect of khat on blood pressure and heart rate among a substantial number of patients with ischaemic heart disease and hypertension [*43*].

The role of khat chewing as a risk factor for acute myocardial infarction in Yemen was investigated by an experimental and clinical study. In the guinea pig, cathinone induced vasoconstriction of the coronary vascular bed which, unlike amphetamine, was not related to a sympathomimetic effect [*44*]. In humans, the circadian rhythm of the timing of acute myocardial infarction was shown to be influenced by khat chewing [*45*]. In non-chewers, there was a progressive increase in number of patients presenting with symptoms of acute myocardial infarction from 03:00 to 09:00 hours, and after 15:00 hours there was a gradual decline until there were none in the last 3 hours of the day. This confirms the previously noted rhythmicity in the timing of the onset of acute myocardial infarction which peaks in the early hours of the day. By contrast, the peak period of presentation of acute myocardial infarction in khat chewers was during the afternoon, commencing at 15:00 hours, continuing until 21:00 hours, and then declining to a trough at 03:00 hours. This finding illustrates the shift in the circadian rhythm of acute myocardial infarction presentation associated with khat chewing [*45*].

Khat and the digestive system

The effects of habitual khat chewing on the digestive system mentioned in older studies were based on the clinical observation that khat chewers often complained of symptoms suggestive of stomatitis, oesophagitis and gastritis. These effects were believed to be caused mainly by the strongly astringent tannins in khat [*17,46*].

Stomatitis is discussed later. Gastric symptoms were attributed to a hypotonic stomach resulting from the sympathomimetic action of cathine and its precursor [*17*]. Recent evidence has shown that khat chewing does indeed delay gastric emptying of a semi-solid meal, probably as a result of the sympathomimetic action of cathinone in khat [*19*]. Delayed gastric emptying may contribute to an increased rate of gastro-oesophageal reflux manifested as heartburn and acid regurgitation, and to an increased risk of Barrett oesophagus, a precancerous condition (see khat and cancer below).

Anorexia frequently follows a khat session and chewers seldom eat a further significant meal on the same day. A significant reduction of appetite after khat chewing was recently noted in a study on the subjective effects of khat chewing [*18*]. This anorectic effect is not due to an effect on ghrelin or peptide YY levels [*47*] but may be attributed to combined direct central and gastric effects of cathinone in fresh leaves of khat [*19*].

A common complaint of khat chewers is constipation, probably caused by a combination of the astringent properties of the khat tannins and the sympathomimetic properties of cathinone [*8*]. Habitual users try to attenuate this undesirable effect by food adaptation, notably by eating a meal with high fat content prior to the khat session in order to facilitate intestinal transit [*48*]. The constipating effect of khat was suggested by the observation that when a ban was imposed on khat in Aden in 1957, the sales of laxatives decreased by 90%, but returned to the original level soon after the ban was lifted [*4*]. Recent evidence has shown that chewing khat leaves significantly slows both the orocaecal transit time [*49*] and the whole gut transit time [*50*]. These 2 mechanisms may contribute to the constipating effect of khat. Moreover, khat chewing was found to interfere with the absorption of some orally administered antibiotics, particularly ampicillin [*51*] and tetracycline [*52*] resulting in low bioavailability. Khat chewing has no effect on gall bladder contraction [*53*].

The liver has been suspected to be particularly vulnerable to the harmful effects of khat use [*3,4*], and a disturbance in liver function and architecture has been described in experimental animals both on short-term [*54*] and long-term [*55*] feeding with *Catha edulis* leaves. Hepatitis B and C viruses are a cause of major health problems in Yemen; however, no significant relationship was found between hepatitis B surface antigen positivity and khat use in one study conducted in a rural community in Taiz province [*56*]. In a recent study on acute sporadic hepatitis in adults in Yemen, it was found that hepatitis viruses A to E accounted for only 48.7% of the cases, and in 51.3% of cases no viral cause was identified. There may be an unknown virus responsible or some environmental toxins, such as pesticides in khat leaves [*57*]. Certainly we have seen patients with abnormal liver function which resolved after khat chewing was suspended and a prospective study is underway.

Khat and the genitourinary system

One of the obvious side-effects of chewing khat leaves in males is temporary interference with micturition with hesitancy and poor flow. Overall urine flow rates were recently found to be significantly lower in khat users [*58*]. This effect is probably mediated through stimulation of α_1 adrenoceptors in the bladder neck by the sympathomimetic alkaloid cathinone. These effects were abolished by the α_1 adrenoceptor blocker, indoramin. The consumption of khat is also said to induce an increase in libido, spermatorrhoea and erectile dysfunction [*7*] but this has not been adequately studied.

Khat and fetal and neoatal health

In the domain of reproductive health, epidemiological data derived from 1181 deliveries in Yemen showed that at birth the mean weight of full-term single infants from mothers who chewed khat habitually or occasionally was below average [*59*]. A study on pregnancy outcome and khat showed a significantly increased incidence of low-birth-weight full-term infants among the offspring of women who chewed khat during pregnancy in comparison to those who were non-chewers during pregnancy [*60*].

Recent evidence indicates that neonates of mothers who chewed khat during pregnancy had a significant decrease in all neonatal parameters such as birth weight, length, head circumference and Apgar score at 1 and 5 minutes in comparison with those of mothers who did not chew khat during pregnancy [*61*]. This effect was found to increase in severity with the increased frequency and duration of khat chewing during pregnancy. Results obtained from the above-mentioned studies indicate that frequent use of khat during pregnancy may impair intrauterine fetal growth. An experimental study in rats has recently proved that khat can affect intrauterine fetal growth by reducing total fetal fat and weight and by inducing some changes in the chemical composition of fetal organs, particularly the liver, heart and kidneys [*62*]. This effect was attributed to depletion of carbohydrate material and suppression of DNA and protein synthesis in the fetal organs.

Nursing mothers in Yemen frequently complain of poor lactation. Some authors believe that this phenomenon may be related to the use of khat as cathine in khat

may inhibit prolactin secretion [*3*]. Interestingly, it has been found that the breast milk of khat-chewing mothers contains cathine, and this compound could even be detected in the urine of one breastfed infant [*63*].

Khat and diabetes mellitus

The effect of khat chewing in diabetic patients is unclear. The very few published papers on this issue make it difficult to draw a conclusion. Some authors believe that the overall effect of khat on diabetic patients is deleterious because the user is less likely to follow dietary advice, and the consumption of sweetened beverages with khat aggravates hyperglycaemia [*3*]. A clinical study was conducted on diabetic patients in Yemen over 20 years ago [*64*]. It showed that when khat-extract was mixed with the glucose given for the glucose tolerance test, there was a significant lowering of blood glucose level in comparison to the non-khat (control) arm of the experiment. This effect was attributed to delayed glucose absorption from the intestine by the action of khat tannins and inorganic ions, particularly magnesium, which produces a substantial inhibitory action upon gastrointestinal function. It seems that khat-induced delay of gastric emptying may also play a role in reducing postprandial hyperglycaemia in patients with type 2 diabetes mellitus [*19*]. By contrast, a similar study on nondiabetic subjects in Somalia showed that khat did not influence to any significant extent blood glucose levels in man [*65*].

Khat and cancer

Since khat use is widespread and often persists throughout adult life, a number of studies have been made on the toxicological aspects of habitual khat use. Owing to its mode of consumption, khat frequently affects the oral cavity and digestive tract. Its effect was found to be clearly dependent on the level of khat consumption [*7*]. Tumours of the oral cavity (lower maxilla, buccal mucosa and lateral surface of the tongue) were reported in 0.13% of patients seeking treatment over a 2-year period in a stomatology clinic in Hodeida, Yemen [*66*]. Most of them had been habitual khat chewers for more than 20 years, and some of them also chewed *shamma* (tobacco powder). A similar review of oral cancers presenting over a 2-year period in Asir region of Saudi Arabia showed strong circumstantial evidence linking the long-term use of khat with an increased rate of oral malignancies [*67*].

Tannins in khat can thicken the mucosa of the oropharynx and oesophagus [*68*] and may be carcinogenic [*69*]. A recent study in Yemen has shown that oesophageal and gastric carcinoma accounted for 6% of all patients who had an upper gastrointestinal endoscopy (183 out of 3064 patients) over a period of 1 year [*70*]. A preponderance of women with carcinoma of the mid-oesophagus was noted, which was previously only recorded in areas of high prevalence of oesophageal carcinoma. A high frequency of khat chewing and water-pipe smoking (*mada'a*) was found among both men and women and among a group with tumours of the gastro-oesophageal junction or cardia. This apparent association of khat with carcinoma of the lower oesophagus might be related to the khat-induced delay of gastric emptying with a subsequent increased risk of gastro-oesophageal reflux and Barrett oesophagus [*19*].

The effect of chewing khat on the mucosal histology of the upper gastrointestinal tract was explored in Yemeni patients presenting with dyspepsia [*71*]. Regular daily khat chewing was not associated with any major effect on the oesophagus or stomach

but duodenal ulcers were common in chewers. This may have been associated with the high prevalence of smoking in this group. Gastric-type mucosa at the lower end of oesophagus is thought to increase the risk of developing adenocarcinoma 30–125-fold. Although its presence was not related to the intake of khat, its overall prevalence in Yemeni patients was comparatively high (18%). To clarify this point, a case–control study on oesophageal carcinoma in Yemen is planned.

Khat and oral–dental tissues

The association with mouth cancer has been discussed earlier.

The adverse effects of khat chewing on oral–dental tissues were first observed by Laurent [*72*], Halbach [*4*] and Luqman and Danowski [*3*]. They reported that long-term khat chewing caused stomatitis followed by secondary infection. These might be related to mechanical strain on the cheek and other oral tissues as well as chemical irritation of the mucosal surfaces. A high rate of periodontal diseases and low rate of dental caries has been observed among male Yemeni khat chewers [*3*]. Mouth dryness, the major complaint following khat chewing, might be due to the sympathomimetic effect of cathinone and/or to excess secretion of saliva during chewing [*73*]. Hill and Gibson observed the effects on oral and dental tissue among Yemeni males with an average age of 35 years who chewed khat for of 20 years [*74*]. They found a low prevalence of caries, but universal attrition, temporomandibular joint pain and increased periodontal pocket depth on the khat-chewing side compared with the non-khat chewing side. They also reported increased keratosis on the buccal mucosa in 50% of the cases. In Kenya, Macigo and his colleagues showed that khat chewing was not significantly associated with leukoplakia compared with tobacco and alcohol consumption [*75*].

Recently, a cross-sectional hospital study among Yemeni khat and non-khat chewers showed an increased risk for a number of oral and paraoral lesions [*76*]. The study revealed that khat chewing caused many lesions to the supporting structures of the teeth, namely gingivitis, periodontal pocket formation, gingival recession, tooth mobility and tooth mortality. Khat chewing caused clicking and pain in the temporomandibular joints and led to attrition and staining of teeth and cervical caries, particularly among crystallized sugar consumers. Due to continuous mechanical friction and/or the chemical content, khat chewing caused white lesions on the buccal and gingival mucosa. Histopathological study revealed changes to the oral mucosa, such as acanthosis, papillomatosis, ortho- and para-keratosis and intercellular oedema, but not leukoplakia.

Concerning saliva and salivary glands, khat chewing results in mouth dryness, enlargement of salivary glands, inflammation and folding of the parotid papilla at the site of khat chewing. Khat chewing also causes obvious facial asymmetry of facial tissues.

Conclusion

To conclude, khat chewing appears to pose the following potential health risks.

- It may induce disturbance of mood (anxiety and/or depression, insomnia).
- In psychotic patients, it may aggravate thought disturbances (hallucination and delusions), induce aggressive behaviour and create difficulties in treating these patients.
- It may cause elevation of arterial blood pressure and pulse rate with subsequent

increased cardiovascular risk, particularly in hypertensive patients.

- It seems to be a common cause of stomatitis and other problems in the mouth as well as gastro-oesophageal reflux.
- It may be associated with increased risk of carcinoma of the mouth and oesophagitis.
- It may interfere with absorption of some orally administered antibiotics.
- It causes anorexia.
- It causes constipation.
- It may have a toxic effect on the liver, possibly as a result of pesticides used in khat cultivation.
- It is associated with an increased risk of low birth weight infants in khat-chewing pregnant women.

Recommendations

Since khat chewing is widespread in Yemen, the following actions are recommended.

1. Increase public awareness of the potential health hazards of khat chewing.
2. Support scientific research on khat in different institutions and universities to explore the different effects of khat on public health.
3. Integrate education about khat into the curricula of primary and secondary schools.
4. Legislate on the use of pesticides in the cultivation of khat in view of their potentially harmful effects on human health.

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Report

Tobacco control in Bahrain: an overview

I. Fadhil[1]

مكافحة التبغ في البحرين: نظرة عامة

ابتهال محمد فاظل الريفي

الخلاصة: بدأت مداخلات مكافحة التبغ في البحرين منذ أواخر سبعينات القرن العشرين، وبدأ سَنُّ التشريعات المتعلِّقة بالتبغ في عام 1994. ويعتمد أسلوب مكافحة التبغ على الاستراتيجيات الدولية المُوصَى بها من قِبَل مجلس التعاون الخليجي ومنظمة الصحة العالمية. وقد تمت مؤخراً مراجعة خطة مكافحة التبغ والتشريعات المتعلقة به، وطرحت خطة وطنية شاملة جديدة لتنفيذها من قِبَل وزارة الصحة. ويناقش هذا التقرير أسلوب مكافحة التبغ في البحرين، مع التركيز على التشريعات المتعلِّقة بالتبغ، وتدخين الشباب، وتدخين الشيشة، وترصُّد التبغ، وخطة الإقلاع عن التدخين. كما يناقش التقرير عدداً من التوصيات بُغْيَةَ التحسين.

ABSTRACT Tobacco control interventions in Bahrain started in the late 1970s and tobacco legislation was introduced in 1994. The tobacco control approach incorporated the international recommended strategies according to the Gulf Cooperation Council and World Health Organization. Recently the tobacco control plan and tobacco legislation were reviewed. A new national comprehensive plan is put forward for implementation by the Ministry of Health. This report examines the Bahrain tobacco control approach, focusing on tobacco legislation, youth smoking, waterpipe smoking, tobacco surveillance and the smoking cessation plan. A number of recommendations for further improvement are discussed.

La lutte contre le tabagisme à Bahreïn : synthèse

RÉSUMÉ À Bahreïn, les premières interventions contre le tabagisme ont été lancées dès la fin des années soixante-dix et la législation antitabac est entrée en vigueur en 1994. Cette politique de lutte contre le tabagisme a intégré les recommandations stratégiques, de portée internationale, émises par le Conseil de Coopération du Golfe et l'Organisation mondiale de la Santé. Le plan et la législation antitabac ont récemment fait l'objet d'une révision. Le Ministère de la Santé propose la mise en œuvre d'un nouveau plan global national. Le présent rapport analyse le plan d'action du Bahreïn contre le tabagisme, s'attachant tout particulièrement à la législation antitabac, au tabagisme chez les jeunes, à l'utilisation du narguilé, à la surveillance du tabagisme et au programme de sevrage tabagique. Différentes recommandations pour l'amélioration de certains aspects sont discutées.

[1]*Non-Communicable Diseases Unit, Ministry of Health, Manama, Bahrain (Correspondence to I. Fadhil: ifadhil@hotmail.com).*

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Introduction

Tobacco use has been identified as one of the major avoidable causes of morbidity and mortality in society [*1,2*]. Tobacco use is a known cause of cancer, heart disease, stroke and chronic obstructive pulmonary disease [*2*]. In Bahrain, despite decades of health promotion and tobacco control legislation, tobacco use is still prevalent among adults and teenagers.

The national family health survey in Bahrain in 1995 reported that the overall prevalence of smoking among Bahraini male adults was 22.8% and among adult females was 8.8% [*3*]. The latest global health professional survey in 2004 showed that 23.8% of Bahraini male physicians were cigarette smokers, while only 0.9% of Bahraini female physicians were smokers [*4*]. This is lower than earlier studies, in which 26.6% of male physicians and 6.9% of female physicians were smokers [*5,6*].

Moreover, the prevalence of smoking among youth appears to be rising [*7*]. Smoking among high-school males has risen from 14.8% in the early 1980s to 25.8% in the late 1990s, although the reasons for this increase are unclear [*8,9*]. In a more recent survey, 33.5% of young males and 11.9% of young females reported being smokers [*10*]. Smoking is prevalent among medical students, with 27.5% of male medical students and 2.3% of female students reporting being smokers [*11*].

The recent trend towards waterpipe smoking is also a source of concern. Anecdotal evidence suggests a rise in the prevalence of this type of tobacco use in Bahrain, particularly among women and teenagers. The prevalence of waterpipe smoking was 9.7% among Bahraini male physicians and 3.1% among Bahraini female physicians [*4*].

The aim of this report is to describe the tobacco control approach in Bahrain, focusing on tobacco legislation, youth and waterpipe smoking, tobacco surveillance, and smoking cessation, exploring the main limitations and suggesting action for further improvement.

Tobacco control strategy

The history of tobacco control in Bahrain dates back to 1978, when a number of control measures were implemented for the first time, including raising custom duties on cigarettes to 70%, regulating the permissible level of tar and nicotine per cigarette and restricting cigarette advertising. The following year (1979) a nongovernmental organization (NGO), the Bahrain Antismoking Society, was formed [*12*]. The society works in collaboration with the Bahrain government to advocate for tobacco control through prevention activities and lobbying for law review and law enforcement.

In 1994 a tobacco control decree was issued by the Emir of Bahrain to reinforce the antismoking measures [*13*]. It stated the following:

- No tobacco to be cultivated in Bahrain.
- Smoking to be banned in closed public transport and aeroplane flights.
- Smoking to be banned in closed public places, government institutions, hospitals, educational institutions and airports.
- No sponsorship by tobacco companies to be allowed for any kind of sports or competitions.
- No tobacco factories to be built.
- No vending machines for cigarettes to be allowed.
- No sale of tobacco to under 18-year-olds.

The law also called for the formation of a committee to include members represent-

ing different parties involved in the tobacco control plan. The National Tobacco Control Committee was established in 1995. The committee was headed by the Minister of Health and members of various ministries involved in tobacco control plus NGO representatives. The committee was assigned various responsibilities, such as identifying the upper limit for nicotine, tar and other toxic substances in cigarettes, limiting advertisements and putting warning signs on advertisements. Despite having been inactive from 1997 until 2005, the committee finally resumed its operation with new members.

It is worth noting that the tobacco control approach in Bahrain incorporates the Gulf Cooperation Council, World Health Organization and other internationally recommended strategies of legislation and health promotion. In general, primary prevention activities dominated the tobacco control plan in Bahrain. Activities such as media advocacy, school education and community awareness are dominant. The implementation plan is multisectoral, involving the Ministry of Health as the leader, plus other members (Ministry of Education, Ministry of Information, municipal government, NGOs, private companies, etc.).

In terms of tobacco research, Bahrain has participated in two global tobacco surveys, the Global Youth Tobacco Survey in 2003 and the Global Health Professional Tobacco Survey in 2002 [*10,14*]. In addition, a few local studies [*5,6,8,9,11*] and a national survey [*3,15*] have been carried out to assess the prevalence of smoking in Bahrain.

Bahrain participates at regional and international level conferences and meetings concerned with tobacco control and lately at the negotiations for the WHO Framework Convention on Tobacco Control (FCTC) [*16*]. However, as Bahrain hosts the Formula One motor racing sport, which is sponsored by the tobacco industry, ratification the FCTC has been delayed. The text is currently being submitted to a special ministerial committee for consideration and approval [*12*].

Youth smoking

Smoking uptake in youth is of particular concern for tobacco control programmers [*10,14*]. Data show that around three-quarters of ever-smokers, including current smokers and ex-smokers, reported that they started to smoke regularly between the ages of 15 and 18 years. A further 1 in 5 of these said they started to smoke before age 15 years [*14*].

Intervention directed at youth smoking in Bahrain is focused on risk awareness and education on the negative consequences of smoking. A number of school-based programmes have been implemented in recent decades, plus mass media messages and other community-focused programmes [*17*].

The latest survey among youth in Bahrain indicated that the prevalence of smoking is 33.5% among male high-school students and 11.9% among females (Table 1) [*10*]. The mean age at which smoking began has been reported to be 16.8 (SD 1.1) years [*8*]. The survey showed that over half (52.4%) of under-18-year-olds purchase their cigarettes from local stores, and 75.3% were not stopped from purchasing because of their age. With regards to mass media campaigns, it appears that 7 in 10 teenagers saw pro-tobacco messages in the media [*7*].

Based on the above data, it is evident that there has been a failure of tobacco legislation and there is a need to review the current strategies and legislative ac-

Table 1 **Percentage of students aged 13–15 years who use tobacco by sex from the Global Youth Tobacco Survey, Bahrain, 2003 [*10*]**

Variable	Males	Females	Total
Ever smoked cigarettes[a]	41.5	14.1	28.4
Currently smoke			
Any tobacco product	33.5	11.9	23.3
Cigarettes	23.1	4.6	14.3
Other tobacco products	24.9	10.6	18.2

[a]*Even 1 or 2 puffs.*

tion focused on youth smoking, and devise with new interventions. Evidence elsewhere shows that legislative strategies and penalties are important for reducing youth smoking [*18*]. This can discourage both uptake and continuation of tobacco use.

Waterpipe smoking

Smoking tobacco in a waterpipe (*shisha, nargile, hookah*) seems to be a rising trend among both sexes and teenagers and is a major concern to the public health system [*10,19,20*]. Anecdotal evidence in Bahrain indicates that waterpipe smoking has increased in popularity in Bahrain recently, particularly among women and teenagers. In contrast to cigarette smoking, waterpipe smoking has become an accepted social behaviour and has gained more public tolerance [*4*]. The majority of smokers believe that waterpipe smoking is not damaging to health and many cigarette smokers switch to the waterpipe while they attempt to quit [*21–23*].

There are few studies concerned with waterpipe smoking and its patterns and trends in Bahrain. Data from the national morbidity survey showed that waterpipe smoking is more prevalent among females (8.9%) compared with males (2.0%) (Table 2) [*24*]. The Global Youth Tobacco Survey showed that among young people the prevalence of tobacco consumption in the category "other tobacco products" was 18.2% [*10*]; this is likely to comprise mostly waterpipe use.

Tobacco market

Bahrain does not grow tobacco or manufacture cigarettes, and thus all cigarettes available in the market are imported, almost exclusively from Europe and North America. There are four main types of tobacco available in Bahrain (cigarette, waterpipe, cigar and pipe) and two types of tobacco are used in waterpipes (*narjeela* and *kadu*). Females smoke *narjeela* compared with males who commonly use *kadu*. The local

Table 2 **Type of smoking by sex from the National Morbidity Survey, Bahrain, 1981–83 [*15*]**

Type of smoking	Males		Females	
	No.	%	No.	%
Cigarette	981	27.7	19	0.5
Waterpipe	69	2.0	315	8.9
Cigar	3	0.1	0	0.0
Mixed	29	0.8	3	0.1
Non-smoker	2455	69.4	3211	90.5
Total	3537	100.0	3548	100.0

tobacco used in waterpipe smoking (*muasal*) is flavoured and processed in Bahrain. The popularity of Bahrain *muasal* is increasing in the local and regional market [*19,25*].

For cigarettes in Bahrain, by law the maximum permissible limits of nicotine, tar, and carbon monoxide are 0.6 mg, 10 mg and 12 mg per cigarette respectively [*26*]. However, the main challenge here is the absence of local resources to assess the required specification for the new type of imported cigarettes and tobacco, making it difficult to enforce the law in this area. Moreover, random checking on the cigarettes available in the local market is not in operation.

Reviewing the available data [*27*] and Ministry of Health reports [*28*] shows that periodic data on consumption, import and export of tobacco and on smoking locations are missing. Such information is critical for monitoring and evaluating the control plan. Thus, one of the first initiatives is to maintain an effective tobacco surveillance and reporting system with other ministries, such as the Ministry of Commerce, the Ministry of Education and other licensing bodies, such as the local municipality.

Legislative action

Despite the Emiri decree for tobacco control in 1994, law enforcement is weak in general, and special enforcement activities, such as conducting a regular retail compliance check or restrictions on advertising for tobacco and frequent checks on tobacco specifications, are not in operation. Although the 1994 law stated that Ministry of Health inspectors can issue an injunction for law breakers, since then, apart from three warning letters issued by the Ministry of Health, no injunctions have been issued.

Publicity in the media suggests that public pressure is growing against the harmful effects of second-hand cigarette smoke and the smoking of waterpipes in closed public places [*19,24*]. On the other hand, personnel shortages at the Ministry of Health have delayed action and the enforcement of the law in most cases. In addition, the current legislative charges imposed on companies who break the law are hardly significant in terms of business profit for these activities.

Smoking cessation plans

Interventions targeted at individual smokers are only part of the much broader spectrum of strategies to reduce the prevalence of smoking. A wide variety of smoking cessation programmes have been developed and studied over recent years. The two main interventions are pharmacotherapy and behavioural therapy. These contribute about equally to success in quitting. Most evidence indicates that a combination of both methods is the most effective intervention [*29*].

In Bahrain, an anti-smoking clinic was set up by the Bahrain Anti-smoking Society. However, as it operated on a voluntary basis it has been unable to maintain its services over time. In 2004 a smoking cessation clinic was set up by the Ministry of Health, but the clinic operates on a part-time basis on limited resources.

Nicotine replacement therapy and bupropion hydrochloride tablets are available in the local market; however, their use is very limited because they are expensive and the price is not subsidized.

Recently an attempt has been made to formulate national guidelines for smoking cessation [*30,31*]. Building local capacity with regards to smoking cessation interventions is still a big challenge. Affordability

and acceptability need to be addressed. The new tobacco control plan suggested by the Chronic Diseases Control Section of the Bahrain Ministry of Health recommended widening the smoking cessation services and integrating them into primary care services [*32*].

Training of health care staff on measures for dealing with smokers is being given priority. Recently a number of workshops organized by the Ministry of Health and NGOs focused on national capacity-building in tobacco control [Ministry of Health, Bahrain, Quit smoking workshop, unpublished, 2005].

Monitoring and surveillance evaluation

Ongoing surveillance will document any positive future changes. In Bahrain, tobacco use surveillance has been monitored through population surveys and tobacco-specific surveys; these include:

- Global Youth Tobacco Survey, 2003 [*14*];
- Global health professionals survey [*4*];
- Census data and health statistics;
- National family health survey, 1995 [*3*];
- National morbidity survey of 4.5% of the households in Bahrain [*24*].

Individual research has been carried out on different population groups (school-based youth tobacco surveys, surveys of adults, school administrators, teachers, opinion leaders and health care providers, etc.) [*5,6,8,10,11,33*].

Inconsistent methods and irregular survey intervals are two of the issues that have made it difficult to know exactly how smoking patterns are changing in Bahrain.

Furthermore, two significant challenges were noted. First, liaison with other ministries is weak regarding the tobacco market (import, export) and specific data on the amount of tobacco consumed, the type of tobacco permitted, the number of permitted smoking places and other tobacco-related activities. Thus, maintaining collaboration and proper reporting channels with other parties involved in tobacco control are being addressed. A special reporting format is been created and will be processed soon. This would allow for a proper surveillance system to be put in place. Second, baseline data on patterns and trends in waterpipe smoking and second-hand smoke are insufficient.

Giving the importance of the above data for monitoring the tobacco control interventions, further research is required.

Conclusion

Tobacco use still constitutes a public health problem in Bahrain and imposes a huge burden with its associated morbidity and mortality. Although tobacco legislation plays a major role in tobacco control policy, in Bahrain there exist two main limitations facing tobacco legislation: first, the failure to enforce the law in the majority of cases and a lack of qualified manpower to do this; second, the delay in ratification of the FCTC.

Upward trends in youth smoking prevalence highlight the need to diversify the approaches within the tobacco control plan. New legislation and enforcement of existing legislation take priority, and there is a need to reduce availability of tobacco products to young people and regulate supply. In addition, teenagers need an alternative to occupy their free time, particularly at school breaks; therefore it is highly recommended to provide special programmes focused on youth during the breaktime. The implemen-

tation of such programmes would minimize the peer pressure effect on tobacco intake.

The smoking cessation plan needs to be strengthened within the context of primary health care. However, implementation of a cessation plan requires adequate staff training and more resources, such as medication to support smokers who want to quit. It is essential as well to equip medical students and other health professional students with the skills to help smokers to quit smoking.

Implementation of a tobacco control plan is multisectoral, involving government and NGOs. Hence, it is recommended to maintain collaboration and surveillance through periodic reporting systems, with the Ministry of Health taking the leadership role. Data collated from various implementation agencies should be analysed and disseminated for policy use.

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Short communication

Health research priority setting in developing countries of the Eastern Mediterranean Region: partnering with The Cochrane Collaboration

Z. Fedorowicz,[1] E. Waters,[2] P. Tugwell[3] and M. Nasser[4]

تحديد أولويات البحوث الصحية في البلدان النامية في إقليم شرق المتوسط: الشراكة مع مؤسسة كوكرَن

زبش فيدوروفيتش، إليزابيث ووترز، بيتر تاغويل، منى ناصر

الخلاصة: تتَّصف بحوث الرعاية الصحية في إقليم شرق المتوسط بالتشتُّت، وفي أحيان كثيرة، بالضَعْف، مما يُظهر الحاجة إلى تبنِّي أسلوب مُنَسَّق لتعزيز الجهود في هذا المجال وتركيزها. ففي ضوء انخفاض الموارد، يأتي تحديد الأولويات كعنصر أساسي. وينبغي دعم سياسات وبرامج الرعاية الصحية في إقليم شرق المتوسط ببيِّنات موثوقة حول «ماذا يَصْلُحُ لِمَنْ، ولماذا؟»، مع إيلاء اهتمام خاص للاحتياجات الصحية للفئات المحرومة. ويُعَدُّ التعاون مع منظمات البحوث الصحية الدولية، مثل مؤسسة كوكرَن، أمراً أساسياً، إذْ أن من شأنه أن يتيح الفرصة لفحص البيِّنات، وتحديد الأولويات في ما يتعلَّق بمجالات المعرفة، والتعرُّف على الثغرات الموجودة في الأبحاث.

ABSTRACT Healthcare research in the Eastern Mediterranean Region (EMR) is fragmented and often weak. A coordinated approach is required to strengthen and focus efforts. Given the low resource base, priority-setting is an essential component. Healthcare policy and programmes in the EMR should be underpinned by reliable evidence of "what works for whom and why", with special attention to the health needs of the disadvantaged. Collaboration with international health research organizations, such as The Cochrane Collaboration, is essential and would provide an opportunity to examine evidence, prioritize knowledge areas, and identify research gaps.

Définition des priorités de la recherche en santé dans les pays en développement de la Région de la Méditerranée orientale : le partenariat avec *The Cochrane Collaboration*

RÉSUMÉ Dans la Région de la Méditerranée orientale, la recherche en santé est fragmentée et le plus souvent indigente. Une stratégie coordonnée s'avère indispensable pour concentrer et dynamiser les efforts. Compte tenu de la faiblesse des ressources disponibles, une définition des priorités s'impose. Dans la Région de la Méditerranée orientale, les politiques et programmes de santé doivent impérativement reposer sur une base solide et fiable que l'on peut résumer ainsi : "ce qui marche réellement, pour qui et pourquoi", en accordant une attention toute particulière aux besoins de santé des groupes défavorisés. La collaboration avec des organismes internationaux de recherche en santé, comme *The Cochrane Collaboration*, est cruciale et devrait fournir l'occasion d'évaluer les faits, de privilégier certains domaines de connaissance et d'identifier les lacunes de la recherche.

[1]*Bahrain Branch of the UK Cochrane Centre, The Cochrane Collaboration, Muharraq, Bahrain (Correspondence to Z. Fedorowicz: zbysfedo@batelco.com.bh).*
[2]*School of Health and Social Development, Faculty of Health and Behavioural Sciences, Deakin University, Burwood, Victoria, Australia.*
[3]*Centre for Global Health, Institute of Population Health, University of Ottawa, Ottawa, Ontario, Canada.*
[4]*The Cochrane Developing Countries Network, The Cochrane Collaboration, Tehran, Islamic Republic of Iran.*
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Introduction

Setting appropriate priorities for healthcare research should be an integral component of planning in developed and developing countries alike. However, other priorities all too often take precedence over this, especially in developing countries. Coupled with this, the generally lower levels of funding for healthcare research in developing countries may necessitate a more creative use of existing resources, including as wide a range of collaborative coalitions as possible. This paper makes recommendations for knowledge generation and knowledge application partnerships between developing countries in the Eastern Mediterranean Region (EMR), research organizations elsewhere and, in particular, The Cochrane Collaboration.

Research priority setting in EMR: What do we know already?

The development of healthcare research capacity in the EMR is constrained by factors that have been clearly articulated in the past: "inadequate political commitment; an unfavourable research environment; lack of leadership, and weak management and coordination of research; near absence of linkages and networking among scientists; poorly developed research capacity and inadequate resources" [*1*].

A recent analysis by the World Health Organization (WHO) of 5 developing countries in the EMR confirmed the fragmented and poorly coordinated status of their national health research systems and the wide variation in research priority setting among them [*2*]. The final report recommended that "the development of national health research systems will need to look beyond the Ministry of Health and/or the Department of Medical Research or Medical Research Council in terms of priorities or an agenda for action".

Methods and criteria that could be or are being used to prioritize research

A range of models has been designed for setting priorities for the allocation of health resources and the conduct of research. These have incorporated qualitative and quantitative methods, quantitative formulations, and prioritization matrices but not all have found wide acceptance in developing countries [*3,4*].

Decisions on priorities need to take account of the best available information, including an evidence-based situation analysis or context analysis, to help inform the process. Information needs to be gathered on population health status or burden of disease and contextual data regarding the healthcare system and health research system.

Developing capacity

If countries within the EMR wish to develop research capacity, build sustainable institutions and identify solutions to key national health problems, the research conducted must be grounded on robust scientific data on population morbidity and mortality, as well as the crucial evidence of what works, for whom, and why. Moreover, if the development of indigenous capacity for research in developing countries within the EMR ran in tandem with policies ensuring that research funding is allocated to addressing

local priorities (specifically the most important determinants of health), this might ensure that the limited expertise within these countries and the new expertise that will be created, is used to maximum benefit locally, In this way, priority setting would not only crystallize the immediate health goals but would also serve to empower, energize, retain and attract researchers.

Partnering with The Cochrane Collaboration to identify priorities for research and practice

The Ministerial Summit on Health Research in Mexico City in 2004, convened by the WHO, called for action by national governments to, "promote access to reliable, relevant, and up-to-date evidence on the effects of interventions, based on systematic reviews of the totality of available research findings" [*5*].

The Cochrane Collaboration is well placed to work with national governments to achieve this goal. The Collaboration is an international organization dedicated to improving health care for the world's population by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions. These high quality Cochrane reviews are available online in The Cochrane Library, and are being used increasingly by policy-makers in the developing world not only to make decisions about service provision but also to help set research priorities.

Systematic reviews allow one to examine what research has been done, where, and to what effect. They can underpin decision-making about healthcare interventions and research because they summarize large amounts of information, identify beneficial, harmful or unproven interventions, and highlight gaps in research.

Recent initiatives within The Cochrane Collaboration are of increasing relevance to developing countries; for example the Developing Country Network and the Cochrane Health Equity Field & Campbell Equity Methods Group whose mandate is to ensure that reviews relevant to lower- and middle-income countries, including EMR countries, apply an "equity lens" that ensures the results relate to the disadvantaged. These entities are developing further methods of examining equity in evidence on the effects of interventions, in addition to ways of integrating differing methods, thereby answering the "for whom and why" elements of what works [*6*]. This builds on the Collaboration's commitment to engage with the generators and users of research in developing countries, and now is an ideal time to combine this work with the establishment of a priority-driven approach to health research in the EMR.

Therefore, given the limited resources currently available to prepare and maintain systematic reviews, there is an urgent need to identify the priorities for this form of research. These reviews will clarify the benefits and harms of interventions studied in randomized trials, and identify the gaps and priorities for further trials in the EMR.

We believe that priorities for future health research should be based on the most important gaps in current knowledge in the relevant part of the world. We propose that the following approach be integrated into regional planning.

1. Analysis of the relevant health burden, using the burden of disease approach, in the context of equity and health inequalities.

2. Systematic reviews of the evidence on the effects of interventions, relevant to the health outcomes sought in the region, with special attention to the disadvantaged.
3. Consultation on a process of identifying the matches and gaps, with the aim of undertaking a priority setting exercise to:
   - identify priority topics for Cochrane systematic reviews
   - examine processes within the agency and among agencies for funding relevant new research.
4. Undertaking of a process of knowledge translation for dissemination to, and engagement with, users and key stakeholders, with a strategy to update this at least every 5 years.

Conclusion

We contend that this approach has the potential to make a meaningful difference to people in the EMR, whilst allowing the countries of this Region to develop and retain the capacity to set their own research priorities.

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Case report

Pseudomonas stutzeri: a rare cause of neonatal septicaemia

C.S.S. Bello[1]

Introduction

Gram-negative sepsis is a life-threatening disease especially in an already debilitated patient. The presence of Enterobacteriaceae or any Gram-negative bacteria in the bloodstream may lead to endotoxic shock, systemic disease and multiple organ failure.

The pseudomonads are among the most common organisms causing nosocomial infections [*1*]. Although *Pseudomonas aeruginosa* is by far the most commonly isolated species, several other species are occasionally isolated from clinical human specimens as opportunistic pathogens, such as *P. stutzeri* [*2*]. *P. stutzeri* was recently isolated in a newborn pre-term baby in our hospital. This is the first time this organism has been isolated in our laboratory over the past few years. The organism was almost discarded as a plate contaminant, but for its unusual features. It is being reported here in order to alert microbiologists to be vigilant concerning such unusual organisms so that they are not missed and that prompt and appropriate antibiotic therapy can be instituted.

Case report

T.B. was a male twin delivered in our hospital by emergency caesarean section on 16th December, 2004. The mother was 34 weeks pregnant and had had pre-eclampsia and premature rupture of the membranes for 8 hours before she underwent caesarean section. The babies' presentation was breach.

At delivery, baby T.B. weighed 1.8 kg. On examination, he was pink and cried normally. His Apgar scores were 6/1 and 8/5. He had mild tachypnea. His heart sounds I and II were normal and there were no murmurs. No abnormality was found in his chest, his abdomen was soft, not distended, and there was no organomegaly. His hip joints were normal. The second twin, a female, was normal. Because of the baby's tachypnea, neonatal sepsis was suspected.

The following investigations were carried out: complete blood count (CBC), chest X-ray, erythrocyte sedimentation rate, blood and urine culture, electrolytes, C-reactive protein, TORCH (*Toxoplasma gondii*, other microorganisms, rubella virus, cytomegalovirus and herpes simplex virus) and occult blood. The baby was then started on intravenous ampicillin 45 mg every 12 hours (which was increased to 90 mg every 12 hours after 48 hours) and intravenous amikacin 13.5 mg every 12 hours.

Blood culture was performed in the BACTEC 9240 blood culture system. After 48 hours, the machine indicated a growth, which on Gram stain showed Gram-negative bacilli. A subculture was done as well as direct sensitivity testing using the

[1]*Abha General Hospital, Abha, Saudi Arabia (Correspondence to C.S.S. Bello: cssbello@hotmail.com)*
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disc-diffusion technique. The organism was sensitive to all routine antibiotics for Enterobacteriaceae. It grew well on blood agar, Mueller–Hinton agar and on MacConkey agar as a non-lactose fermenter. It was motile and oxidase positive. It grew at 42 °C but not at 4 °C. The colonies were dry, wrinkled and brownish in appearance. If not for the good growth on MacConkey agar, it could pass for a contaminant, such as aerobic spore-bearers. When attempts were made to make new smears and suspension for biochemical tests, removing the colonies from the plates proved difficult. This aroused further suspicion. After much difficulty, a few colonies were removed for Gram-stain, oxidase test and biochemical tests with the API system (bioMérieux, France). The next day, API reactions were all negative. It was thought that this might be due to insufficient organisms in the suspension used.

A repeat API was done and the result came out the same as before. Meanwhile, a preliminary report was sent to the nursery as Gram-negative bacilli, possibly *Pseudomonas* species, sensitive to both amikacin and ampicillin, which the baby was being treated with. After 3 unsuccessful attempts at identification using the API system, the isolate was sent to the Aseer Central Hospital for identification using the Microscan system (Dade Behring, West Sacramento, USA). After 48 hours the organism was identified as *P. stutzeri*, sensitive to a large number of antibiotics.

The results of the other investigations carried out were as follows: blood urea nitrogen 3 mg/dL (low) (normal 6–20); sodium 135.3 mmol/L (low) (normal 136–145); total bilirubin 9.38 mg/dL (high) (normal 0.00–1.00); direct bilirubin 0.39 mg/dL (high) (normal 0.00–0.30). The results of the remaining tests were normal.

The baby was continued on amikacin plus ampicillin since the organism was sensitive to both agents. He made rapid progress and the results of the repeat tests were all normal within 2 weeks. The antibiotics were discontinued after 10 days of therapy. Repeat blood cultures were carried out on days 13 and 15 and were both negative. The baby was discharged home 1 week thereafter. Before discharge, the electrolytes became normal, haemoglobin was 13.4 g/dL, white blood cell count was $9.1 \times 10^3/\mu L$ and platelets $411 \times 10^3/\mu L$.

Discussion

P. stutzeri group of pseudomonads consists of 3 organisms: *P. stutzeri*, CDC group Vb-3 and *P. mendocina* [*3*]. Among this group, *P. stutzeri* is the most frequently encountered in clinical specimens. A review of the literature shows that *P. stutzeri* is most frequently isolated from blood, wounds, the respiratory tract and urine [*4*]. *P. stutzeri* has distinctive features. On sheep blood agar, strains appear buff to brown in colour with dry, wrinkled, tough and adherent colonies. The adherence of *P. stutzeri* makes the removal of colonies from agar medium difficult. Because of the difficulty in making suspensions of specific turbidity, identification and susceptibility systems do not work well with this organism [*3*]. However, *P. stutzeri* may be identified using the following criteria: presence of oxidase, ability to oxidize but not ferment dextrose, growth on MacConkey agar and demonstration of motility by polar flagella [*5*].

P. stutzeri is a ubiquitous organism found in soil, water and the hospital environments [*5*]. It is a saprophytic microorganism that rarely causes severe infections [*6*]. Isolation of *P. stutzeri* indicates contamination or

colonization in hospitalized patients. However, patients with *P. stutzeri* infections have generally been found to have serious underlying diseases or predisposing risk factors such as haemodialysis [*1*], meningomyelocele [*6*], human immunodeficiency virus infection [*7*] and chronic obstructive pulmonary disease [*8*]. All isolates to date have responded well to a wide range of antibiotics including the aminoglycosides, the antipseudomonal penicillins, trimethoprim–sulfamethoxazole and the third generation cephalosporins [*4,5*]. The isolate from our patient was sensitive to all of these drugs.

Whenever a laboratory encounters an unusual organism such as this, every effort should be made to identify it, including sending it to the nearest reference centre. Besides, every clinical isolate must be correlated with the patient's symptoms before arriving at a decision.

Samples were taken from the baby's intravenous fluid and line, suction machine, cot, surrounding floor and walls, the sink, and attending physicians and nurses but none of these grew *P. stutzeri*. The mother however was not sampled due to cultural practices in our area. However, the twin sister who was also admitted into the nursery at about the same time for observation was free of the organism. Although we were unable to identify the exact source of the organism, the probability of the organism coming from the mother's vagina cannot be excluded, with acquisition by the baby during parturition. This view is supported by an earlier report from this hospital by Asindi et al. [*9*] on neonatal sepsis in pre-labour rupture of membranes.

At the same time, given that *P. stutzeri* is an environmental organism, attending healthcare workers should be reminded to observe strictly infection control guidelines, especially scrupulous washing of hands.

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Infant and meonatal health and development

A healthy start in life is important to every newborn baby. The first 28 days, the neonatal period, is critical. It is during this time that fundamental health and feeding practices are established. It is also during this time that the child is at highest risk for death.

One of the aims of the Infant and Neonatal Health (HNI) team within the WHO Department of Child and Adolescent Health and Development (CAH) is to reduce infant mortality and to ensure that newborns and infants have the opportunity for a healthy start in life. Further information about the work of the team can be found at: http://www.who.int/child-adolescent-health/OVERVIEW/HNI/neonatal.htm

Letter to the Editor

Spontaneous splenic rupture in a pregnant Sudanese woman with falciparum malaria: a case report

Sir

In Sudan, 13.7% of women attending antenatal care are reported to have *Plasmodium falciparum* malaria, irrespective of age or parity, some of them severe cases [*1*]. Malaria can have serious adverse effects on pregnancy, e.g. low birth weight and maternal anaemia, and is the leading cause of maternal and perinatal mortality in Sudan [*2–4*].

Splenic rupture can occur with any degree of trauma to a normal spleen or a minimal trauma to a diseased spleen. To be labelled as spontaneous, the splenic rupture should not be associated with any degree of trauma or evidence of gross pathology at the time of exploration [*5*]. A high index of suspicion of splenic rupture is imperative because delay in diagnosis may lead to catastrophic consequences. Therefore, preoperative diagnosis and rapid intervention are important.

A 29-year-old pregnant Sudanese woman presented to New Halfa Teaching Hospital, Sudan with a history of fever, headache, backache, sweating, nausea and abdominal pain for 18 hours. She was in her 3rd pregnancy (parity 2) and the 26th week of gestation. There was no history of trauma, her pulse was 110/min, blood pressure was 100/60 mmHg, she was pale and her temperature was 38.7 °C.

A Giemsa-stained peripheral blood film confirmed the provisional diagnosis of falciparum malaria. The haemoglobin level was 6.8 g/dL and the total white blood cell count was 6800 cells/μL. The presence of distended, tender abdomen with absent bowel sounds, plus her pregnancy, necessitated urgent ultrasound that revealed a single viable baby with upper segment placenta and 22 cm splenomegaly and free fluid in the peritoneal cavity.

Laparotomy revealed an enlarged spleen with several tears. An emergency splenectomy was performed and no other abnormalities were seen. The patient received 2 L of blood and quinine 30 mg/kg daily for 7 days and 1 g of ceftriaxone intravenously. She was discharged after 8 days in good health and seen every 15 days in the antenatal clinic until delivery. She delivered vaginally at 39 weeks gestational age and the outcome was a male with birth weight 2.8 kg.

This patient presented with large ruptured spleen that was most likely due to the falciparum malaria. Spontaneous rupture of the spleen is an extremely rare complication of falciparum malaria [*6*].

In the New Halfa area of eastern Sudan it has been previously documented that *P. falciparum* is the predominant malaria species in the area, which is characterized by high antimalarial drug resistance [*7*]. Thus malaria should be remembered among the causes and differential diagnosis of splenic rupture. These other causes include: haematological disorders (e.g. haemophilia, haemolytic anaemia), metabolic disorders (e.g. amyloidosis, Wilson disease), drug-induced disorders (e.g. due to heparin and warfarin), vomiting, uraemia, systemic lupus erythaematosus and infectious mononucleosis which is considered the most common cause of spontaneous rupture of the spleen [*8*].

Emergency splenectomy was performed for this patient and this is the standard management. However, a more conservative approach in selected cases has been reported [9].

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I. Adam
Department of Obstetrics and Gynaecology, Faculty of Medicine University of Khartoum, and Academy of Medical Sciences and Technology, Khartoum, Sudan (Correspondence to I. Adam: ishagadam@hotmail.com).

E.S. Adam
New Halfa Teaching Hospital, New Halfa, Sudan.

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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. وتقدَّم الطلبات للحصول على المزيد من النسخ، أو على معلومات حول الأسعار، إلى رئيس التحرير.

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Livre : Al Hamza B, Smith A. *The fifth sign of identity*. Cairo, American University Press, 1990.

Article de Revue : Jones A et al. One day in Tibet. *Journal of tautology*, 1993, 13(5):23–7.

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Correspondence

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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

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