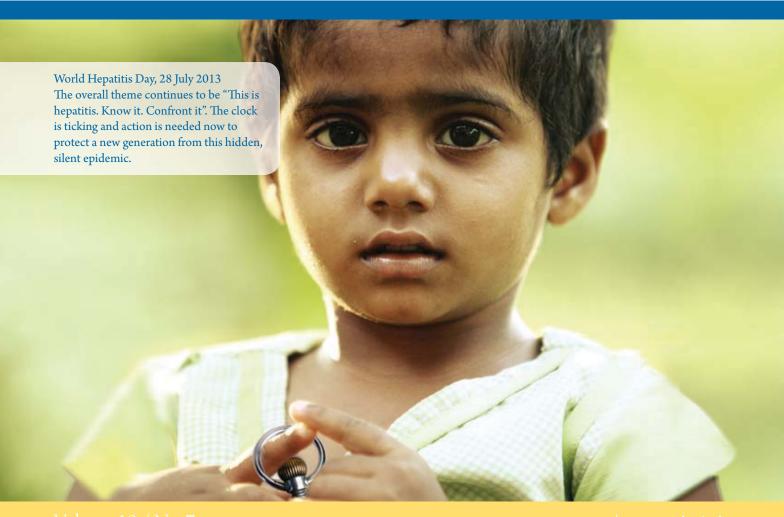




# **EMHJ**

Eastern Mediterranean Health Journal

La Revue de Santé de la Méditerranée orientale



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هى المجلة الرسمية التى تصدر عن المكتب الإقليمي لشرق المتوسط بمنظمة الصحة العالمية. وهي منبر لتقديم السياسات والمبادرات الجديدة في الخدمات الصحية والترويج لها، ولتبادل الآراء والمفاهيم والمعطيات الوبائية ونتائج الأبحاث وغير ذلك من المعلومات، وخاصة ما يتعلق منها بإقليم شرق المتوسط. وهي موجهة إلى كل أعضاء المهن الصحية، والكليات الطبية وسائر المعاهد التعليمية، وكذا المنظات 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 ser-vices 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



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**Editorial** 

# Hepatitis B infection in Eastern Mediterranean Region: challenges and the way forward

Huma Qureshi1

In all the countries of the World Health Organization's (WHO) Eastern Mediterranean Region (EMR), hepatitis B infection is endemic [1]. In low-risk countries, hepatitis B infection occurs in teenagers and young adults as a result of risky behaviours. Effective vaccination, better blood screening and proper sterilization/disinfection has contributed considerably in its control [2]. In endemic countries, including EMR countries, however, the infection tends to occur in infants and children from maternal-fetal transmission, close contacts from persons nursing the infected patient's wounds and the percutaneous route (unsafe injections, improperly sterilized invasive medical devices and improperly screened blood transfusions) [3,4]. Unfortunately in endemic countries, the disease in children is generally unrecognized because the signs and symptoms are negligible. These cases are unlikely therefore to be recorded in the surveillance data. As a result, endemic countries bear the brunt of hepatitis B infection as adult chronic disease, cirrhosis and its complications and hepatocellular carcinoma [5].

According to WHO and the Centers for Disease Control and Prevention (CDC) [1], the major interventions that can control the spread of hepatitis B include: a) Hepatitis B vaccination (universal immunization of all neonates, catch-up vaccination of all children who have missed the universal vaccination and vaccination of high-risk groups); b) Safe blood transfusion; c) Injection safety; d) Infection control including

hospital waste management; and e) Surveillance for new cases.

Routine infant immunization programmes will ultimately achieve a wide coverage and increased immunity in the population and hence prevent disease spread and the chronic complications of hepatitis B infection [6]. Reduction in the prevalence of hepatitis B infection has already been reported from many highly endemic countries after the launch immunization programmes [7–11].

Protective antibody titres ( > 10 IU) are achieved after vaccination which fall after some time but antibodies are boosted following exposure to hepatitis B virus [12,13]. Antibody titres generally remain viable for 15 years and to date a booster dose is not recommended. Maternal—fetal transmission to infants born to HBsAg positive mothers can be drastically reduced with the administration of hepatitis B immune globulin (HBIG) and hepatitis B vaccine given at different sites [14] within 24 hours of birth [12].

The cost of treatment of hepatitis B infection and its complications is huge and cost—benefit studies show vaccination to be very cost-effective, even in low-endemic counties when compared with the treatment costs and life lost. However, although the cost of each hepatitis dose is less than US\$ 1, with 3 doses the overall cost is higher when compared with the other 6 vaccines recommended by WHO and given through the Expanded Programme on Immunization (EPI) [12] and this is a concern of many developing countries.

While hepatitis B vaccine has been introduced into EPI in all countries of the Region except Somalia and South Sudan, only 14 countries give a dose at birth. Nonetheless, over 85% of infants born in the Region have received 3 doses of hepatitis B vaccine [3] although some countries are reporting low figures [15]. As well as infant immunization, WHO recommends vaccination of high-risk groups, such as health care workers; however, in most EMR countries health workers are either not vaccinated or not fully vaccinated [16,17].

An issue of concern in EMR countries is the viability of the vaccine at high temperatures as in most EMR countries, temperatures in summer reach 40 °C and higher. Fortunately, the hepatitis B vaccine is thermostable and remains effective for 1 week at temperatures of 45 °C and for 1 month at 37 °C [12].

The challenges for hepatitis B vaccination in EMR are to achieve > 95% coverage in all neonates and to administer catch-up vaccination to those not yet covered and adult vaccination of highrisk groups, such as health workers. Each country should examine the reasons for low coverage at birth and address the issues accordingly and implement catch-up vaccination at schools, work places and homes. High-risk groups in particular need to be identified, motivated and vaccinated.

For countries with unregulated blood banking, a national strategy should be implemented on a priority basis with standardization of testing kits. Unnecessary therapeutic injections should be discouraged by improving people's perception about injections.

Surveillance of hepatitis should be added in the health information and management system of EMR countries

to identify new cases arising in the population as the ultimate aim is to stop emergence of new cases.

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**Editorial** 

## Hepatitis C in the Eastern Mediterranean Region

Gamal Esmat<sup>1</sup>

Hepatitis C virus (HCV) infection is still one of the major causes of mortality and morbidity worldwide and is the main cause of liver cirrhosis, hepatocellular carcinoma and liver transplantation in developing countries [1]. The World Health Organization (WHO) has estimated a 3% worldwide prevalence of the virus affecting more than 170 million people worldwide [2].

A clear geographical distribution of the virus exists due to many factors. The Middle East region is the geographical area traditionally consisting of southwest Asia and parts of North Africa. This area shows a heterogeneous distribution of HCV with at least 23 million people estimated to have HCV infection in the countries of the Eastern Mediterranean Region of WHO [3]. This is close to the number of infected people in the Americas and Europe combined. The average overall prevalence in most countries of the Region ranges from 1% to 2% with the exception of Egypt which is considered to have the highest prevalence worldwide with an estimated 14.7% of the total population seropositive for HCV [4,5]. The epidemic of HCV in Egypt is always explained by the previous long use of parenteral antischistosomal treatment campaigns for more than 30 years; this could explain in the higher rates in the age group 40–60 years in comparison with younger age categories [6]. No published data are available about the prevalence and risk factors of HCV transmission in some countries of the Region.

HCV has six major genotypes and the genetic diversity of HCV has been clearly linked to the geographic distribution of the virus in different populations, as well as in specific risk groups. Genotype is of clinical importance because of the impact it may have on the response to the current standard therapy for HCV, combined pegylated interferon and ribavirin. Genotype is also considered to be an important epidemiological marker as it may help trace the sources of infection and elucidate the possible modes of transmission [7]. The genotypes of HCV in Middle East countries take two main distribution patterns; the first is limited mostly to the Arab countries (except Jordan) with genotype 4 being predominant. The other pattern which exists in non-Arab countries (Islamic Republic of Iran, Israel and Turkey) is characterized by the dominance of genotype 1 [8]. Although varying prevalence rates of genotype 4 have been reported in the Arab countries, it is noteworthy that genotype 4 is quasi-exclusive (93%) in Egypt [9]. Jordan, the Arab country that is the exception to this rule, shows a heterogeneous distribution of genotypes with 1a the dominant subtype (40%), followed by 1b (33.3%) and genotype 4 (26.6%) [10]. A clear indication of the existence of the 2 patterns of genotypes in Middle East countries came from a study conducted to investigate genotypes of HCV in the Gaza Strip and southern Israel. The most common genotypes found were type 1b (62%) in southern Israel and type 4 (78%) in the Gaza Strip, which is the same dominant genotype in Egypt [11]. Both prevalent genotypes in the region (4 and 1) were considered the genotypes most difficult to treat in terms of response

to the standard therapy. Since the development of new antiviral drugs and the approval of these drugs for managing genotype 1, response to treatment has improved for this genotype, leaving genotype 4 the most resistant type to treat [12].

The most challenging obstacles to managing HCV are the continuous transmission of infection due to lack of effective infection control measures and prevention programmes as well as the high cost of treatment. The financial burden of treatment in the Region is problematic in view of the limited resources of many of the countries. The expected directly acting antiviral drugs could add more to this in the near future. An example of a relatively integrated programme for managing HCV came from Egypt. In 2006, the Egyptian authorities launched the national control strategy for managing viral hepatitis. The programme aimed to improve access to HCV treatment through a specialized network of viral hepatitis treatment centres covering the entire country and providing antiviral treatment at very affordable prices to people in need. Despite success in improving access to treatment and delivery of treatment to almost 200 000 people in the past few years, more programmes for preventing transmission and optimizing the treatment strategies provided are needed [13].

HCV remains a considerable challenge in the Middle East region imposing both a health and a financial burden and more efforts are required to highlight the problem and augment both prevention and treatment programmes.

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# Prevalence of hepatitis B and C virus infections and their related risk factors in Libya: a national seroepidemiological survey

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معدل انتشار العدوى بفيروسات الالتهاب الكبدي "بي" و"سي" وعوامل الاختطار ذات الصلة بها في ليبيا: مسح وطني مصلي وبائي عبد الناصر الزوكي، محمد نجيب أسميو، محمد صمود، عمر الأحمر، محمد ضوّ، عبد الرحمن فرارة، عبد الخفيظ أبو ظهير، مصطفى كهال محمد

الخلاصة: أشارت التقارير إلى وجود معدلات انتشار مرتفعة للعدوى بفيروسات الالتهاب الكبدي "بي" و"سي" بين مجموعات معينة من المرضى في ليبيا، فأجرى الباحثون مسحاً تم تصميمه للتعرف على مدى اتساع نطاق المشكلة على المستوى الوطني. وقد طبق الباحثون تصميماً للعينة المتعددة المراحل التي تغطي جميع المناطق الإدارية في ليبيا، وشملت العينة أكثر من 65000 فرد من جميع المجموعات العمرية. وقد أخذت عينات الدم من جميع المرضى، مع استكهال الاستبيان حول المعطيات لعوامل الاختطار الديموغرافية والسلوكية. واتضح أن معدل انتشار المستضد السطحي للالتهاب الكبدي "سي" 12.3٪، وأن معدل انتشار الضد المضاد للالتهاب الكبدي "سي" يزداد الكبدي "بي" 2.2٪، ومعدل انتشار الضد المضاد للالتهاب الكبدي "سي" يزداد بتقدم العمر، وأنه يزداد تدريجياً بعد عمر الثلاثين عاماً، وفي المقابل فإن المستضد السطحي للالتهاب الكبدي "بي" ثابت في جميع المجموعات العمرية التي تزيد على العاشرة من العمر. أما عوامل الاختطار المعدَّلة حسب العمر للعدوى بفيروس الالتهاب الكبدي "سي" فهي الإدخال السابق إلى المستشفى، والعمليات الجراحية، ونقل الدم السابق، وتعاطي المخدرات بالحقن، ولم يتعرف الباحثون على عوامل الاختطار المرافقة للعدوى بفيروس الالتهاب الكبدي "بي" سوى التعرض الأسري أو مخالطة حالة مصابة بالعدوى بفيروس الالتهاب الكبدي "بي" سوى التعرض الأسري أو مخالطة حالة مصابة بالعدوى بفيروس الالتهاب الكبدي "بي".

ABSTRACT A high prevalence of hepatitis B (HBV) and C virus (HCV) infections has been reported among specific patient groups in Libya; a survey was thus designed to determine the extent of the problem at the national level. A multistage sampling design covering all administrative areas of Libya was applied, covering > 65 000 individuals of all age groups. All subjects gave a blood sample and completed a questionnaire on demographic and risk behaviour data. The prevalence of HBV surface antigen (HBsAg) and anti-HCV were 2.2% and 1.3% respectively. The prevalence of anti-HCV increased with age, rising gradually after age 30 years, in contrast to a stable prevalence of HBsAg in all age groups 10+ years. Age-adjusted risk factors for HCV infection were previous hospitalization, surgical operations, previous blood transfusions and intravenous drug use; for HBV infection only family exposure or contact with HBV case were identified.

## Prévalence des infections par les virus de l'hépatite B et C et des facteurs de risque associés en Libye : enquête séro-épidémiologique nationale

RÉSUMÉ Une forte prévalence des infections par les virus de l'hépatite B et C a été signalée dans des groupes de patients spécifiques en Libye et une enquête a par conséquent été préparée pour évaluer l'étendue du problème à l'échelle nationale. Un plan d'échantillonnage à plusieurs degrés couvrant toutes les zones administratives de Libye a été appliqué, impliquant plus de 65 000 personnes de tous les groupes d'âge. Tous les sujets ont fourni un échantillon de sang et rempli un questionnaire concernant leurs données démographiques et leur comportement à risque. La prévalence de l'antigène de surface du virus de l'hépatite B (AgHBs) et des anticorps anti-hépatite C était de 2,2 % et 1,3 % respectivement. La prévalence des anticorps anti-hépatite C augmentait progressivement avec l'âge, enregistrant une progression à partir de 30 ans contrairement à la prévalence de l'AgHBs qui restait stable dans tous les groupes d'âge de plus de dix ans. Les antécédents d'hospitalisation, d'interventions chirurgicales, de transfusions sanguines et de consommation de drogue par voie intraveineuse étaient les facteurs de risque corrigés selon l'âge pour une infection par le virus de l'hépatite C, alors que pour l'infection par le virus de l'hépatite B, une exposition familiale ou le contact avec un cas infecté étaient les seuls facteurs identifiés.

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#### Introduction

Hepatitis B virus (HBV) and C virus (HCV) infections are a major global public health problem warranting high priority efforts for prevention, control and treatment [1,2]. In developing countries the mode of transmission of these 2 bloodborne viruses tends to be from perinatal transmission or household contacts, while in developed countries sexual contact, shared needles among intravenous drug users and contaminated blood or organ transplants are more likely to be responsible for transmission. However, screening tests have reduced dramatically the risk of transmission worldwide [3-5].

Libya, a developing country of approximately 6 million people, belongs to the intermediate endemicity countries with a wide variance of seropositivity among different regions and populations. Previous studies of blood donors from serum screening in Libya revealed prevalence rates varying between 1.9%-5.8% for HBV and 1.2%-7.9% for HCV [6-11]. In one of these studies, a high prevalence of HCV infection in the apparently healthy Libyan population was reported (7.9%) [9]. Nosocomial outbreaks of multiple bloodborne viral infections was reported in 2001 by Yerly et al. involving approximately 400 children. While all were infected with HIV, coinfection with HCV or HBV was found in 47% and 33% respectively after testing a subgroup of 148 children [10]. The prevalence of HCV antibodies among different populations in 1999–2001 was found to be 1.6% among healthy adults, 1.2% among blood donors, 2.0% among hospital health care workers, 10.8% in multiple blood transfusion patients and 20.5% among renal dialysis patients [11]. Furthermore, in Benghazi city the prevalence of anti-HCV in 153 chronic renal dialysis patients was found to be 21% [12]. It is well known that such a high prevalence of HCV infection could lead to a substantial

increase in future morbidity and mortality from HCV-related diseases such as liver cirrhosis and hepatocellular carcinoma.

These high figures of HBV and HCV infection among different patients groups in Libya have raised questions about whether the general population has a similar high prevalence from sources as exposure to blood during the period before initiation of routine testing for blood units for anti-HCV in 1997. We conducted the present national seroepidemiological investigation to determine the prevalence and risk factors of HBV and HCV infection among the general population in Libya.

#### Methods

#### Sample

Sample size calculations were based on the prevalence of hepatitis B surface antigen (HBsAg) and HCV infection in previous studies in Libya. To detect a 2-fold increase in prevalence among the lowest prevalence expected for HCV (1/1000) in each age group as compared with the next age one a sample size of 25 476 has a power of 80% (i.e. beta error of < 0.2) to detect this difference at the alpha = 0.05 level (1-sided). This sample size allows for estimating a prevalence of 2/10 000 for HBsAg with a power of > 96%. A total sample of 51 000 would allow estimation of these parameters independently for males and females.

A multi-stage sampling technique was applied in the year 2005 to select a large, representative sample of sex and age groups from all administrative regions of Libya and to minimize refusals. The following age strata were targeted in each administrative region for both males and females:

 Pre-school children (< 6 years) at maternal and child care centres as

- well as other health facilities and child care centres.
- School-age children below university levels (6–18 years) at schools of the 3 levels (primary, preparatory and high schools).
- University age group for graduate and postgraduate students (19–45 years) at university health service centres.
- Employment age (20–62 years), and above retired age (> 62 years) at schools for teachers, outpatient clinics at public sector facilities, outpatient clinics at general hospitals, work places at government facilities and inpatient health care facilities.

For regional representativeness, Libya was classified into 12 regions including all 32 administrative sections with a cluster sampling technique with population proportional to all age groups and both sexes. Several sampling frames were established in all targeted sectors in the 12 regions. The sampling units for schools were the class level in a frame including all schools and classes in each region. In health care facilities the unit was the health care centre in a frame including all health care facilities in the region. In administrative and employment places the unit was an office in a frame including all administrative buildings and offices in the region. The sample size for males and females and age strata was determined in each region proportional to regional population according to the latest national census in 2003–04. The target cluster sample was calculated for each sampling age and sex group in each region in proportion to its size within the region based on the national census.

The total sample in each region was set ahead of the survey and recruitment continued till the sampling teams fulfilled the required sample according to Table 1. Sample weighting was later performed and a weight was calculated according to age and sex within each region.

Table 1 Geographical sample allocation			
Province	Total s	sample	
	No.	%	
Derna	4 996	7.6	
Aljabal Al-Akhdar	5 944	9.0	
Benghazi	6 938	10.6	
Ijdabia	4 963	7.5	
Sirt	3 871	5.9	
Misrata	4 966	7.6	
Almergeb	4 913	7.5	
Tarhouna	5 023	7.6	
Tripoli	8 013	12.2	
Alzawia	5 022	7.6	
Aljabal Al-Garbi (Nafosa)	5 752	8.7	
Fezan	5 3 6 0	8.2	
Total	65 761	100.0	

#### **Data collection**

An anonymous questionnaire was filled out for each participant, including information on age, sex, education, residence and occupation. It also included lifetime history of major invasive exposures, use of recreational intravenous drugs and multiple sexual partners.

A 5–10 mL blood was collected on site and transported within a few hours to the local laboratory in a general hospital in the region for separating serum aliquots and stored in a –20 °C deep freezer until testing. Serum samples were tested for anti-HCV antibodies by using a 3rd-generation microparticle enzyme immunoassay (Axsym System) (i.e. HCV EIA 3.0, Abbott Laboratories) and HBsAg (Axsym). Samples that initially gave a positive HBsAg and anti-HCV antibodies result were repeatedly tested for confirmation. Only

cases that tested repeatedly positive were considered as positive for HBsAg and anti-HCV antibodies.

The study protocol and a questionnaire were approved by the Libyan National Center for Disease Control ethics committee and an informed consent was prepared to be signed by the individual or a witness from the local health office before initiating collection of data or blood samples. Serum samples and associated demographic data were coded so that data were collected without any need for personal identifiers.

#### Statistical analysis

Data were coded and using a computer data entry program the database was cleaned and verified. Data were analysed by using the chi-squared test with Yates' correction or Student *t*-test for univariate analysis. Multivariate analysis

was conducted using logistic regression, with anti-HCV serologic results as the dependent variable, using *SPSS*, version 17. Prevalence estimates were reported with 95% confidence intervals (CI) by using the Poisson distribution approximation. A type I error of alpha = 0.05 was assumed.

There was a good agreement between sample structure after weighting and population structure at all age groups for both males and females (data on request).

#### Results

The overall unweighted prevalence of anti-HCV was 1.2% (95% CI: 1.1%-1.3%), which rose to 1.3% after weighting. The overall prevalence of HBsAg for the whole sample was 2.2% (95% CI: 2.1%-2.3%), with a significantly higher rate among males (2.6%; 95% CI: 2.4%-2.7%) than females (1.8%; 95% CI: 1.6%–1.9%). The risk for being HBsAg positive was 1.4 times higher among males than females (Table 2). The prevalence of anti-HCV increased with age rising gradually after the age of 30 years (from 0.7%-0.9% < 30 years up to  $3.7\% \ge 30$  years) in contrast to a stable prevalence of HBsAg in all age groups 10+ years (2.3%-2.7%) with a reduced prevalence probably due to vaccination of children among those < 10 years (0.8%–0.9%).

The mean age of anti-HCV-positive individuals was 31.7 (SD 18.4) years and 35.6 (SD 20.9) years among females and males respectively, which

Table 2 Weighted hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) prevalence among males and females

Sex	Total sample		Prevaler	ıce	
		НВ	sAg +ve	Anti-	HCV +ve
	No.	No.	% (95% CI)	No.	% (95% CI)
Total	65 671	1 431	2.2 (2.1–2.3)	780	1.2 (1.1–1.3)
Female	32 996	591	1.8 (1.6–1.9)	413	1.3 (1.1–1.4)
Male	32 765	840	2.6 (2.4-2.7) <sup>b</sup>	367	1.1 (1.0-1.2) <sup>a</sup>

<sup>&</sup>lt;sup>a</sup>P > 0.05 males vs females; <sup>b</sup>P < 0.001 males vs females (OR 1.4; 95% CI: 1.3–1.6).

CI = confidence interval.

Table 3 Mean age of hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) positive groups among males and females

Sex				Age (years)		
	Total	sample	н	BsAg +ve	Anti-	HCV +ve
	Median	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)
Total	22	25.3 (16.4)	25	28.5 (17.4)	32	33.5 (19.7)
Female	22	24.7 (15.5)	23	26.3 (16.8)	30	31.7 (18.4)
Male	23	25.9 (17.2) <sup>a</sup>	27	30.0 (17.6) <sup>a</sup>	36	35.6 (20.9)

*aP* < 0.001, t-test for mean age SD = standard deviation.

was higher than for HBsAg-positive individuals, 26.3 (SD 16.8) years and 30.0 (SD 17.6) years among females and males respectively (P < 0.001) (Table 3). The mean age of anti-HCV-positive individuals was significantly higher than that for anti-HCV-negative individuals for both males (by almost 10 years) and females (by 7 years). The mean age of HBsAg-positive individuals was also significantly higher but to a lesser degree among females (by < 2 years) and males (by < 4 years).

Table 4 summarizes the seroprevalence of HBsAg and anti-HCV antibodies among the general population according to demographic characteristics and risk factors. Although there was no significant difference between males and females in the prevalence of anti-HCV positivity, HBsAg was significantly higher in males than females (P < 0.001). The frequency of HBsAg and anti-HCV antibodies significantly increased with increasing age group (P < 0.001), and significantly decreased with increasing the level of education (P < 0.001). Among known risk factors, previous history of jaundice and history of contact with infected patients were significantly higher in both HBsAg and anti-HCV positives (P < 0.001 respectively). In contrast, history of blood transfusion, previous hospital admission, previous surgical operation and history of skin piercing were the major risk factors for transmission of anti-HCV (P < 0.001, for all comparisons).

As shown in Table 5, there was little difference in the estimated proportions of cases between males and females for

HCV but more than 60% of the estimated HBsAg cases were among males. More than 50% of the estimated HBsAg were < 30 years and around 40% of HCV cases were also below that age. In terms of educational level and HBV and HCV, the highest level of infection by both viruses was among illiterate individuals (weighted prevalence 2.6% for HBsAg representing 12.3% of all estimated cases and 3.0% for anti-HCV antibodies representing 21.8% of all estimated cases).

There was a very clear-cut difference in the age distribution of HBsAg-positive cases at the 10-years age cut-off and of anti-HCV positive at the 30-years age cut-off. The estimated numbers of anti-HCV positive cases aged 30+ years were > 40 000 and for HBsAg positive age 10+ years were > 100 000 (Table 6).

# Regional variations in HBsAg and HCV prevalence

As for regional differences in the prevalence of HBsAg and anti-HCV, there were significant variations from 0.6% in Misrata, up to 2.1% in Fezan for anti-HCV and from 1.0% in Benghazi and Aljabal Al-Akhdar to 6.6% in Sirt for HBsAg (Table 7).

#### **Risk factors for HCV infection**

Data from the present national survey were analysed by logistic binary regression analysis for HCV seropositivity to determine which risk factors were significantly associated with risk of infection. All invasive exposures were entered into the regression equation including dental treatment, traditional exposures

such as tattooing and bloodletting or skin piercing. However, these were not significantly associated with increased risk of HCV infection. Similarly there was no significant difference of risk of infection according to sex. An increased risk was associated with increasing age for all subjects and among males and females (a significant risk for all age groups 50+ years compared with < 5 years (data not presented). Among all subjects, hospitalization and surgical operation, blood transfusion, intravenous drug use and haemodialysis were all significantly associated with an increased age-adjusted risk compared with those not exposed. The increased risk for hospitalization and surgical operation and blood transfusion were modest (an increase of 29%, 32% and 48% respectively) with proportion of exposed in the community of 26%, 14.8% and 5.5% of all subjects respectively. The risk associated with intravenous drug use and haemodialysis were much higher (5.9 times and 3.5 times respectively), but their exposure frequency was only 0.1% of all subjects (Table 8).

Among males, similar increased risks were found but these were only statistically significant for intravenous hospitalization and diabetes treatment. Male drug abusers had an 9.4 times increased risk with an exposure frequency of 0.2% of all males. Hospitalization was significantly associated with increased risk of HCV infection of 39% with an exposure rate of 24.3%, and diabetes treatment was associated with an increased risk of 53% with an exposure frequency of 3.7% among all males. The

Table 4 Seroprevalence of hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) antibodies among Libyans according to demographic characteristics and risk exposures

Variable	Total sample		HBsAg +	-ve		Anti-HC	/ +ve	P-va	alues
				Weighted			Weighted	HBsAg	Anti-HCV
	No.	No.	%	%	No.	%	%		
Total	65 761	1 431	2.2	2.0	780	1.2	1.3		
Sex									
Female	32 996	591	1.8	1.6	413	1.3	1.3	< 0.001	0.119
Male	32 765	840	2.6	2.4	367	1.1	1.2		
Age (years)									
5	6 530	55	0.8	0.9	57	0.9	0.8		
10	4 091	38	0.9	0.8	28	0.7	0.7		
20	20 658	520	2.5	2.3	168	8.0	0.8		
30	13 883	289	2.1	2.3	119	0.9	0.9		
40	9 775	220	2.3	2.3	140	1.4	1.6		
50	5 359	150	2.8	2.4	108	2.0	2.0		
60	3 427	91	2.7	2.7	86	2.5	2.6		
70	1344	35	2.6	2.1	50	3.7	3.7		
75	694	33	4.8	3.1	24	3.5	2.7	< 0.001	< 0.001
Education									
Below age	6 485	56	0.9	0.9	60	0.9	0.9		
Illiterate	5 084	146	2.9	2.6	156	3.1	3.0		
Preparatory	22 431	520	2.3	2.0	236	1.1	1.2		
High school	20 646	458	2.2	2.3	212	1.0	1.1		
University	8 592	184	2.1	2.2	90	1.0	1.0		
Postgraduate	1 007	16	1.6	1.9	13	1.3	1.0		
Unknown	1 516	51	3.4	2.0	13	0.9	1.3	< 0.001	< 0.001
Marital status									
Married	17 862	472	2.6	2.5	351	2.0	2.1		
Single	26 634	576	2.2	2.2	230	0.9	0.9		
Widowed	808	15	1.9	1.4	26	3.2	3.4		
Divorced	337	6	1.8	2.9	6	1.8	1.5		
Below age	18 994	330	1.7	1.4	156	0.8	0.8		
Unknown	1126	32	2.8	2.1	11	1.0	1.4	< 0.001	< 0.001
Type of dwelling									
Villa	9 998	218	2.2	2.2	96	1.0	1.2		
Apartment	7 350	135	1.8	1.6	103	1.4	1.6		
Rural house	46 088	1 035	2.2	2.1	567	1.2	1.3		
Other	120	1	0.8	1.1	1	0.8	1.0		
Unknown	2 205	42	1.9	1.6	13	0.6	0.7	0.078	0.011

increased risk associated with surgical operation and blood transfusion did not reach statistical significance (P = 0.071 and P = 0.068 respectively). Among females, similar increased risks were found, but only blood transfusion was statistically significantly associated with increased risk of HCV (69%). It

was also clear that married women had a 69% increased risk of acquiring HCV (Table 8).

## Risk factors for HBV transmission

Unlike HCV, there were no invasive risk factors associated with being

HBsAg-positive. The age-adjusted risk factors for HBV infection included only family exposure to HBV case or contact with HBV case with an increased risk of 2.1 (2.0 among females and 2.4 among males). Being vaccinated against HBV was protective and those who

Table 4 Seroprevalence of hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) antibodies among Libyans according to demographic characteristics and risk exposures (concluded)

Variable	Total sample		HBsAg +	ve	,	Anti-HC\	/+ve	P-v	alues
				Weighted			Weighted	HBsAg	Anti-HCV
	No.	No.	%	%	No.	%	%		
Clinical history									
Hospital admissions	16 946	395	2.3	2.3	326	1.9	2.1	0.115	< 0.001
Surgical operations	9 586	233	2.4	2.3	218	2.3	2.6	0.077	< 0.001
Blood transfusion	3 557	74	2.1	2.0	96	2.7	2.8	0.681	< 0.001
Dental procedures	23 220	500	2.2	2.1	299	1.3	1.4	0.767	0.089
Skin piercing	7 451	189	2.5	2.4	130	1.7	1.9	0.073	< 0.001
Skin tattoo	1 243	36	2.9	2.5	22	1.8	2.3	0.532	0.283
IV drug use	54	0	0.0	0.0	4	7.4	15.4	0.266	< 0.001
Illegal sex	193	3	1.6	1.3	3	1.6	2.6	0.464	0.814
HBV vaccination	13 242	167	1.3	1.1	147	1.1	1.0	< 0.001	0.376
HBV contact	1 423	57	4.0	3.8	26	1.8	2.6	< 0.001	0.006
History of jaundice	2 421	88	3.6	3.6	51	2.1	2.5	< 0.001	< 0.001

IV = intravenous.

were vaccinated had a 44% lower risk of being infected (38% among females and 49% among males) (Table 9).

#### Discussion

The present study reports the results of a national seroepidemiologic study in Libya on the prevalence of HBV and HCV infections and the related risk factors. Previous studies in Libya were based on selected populations such as hospitalized patients, health care workers and blood donors. Blood donor groups are usually young male adults, hence the seroprevalence in females and other age groups such as children and elderly people have not previously been estimated. The present study is the first survey of a representative, random, community-based sample of the general population of Libya. It is unique because a large sample size was tested (65 761), the evaluation was conducted

in 12 distinct administrative regions of the country, the study comprised all age groups of both sexes in the Libyan general population and the risk factors for transmission for both HBV and HCV infections were identified. A multi-stage sampling technique was applied and the high participation rate from all age groups of both sexes in all administrative regions of Libya suggests the absence of selection bias and may provide an accurate assessment of HB-sAg and anti-HCV prevalence and their associated risk factors in this developing country.

Since 1997 blood units were routinely examined for anti-HCV in all blood banks in Libya, which should reduce the transmission through blood transfusion. The relatively low overall prevalence of anti-HCV antibodies (1.3%) among Libyans is still higher than Canada (0.8%), Australia (1.1%) and some western European countries including France (1.1%) and Germany (0.6%) [13–17] and is close to that

reported from large studies of the general population in the United States of America (1.8%–2.2%) [18–21] and much lower than the figures reported for Pakistan (5%–7%) [22,23] and Egypt (22%) [24], a neighbouring country with a high movement of workers every year. The results of this study also are consistent with previously published studies of selected Libyan populations [6-11]. The relatively low level of HCV infection among the general population in this country can be contrasted with the high prevalence among those who reported use of intravenous drugs (15.4%) and may suggest that this route of transmission is potentially an important risk factor for future transmission of HCV in Libya, as in the USA where it is the major mode of HCV transmission [25-28].

The prevalence of anti-HCV antibodies increased with age, rising gradually after the age of 30 years (from 0.7%–0.9% at age < 30 years up to 3.7% at 30+ years). This suggests that HCV

Table 5 Weighted hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) antibodies prevalence and population estimates of hepatitis B virus (HBV) and C virus (HCV) infections

Variable Variable		onal HBSAg +ve	Estimated nat	ional HCV +ve
	No.	%	No.	%
Total	107 848	100.0	68 275	100.0
Sex				
Female	42 297	39.2	34 845	51.0
Male	65 551	60.8	33 430	49.0
Age (years)				
5	4 861	4.5	4 699	6.9
10	4 110	3.8	3 881	5.7
20	26 148	24.2	8 889	13.0
30	26 153	24.2	10 147	14.9
40	20 139	18.7	13 966	20.5
50	11 436	10.6	9 738	14.3
60	6 856	6.4	6 633	9.7
70	3 613	3.4	6 415	9.4
75	4 532	4.2	3 907	5.7
Education				
Below age	4 957	4.6	5 235	7.7
Illiterate	13 318	12.3	14 850	21.8
Preparatory	34 927	32.4	20 685	30.3
High school	34 389	31.9	17 214	25.2
University	16 118	14.9	7 544	11.0
Postgraduate	1769	1.6	981	1.4
Unknown	2 370	2.2	1766	2.6
Marital status				
Married	39 844	36.9	32 605	47.8
Single	42 551	39.5	17 845	26.1
Widowed	1 425	1.3	3 403	5.0
Divorced	913	0.8	470	0.7
Below age	21 434	19.9	12 828	18.8
Unknown	1 681	1.6	1 124	1.6
Type of dwelling				
Villa	13 545	12.6	6 944	10.2
Apartment	10 491	9.7	10 480	15.3
Rural house	80 646	74.8	49 398	72.4
Other	118	0.1	104	0.2
Unknown	3 048	2.8	1349	2.0

screening needs to be targeted on people aged 35+ years old.

Although the results of the present study did not show a significant difference in the prevalence of anti-HCV antibodies according to sex, a higher prevalence of HBsAg in males and older ages was detected. The infection rate was higher in individuals aged 10+ years

and was more obvious at age 75+ years, with a prevalence of 3.1%. Individuals in the older age groups were most likely to have been exposed to HBV infection before the risks were well recognized, through hospital care, exposure to blood transfusion and blood products or family contacts. On the other hand, the lower HBsAg prevalence in individuals

aged < 20 years (0.8%–0.9%) was probably due to the universal vaccination programme of newborns and adolescents against hepatitis B in Libya since 1992 according to World Health Organization criteria.

The present study showed that close contact with infected family members, particularly the mother, was probably

Table 6 Weighted hepatitis B virus (HBV) and C virus (HCV) population prevalence estimates according to age strata

Variable	Sample	Total	Estimated in population	Weighted +ve	OR (95% CI)
	No.	No.	No.	%	
HCV estimated national caseload					2.5 (2.5-2.6)
Age < 30 yrs	43 240	352	25 786	0.8	
Age 30+ yrs	22 521	428	42 489	2.0	
Total	65 761	780	68 275	1.3	
HBV estimated national caseload					3.3 (3.2–3.3)
Age < 10 yrs	76	9 459	7 006	0.7	
Age 10+ yrs	1355	56 302	100 842	2.3	
Total	1 431	65 761	107 848	2.0	

OR = odds ratio; CI = confidence interval.

a major source of HBV infection, suggesting that intrafamiliar transmission is a significant risk factor. Screening of family members in direct contact with infected patients and subsequent vaccination is needed to minimize intrafamiliar transmission of HBV.

Comparison of invasive exposures between HBsAg-positive and-negative individuals did not reveal any factors that were significantly associated with HBV infection, except having family contact with an HBV-infected person and previous history of jaundice. In addition, this study did not find

dental procedures or tattooing to be associated with transmission of HCV. However, body piercing was a statistically significant risk factor for HCV but not for HBV transmission. HCV was significantly associated with a history of hospital admissions, surgical operations and blood transfusions, with prevalence rates among exposed individuals of at least twice the general population rate. Haemodialysis was reported among a very small number of individuals, which did not allow for a sufficient power for detecting its risk. The above findings may suggest that nosocomial infection may have an important role in transmission of HCV infection in a considerable number of individuals in Libya. Contaminated injection equipment seems to be the major risk factor for HCV infection in many developing countries. In Egypt, the country with the highest reported prevalence of HCV in the world, transmission has been attributed to contaminated glass syringes used in nationwide schistosomiasis treatment campaigns from 1960 to 1987 [23]. A high prevalence of HCV (31.1%) has been also reported from India among patients receiving multiple injections to treat leishmaniasis [29] and among

Table 7 Regional anti-hepatitis C virus (HCV) and hepatitis B surface antigen (HBsAg) prevalence

Province	Total sample	ŀ	ICV	HI	BsAg
		Weighted	Estimated +ve	Weighted	Estimated +ve
	No.	%	No.	%	No.
Derna	308 178	1.77	5 467	1.59	4 904
Aljabal Al-Akhdar	335 025	0.86	2 877	1.00	3 364
Benghazi	656 083	1.32	8 686	1.04	6 810
Igdabia	208 044	1.30	2 703	1.35	2 811
Sirt	132 174	0.99	1 314	6.61	8 743
Misrata	512 532	0.59	3 042	1.73	8 870
Almergeb	203 320	1.36	2 759	1.43	2 914
Tarhouna	200 523	1.20	2 397	3.42	6 858
Tripoli	1 422 204	1.40	19 854	2.27	32 316
Alzawia	541 136	1.32	7 150	2.42	13 089
Aljabal Al-Garbi	434 406	1.10	4 768	2.25	9 760
Fezan	348 606	2.08	7 258	2.13	7 409
Total	5 302 231	1.29	68 275	2.03	107 848

Table 8 Regression analysis for risk factors of hepatitis C virus (HCV) in	nalysis for risk	k factors o	of hepatitis C virus	(HCV) infe	nfection							
Variable		Total san	Total sample ( <i>n</i> = 65 761)			Female	Females ( <i>n</i> = 32 780)			Male	Males $(n = 32.391)$	
	Exposed %	Exp(B)	Exposed % Exp(B) 95% CI for ExpB P-value	<i>P</i> -value	Exposed %	ExpB	95% CI for ExpB	<i>P</i> -value	Exposed %	ExpB	95% CI for ExpB	<i>P</i> -value
Age		1.02	1.01-1.02	< 0.001		1.01	1.00-1.02	0.014		1.02	1.02-1.03	< 0.001
Married vs single	29.0	1.25	1.02-1.54	0.031	26.4	1.69	1.26-2.25	< 0.001	32.0	96.0	0.71-1.28	0.756
Hospitalization	26.0	1.29	1.06-1.56	0.011	27.0	1.12	0.86-1.47	0.404	24.3	1.39	1.04-1.84	0.024
Surgical operation	14.8	1.32	1.06-1.63	0.011	15.5	1.28	0.96-1.72	0.094	14.1	1.34	0.98-1.84	0.071
Blood transfusion	5.5	1.48	1.17–1.87	< 0.001	4.5	1.69	1.21-2.36	0.002	6.4	1.36	0.98-1.90	0.068
IV drug abuse	0.1	5.94	2.12-16.7	0.001		0.00	0.00-0.00	0.999	0.2	9:36	3.29-26.7	0.000
Haemodialysis	0.1	3.54	1.25-10.0	0.017	0.1	3.64	0.84-15.8	0.084	0.1	3.43	0.78-15.1	0.104
Diabetes treatment	0.4	1.25	0.95-1.64	0.107	0.4	1.03	0.70-1.52	928.0	0.37	1.53	1.05-2.23	0.028
Constant		0.055		0.000		0.009		0.000		0.056		< 0.001

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Table 5 reglession analysis for the records of the parties by the condition	I NEIL IOI EIE	acto13 01	incpatitis b vii as (i in	) IIIICCEIO								
Variable		Total sa	Total sample ( $n = 65761$ )			Fen	Females $(n = 32780)$			Males	Males $(n = 32.391)$	
	Exposed %	Exp(B)	Exposed Exp(B) 95% CI for Exp(B) %	<i>P</i> -value	Exposed %	Exp(B)	Exp(B) 95% CI for Exp(B)	<i>P</i> -value	Exposed %	Exp(B)	95% CI for Exp(B)	<i>P</i> -value
Age		1.01	(1.00-1.01)	< 0.001		1.00	(0.99–1.01)	0.665		1.01	1.01-1.02	< 0.001
Hospitalization	26.0	0.98	(0.84-1.14)	0.756	27.0	1:11	(0.88-1.40)	0.394	24.3	0.94	0.76-1.15	0.543
Surgical operation	14.8	1.02	(0.84-1.23)	0.868	15.5	1.02	(0.77-1.35)	0.887	14.1	1.04	0.81-1.34	0.745
Blood transfusion	5.5	0.81	(0.63-1.05)	0.107	4.5	98.0	(0.56-1.32)	0.485	6.4	0.74	0.54-1.01	0.054
IV drug use	0.1	0.00	I	0.997		0.00	ı	0.999	0.2	0.00	-00.0	0.998
Haemodialysis	0.1	1.50	(0.36–6.23)	0.578	0.1	1.72	(0.23-12.9)	0.599	0.1	1.35	0.18-10.2	692.0
Diabetes treatment	3.8	1.02	(0.79-1.33)	0.869	3.9	1:1	(0.73-1.68)	0.629	3.7	1.02	0.73-1.43	0.907
Family hepatitis B cases	2.0	2.10	(1.70–2.61)	< 0.001	2.2	1.99	(1.45–2.73)	< 0.001	1.6	2.43	1.80-3.26	< 0.001
HBV vaccination	20.4	0.56	(0.47–0.66)	< 0.001	28.4	0.62	(0.48-0.80)	< 0.001	24.1	0.50	0.40-0.63	< 0.001

W = intravenous.

individuals with frequent visits to unlicensed practitioners [30] as well as among those with history of therapeutic injections using reusable syringes [31].

Sexual contact could also be a source of infection, although this was not detected in this national survey data analysis. However, HCV infections in some population groups may be due to high-risk sexual activity (e.g. multiple partners) similar to the findings of studies other countries [32–34].

In conclusion, the results of this general population-based survey suggest

the need for continuous implementation of stringent measures for prevention and control of these infections in Libya, including screening and vaccination focused on high-risk groups, such as contacts for HBV cases. The higher prevalence of HCV infection in older age groups suggests that the Center for Disease Control of Libya needs to implement a targeted risk-based HCV screening programme for persons who are 35+ years of age for early detection and specific treatment of this insidious infection. Even though the risk of HCV infection was relatively low compared with that of HBV, the future health care burden of prior HCV infections in Libya could be substantial in the general community.

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**Competing interests:** None declared.

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# Serological pattern of hepatitis B virus among HBsAg negative blood donors in Alexandria, Egypt

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النموذج المصلي لفيروس التهاب الكبد"بي" بين المتبرعين بالدم السلبيين للمستضّد السطحي لفيروس التهاب الكبد في الإسكندرية، مصر إنجي محمد الغيطاني، عزة جلال فرغلي

الخلاصة: أجرَت الباحثتان هذه الدراسة في الإسكندرية، مصر، للتعرُّف على توزُّع ختَلف واسيات فيروس الالتهاب الكبدي "بي" بين المتبرعين بالدم الذين يبدون أصحاء، ويكون لديهم المستضد السطحي لفيروس التهاب الكبد سلبياً، وللتعرُّف على عوامل الاختطار المستقلة الكبرى. وقد اتضح وجود بيِّنات على تعرُّض سابق بفيروس الالتهاب الكبدي "بي" لدى 148 متبرعاً من بين 508 متبرعين تم تحرِّي الفيروس لديهم (29.1٪). وقد كان أكثر الواسيات شيوعاً هو المضاد اللبي لفيروس الالتهاب الكبدي الذي لوحظ لدى 124 متبرعاً من أصل 124 متبرعاً من أصل 124 من بين 508 من المتبرعين بالدم (24.4٪)، وكان لدى نصفهم (63 متبرعاً من أصل 124 متبرعاً) إيجابية تقتصر على المضاد اللبي لفيروس الالتهاب الكبدي "بي" في المناد اللبي لفيروس الالتهاب الكبدي "بي" في 12.0٪، بينها كان مع المضاد البائي للالتهاب الكبدي "بي" في 5.7٪. وكانت عوامل الاختطار المستقلة المرتبطة بوجود واحد على الأقل من الواسيات هي: الزواج (نسبة الأرجحية 28.8)، وسوابق نقل الدم (نسبة الأرجحية 20.4)، ومعالجة بالحقن المضادة للبلهارسيا (نسبة الأرجحية 28.8)، وسوابق نقل الدم (نسبة الأرجحية 20.4)، ومعالجة بالحقن المضادة للبلهارسيا (نسبة الأرجحية 28.6)، وسوابق نقل الدم (نسبة الأرجحية 20.4)، ومعالجة بالحقن المضادة للبلهارسيا (نسبة الأرجحية 28.6)، وسوابق نقل الدم (نسبة الأرجحية 20.4)، ومعالجة بالحقن المضادة المنادة لفيروس الالتهاب الكبدي البائي يجعل من الضروري اتخاذ التدابير الصارمة لمكافحة العدوى ولتوعية البالغين ببرنامج التلقيع. إن الارتفاع النسبي لمعدّل انتشار التعرُّض لفيروس الالتهاب الكبدي البائي يجعل من الضروري اتخاذ التدابير الصارمة لمكافحة العدوى ولتوعية البالغين ببرنامج التلقيع.

ABSTRACT This study in Alexandria, Egypt was conducted to investigate the distribution of different hepatitis B virus (HBV) markers in apparently healthy blood donors who were hepatitis B surface antigen (HBsAg) negative, and to determine the major independent risk factors. Evidence of past exposure to HBV was found in 148/508 screened donors (29.1%). The most prevalent marker was anti-HBc in 124/508 donors (24.4%), half of whom (63/124) showed anti-HBc only. Anti-HBs prevalence was 15.9%, combined anti-HBc and anti-HBs was 12.0% and anti-HBe was 5.7%. Independent risk factors associated with the presence of at least 1 marker were: being married (OR 3.82), history of blood transfusion (OR 3.04) and parenteral antibilharzial treatment (OR 2.49). Receiving a full HBV vaccination schedule was reported by 39 donors, but only 1 of them had isolated anti-HBs. The relatively high prevalence of HBV exposure necessitates solid infection control measures and adult vaccination programme awareness.

# Sérologie du virus de l'hépatite B chez des donneurs de sang négatifs pour l'antigène de surface du virus de l'hépatite B à Alexandrie (Égypte)

RÉSUMÉ La présente étude, menée à Alexandrie (Égypte), a évalué la répartition des différents marqueurs du virus de l'hépatite B chez des donneurs de sang apparemment en bonne santé qui étaient négatifs pour l'antigène de surface de l'hépatite B, et a identifié les principaux facteurs de risque indépendants. La preuve d'une exposition antérieure au virus de l'hépatite B a été retrouvée chez 148 des 508 donneurs dépistés (29,1 %). Le marqueur le plus prévalent était l'anti-HBc, observé chez 124 des 508 donneurs (24,4 %), dont la moitié (63/124) ne présentait que ce marqueur. La prévalence de l'anti-HBs était de 15,9 %, celle de l'anti-HBc et anti-HBs combinés était de 12,0 % et celle de l'anti-HBe de 5,7 %. Les facteurs de risque indépendants associés à la présence d'au moins un marqueur étaient les suivants : le fait d'être marié(e) (OR 3,82), d'avoir des antécédents de transfusion sanguine (OR 3,04) et d'être sous traitement parentéral contre la schistosomiase (OR 2,49). Trente-neuf donneurs ont indiqué avoir reçu toutes les injections du vaccin contre le virus de l'hépatite B, mais seul l'un d'entre eux avait des anti-HBs isolés. La prévalence relativement élevée de l'exposition au virus de l'hépatite B requiert des mesures de lutte contre les infections qui soient robustes et une sensibilisation au programme de vaccination des adultes.

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#### Introduction

Hepatitis B virus (HBV) infection is a serious global health problem, with 2 billion people infected worldwide, and 400 million suffering from chronic HBV infection. Approximately 2 people die each minute from HBV infection; representing the 10th leading cause of death worldwide [1]. Although the prevalence of HBV has declined due to the effectiveness of vaccination programmes, HBV infection is still a significant health concern in the world [2]. The prevalence of HBV infection in Egypt showed a massive decline after the application of the vaccination programme in 1991, from 10.1% in 1985 [3] to 1.3% in a recent study in 2009 on blood donors [4].

The presence of hepatitis B virus surface antigen (HBsAg) is an essential serological marker for diagnosing ongoing HBV infection; however, the presence of IgG antibodies against core antigen (anti-HBc), alone or in combination with antibodies against surface antigen (anti-HBs), indicates previous exposure to the virus [5]. Absence of HBsAg can be interpreted in a number of ways: no current or past HBV infection if no other HBV markers are detected; recovered past infection with detectable anti-HBs and anti-HBc; immunity due to vaccination with only detectable isolated anti-HBs; occult HBV infection in the presence of HBV-DNA in serum or liver with or without other markers; or false occult HBV infection if the serum DNA is comparable to that of overt infection in case of HBsAg mutants [6-8]. The persistent presence of anti-HBc is associated with chronic HBV infection and can be selective for HBVinfected samples even in the absence of HBsAg [9]. These patients who remain HBsAg negative/anti-HBc-positive are at risk of transmitting the disease on rare occasions, such as donation of solid organ tissue, or of reactivation of HBV disease if they are immunosuppressed [10].

Screening for HBV status using these markers provides an overview of the exposure, probability of transmission and immune status of the general population. This is crucial to anticipating the future impact of the disease on the health system and also to ensure adequate allocation of financial resources. We therefore conducted this study to investigate the distribution of anti-HBc and other HBV markers in apparently healthy blood donors who were HBsAg negative and to determine the major independent risk factors beyond HBV exposure with the goal of improving blood donation safety.

#### Methods

#### Sample

The study population (n = 508) was randomly selected from among Egyptian donors from blood banks in Alexandria. Assuming a 50% prevalence of anti-HBc among blood donors, the minimum required sample size was estimated by Epi Info, version 6 to be 474 blood donors with a precision = 4.5%, an  $\alpha$ -level = 0.05 and a power = 80%. The researchers visited the blood banks at least 4 times weekly for a period of at least 4 hours. All donors attending blood banks during the researchers' visits and who consented to participate were included. Blood bank laboratory results were collected thereafter and only the eligible donors were included. The donors were screened continuously and the results from the blood banks were obtained a week later and those who had positive HBsAg were excluded (n = 13). There were 73 people who refused to participate.

#### **Data collection**

The study was conducted from September 2009 to March 2011. An interview using a structured questionnaire

was conducted at the time of the participant's blood donation after getting his/her informed consent. The questionnaire included information about demographic, social and behavioural factors. Blood samples were taken from each participant and sera were stored at –20 °C until tested. After obtaining the blood bank results, HBsAg reactive sera were excluded and the final number of participants included in the study was 508 HBsAg non-reactive blood donors.

Serology comprised anti-HBc, anti-HBs, hepatitis B e antigen (HBeAg) antibodies against HBeAg (anti-HBe) and IgM antibody to hepatitis B core antigen (anti-HBc IgM). Every test was performed twice using enzyme-linked immunosorbent assay (Dialab GmbH) in accordance with the manufacturer's instructions.

The study protocol was approved by the research ethics committee of the High Institute of Public Health, University of Alexandria.

#### Data entry and analyses

Data entry and analyses were performed using SPSS software, version 15.0. The prevalence of each HBV serological marker was calculated as a percentage of the total population included in the study. The confidence intervals (CI) were calculated manually at the 95% level with continuity correlation. The blood donor was considered exposed if at least 1 positive marker was detected. The titres of different markers in serum were categorized according to quarter percentiles. Cut-off values for low titres were < 50th percentile and for high titres were ≥ 50th percentile. The association between the demographic and social variables and the prevalence of HBV markers was evaluated using the chi-squared test. Multivariate logistic regression analyses were done to reveal the independent predictors of past exposure with or without immunity. A 2-sided P-value < 0.05 was considered statistically significant.

#### Results

The total number of people with evidence of exposure to HBV infection among the study group (i.e. presence of at least 1 serologic marker) was 148/508, a prevalence of 29.1%. They will be referred to as the exposed group. The prevalence of each marker is shown in Table 1. The most frequent marker was anti-HBc (24.4%), followed by anti-HBs (15.9%) and anti-HBe (5.7%). The number of individuals who had combined anti-HBs and anti-HBc was 61 (12.0%), making the anti-HBc alone (without anti-HBs) 50.8% (63/124) of the total positive anti-HBc. The majority of anti-HBs seropositive donors (n = 49; 60.5%) had high titres compared with almost half of the anti-HBc positive sera (n = 61; 49.2%). Anti-HBc IgM and HBeAg were detected in 3 (0.6%) and 2 (0.4%) individuals respectively; all of them had borderline cut-off levels.

As shown in Table 2, although most of the exposed group were males (114/148), female sex was significantly associated with exposure (P = 0.006). The mean age of the exposed group was 38.9 (SD 9.9) years, with 44.2% being older than 35 years. The exposed donors were significantly older than the unexposed group (P < 0.001). Marriage and rural residence were significantly associated with exposure (83.1% and 41.9% versus 61.9% and 31.1% in the

exposed and unexposed groups respectively) (P < 0.001, P = 0.02 respectively). Neither education level nor type of work showed any association with the presence of HBV markers. Other factors that showed significance in the univariate analysis (Table 3) were: history of circumcision using traditional practices (P = 0.047), travelling to HBV-endemic area (P = 0.008), a history of frequent blood transfusion, even after 1992 (when screening began in blood banks) (P = 0.01), frequent dental manipulation (P = 0.002), history of jaundice (P =0.009), reporting elevated liver enzymes (P=0.04) and receiving schistosomiasis treatment by injection (P < 0.001). The independent risk factors revealed in the logistic regression analysis are shown in Table 4.

Among all participants, 461 (90.7%) gave no history of receiving HBV vaccine. No significant relation was found between seropositivity with isolated anti-HBs and self-reported history of receiving HBV vaccine (Table 5). Of the 37 who reported history of complete HBV vaccination, none had HBeAg, 1 had anti-HBc IgM, 4 (10.8%) showed anti-HBe and 9 (24.3%) were anti-HBcpositive. Surprisingly, 8/37 (21.6%) of them showed anti-HBs, of whom 1/37 showed only anti-HBs. Most of the blood donors showing anti-HBs alone (16 out of 18; 88.9%) did not report any history of vaccination.

Table 1 Prevalence of hepatitis B virus (HBV serological markers in HBsAg-negative blood donors

biood dollors			
HBV marker	No.	% (n = 508	95% CI
Anti-HBc	124	24.4	20.8-28.3
Anti-HBs	81	15.9	12.9-19.5
Anti-HBe	29	5.7	3.9-8.2
Anti-HBc IgM	3	0.6	0.2-1.9
HBeAg	2	0.4	0.3-1.6
Total	148ª	29.1	23.9-34.2

<sup>&</sup>lt;sup>a</sup>Presence of more than 1 marker was common.

Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; anti-HBc = antibody to hepatitis B envelope antigen; anti-HBc IgM = IgM antibody to hepatitis B core antigen; HBeAg = IgM antibody to hepatitis B core antigen.

#### Discussion

The assumed rarity of hepatitis transmission by blood transfusion has been attributed to the screening of blood for markers of HBV and HCV, which has been universally applied in blood banks worldwide since 1992. However, the univariate analysis of different risk factors for hepatitis infection in the present study documented that positive history of frequent blood transfusion especially after 1992 was a significant risk factor for evidence of HBV exposure. Meanwhile, the logistic regression analysis showed that history of blood transfusion was one of the independent risk factors for HBV infection. This latter finding matches well with other published data [11]. It has been reported that despite continued improvements in the selection criteria of blood bank donors and of the applied serological tests protocol in sample evaluation, the transmission of HBV infection by blood transfusion still occurs in a proportion of cases even if the transfused blood tested negative for HBsAg using highly sensitive assays [12].

The most prevalent marker among exposed people in this study was anti-HBc (24.4%). It should be noted that false positivity is unlikely in the present work as the test was double-checked and was considered positive only if both assays clearly indicated that. Anti-HBc is the first antibody to appear following acute HBV infection and persists at high levels following resolution of infection [13]. It is a marker of acute, chronic or resolved infection and remains detectable for life [14]. The reported prevalence of anti-HBc markers among donors at blood banks varies in other published studies depending on the local prevalence of HBV, ranging from 0.4% in low-endemic areas to 70% in high-endemic areas [11,15–17].

As the safety of blood products is one of the major issues in the area of transfusion medicine, the combined strategy of testing for both HBsAg and

CI = confidence interval.

Table 2 Demographic characteristics and clinical history in relation to exposure to hepatitis B virus (HBV) infection

Variable		Exposed ( <i>n</i> = 148)		xposed 360)	<i>P</i> -value	
	No.	%	No.	%		
Sex						
Male	114	77.0	313	86.9	0.006	
Female	34	23.0	47	13.1		
Age (years)ª						
< 25	18	12.2	84	23.5		
25-	64	43.5	183	51.3	< 0.001	
35-	26	17.7	52	14.6		
45+	39	26.5	38	10.6		
Mean (SD)	38.	.9 (9.94)	33	.2 (9.25)	< 0.001	
Marital status						
Single	24	16.2	127	35.3		
Married	123	83.1	223	61.9	< 0.001	
Divorced	0	0	3	0.8		
Widowed	1	0.7	7	1.9		
Residence						
Rural	62	41.9	112	31.1	0.020	
Urban	86	58.1	248	68.9		
Education						
Illiterate	39	26.4	72	20.0		
Read & write	12	8.1	21	5.8		
Primary	17	11.5	24	6.7	0.113 <sup>b</sup>	
Preparatory	22	14.9	65	18.1		
High	34	23.0	100	27.8		
University	24	16.2	78	21.7		
Employment status						
Health care	4	2.7	7	2.0		
Armed force	2	1.4	10	2.8		
Emergency service	0	0.0	4	1.1		
Beautician or barber	1	0.7	3	0.8	0.102h	
Institution work (daycare, nursery)	1	0.7	0	0.0	0.182 <sup>b</sup>	
Employee	23	15.5	79	21.9		
Manual	55	37.2	123	34.2		
Uneployed	35	23.6	59	16.4		
Others	27	18.2	75	20.8		

<sup>°1</sup> in the exposed group and 3 in the unexposed group were missing data giving a total of 147 and 357 respectively.
bMonte-Carlo test.

anti-HBc is practised worldwide and testing for anti-HBc was adopted in some areas in the world. This strategy has been found to markedly minimize the possibility of HBV transmission via blood transfusion [14]. On the other hand, it may lead to the exclusion of a significant number of donors' blood, as reported in Brazil where high levels of

anti-HBc were recorded (up to 57%) [18].

There has recently been concern about "anti-HBc only" or isolated anti-HBc individuals, i.e. those in whom anti-HBc is the only detectable HBV marker with no evidence of HBsAg or anti-HBs [19]. A serological pattern of anti-HBc

as a sole marker is not infrequent. It was reported that 3.7% of randomly selected Lebanese blood donors were confirmed as isolated anti-HBc [20]. Similarly, isolated anti-HBc was reported in 125 out of 6035 (2.1%) of Saudi blood donors [21]. Another study performed on 545 Iranian blood donors; 8% of them were positive for isolated anti-HBc [22]. The

Risk factor	Exposed ( <i>n</i> = 148)			exposed = 360)	<i>P</i> -value	
	No.	%	No.	%		
Tattooing	8	5.4	10	2.8	0.146	
Body piercing	2	1.4	7	1.9	1.000	
Acupuncture	8	5.4	18	5.0	0.851	
Sharing razor, toothbrush, comb or any potentially infecting items	5	3.4	18	5.0	0.424	
Public barber or manicure	106	71.6	263	73.1	0.742	
Circumcision	100	7 1.0	203	75.1	0.7 12	
No	81	54.7	51	14.2		
Doctor	20	13.5	80	22.2	0.047 <sup>c</sup>	
Folk	110	74.3	229	63.6		
Traveled abroad <sup>a</sup>	45	30.4	69	19.2	0.008	
Undergone surgery	.5	3011	03	.5.2	0.000	
No	70	47.3	195	54.2		
Minor	43	29.1	108	30.0	0.104 <sup>c</sup>	
Major	35	23.6	57	15.8		
Time since surgery (years)						
< 20	58	74.4	132	80.0	0.264	
20+	15	19.2	21	12.7		
History of blood or blood products transfusion						
No	133	89.9	346	96.1		
Before 1992	3	2.0	4	1.1	0.016 <sup>c</sup>	
After 1992	12	8.1	10	2.8		
Infrequent	7	4.7	10	2.8		
Frequent	8	5.4	4	1.1	0.010 <sup>c</sup>	
Undergone dental manipulation			·			
No	54	36.5	177	49.2		
Infrequent	50	33.8	122	33.9	$0.002^{c}$	
Frequent	44	29.7	61	16.9		
Undergone invasive intervention						
No	139	93.9	342	95.0		
Endoscopy	7	4.7	17	4.7	0.365	
Catheterization	2	1.4	1	0.3		
History of jaundice	- 17	11.5	18	5.0	0.009	
Reported elevated liver enzymes <sup>b</sup>	17	13.4	24	7.3	0.040	
Been hospitalized						
No	88	59.5	248	68.9	0	
Once	43	29.1	86	23.9	$0.090^{\circ}$	
More	17	11.5	26	7.2		
Vaccination for HBV						
No	133	89.9	328	91.1		
Incomplete	3	2.0	7	1.9	0.917 <sup>c</sup>	
Complete	12	8.1	25	6.9		
Had antibilharzial treatment by injection	50	33.8	45	12.5	< 0.001	
Parenteral injections or infusion						
No	106	71.6	260	72.2		
Once	22	14.9	55	15.3	0.951	
More	20	13.5	45	12.5		
HIV-Ab positive	1	0.7	2	0.6	1.00	

None had organ transplantation or been on haemodialysis

The total number is less than those traveled as the rest were missing data.

Note all participants had previously measured aspartate/alanine aminotransferase, so the totals were 127 and 331 for the exposed and unexposed participants respectively. <sup>c</sup>Monte-Carlo test.

Table 4 Logistic regression analysis of different risk factors of exposure to hepatitis B virus (HBV infection)

Variable	OR	SE	z-value	<i>P</i> -value	95% CI
Married	3.82	2.13	2.41	0.016	1.28-11.4
History of blood or blood product transfusion	3.04	1.62	2.09	0.037	1.07-8.65
History of schistosomiasis treatment by injection	2.49	0.91	2.49	0.013	1.21-5.12

Logistic regression analysis of different risk factors significantly associated with exposure to HBV shows that marriage and history of blood transfusion had more prominent effect (OR 3.82 and 3.04 respectively that was followed by history of anti-bilharzial treatment by injection OR = odds ratio; SE = standard error; CI = confidence interval.

results of the present study further confirmed the high rate of isolated anti-HBc among tested blood donors 63/508 (12.4%).

Besides false positive results of anti-HBc assays [23], emergence of 's' mutants which could occur during therapy with nucleoside inhibitors was also suggested as a possible explanation for the presence of isolated anti-HBc [24]. It was declared that mutations occur in HBsAg making it undetectable by conventional assays [25]. Alhababi et al. suggested that in communities where the circulation of antigenic determinant mutants are increasing, surveillance of isolated anti-HBc cases may be a valuable tool to identify the mutants [26]. Some authors considered anti-HBc alone as evidence of past infection with HBV when the anti-HBs level has fallen below the detection level [20]. Others concluded that many years after chronic carriage the level of HBsAg in the circulation becomes too low to be detected [16]. Finally, anti-HBc alone has also been attributed to an acute HBV infection during the so-called "window

period" between the disappearance of HBsAg and the appearance of HBsAb. In this case, if the individual is followed up, anti-HBs will appear [13].

In the present study, combined anti-HBc and anti-HBs was present in almost half of those showing anti-HBc (61/124), constituting 12.0% of the total population tested for HBV markers. A similar high frequency was found by Aguiar et al. [18]. These cases were considered to be previously infected and to have become immune to HBV infection, although we need to bear in mind that the degree of protection depends on the level of anti-HBs. Kaminski et al. reported that 22 out of 41 donors with evidence of anti-HBc had anti-HBs level > 100 mIU/mL, a level generally considered protective against HBV infection [11]. Other investigators stressed the fact that blood components positive for anti-HBc and anti-HBs do not appear to transmit HBV and there is clearly an inverse correlation between anti-HBs level and infectivity [27]. The above explanations could be applied to the combined anti-HBc and anti-HBs cases found in this study, as we also found that a high proportion of anti-HBs subjects (60.5%) had high titres.

Older age was significantly associated with the detection of HBV markers. Similarly, Dettori et al. reported that the prevalence of markers of a previous HBV infection was low in young persons, whereas in those aged > 50 years the prevalence of markers of previous HBV infection was high [28]. Other authors also showed that anti-HBc prevalence increased with age, suggesting that sexual activity may contribute to horizontal transmission of this infection among adults [29]. This latter explanation finds support in the present work, as being married was a significant risk factor for HBV infection [30]. The significant association of HBV markers with older age could also be due to the greater number of years of potential exposure, lack of awareness of HBV infection and lack of awareness and eventually infrequent HBV vaccination in adults. The latter finding was supported in the present study as 90.7% of our total sample did not report any

Table 5 Relation between history of hepatitis B virus (HBV) vaccination and detection of HBV markers

HBV markers		No HBV vaccination (n = 461)		Incomplete HBV vaccination (n = 10)		ete HBV nation = 37)	<i>P</i> -value
	No.	%	No.	%	No.	%	
Anti-HBs	71	15.4	2	20.0	8	21.6	0.573
Isolated Anti-HBs	16	3.5	1	10.0	1	2.7	0.521
HBeAg	2	0.4	0	0.0	0	0.0	1.000
Anti-HBe	24	5.2	1	10.0	4	10.8	0.189
Anti-HBc IgM	2	0.4	0	0.0	1	2.7	0.253
Total anti-HBc	113	24.5	2	20.0	9	24.3	0.947

Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; anti-HBe = antibody to hepatitis B envelope antigen; anti-HBclgM = IgM antibody to hepatitis B core antigen; IgM and IgM antibody to hepatitis B core antigen; IgM and IgM antibody to hepatitis B core antigen; IgM and IgM and IgM antibody to hepatitis B core antigen; IgM and IgM antibody to hepatitis B core antigen; IgM and IgM antibody to hepatitis B core antigen; IgM and IgM antibody to hepatitis B core antigen; IgM antibody to hepatitis B core antigen; IgM and IgM and IgM antibody to hepatit

history of vaccination. The very poor response to vaccine among those who reported full vaccination suggests the possibility of incorrect reporting by the participants or poor vaccination practices. It could also be attributed to being infected before vaccination (when other markers were detected) as no screening was done before vaccination. Another explanation is if a long time had elapsed since vaccination (although no data were obtained to confirm this), leading to low undetectable levels of anti-HBs in individuals who did not show anti-HBs.

Although several published studies concluded that male sex seemed to play an important role in acquisition of HBV infection [29,31,32], the results of the present study revealed that females were more prevalent among the exposed group compared with the unexposed group (23.0% and 13.1%).

The other risk factors revealed in this study, namely circumcision in traditional facilities, rural residence and receiving parenteral schistosomiasis treatment denote a lack of hygiene and poor infection control practices in circumcisions and injections. Similar conclusions were reported by other authors who documented community delivery with traditional birth attendants as an important route of horizontal spread of HBV. They suggested that this may be attributed to the procedure being practised under poor hygiene conditions with sharing of ancillary supply equipment such as scissors [33]. This was further documented in another study, which revealed that the main risk factors for HBV transmission was syringe exchange, sexual exposure, nosocomial exposure and more rarely blood transfusion [28].

#### Conclusion

The prevalence of exposure to HBV infection in this study in Egypt was higher than expected. Public health

measures should be adopted for HBV control including proper infection control measures and better awareness and evaluation of adult vaccination programmes. The need for screening of HBsAg negative donated blood for anti-HBc needs to be evaluated.

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#### Hepatitis B transmission

Hepatitis B virus is transmitted between people by direct blood-to-blood contact or semen and vaginal fluid of an infected person. Modes of transmission are the same as those for the HIV, but the hepatitis B virus is 50 to 100 times more infectious. Unlike HIV, the hepatitis B virus can survive outside the body for at least seven days. During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. In developing countries, common modes of transmission are:

- perinatal (from mother to baby at birth)
- early childhood infections (inapparent infection through close interpersonal contact with infected household contacts)
- unsafe injection practices
- unsafe blood transfusions
- unprotected sexual contact.

Source: WHO Fact sheet No. 204

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# Hepatitis E virus seroprevalence in haemodialysis patients in Zanjan province, Islamic Republic of Iran

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# معدّل الانتشار المصلي لفيروس التهاب الكبد "ئي" بين مرضى الديال في زنجان، في جمهورية إيران الإسلامية أحمد رضا مُبيّن، رامين محمدي، رحيم سروري، كيانا صادقي

الخلاصة: إن فيروس التهاب الكبد "ئي" عهو الأكثر شيوعاً بين أسباب التهاب الكبد الحاد بين البالغين في المناطق الموطونة به في آسيا. وقد أجرى الباحثون هذه الدراسة الوصفية المستعرضة لقياس أضداد فيروس التهاب الكبد "ئي" لدى المرضى المحوَّلين إلى مركزين للديال في مدينة زنجان في جمهورية إيران الإسلامية، وشملت الدراسة 93 مريضاً بالفشل الكلوي المزمن، بعمر وسطي 57.0 عاماً (الانحراف المعياري 18.5)، فوجدوا أن أضداد فيروس التهاب الكبد اليائي إيجابية في 25 مريضاً (6.92٪). ولم يكن هناك ارتباط يُعتدُّ به إحصائياً بين العدوى بفيروس التهاب الكبد اليائي وبين الجنس أو العستوى التعليمي أو مكان الإقامة أو مصدر المياه. وكان معدل إيجابية فيروس التهاب الكبد اليائي أعلى لدى المرضى الذين أمضوا فترة تزيد على العام الواحد في الديال (15.4٪)؛ إلا أن ذلك لم يكن له اعتداد إحصائي. ولم يكن على العام الواحد في الديال (15.4٪)؛ إلا أن ذلك لم يكن له اعتداد إحصائي. ولم يكن لدى أحد من المرضى عدوى مزمنة بالتهاب الكبد سي أو بفيروس الإيدز، وكان اثنان منهم يعانون من العدوى بالتهاب الكبد (بي) أو البائي المن ونظراً لارتفاع معدلات انتشار فيروس التهاب الكبد اليائي بين مرضى الديال في زنجان فإن الحاجة ماسة إلى المزيد من الاهتام بالسهات الوبائية لفيروس الالتهاب الكبدي اليائي ومكافحته والوقاية منه مع التدريب على ذلك في غرب جمهورية إيران الإسلامية، وربيا في البلدان المجاورة.

ABSTRACT Hepatitis E virus (HEV) infection is the most common form of acute hepatitis in adults in endemic regions of Asia. In a descriptive, cross-sectional study, anti-HEV antibody was measured in patients referred to the 2 haemodialysis centres in Zanjan city, Islamic Republic of Iran. Among 93 patients with chronic renal failure, mean age 57.0 (SD 18.5) years, antibodies against HEV were positive in 25 (26.9%) patients. HEV infection was not significantly associated with sex, age, educational level, residence or water source. The rate of HEV positivity was higher in patients with > 1 than  $\leq$  1 year of haemodialysis (31.3% versus 15.4%) but this was not statistically significant. None of the patients had chronic hepatitis C or HIV infection, and only 2 were suffering from chronic hepatitis B infection. Given the high prevalence of HEV in haemodialysis patients in Zanjan, more attention is needed towards HEV epidemiology, control, prevention and training in the west of the Islamic Republic of Iran and possibly neighbouring countries.

# Séroprévalence du virus de l'hépatite E chez des patients hémodialysés dans la province de Zanjan (République islamique d'Iran)

RÉSUMÉ L'infection par le virus de l'hépatite E (VHE) représente la forme la plus fréquente de l'hépatite aiguë chez l'adulte dans les régions endémiques d'Asie. Dans une étude descriptive transversale, les anticorps anti-VHE ont été mesurés chez des patients orientés vers deux centres d'hémodialyse de la ville de Zanjan (République islamique d'Iran). Sur 93 patients atteints d'une insuffisance rénale chronique, âgés en moyenne de 57,0 ans (ET 18,5), 25 patients (26,9 %) étaient positifs pour les anticorps anti-VHE. L'infection par le VHE n'était pas significativement associée au sexe, à l'âge, au niveau d'études, au lieu de résidence ni à une source d'eau. Le taux de positivité pour le virus de l'hépatite E était supérieur chez les patients sous hémodialyse depuis plus d'un an, par rapport à ceux traités depuis un an ou moins (31,3 % contre 15,4 %), mais la différence n'était pas statistiquement significative. Aucun des patients n'était infecté par le virus de l'hépatite C chronique ou le VIH, et seulement deux patients souffraient d'une infection chronique par le virus de l'hépatite B. Étant donné la forte prévalence du VHE chez les patients hémodialysés à Zanjan, une attention accrue est requise vis-à-vis de l'épidémiologie du VHE, de la lutte, de la prévention mais aussi de la formation en la matière dans l'ouest de la République islamique d'Iran, voire éventuellement dans les pays voisins.

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#### Introduction

Hepatitis E is a self-limiting acute hepatitis caused by hepatitis E virus (HEV), which can occur both in sporadic or epidemics forms [1]. In terms of clinical symptoms, hepatitis E cannot be differentiated from other viral hepatitis cases. The spectrum of symptoms ranges from asymptomatic to fulminate disease; most patients suffer from pain, abdominal tenderness, nausea, vomiting and fever. Hepatitis E does not become chronic and often shows no recurrence. The most important complication is a severe fulminate and fetal hepatitis in pregnant women and people with chronic liver disease [2]. While in the industrialized countries, including the United States, HEV is rarely detected, it is the most common form of acute hepatitis in adults in the endemic areas in Asia. The transmission mode of HEV is mainly fecal-oral, and epidemics are typically caused by contamination of water [1]. There is disagreement about other means of viral transmission, and some researchers have maintained that fecal-oral transmission is the only route [1,2]. However, recently other means of transmission such as skin contact, blood transfusion [3-5] and mother-to-infant transmission have been proposed [6].

In a number of studies, the seroprevalence of HEV in various community groups have been compared. However, the published results have been inconsistent. While one study rejected a higher HEV seroprevalence in injecting drug users [6], another study supported it [7,8]. There have also been contradictory reports concerning haemodialysis patients. While some studies claimed that there were no significant differences between haemodialysis patients and the normal population [9], others reported significant differences [10]. The major causes of these contradictions appear to be due to a lack of matched criteria between selected groups, issues including socioeconomic status, age and so on [11].

Based on several recent studies, while the prevalence of hepatitis E in the Islamic Republic of Iran is lower than in Turkey, it is higher than Saudi Arabia, Pakistan and Iraq [12,13]. Because the city of Zanjan is near the endemic hepatitis E areas of the 2 neighbouring countries of Iraq and Turkey, and also due to the limited number of studies related to this disease in dialysis patients in Islamic Republic of Iran [12–20], we decided to analyse the prevalence of anti-HEV antibody (Ab) in a cohort of Iranian haemodialysis patients.

#### Methods

#### Study design and sample

In this descriptive, cross-sectional study, all the haemodialysis patients referred to Zanjan haemodialysis centres (Valie-Asr and Shahid Beheshti hospitals) in 2011, who were willing to participate, were included on a census basis.

#### **Data collection**

Demographic and clinical variables were recorded using a questionnaire survey designed for that purpose, including age, sex, educational level, residency, source of drinking water and duration and frequency of haemodialysis. Histories of hepatitis B (HBV) and C virus (HCV) or human immunodeficiency virus (HIV) infection were extracted from the patient records.

A sample of blood (3 mL) was taken from each patient, quickly centrifuged and kept at -70 °C. Following sample collection, the anti-HEV-Ab level was measured by an enzyme-liked immunosorbent assay method by using Bindlaver kit (ELISA, DiaPro, Diagnostic Bioprobes) and the results were recorded on a checklist. All positive samples were tested a second time for conformation

The study was approved by the ethics committee of Zanjan University of Medical Sciences, and informed consent was obtained from each

participant. No intervention outside of routine procedures was done, and there were no additional costs imposed on the participants. Specifications and information about all patients were kept confidential.

#### Data analysis

The chi-squared test was performed for statistical analysis using *SPSS*, version 16. A *P*-value < 0.05 was considered significant.

#### Results

A total of 93 patients [49 males (52.7%) and 44 females (47.3%)] with chronic renal failure with a mean age of 57.0 (SD 18.5) years (range 16–88 years) who had been admitted to the Zanjan haemodialysis centres (Vali-e-Asr and Shahid Beheshti hospitals) were studied. A summary of the patients' important demographic data including sex, residence, education level and source of drinking water is shown on Table 1.

Antibodies against HEV were positive in 25 (26.9%) patients and negative in 68 (73.1%). Patients who were anti-HEV-Ab positive were slightly more likely to be male, older age, illiterate, living in a village and using unfiltered water. However none of these differences were statistically significant (P = 0.698, P = 0.298, P = 0.769, P = 0.335 and P = 0.081 respectively) (Table 1).

The mean duration of dialysis in patients who were positive for anti-HEV-Ab was 39 months (range 1–24 months) compared with 38 (SD 43) months (range 1–220 months) for anti-HEV-Ab negative patients. A higher rate of HEV infection was seen in patients who had undergone > 1 year of haemo-dialysis (31.3%) than those who had  $\leq$  1 year of dialysis (15.4%) but the difference was not statistically significant (P = 0.365) (Table 1).

Only 2 people were suffering from chronic HBV, 1 of them was positive for anti-HEV-Ab. None of the patients showed evidence of chronic HCV or HIV infection

#### Discussion

Among the 93 participants enrolled in the study, 25 (26.9%) were found to be positive for anti-HEV-Ab. Only 1 of the patients had chronic HBV in addition to HEV, and none were positive for HCV or HIV. Statistical analysis of the relationship between the variables including sex, age, education, water, residency and history of HBV infection, showed no significant relationship between these variables and HEV infection. This observation is in line with a

2008 study in the province of Isfahan, reporting no significant difference between the sexes [3].

In several studies conducted on the general population in Islamic Republic of Iran, the prevalence of HEV infection was reported to be between 1.1% and 30.8% (Table 2) [12-20]. Only one of these studies, however, was performed on haemodialysis patients: Taremi et al., reporting a 7.4% HEV infection prevalence in Tabriz [13]. By contrast, our estimate indicated almost a 4-fold (26.8%) higher prevalence of HEV infection in haemodialysis patients in Zanjan, a figure that is also much higher than the average estimate for the general population. In line with our results, Rostamzadeh Khameneh et al. reported a high prevalence of HEV infection (30.8%) among kidney

transplant recipients in Urmia, located in the north-west of Islamic Republic of Iran [20]. A possible explanation could be that Zanjan and Urmia are geographically close to the endemic areas of the 2 neighbouring countries to the west of Islamic Republic of Iran, Turkey and Iraq. It is also possible that this high seroprevalence of HEV might be due to infection with an unknown virus, which creates antibodies cross-reacting with HEV [21]. Finally, some studies have proposed blood transfusion as a potential route of HEV transmission, particularly in highly endemic areas [5,22].

Because of a 4-fold higher HEV infection prevalence in Zanjan compared with the normal population of Islamic Republic of Iran, we should pay special attention to the high risk of

Table 1 Demographic and clinical characteristics of haemodialysis patients in relation to their anti-hepatitis E virus (HEV) status

Variable	Total	Anti-HEV -ve		Anti-l	HEV +ve	<i>P</i> -value <sup>a</sup>
	No.	No.	%	No.	%	
Total	93	68	73.1	25	26.9	
Sex						
Male	49	35	71.4	14	28.6	0.698
Female	44	33	75.0	11	25.0	0.050
Education						
Illiterate	54	37	68.5	17	31.5	
Secondary school or lower	28	22	78.6	6	21.4	0.769
Highschool diploma	4	3	75.0	1	25.0	0.709
Bachelor degree or higher	7	6	85.7	1	14.3	
Age (years)						
< 50	31	27	87.1	4	12.9	
50-59	15	9	60.0	6	40.0	0.298
60-69	20	13	65.0	7	35.0	0.290
> 70	27	19	70.4	8	29.6	
Location						
City	73	54	74.0	19	26.0	0.335
Village	20	14	70.0	6	30.0	0.555
Drinking water						
Filtration	83	63	75.9	20	24.1	0.001
No filtration	10	5	50.0	5	50.0	0.081
Duration of haemodialysis (years)						
≤1	26	22	84.6	4	15.4	0.365
>1	67	46	68.7	21	31.3	0.303

<sup>&</sup>lt;sup>a</sup>Pearson chi-squared test.

9.3

11.5

30.8

Taremi M et al. [18]

Assarehzadegan MA et al. [19]

Rostamzadeh Khameneh Z et al. [20]

lable 2 Seroepidemiology of hepatitis E virus (HEV) in various studies in the Islamic Republic of Iran					
	Study [reference]	Province	Year	Population	Prevalence of anti-HEV+ %
	Aminiafshar S et al. [12]	Tehran	2004	Blood donors	7.8
	Safar MJ et al. [14]	Mazandaran	2005	General population	7.2
	Taremi M et al. [13]	Tabriz	2005	Haemodialysis patients	7.4
	Taremi M et al. [15]	Tabriz	2007	Blood donors	7.8
	Ghorbani GA et al. [16]	Tehran	2007	General population	1.1
	Ataei B et al. [17]	Isfahan	2008	General population	3.8

2008

2008

2011

Nahavand

Khuzestan

Urmia

Table 2 Sava anidemialary of honotitic E virus (HEV) in various studies in the Islamic Popublic of Iran

transmission in this region, as well as the possible means of prevention. Two particular vulnerable groups at risk include pregnant women and those already affected with HBV. Unfortunately, at the moment, HEV vaccines have not been mass produced and are not available for public use [23]. However, if a vaccine became available, HEV vaccination should be a health priority in areas such as Zanjan.

Our data indicated a tendency towards a higher rate of HEV infection among patients with > 1 year of haemodialysis versus ≤ 1 year. It is possible that this is an indication of a rising trend

for HEV infection, or that patients who started dialysis in the previous year were somehow more exposed to the risk of infection, or that the risk of infection was simply higher for patients with a longer period of dialysis.

To summarize, the results of our study showed that particular attention should be paid to the problem of HEV epidemiology in the west of Islamic Republic of Iran and possibly in neighbouring countries. We recommend that health officials provide HEV awareness programmes in such areas. Furthermore, because chronic patients may have normal liver enzymes or remain seronegative [24], long-term follow-up of haemodialysis patients seems advisable.

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General population

**Blood donors** 

recipients

Renal transplant

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#### Hepatitis E

The hepatitis E virus is transmitted mainly through the faecal-oral route due to faecal contamination of drinking water. Other transmission routes have been identified, which include:

- foodborne transmission from ingestion of products derived from infected animals;
- zoonotic transmission from animals to humans;
- transfusion of infected blood products;
- vertical transmission from a pregnant woman to her fetus.

The highest seroprevalence rates of hepatitis E are observed in regions where low standards of sanitation increase the risk for transmission of the virus. Over 60% of all hepatitis E infections and 65% of all hepatitis E deaths occur in East and South Asia, where seroprevalence rates of 25% are common in some age groups. In Egypt, half the population aged above 5 years is serologically positive for the hepatitis E virus.

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# Experience of malaria in children of a flood affected area: a field hospital study

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# معاناة الأطفال من الملاريا في المناطق المتضررة من الفيضان: دراسة لمستشفى ميداني محمد فهيم أفضل، محمد أشرف سلطان

الخلاصة: تهدف هذه الدراسة إلى التعرف على تواتُر وقوع الملاريا بين الأطفال الذين يعانون من الحمى في المناطق المتضررة بالفيضان، وعلى تواتُر المتصورة النشيطة والمتصورة المنتجلية بين الحالات. وقد غطت هذه الدراسة المستعرضة المدة بين 1 أيلول/ سبتمبر 2010 و15 كانون الثاني/ يناير 2011 في مستشفى المخيم الميداني الأسترالي والمستشفى الميداني لإحساس؛ في كوت أدو، مقاطعة مظفر آغا في جنوب البنجاب، في باكستان. وقد استقصى الباحثان كل طفل يعاني من الحمى ويقل عمره عن 15 عاماً ويفي بالتعريف السريري لحالة ملاريا مشتبهة غير مترافقة بمضاعفات، وذلك من خلال اختبار تشخيصي سريع. وقد شملت الدراسة 288 20 طفلاً تم فحصهم، من بينهم 3198 طفلاً (16٪) يعانون من الحمى ويفون بتعريف الحالة السريرية، وكان 2016 أطفال (75٪)، وبالمتصورة المنجلية المدى 759 طفلاً (16٪)، والعدوى المشتركة بكليها معاً لدى 85 طفلاً (4٪)، وكانت المتصورة النشيطة هي النوع الأكثر شيوعاً تتلوها المتصورة المنجلية. وقد وفت 27 حالة (4٪) ناجمة عن المتصورة المنجلية بتعريف حالة الملاريا الدماغية. أما الفئة العمرية الأكثر إصابة فكانت 5-9 سنوات (14٪).

ABSTRACT To determine the frequency of malaria among children presenting with fever in a flood affected area, and the frequency of *Plasmodium vivax* and *P. falciparum* among cases, this cross-sectional study was conducted from 1 September 2010 to 15 January 2011 in the Australian Field Camp and Ehsas Field Hospital, Kot Addu, Muzaffargarh District, Southern Punjab, Pakistan. Each febrile child aged  $\leq$  15 years fulfilling the clinical case definition of suspected uncomplicated malaria was investigated by rapid diagnostic test. Of 20 288 children examined, 3198 (16%) febrile patients fulfilled the clinical case definition and 2406 (75%) cases were positive for malaria. *P. vivax, P. falciparum,* and co-infection were present in 1562 (65%), 759 (31%) and 85(4%) cases respectively. *P. vivax* was the most prevalent species followed by *P. falciparum.* Twenty seven (4%) cases of *P. falciparum* fulfilled the case definition of cerebral malaria. The age group most affected was 5–9 years (41%).

## Le paludisme chez des enfants vivant dans une zone touchée par des inondations : étude dans des hôpitaux de terrain

RÉSUMÉ Afin de déterminer la fréquence du paludisme chez des enfants souffrant de fièvre dans une zone touchée par des inondations et la fréquence de *Plasmodium vivax et P. falciparum* parmi les cas, la présente étude transversale a été menée entre le 1er septembre 2010 et le 15 janvier 2011 à l'*Australian Field Camp* et l'*Ehas Field Hospital*, à Kot Addu, dans le district de Muzaffargarh, dans le sud du Pendjab (Pakistan). Chaque enfant fébrile âgé de 15 ans ou moins correspondant à la définition de cas clinique suspect de paludisme simple a subi un test diagnostique rapide. Sur les 20 288 enfants examinés, 3198 patients fébriles (16 %) correspondaient à la définition de cas clinique et 2 406 cas (75 %) étaient positifs pour le paludisme. *P. vivax* a été retrouvé chez 1 562 enfants (65 %), *P. falciparum* chez 759 enfants (31 %) et une co-infection chez 85 cas (4 %). *P. vivax* était l'espèce la plus prévalente suivie par *P. falciparum*. Vingt-sept cas d'infection par *P. falciparum* (4 %) correspondaient à la définition de neuropaludisme. Les enfants âgés de cinq à neuf ans constituaient la tranche d'âge la plus touchée (41 %).

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#### Introduction

The World Health Organization (WHO) reported about 3.3 billion people at risk of malaria globally; this leads to about 250 million malaria cases and nearly 2 million deaths every year. The estimated number of annual malaria episodes in Pakistan is 1.5 million [1].

Malaria transmission risk can increase in natural disasters such as floods. During flooding, changes in human behavior and in the habitat can promote mosquito breeding. (e.g. river damming, and rerouting) [2].

The monsoon flood 2010 in Pakistan was the biggest disaster in history of the country. The National Disaster Management Authority estimated that over 17.6 million people were affected, exceeding the combined total of individuals affected by the 2004 Indian Ocean tsunami, the 2005 earthquake in northern areas of Pakistan and Kashmir and the 2010 Haiti earthquake [3]. The United Nations reported nearly 300 000 suspected malaria cases in flood-affected areas from the end of July 2010 to October 2010 [4].

This study was conducted in 2 outreach field hospitals in Kot Addu to determine the frequency of malaria among children presenting with fever in the flood-affected area, and the frequency of Plasmodium vivax and P. falciparum among the malaria cases. Determining the species of Plasmodium in a community settings suffering from a disaster, where microscopy is not possible, is crucial. Healthcare personnel would thus be guided by the results of the malaria rapid diagnostic testing to decide on the most suitable course of treatment: chloroquine or artemisinin-based coms bination therapy.

#### Methods

This cross-sectional study was conducted from 1 September 2010 to 15 January 2011 in the Australian Field

Camp and Ehsas Field Hospital, Kot Addu, Muzaffargarh District, Southern Punjab, Pakistan. Kot Addu is a remote area along the river Indus in Southern Punjab, Pakistan which was among the regions most affected by flooding. The Australian Government established a medical relief camp in Kot Addu in September 2010. Later on, the 100-bed mobile Ehsas Field Hospital was established at the end of September 2010 in partnership with the Government of the Punjab and King Edward Medical University/Mayo Hospital, Lahore. The paediatric department of this field hospital was under the Department of Paediatrics, King Edward Medical University/Mayo Hospital, Lahore.

All children aged ≤ 15 years who presented with a febrile illness were included in the study. A trained paediatric resident was deputed for patient evaluation. A total of 20 288 children aged ≤ 15 years were examined in the paediatric outpatient departments of both hospitals. Each febrile child was evaluated according to the clinical case definition of suspected malaria (history of recent fever, with  $\geq 1$  among chills, headaches, body aches, perspiration, tiredness, and pallor) [5]. Thereafter, each child was investigated for evidence of malaria infection by CareStart malaria pLDH/HRP2 combo rapid diagnostic test (RDT). The CareStart malaria pLDH/HRP2 combo RDT kits were provided by the WHO to detect P. falciparum and non-falciparum infections (or both) in community setting, distant from microscopy facilities [6]. These RDTs had a sensitivity of 96% and a specificity of 97% (manufacturer's data) [7]. Supervisors from the local Centre for Disease Control (CDC) and laboratory technicians from the field hospital were trained in the use of the CareStart malaria pLDH/HRP2 combo RDT and the interpretation of the results. Results were read after 20 minutes. A patient was labelled as a confirmed malaria case if they tested positive for one or both *Plasmodium* spp. [5]. Cases of cerebral malaria were also identified in line with the clinical case definition (fever, confusion, seizures, coma, and/or focal neurological signs) [5]. The information was recorded on a structured questionnaire.

Data were entered in SPSS, version 17. Each patient was treated on an individual basis. Cases of uncomplicated *P. vivax* malaria were treated with chloroquine and primaquine, while *P. falciparum* cases were treated with artemisinin-based therapy (Artesunate). Cases of cerebral malaria were referred to nearby tertiary care hospitals after initial emergency management.

#### Results

Out of 20 288 children aged ≤ 15 years presenting with fever, 3198 (16%) fulfilled the clinical case definition of suspected uncomplicated malaria; 2406 (75%) of these tested positive for malaria (confirmed cases). *P. vivax* was present in 1562 (65%) cases, *P. falciparum* in 759 (31%) and co-infection in 85 (4%) (Table 1). Twenty seven (4%)

Table 1 Distribution of malaria cases and *Plasmodium* species (n=2406)

Cases	No.	%
Total examined	20 288	100
Clinically suspected malaria	3198	16
Confirmed malaria	2406	12
P. vivax	1562	65 <sup>a</sup>
P. falciparum	759	31 <sup>a</sup>
Co-infection	85	<b>4</b> <sup>a</sup>

<sup>&</sup>lt;sup>a</sup>As percentage of confirmed cases.

cases of *P. falciparum* malaria fulfilled the clinical case definition of cerebral malaria.

The most common age group affected was 5–9 years (41%), followed by 10–15 years (31%), 1–4 years (19%) and < 1 year (9%) (Figure 1).

#### Discussion

Our study shows that in children who presented with fever in the flood-affected region of Pakistan in 2010/2011, the incidence of suspected malaria was 16%. The disease early warning system (DEWS) of the WHO estimated that out of 13 095 799 total consultations reported throughout the country from 29 July 2010 to 13 January 2011, 752 637 (6%) were for suspected malaria [8]. Similarly, in Punjab over the same period, of 29 728 93 total consultations (all age groups), suspected malaria was reported in 151 785 (5%) cases [8]. The difference may be due to the fact that our study focused on Southern Punjab while the WHO data was for whole province.

Our findings in regard to *Plasmo-dium* infection in febrile children in a flood-affected area are in accordance with those from WHO, which reported both *P. vivax* and *P. falciparum* cases in Muzaffarghar district in Southern

Punjab [8]. Looking at the international data from other flood-affected regions, we find epidemics of malaria in Costa Rica's Atlantic region in 1991, the Dominican Republic in 2004 [2], Surat, India in 2006 [9] and in eastern Yemen in 2008 [10].

Malaria case management remains a vital component of the malaria control strategies. This entails early diagnosis and prompt treatment with effective antimalarial medicines. In the present study, cases of uncomplicated P. vivax malaria were treated with chloroquine and primaquine, while P. falciparum cases were treated with artemisininbased therapy provided by WHO for disaster areas [6]. WHO recommends chloroquine combined with primaquine for uncomplicated P. vivax as treatment of choice for chloroquine-sensitive infection and artemisinin-based combination therapy (ACT) for treatment of uncomplicated P. falciparum malaria [11]. The National Malaria Control Programme in Pakistan has similar recommendations for the treatment of malaria infection [12]. However, WHO has also recommended that where ACT therapy has been adopted as the first line treatment for P. falciparum malaria, it may also be used for P. vivax malaria in combination with primaquine for radical cure [11]. A regional study reported

only 1.3% resistance to chloroquine for *P. vivax* and *P. falciparum* co-infection in 2006 [13] whereas the National Malaria Control Programme reported in 2007 that 40% of cases of *P. falciparum* were resistant to chloroquine [12].

In our population, even in disaster circumstances, P. vivax was more common (65%). The National Malaria Control Programme also reported *P.* vivax as the dominant species (75%) [12]. Similarly, studies in stable populations in Pakistan have shown a predominance of P. vivax in children [13,14]. Therefore, to guide the treatment of malaria, the correct approach would be to request confirmatory diagnosis of malaria in all suspected cases using microscopy, but in community settings like disaster areas, where microscopy is not possible, combination RDTs with high diagnostic performance for P. falciparum and P. vivax should be used to identify the species. Treatment with chloroquine or ACTs should then be guided by the results.

The strength of the present study is in being the first field hospital study from a disaster area to report on malaria infection along with *Plasmodium* spp. from one of the regions most affected by the floods in southern Punjab. The main limitation of our study was the lack of clinical follow-up of cases owing to the mass displacement and loss of communication in the disaster situation.

# 700 600 500 Co-infection R. vivax P. falciparum Co-infection

Figure 1 Age distribution of children (*n* = 2406) with clinically confirmed malaria in a flooded area in southern Punjab, 2010–2011

#### Recommendations

Suspicion for malaria among febrile children must be kept in mind in disaster circumstances. In the fields of community setting, distant from microscopy, it is recommended that combination RDTs with high diagnostic performance to *P. falciparum* and *P. vivax* should be used for the diagnosis. Treatment with either chloroquine or ACTs should be guided by the results. Early referral of non-responders is also recommended. We believe that malaria

prevention awareness campaigns be launched in malaria-endemic and disaster-prone areas of the region.

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## Diarrhoeagenic *E. coli* pathotypes in children with and without diarrhoea in an Iranian referral paediatrics centre

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#### تكرار الأنهاط المسببة للمرض وللإسهال من الإشريكية القولونية لدى الأطفال المصابين بالإسهال وغير المصابين به في أحد المراكز الإيرانية للإحالة في طب الأطفال

بابك بور أكبري، حسين حيدري، شيها محمودي، فرح صابوني، مصطفى تيموري، فرزاد فردوسيان، محمد تقي حقى أشتياني، ستاره مميشى الحلاصة: يمكن اعتبار الإشريكية القولونية المسببة للإسهال أهم العوامل المسببة للمرض وللإسهال في جمهورية إيران الإسلامية، ولاسبًا لدى الأطفال. وتهدف هذه الدراسة إلى التعرف على تكرار مستفردات الإيشريكيات القولونية المسببة للإسهال التي جُعِعَتْ من خمسين طفلاً ممن الأطفال الشواهد، وذلك في مركز للإحالة في طب الأطفال في إيران على مدى سنة واحدة. واستخدم الباحثون الاختبار المتعدد للتفاعل السلسلي للبوليمراز للتعرف على الإشريكيات القولونية المسببة للإسهال، فاكتشفوها لدى 90٪ من مجموعة الحالات، ولدى 20٪ من مجموعة الشواهد. وكانت الإشريكية المولّدة للذيفانات المعوية هي النمط المسبب للمرض الأكثر تكراراً الذي تم التعرف عليه لدى كلتا المجموعتين (26٪ لدى مجموعة الحالات و 10٪ لدى مجموعة الشواهد)، واحتلت الإشريكيات القولونية المنتجة لذيفان شيغا المرتبة الثانية بين الأنهاط المستفردة المسببة للأمراض (17٪)، تلاها الإشريكيات القولونية المعونية المحتفرة المسببة للأمراض (17٪)، تلاها الإشريكيات القولونية المعونية المعاء أو محرضة للأمعاء. وقد وُجِدَ في أكثر من 80٪ من المستفردات جين fimH. ويرى الباحثون أن النسبة المرتفعة للإشريكيات القولونية المسببة للإسهال وتنوع أنهاط الإشريكيات القولونية يؤكّد الحاجة إلى الترصّد المعودي المعاء. وقد وُجِدَ في أكثر من 80٪ من المستفردات جين fimH. ويرى الباحثون أن النسبة المرتفعة للإشريكيات القولونية إلى النرصّد المعاء وتنوع أنهاط الإشريكيات القولونية يؤكّد الحاجة إلى الترصّد المعود التي تسبب التهابات المعدة والأمعاء لدى الأطفال في إيران.

ABSTRACT Diarrhoeagenic *Escherichia coli* can be considered as the most important etiologic agents of diarrhoea in the Islamic Republic of Iran, particularly in children. This study determined the frequency of diarrhoeagenic *E. coli* isolates collected from children with acute diarrhoea (*n* = 50) and a control group (*n* = 50) at an Iranian referral paediatric centre during a 1-year period. Using multiplex PCR, diarrhoeagenic *E. coli* was identified in 90% of the case group and 20% of controls. Enterotoxigenic *E. coli* was the most frequently identified pathotype in both groups (26% in cases; 10% in controls). Shiga toxin-producing *E. coli* was the second most isolated pathotype (17%), followed by enteroaggregative *E. coli* (12%). No enteroinvasive *E. coli* and enteropathogenic *E. coli* strains were recovered. More than 80% of isolates harboured the *fimH* gene. This high proportion of diarrhoeagenic *E. coli* and diversity of *E. coli* types highlights the need for enhanced surveillance of gastroenteritis agents in children in this country.

## Pathotypes *Escherichia coli* diarrhéogènes chez des enfants souffrant ou non de diarrhées dans un centre pédiatrique d'orientation-recours iranien

RÉSUMÉ Les souches d'*Escherichia coli* diarrhéogènes peuvent être considérées comme les agents étiologiques les plus importants à l'origine de diarrhées en République islamique d'Iran, notamment chez l'enfant. La présente étude a déterminé la fréquence d'*E. coli* diarrhéogènes à partir d'isolats recueillis chez des enfants souffrant de diarrhées aiguës (n = 50) et dans un groupe témoin (n = 50) au sein d'un centre pédiatrique d'orientation-recours iranien pendant un an. À l'aide de la PCR multiplexe, *E. coli* diarrhéogène a été identifié chez 90 % des patients et 20 % des témoins. *E. coli* entérotoxinogène était le pathotype le plus fréquemment identifié dans les deux groupes (26 % des cas ; 10 % des témoins). *E. coli* producteur de shiga-toxine était le deuxième pathotype le plus fréquemment isolé (17 %), suivi par *E. coli* entéroagglutinant (12 %). Aucune souche d'*E. coli* entéroenvahissant ni d'*E. coli* enteropathogène n'a été découverte. Plus de 80 % des isolats hébergeaient le gène fimH. La proportion élevée de souches *E. coli* diarrhéogènes et la diversité des types d'*E. coli* soulignent la nécessité d'une surveillance accrue des agents de gastro-entérites chez les enfants de ce pays.

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#### Introduction

Diarrhoeal disease is still a major health problem, especially in developing countries, where it is considered one of the leading causes of morbidity and mortality especially in children aged less than 5 years [1]. Among the bacterial causes of diarrhoea, diarrhoeagenic *Escherichia coli* is the most important etiologic agent of children's diarrhoea in the Islamic Republic of Iran [2,3].

Identification of *E. coli* pathotypes is limited in many developing countries because conventional microbiological testing is unable to distinguish between normal flora and pathogenic strains [4]. Molecular identification and classification of diarrhoeagenic E. coli is based on the presence of different chromosomal or plasmidencoded virulence genes, which are absent in the commensal *E. coli* [5]. Five categories of *E. coli* have been associated with diarrhoea in several epidemiological studies: enteropathogenic E. coli (EPEC), enteroaggregative E. coli (EAEC), enterotoxigenic E. coli (ETEC), enteroinvasive E. coli (EIEC) and Shiga toxin-producing E. coli (STEC) [5]. Infections caused by pathogenic *E. coli* are often initiated by binding of the bacteria to the host cell surface via specific bacterial adhesins. Binding of fimbrial adhesins enabling bacteria to adhere to host cells. Type 1 fimbriae were the adhesins first described in E. coli [6].

The features of acute diarrhoea vary from place to place depending on local meteorology, geography and socioeconomic variables. Knowledge of the major etiologic agents of this disease is important for epidemiological surveillance and correct treatment. The goal of our study was to evaluate the frequency of *E. coli* pathotypes and type 1 fimbriae in children attending a referral hospital in Tehran, Islamic Republic of Iran.

#### Methods

#### Study design and setting

In this study, a total of 100 random *E. coli* isolates of stool samples were collected and processed during a 1-year period (2010–11) from patients attending the Children's Medical Centre. In addition to being a referral tertiary care centre this is one of the major teaching hospitals of Tehran University of Medical Sciences. It admits patients from all regions of Islamic Republic of Iran, representing a wide spectrum of socioeconomic levels.

#### Sample

A random sample of 50 children aged > 1 month to 12 years old with acute diarrhoea referred to the Children's Medical Centre over a 1-year period were selected as case patients and enrolled into the study. Diarrhoea was defined, according World Health Organization guidelines as the occurrence of 3 or more, loose, liquid or watery stools within 24 hours [7]. To ensure optimum recovery of E. coli all specimens were obtained within 24 h of the onset of illness and before any antimicrobial treatment had begun. During the same period, 50 children with no evident signs and symptoms of gastroenteritis were recruited from the general population as controls. These patients were apparently healthy, with the same age range and sex, and included healthy volunteers, individuals presenting to clinics for routine health maintenance visits and individuals presenting to the emergency department.

#### Data collection

After informed consent was obtained from each child's parent, stool samples were collected and transported immediately to the microbiology laboratory for analysis within 2 hours of collection.

#### Bacteriological procedures

All bacterial isolates were microbiologically identified in the microbiology

laboratory of the hospital using standard identification methods [8].

#### DNA extraction

*E. coli* clinical isolates were processed for isolation of genomic DNA as previously described [9].

## Detection of fimH gene and E. coli pathotypes

Detection of specific virulence genes by polymerase chain reaction (PCR) is frequently used because this method gives rapid, reliable results with a high sensitivity and a high specificity [5,10]. Having confirmed the specificity of each primer set by single PCR, we combined primer sets and tested the control strains in several PCR cycling protocols. The targets selected for each category were fimH for type 1 fimbriae, aggR for EAEC, eae for EPEC, stx1 and stx2 for STEC, lt and st for ETEC, and invE for EIEC. For each of the target genes, different pairs of primers were selected from the literature [11,12].

The multiplex PCR reactions were performed using 10× PCR buffer; 100 mM MgCl<sub>2</sub>; 10 mM dNTP; 1.5 U Taq DNA polymerase and each of primers. The PCR programme was 94 °C for 30 s, 55 °C for 30 s, and 72 °C for 30 s, for 30 cycles, and 72 °C for 3 min. PCR products were then electrophoresed on a 1.5% agarose gel.

#### Results

## Background characteristic of patients

In this study, multiplex PCR was used to detect pathotypes of *E. coli* in 50 children with diarrhoea and 50 control children. The patients were analysed in 4 age groups < 6 months (n = 11), 6–11 months (n = 20), 12–23 months (n = 50) and  $\geq 24$  months (n = 19). There were 32 males and 68 females. Children were enrolled during all seasons: spring (n = 21), summer (n = 27), fall (n = 22), and winter (n = 30).

### Diarrhoeagenic *E. coli* strains isolated

A total of 55 isolates of diarrhoeagenic *E. coli* were isolated from the 100 children, including 45/50 (90%) from patients with diarrhoea compared with 10/50 (20%) from the control group.

ETEC was the most common pathotype, found in 26/100 (26%) of the total children: 21/50 (42%) cases with diarrhoea and 5/50 (10%) controls. Among 26 ETEC strains, 8/26 were positive for the *lt* gene (7 cases; 1 controls) and 15/26 for the st gene (11 cases; 4 controls), while 3/26 strains possessed both genes (3 cases; 0 controls) (Table 1). STEC was found in 17/100 (17%) children (14 cases; 3 controls) (Table 1). stx1 in combination with stx2 was seen exclusively in the case group (10/50 cases). EAEC was isolated from 12/100 (12%) children. Among the EAEC isolates, the aggR gene was seen in 10/50 (20%) cases and 2/50 (4%) controls. We did not find any eae and invE positive strains. No EIEC or EPEC strains were recovered.

Two different types of diarrhoeagenic *E. coli* were isolated from 8/50 (16%) cases and none of the controls. The most frequent combination was

Table 1 Frequency of different diarrhoeagenic *Escherichia coli* strains isolated from the case group of children with diarrhoea and the control group

Pathotype	N	o. of strains isolate	ed
	Cases (n = 50)	Controls ( <i>n</i> = 50)	Total ( <i>n</i> = 100)
STEC			
Stx1-producing	1	1	2
Stx2-producing	3	2	5
Stx1 + stx2-producing	10	0	10
ETEC			
lt-producing	7	1	8
st-producing	11	4	15
lt + st-producing	3	0	3
EAEC	10	2	12
EIEC	0	0	0
EPEC	0	0	0
Total isolates	45	10	55

STEC = Shiga toxin-producing E. coli; ETEC = enterotoxigenic E. coli; EAEC enteroaggregative E. coli; EIEC = enteroinvasive E. coli; EPEC = enteropathogenic E. coli.

n = total number of children.

STEC with ETEC in 7/8 of these cases (Table 2).

In our study, type 1 fimbriae was expressed by the majority of ETEC isolates (19/26, 73%). In addition, this gene was detected in 14/17 (82%) STEC isolates (Table 2).

#### Variations by age and season

No difference in the rate of detection of diarrhoeagenic *E. coli* proportion was

found between the dry (summer) and rainy season (autumn) samples. Of the faecal strains obtained in winter, 24/30 (80%) were diarrhoeagenic *E. coli*: 18/30 (60%) cases and 6/30 (20%) controls.

We divided the samples according the age (Table 2). Despite detection of diarrhoeagenic *E. coli* in faecal specimens from children in all ages, there was

Table 2 Frequency of different diarrhoeagenic *Escherichia coli* strains isolated from the case group of children with diarrhoea and the control group, by age group

Pathotype	No. of strains isolated									
		C	ontrol group					Case group		
	0-5 yrs	6-11 yrs	12-23 yrs	≥ <b>24</b> yrs	Total	0-5 yrs	6-11 yrs	12-23 yrs	≥ <b>24</b> yrs	Total
STEC	0	0	0	0	0	1	0	0	1	2
ETEC	0	0	1	0	1	0	1	3	1	5
EAEC	0	0	1	0	1	0	0	3	0	3
STEC + EAEC	0	0	0	0	0	0	0	1	0	1
STEC + fimH	0	1	2	0	3	0	1	3	1	5
ETEC + fimH	1	1	2	0	4	0	2	4	3	9
EAEC + fimH	0	0	1	0	1	0	2	3	1	6
STEC + ETEC + fimH	0	0	0	0	0	1	0	3	2	6
STEC + ETEC	0	0	0	0	0	0	0	1	0	1
Total children	4	11	25	10	50	7	9	25	9	50

STEC = Shiga toxin-producing E. coli; ETEC = enterotoxigenic E. coli; EAEC enteroaggregative E. coli; EIEC = enteroinvasive E. coli; EPEC = enteropathogenic E. coli; fimH = type 1 fimbriae.

a higher frequency of recovery of strains among children aged 12-23 months in the case group [21/25 (84%)] than the control group [7/25 (28%)].

#### Discussion

Knowledge of the status of the enteropathogenic bacteria responsible for diarrhoea in the Iranian population is essential for implementation of appropriate public health measures to control these diseases [3]. The present study was performed to identify the frequency of diarrhoeagenic *E. coli* as a potential etiologic agent of diarrhoeal disease in an Iranian referral paediatrics centre. The most frequent *E. coli* pathotype in our study was ETEC, which corresponded to 26% of the total children studied (81% of the case group and 19% of the control group). Among diarrhoeagenic *E. coli*, ETEC has been noted as the most common, particularly in the developing world [13]. Variation in the prevalence of ETEC toxin types may occur from year to year and among different geographic areas. In our study, strains carrying only the st gene were more

prevalent (15/26, 58%) than those carrying genes for lt (8/26, 31%) or both st and lt genes (3/26, 11%). This result agrees with the report of other studies in Egypt and Tunisia that the st-expressing ETEC was the most common form [14,15].

STEC was the second most common diarrhoeagenic *E. coli* pathotype, isolated from 17% of children. According to a previous report from the Islamic Republic of Iran, this organism has high frequency in the Iranian population [16]. Although EPEC was the third most abundant E. coli after STEC and EAEC in previous studies in our country, we did not find this pathotype in this study [11,12]. The lack of EIEC isolates in our study and the low rate of its recovery in other studies suggests that this pathotype may play a less important role in childhood diarrhoea in developing countries [17,18].

Isolation of combinations of 2 diarrhoeagenic *E. coli* types in our study (8% of children, 16% of cases) was higher than the recent report in León, Nicaragua. In our study, the combination of ETEC and STEC was the most frequent, while in Vilchez et al.'s study

coinfection with EAEC and EPEC was common and reported in 3.9% of cases [19].

A high frequency of diarrhoeagenic *E. coli* was found in the age group 12–23 months in the case group: 18/30 (60%). In addition, 7/25 (28%) of the control group in this age had diarrhoeagenic *E. coli* pathotypes. We speculate that children at this age are immunologically naive and may not possess a specific immune response to new pathogens. In addition, the behaviour of children in this age group might be another factor that exposes them to more risk factors compared with younger and older children.

#### Conclusion

Our results show a high rate of diarrhoeagenic *E. coli* among Iranian children with diarrhoea. The finding of diverse *E. coli* types, even within a small number of *E. coli* isolates, focuses attention on the importance of pathogenic *E. coli* and stresses the need for enhanced surveillance of gastroenteritis agents in children in the Islamic Republic of Iran.

**Competing interests:** None declared.

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#### Diarrhoeagenic diseases

Diarrhoeal diseases represent a major health problem in developing countries. The wide diversity of bacterial and viral infections that may cause diarrhoea [5] complicates accurate surveillance and diagnosis, especially in developing countries with little or no access to modern laboratory procedures

Numerous types of diarrhoeagenic E. coli strains have been identified worldwide, including enteropathogenic (EPEC), enterohaemorragic (EHEC), enteroinvasive (EIEC), enterotoxigenic (ETEC), Shiga toxin-secreting (STEC), diarrhoea-associated haemolytic (DHEC), entero-aggregative (EAAggEC), and cytolethal distending toxin-secreting (CDTEC) E. coli strains. The prevalence of these strains and the burden of disease they cause are however unequal.

Further information on diarrhoeal diseases can be found at: http://www.who.int/vaccine\_research/diseases/diarrhoeal/en/index.html

## Awareness of World Health Organization methicillinresistant *Staphylococcus aureus* guidelines at Alexandria University hospitals

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الوعي بالدلائل الإرشادية لمنظمة الصحة العالمية حول العنقوديات الذهبية المقاومة للميثيسيلين في مستشفيات جامعة الإسكندرية جيرمين سامح سليان، راندة محمود أبو يوسف، بيشوي فهمي صليب، أحمد محمد المغازي، عادل زكي

الخلاصة: تهدف دراستنا المستعرضة هذه إلى تقييم معارف العاملين الطبيين في مستشفيات جامعة الإسكندرية حول طرق السراية، والمعرفة بالدلائل الإرشادية لمكافحة العنقوديات الذهبية المقاومة للميثيسيلين، وأسباب عدم الامتثال لتلك الدلائل الإرشادية. وقد شملت العينة العشوائية 158 طبيباً 67.4%، محرضة أجابوا على استبيان يدار ذاتياً، وتبيَّن للباحثين أن الوعي الإجمالي بالدلائل الإرشادية لمكافحة العنقوديات الذهبية المقاومة للميثيسيلين يبلغ 67.3%، وأن الممرضات أكثر وعياً (15.5%) من الأطباء (60.0%)، وكان أخفض مستوى للوعي بين أطباء التخدير، إذ لم يعرف سوى 54.4% منهم طرق السراية الصحيحة. وقد تقبَّل 70% من الأطباء العاملين الطبيين ضرورة اتخاذ تدابير التحري لدى المرضي المعرضين لاختطار مرتفع، كما تقبَّل 8.55% من الأطباء استخدام القفازات ذاتها عند رعاية مواضع مختلفة من الجسم لدى نفس المريض. واتضح أيضاً أن نقص الموارد هو التبرير الأكثر شيوعاً لعدم بلوغ الحد القريب من الأمثل في الامتثال. وتظهر الدراسة انخفاض مستوى الوعي بالدلائل الإرشادية حول مكافحة العنقوديات الذهبية المقاومة للميثيسيلين.

ABSTRACT This cross-sectional study aimed to assess knowledge of routes of transmission, awareness of MRSA control guidelines and reasons for non-adherence to guidelines among medical staff at Alexandria University hospitals. A random sample of 158 physicians and 47 nurses answered a self-administered questionnaire. Overall awareness of MRSA control guidelines was 67.3%, and nurses were significantly more aware than physicians (91.5% versus 60.1%). The lowest awareness level was among anaesthesiologists; only 54.4% knew the correct transmission routes. Among medical staff overall, 70.0% accepted the necessity of screening measures for high-risk patients and 35.8% of doctors accepted the use of the same pair of gloves when caring for different body sites on an individual patient. Lack of resources was the most common justification for suboptimum adherence. The study showed low awareness levels of MRSA-related guidelines.

## Sensibilisation aux recommandations de l'Organisation mondiale de la Santé sur la lutte contre *Staphylococcus aureus* résistant à la méthicilline dans des hôpitaux universitaires d'Alexandrie

RÉSUMÉ La présente étude transversale visait à évaluer la connaissance des voies de transmission, la sensibilisation aux recommandations sur la lutte contre *Staphylococcus aureus* résistant à la méthicilline et les motifs du non respect de ces recommandations par le personnel médical des hôpitaux universitaires d'Alexandrie. Un échantillon randomisé de 158 médecins et 47 infirmières ont répondu à un auto-questionnaire. Globalement, la sensibilisation aux recommandations sur la lutte contre *Staphylococcus aureus* résistant à la méthicilline était de 67,3 %, et le personnel infirmier était beaucoup plus sensibilisé que les médecins (91,5 % contre 60,1 %). Le niveau de sensibilisation le plus faible a été retrouvé chez les anesthésistes. Seuls 54,4 % de ces derniers connaissaient les voies de transmission correctes. Au sein du personnel médical globalement, 70,0 % avaient accepté la nécessité de mesures de dépistage pour les patients à haut risque mais 35,8 % des médecins reconnaissaient utiliser une seule paire de gants même lors de soins prodigués sur différents sites corporels d'un même patient. Le manque de ressources était la justification la plus fréquente pour le respect insuffisant de ces recommandations. L'étude a mis en évidence les faibles niveaux de sensibilisation aux recommandations sur la lutte contre *Staphylococcus aureus* résistant à la méthicilline.

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#### Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) is now a major healthcareacquired pathogen, accounting for up to 40% of staphylococcal infections in developed countries [1,2]. Colonization occurs by contact with contaminated wounds, dressings and inanimate objects of infected patients, with another individual's colonized intact skin and by inhalation of aerosolized droplets from chronic nasal carriers [3–5]. Risk factors include surgical site infection, antibiotic use, prolonged hospitalization, intensive care, haemodialysis and proximity to others with MRSA colonization or infection [6-8].

The worldwide MRSA prevalence varies considerably, from less than 1% in Scandinavia to up to 40% in Japan, Israel and elsewhere in Europe [7,9]. In a 2007 study on invasive isolates from southern and eastern Mediterranean countries, the highest proportions of MRSA isolates were reported by Jordan, Egypt and Cyprus. Egypt reported a rate of 52% in comparison with other Mediterranean countries such as Lebanon, Morocco, Algeria, Tunisia and Malta, which reported rates of 12%, 19%, 45%, 18% and 50% respectively, while Jordan and Cyprus reported 56% and 55% respectively [10]. A 2009 study in Alexandria Main University hospitals reported that of 100 S. aureus isolates, 71 were MRSA, mostly from patients in the intensive care unit (ICU) [11].

Countries that have failed to implement early MRSA surveillance and control measures have struggled to control MRSA epidemics [12,13]. The level of awareness of MRSA infection control varies in different countries. A study of medical staff in the United Kingdom (UK) found that knowledge about numerous aspects of MRSA and its management was deficient [14]. In Switzerland a study of adherence to the guideline recommendation of hand washing [15] reported only a 48% adherence rate of health care workers [16].

To the best of our knowledge, there has not been any published study in Egypt investigating the level of awareness among health care workers on MRSA control guideline recommendations. Taking this into account, our study was developed with to assess the level of awareness of health care staff, both physicians and nurses, at Alexandria University hospitals concerning MRSA guideline recommendations, and to determine the reasons, if any, for nonadherence.

#### Methods

#### Study setting and sample

The period of data collection of this cross-sectional study was from September to November 2010 at both the Main University hospital and the Paediatrics and Obstetrics hospitals of University of Alexandria, serving the public sector of the city of Alexandria, Egypt. The units where MRSA was expected to be an important issue were selected, namely: the general ICU, the paediatric ICU (PICU) and neonatal ICU (NICU), the pulmonology medicine department, the anaesthesiology department, the cardiothoracic surgery department and the coronary care unit (CCU). The units totalled 200 beds and the total number of medical staff working in these units was 192 physicians and 75 registered nurses (graduates of the faculty of nursing). Nurses who had graduated from the school of nursing, whose education was in Arabic, did not meet the eligibility requirements for a survey conducted in English. Department heads were informed of the study prior to data collection. A random sample of physicians and registered nurses working in the different selected units were asked to participate in the study.

Those who agreed to complete the questionnaire included a total of 158 physicians and 47 registered nurses. A pilot study of 25 medical staff personnel was conducted to ensure

comprehension and clarity of the questions prior to questionnaire administration.

#### Data collection

Each participant was asked to complete the pre-tested, self-administered questionnaire, which included demographic data such as age, sex, year of graduation, and the unit where he/she worked. The investigator was present to answer any questions.

Initially, using multiple choice questions the questionnaire inquired about knowledge about routes of transmission and the most important risk factor for MRSA infection. Concerning each individual's awareness about the presence of MRSA guidelines, participants were asked: "Have you heard of any guidelines on MRSA and can you mention any?" Medical staff aware of the existence of at least one guideline and able to provide at least one source was deemed "aware"; otherwise "not aware". Those who were not aware of these guidelines did not complete the second part of the questionnaire regarding guideline recommendations.

Regarding their detailed knowledge of the guideline recommendations, each of the World Health Organization (WHO), recommendations was transformed into a true/false question, and the responses were classified as "correct" or "incorrect" [17].

In the final part of the survey, medical staff was asked in an open question format to mention their justification(s) for non-adherence (if any) to MRSA control recommendations in their units. The questionnaire ended by enquiring about methods by which they kept themselves updated on guidelines.

#### Statistical analysis

The data were analysed using *SPSS*, version 15.0. Frequency distributions presenting percentages of different groups of health care professionals interviewed regarding MRSA control guidelines were tabulated. Differences

between percentages of physicians and nurses who gave correct answers for questions covering awareness of guidelines and guideline recommendations were tested using the chi-squared test. For all statistical analyses, the level of significance was set at P < 0.05.

#### Results

Table 1 shows the distribution of respondents (158 physicians and 47 registered nurses) across the different departments. The mean age of the 205 respondents was 32 (SD 7) years; 99 (48.3%) were males and 109 (51.7%) females

### Knowledge about MRSA routes of transmission

Table 2 shows the respondents' awareness of MRSA routes of transmission and main risk factor for MRSA infection in the different units. There was no significant difference between nurses and physicians in their awareness of MRSA routes of transmission (57.4% vs 54.5% respectively, P > 0.05) but significantly more nurses were aware of the main risk factor (23.4% vs 20.3% respectively, P < 0.05). This was particularly evident in the general ICU, CCU and pulmonology departments. In the general ICU 65.2% nurses versus 61.2% of physicians correctly identified MRSA transmission routes, namely airborne mechanisms, contaminated surfaces and skin contact. In the CCU, 60.0% of nurses were aware of the correct MRSA transmission routes, while 55.6% of physicians identified them. Likewise, 40.0% of pulmonology nurses knew how MRSA is transmitted, while only 29.2% of pulmonology physicians knew these routes.

#### Awareness of MRSA guidelines

Medical staff in the NICU and PICU overall showed an 85.7% awareness rate of the MRSA guidelines. This was the highest rate reported from the departments. The general ICU also demonstrated a relatively high rate of awareness (73.3%). In contrast, the rate of guideline awareness was only 45.0% in the anaesthesiology department (Table 3). In each unit, the rate of awareness of nurses was higher than that of physicians, and overall 91.5% of nurses and 60.1% of physicians were aware of the guidelines (*P* > 0.001).

One section of the questionnaire was dedicated specifically to the level of awareness on MRSA guideline recommendations. Notably, 90.7% of nurses and 60.0% of physicians were aware of the importance of screening measures to detect early cases and implement appropriate precautions (P < 0.001). Similarly, 100% of nurses and 90.5% of physicians knew that the detection of cases is mandatory, especially if there is referral from another hospital (P < 0.05). Concerning treatment issues, 86.0% of the nurses acknowledged that airborne precautions should be implemented when caring for a patient

with MRSA pneumonia, while 68.4% of physicians responded similarly (P < 0.05) (Table 4).

More nurses (83.7%) than physicians (64.2%) acknowledged that using only one pair of gloves for each patient when caring for more than one body site is inadequate procedure (P < 0.05). However, 9.3% of nurses and 16.8% of physicians accepted the protocol that the utilization of gloves renders handwashing optional after the care of the patient, according to the severity of the patient's condition (P > 0.05) (Table 4).

The 3 most common justifications given by medical staff for suboptimum adherence to MRSA guideline implementation were: lack of resources (58.2%), lack of staff awareness (32.9%) and non-compliance/negligence (20.3%).

Clinicians used a myriad of sources for learning about and continuing to be updated on MRSA guidelines, namely the Internet in general (23.8%), *UpTo-Date* (20.7%), peers (16.1%), books, journals, *Medscape*, pharmaceutical pamphlets and tutors.

#### Discussion

To the best of our knowledge, this is the first study in Egypt to assess the awareness level of MRSA guidelines, common routes of transmission and the most important guideline recommendations

Table 1 Distribution of the stud	v respondents across	different hospita	l denartments
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Hospital unit	Physicians ( <i>n</i> = 158)	Nurses (n = 47)		otal 205)
	No.	No.	No.	%
Anaesthesiology	20	n/a	20	9.8
Cardiothoracic surgery	13	2	15	7.3
Coronary care unit	18	5	23	11.2
General intensive care unit	67	23	90	43.9
Pulmonology medicine	24	5	29	14.1
Neonatal and paediatric intensive care units	16	12	28	13.7

n/a = not applicable.

Table 2 Awareness of main transmission routes and most important risk factor for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in different units

Unit	Correct MRSA transmission route <sup>a</sup>		factor	oortant risk for MRSA ction <sup>b</sup>
	No.	% correct	No.	% correct
General intensive care unit	56	62.2	18	20.0
Coronary care unit	13	56.5	4	17.4
Neonatal and paediatric intensive care units	18	64.3	8	28.6
Anasthesiology	7	35.0	3	15.0
Cordiothoracic surgery	10	66.7	6	40.0
Internal medicine chest	9	31.0	4	13.8
<i>P</i> -value	<	0.05	> (	0.05

<sup>a</sup>Correct answer: airborne droplets, contaminated surfaces, and skin contact; <sup>b</sup>Correct answer: open skin wounds.

among health care workers at Alexandria University hospitals. Although the study included only hospital departments in which MRSA was considered a major potential infectious threat, the general awareness level towards MRSA guidelines was unexpectedly low (67.3%). Only 20.3% of physicians and 23.4% of nurses correctly identified the most important risk factor for infection, i.e. open skin wounds. Similarly, the correct main routes of transmission were identified by slightly more than half of the medical staff (55.0%). The contrast between the relatively high rate of awareness of MRSA guidelines and the low rates of correct answers about risk factors and routes of transmission may suggest that most of the medical staff

may hear about the existence of MRSA guidelines without actually having adequate, continual access to these guidelines. A Swiss study on hand-washing compliance revealed the consequences of this, in which a lack of awareness of the concepts of a procedure can lead to failure to perform it correctly [15]. Our findings are comparable with a UK study, where only 11.5% of medical staff correctly identified common risk factors for MRSA infection or colonization. Moreover, 25.9% of their staff knew the 2 most common sites of MRSA infection, namely blood and wound/ skin [14].

Our study showed discrepancies in awareness across different hospital departments as well as between physicians

and nurses. Contrary to popular belief, nurses (91.5%) were significantly more aware than physicians (60.1%) about the presence of MRSA guidelines. The lowest awareness levels among physicians were found in the CCU and anaesthesiology units (33.3% and 45.0% respectively), while the highest were in the NICU and PICU (75.0%). Among the nurses, the lowest awareness was in the ICU (82.6%), while 100% in the remaining departments were aware. As to MRSA recommendations, nurses had a significantly higher rate of correct answers compared with physicians about the necessity of screening measures as a strategy for MRSA control (90.7% and 60.0% respectively). Surprisingly, 100% of nurses believed in the principle of early detection of cases, especially those referred from other health care facilities, while only 90.5% of physicians shared the same belief. Since isolation is a pillar of multi-drug resistant infection containment, an absolute consensus for this protocol was expected from medical staff, yet the study revealed that 8.4% of physicians and 4.7% of nurses did not acknowledge this protocol. Reasons behind the higher rates of infection knowledge and awareness of MRSA management practices among nurses compared with physicians should be investigated. Differences in the infection control syllabi at the faculty of medicine and faculty of nursing should

Table 3 Awareness of the guidelines on methicillin-resistant *Staphylococcus aureus* (MRSA) control: comparison of physicians and nurses in different hospital units

Hospital unit	Tot	al	Physi	icians	Nur	ses	<i>P</i> -value
	No. in unit	% aware	No. in unit	% aware	No. in unit	% aware	
General intensive care unit	90	73.3	67	70.1	23	82.6	> 0.05
Coronary care unit	23	47.8	18	33.3	5	100.0	< 0.01
Neonatal and paediatric intensive care units	28	85.7	16	75.0	12	100.0	> 0.05
Anaesthesiology	20	45.0	20	45.0	n/a	n/a	
Cardiothoracic surgery	15	66.6	13	61.5	2	100.0	> 0.05
Pulmonology	29	62.1	24	54.2	5	100.0	> 0.05
Total	205	67.3	158	60.1	47	91.5	< 0.001

n/a = not applicable.

Table 4 Assessment of knowledge of health-care workers on methicillin-resistant *Staphylococcus aureus* (MSRA) control guideline recommendations: comparison of physicians and nurses

Guideline recommendation		rsicians = 95)		urses = 43)	<i>P</i> -value
	No.	% correct	No.	% correct	
Screening of high-risk patients will ensure early detection so that appropriate precautions can be implemented	57	60.0	39	90.7	< 0.001
Detection of cases is necessary, especially if they are admitted from another hospital	86	90.5	43	100.0	> 0.05
Ward transfers of staff and patients must be minimized	90	94.7	40	93.0	> 0.05
Isolation of infected or colonized patients in a single room or isolation unit or cohorting in a larger ward is recommended	87	91.6	41	95.3	> 0.05
Treat patients with MRSA pneumonia with airborne precautions in place	65	68.4	37	86.0	< 0.05
Must not use the same pair of gloves if handling more than one body site when caring for an individual patient	61	64.2	36	83.7	< 0.05
Hand washing after contact with infected or colonized patients is essential	93	97.9	41	95.3	> 0.05
Use of an antiseptic hand washing agent or alcohol hand-rub or hand gel is required	92	96.8	41	95.3	> 0.05
Must wear gloves when attending to patient or when handling MRSA-contaminated materials	92	96.8	42	97.7	> 0.05
Washing hands after taking off gloves when dealing with patients is not optional according to the severity of the patient's condition	79	83.2	39	90.7	> 0.05
Need to wear a gown or apron when attending to patients or when handling contaminated materials	81	85.3	41	95.3	> 0.05
Must ensure that operating surgeons should not perform surgeries until declared negative for carriage	62	65.3	30	69.8	> 0.05

be revised as one of the possible reasons. According to the UK study, doctors were more competent in knowing treatment measures for MRSA patients, while nurses excelled in infection control practices [14]. A similar finding of the superior competence in infection control of nurses over doctors was in the Swiss paper on hand washing compliance in a teaching hospital. In 2834 observed opportunities for hand washing, there was a 48% compliance rate, of which the non-compliance was higher among doctors than nurses [15].

In addition to substantial variation of responses between physicians and nurses, our findings showed that individual departments differed considerably on many guideline recommendations, such as the necessity of airborne precautions when caring for a patient with MRSA pneumonia. The pulmonology department valued this protocol more than other departments.

Hence, protocols tailored according to the nature of work and the priorities of the various departments should be designed to ensure efficient protocol implementation. This is backed by a 2005 Dutch study on MRSA protocols in which a questionnaire and practical tests found that health care workers' knowledge of and attitudes towards protocols were adequate, yet they were inefficient at applying the protocols in their work circumstances, suggesting that it is impractical to use one MRSA protocol for all hospital staff due to the different decisions staff have to take according to their respective circumstances [18].

Our study showed that 35.8% of doctors and 16.3% of nurses considered it acceptable to use the same pair of gloves when caring for different body sites on each individual patient (P > 0.05). These low percentages are comparable to the Swiss study, where hand

washing compliance was found to be higher for low-risk procedures e.g. after wound care, and lower for procedures with a high risk of transmission e.g. 11% for care between dirty and clean body sites and 18% for before respiratory care [15].

Health care institutions striving for standard infection prophylaxis and management practice among their specialist as well as non-specialist staff members must invest their resources in improving generic knowledge of staff, as well as familiarizing them with the utilization of local guidance [14]. About one-third of our medical staff mentioned that lack of awareness was a cause for non-implementation of guidelines. This emphasizes the need for workshops and seminars to focus on key topic areas as well as issues assumed to be generic and trivial and which may therefore be overlooked when designing an infection control

programme. The UK study showed that 68% of medical staff thought that more information was needed within their respective departments on the issues of MRSA colonization, infection, virulence, risk factors, general management and drug treatment, confirming that assumptions should not be made about adequate knowledge and expertise of staff in relation to MRSA [14]. Cabana et al's paper examining reasons why physicians do not follow clinical practice guidelines stated that the first step in improving clinicians' adherence to clinical practical guidelines is the attainment of thoroughly competent knowledge and attitudes, which culminates in the most sustainable change in clinician behaviour among all infection control strategies [19]. There are 4 critical sequential steps of any health education programme for ameliorating the behaviour of health care workers towards adhering to MRSA control guidelines: to be aware of the guidelines; to intellectually agree with them; to decide to adopt them in provided care; and to regularly and properly adhere to these guidelines, comprising the awarenessto-adherence model of clinical guideline compliance [20].

Despite the fact that MRSA guideline implementation by means of personal protective equipment and hand-washing stations is not costly, the most frequent justification given by

medical staff for non-implementation in their departments was the lack of resources (58.2%). This issue needs to be discussed with university hospital administrators.

In the UK study, only 2.3% of interviewees referred solely to the hospital's recommended resource for infection management consultation (a pocketsized prescribing guide booklet handed to all clinicians) [14]. This agrees with our study, where clinicians reported using a myriad of sources for learning about and staying updated on MRSA guidelines, such as (in decreasing order of frequency) the Internet in general, UpToDate, peers, books, journals, Medscape, pharmaceutical pamphlets and tutors. Hospital administrators and medical and nursing faculty staff need to develop a multi-specialty educational source by taking advantage of the varied sources to target key educational needs, incorporating them into undergraduate and postgraduate teaching systems and integrating them into the clinical decision-making of practitioners.

Some medical staff (17.7%) stressed that work overload was a cause for decreased compliance with clinical guidelines. The Swiss study found that hand washing compliance decreases with increased patient care intensity [15]. This is supported by another study claiming that understaffing of wards decreases compliance with isolation

measures [21]. Hospital administrators must be approached in order to address the demands of health care workers for work relief.

We do not known whether our results can be generalized to other regions or even other health care institutions in Egypt, since the infrastructure and work organization of individual health care institutions influence the knowledge, outlook and attitude of health care workers.

#### **Conclusions**

The study showed relatively low levels of awareness of MRSA guidelines among health care workers in Alexandria University hospitals. Concerted efforts by the hospital management administration should be exerted to maintain an influential infection control team whose responsibility is the reinforcement of guideline implementation as well as the undertaking of periodic health education programmes for both the specialist and non-specialist staff members of health care institutions. Medical professionals must be aware of the potential danger of MRSA infection, since countries that did not implement early MRSA surveillance and control measures have struggled to control MRSA epidemics.

Competing interests: None declared.

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#### The evolving threat of antimicrobial resistance - Options for action

In 2012, WHO launched the book *The evolving threat of antimicrobial resistance - Options for action*. This publication examines the experiences with interventions which address the growing threat of antimicrobial resistance (AMR), describes the lessons learnt along the way and highlights the gaps still remaining. It draws attention to areas where knowledge is lacking and where urgent action is still needed.

The aim of the book is to raise awareness about AMR and to stimulate further efforts to meet the recommendations outlined in the WHO 2001 Strategy for Containment of AMR and in the 2011 World Health Day policy package. It does so by examining the current situation, and setting out what has been done and what could still be done around the world, in high-, middle- and low-income countries. While much of what is summarized in this publication is well known to the scientific community, yet awareness at the political level is essential, but often lacking. A specific objective is therefore to encourage policy-makers and the global community to commit to intensified action against AMR.

Further information about this and other WHO publications is available at: http://apps.who.int/bookorders/anglais/home1.jsp

# Evaluation of a community-based drowning prevention programme in northern Islamic Republic of Iran

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## تقييم برنامج مجتمعي المرتكز للوقاية من الغرق في شمال جمهورية إيران الإسلامية على داودي كياكلايه، رضا محمدي، شاهرخ يوسف زاده جابك، بيارنه جانسون

الخلاصة: تقيِّم هذه الدراسة جدوى حزمة من التدخلات للوقاية من الغرق في شهال جمهورية إيران الإسلامية. وقد استخدم الباحثون تصميهاً شبه تجريبي قبل وبعد إجراء الملاحظات على القاطنين والسائحين في مناطق مجموعة التدخلات (الدراسة)، وهي مناطق ساحلية فيها مياه ترفيهية، وفي مناطق مجموعة الشواهد، وهي مناطق تقع بجوار بحر قزوين في منتجعات بجوار الخط الساحلي لبحر خزر. وقد هبط معدل الغرق المميت في المجموعة السكانية القاطنة في تلك الولايات من 4.24 لكل مئة ألف نسمة من السكان إلى 3.04 لكل مئة ألف نسمة من السكان كخط أساسيّ في المجموعة المشوار. واتضح للباحثين أن خطر الموت بسبب الغرق في مناطق التدخل في مناطق المياه الترفيهية كان خلال الفترة السابقة للتدخل أكبر (معدل الأرجحية = 1.1، فاصلة الثقة 95٪، وتتراوح بين 6.66 و2.01). مما صار في فترة تنفيذ التدخل (معدل الأرجحية 2.04، فاصلة الثقة 95٪، وتتراوح بين 6.66 و2.01). مما صار في فترة تنفيذ التدخل (معدل الأرجحية بمستوى الوعي لدى المجتمع.

ABSTRACT This study evaluated the feasibility of a drowning intervention package in northern Islamic Republic of Iran. A quasi-experimental design used pre- and post-observations among residents and tourists in water-recreation beach areas of intervention and control regions by the Caspian Sea and in residents near the Caspian Sea coastline. The fatal drowning rate in the studied resident population in the provinces fell from 4.24 per  $100\ 000\ residents$  at baseline to  $3.04\ per\ 100\ 000\ residents$  at endline. The risk of death from drowning in the intervention areas in the water-recreation area was greater during the pre-intervention (OR = 1.15,  $95\%\ CI$ : 0.66–2.01) than the implementation period (OR = 0.24,  $95\%\ CI$ : 0.15–0.37). The risk of drowning can be reduced by implementing increased supervision and raising community awareness.

## Évaluation d'un programme communautaire de prévention de la noyade dans le nord de la République islamique d'Iran

RÉSUMÉ La présente étude a évalué la faisabilité d'un programme d'intervention contre la noyade dans le nord de la République islamique d'Iran. Un plan quasi-expérimental a été utilisé à partir des observations réalisées avant et après l'intervention auprès de résidents et de touristes dans des zones de plages pour les loisirs aquatiques et des régions témoins près de la mer Caspienne ainsi qu'auprès de résidents à proximité du littoral de la mer Caspienne. Le pourcentage de noyades mortelles au sein de la population résidente étudiée dans les provinces est passé de 4,24 pour 100 000 résidents au début de l'étude à 3,04 pour 100 000 résidents à la fin de l'étude. Le risque de décès par noyade dans les zones d'intervention de loisirs aquatiques était plus élevé avant l'intervention (OR = 1,15, IC 95 % : 0,66–2,01) que pendant la mise en œuvre (OR = 0,24, IC 95 % : 0,15–0,37). Le risque de noyade peut être réduit en renforçant la surveillance et en faisant de la sensibilisation auprès de la communauté.

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#### Introduction

Drowning is a serious public health problem. A recent global burden of disease study revealed that the global mortality rate from drowning was 7% of all injury-related deaths [1]. In the Islamic Republic of Iran, in 2001, the mortality rate due to drowning ranged between 0.9 and 4.1 per 100 000 population (average 2.6 per 100 000 population) with wide variations among the country's 30 provinces [2].

Various drowning prevention measures—pool fencing, parental education, close supervision by parents or lifeguards and cardiopulmonary resuscitation—have been implemented in high-income countries, and these may be applicable to low- and middle-income countries such as the Islamic Republic of Iran. Education is an important factor too. Rahman et al. stated that the risk of childhood drowning was 2.1 times greater for mothers who were illiterate compared with those who had a secondary or higher level of education [3]. This correlates with Fang et al.'s findings in China [4]. Parental education and close supervision by parents have already been examined in rural settings in some lowand middle-income countries including Bangladesh and China [3,4].

A community-based drowning prevention package was implemented in northern Islamic Republic of Iran in 2005, focusing on high-risk groups and selected high-risk areas. The study focused on the feasibility of a drowning prevention package, which was assessed by measurement of both the process and the short-term drowning fatality rate before and after implementation.

#### Methods

#### Study design

To evaluate the feasibility of the drowning intervention package a quasi-experimental community-based trial was performed in 2 separate areas in northern Islamic Republic of

Iran. This comprised: (1) pre- and post-intervention observations in the resident population of areas near the Caspian Sea coastline, without a comparison community; and (2) pre- and post-intervention observations, in an intervention and a comparison region, at water-recreation beach areas at the Caspian Sea. Cross-sectional data were collected at pre-intervention and post-intervention in these areas (Figures 1 and 2). This study proposal was reviewed and approved by the medical ethics committee of the Guilan University of Medical Science.

#### Study areas and populations

#### Residential areas near the Caspian Sea coastline

This study area comprised residential areas along the Caspian Sea coastline of both Guilan and Mazandaran provinces, with data collection limited to natural open water regions, including the sea, rivers, lakes, canals and wells.

## Water recreation areas at the Caspian Sea

This study area encompassed seaside beach areas, in both an intervention region (270 km of seaside beaches in Guilan province) and a control region (270 km of seaside beaches in Mazandaran province). From these sociodemographically similar areas, data were gathered in an area spanning 540 km of coastline during the summer seasons. Information was also supplied by Iranian Red Crescent beach lifeguards at Caspian Sea resorts, who provided first-aid and rescue services. The study included the resident and tourist populations in both provinces.

#### Planning and implementation

The baseline drowning prevention package was applied from March 2005 to March 2006 in order to identify epidemiological aspects of drowning throughout both the provinces. Using the findings from focus group discussions (FGD) and a literature review, and

the data gathered from a cross-sectional survey at baseline, applicable drowning prevention measures were formulated.

During March to July 2006, the intervention package was implemented on a small scale in both study areas (in Anzali county) for 5 months to gauge community feedback. The local provincial government, the lifeguard service, the Guilan University of Medical Sciences and the Red Crescent Society jointly agreed to accept responsibility for the programme. FGD and brainstorming were used to assess the initial community response to the intervention package. The main programme was initiated in July 2006, with the aim of reducing drowning incidents and increasing public awareness in the study area.

The implementation phase evolved from a collaborative effort between the FGD and brainstorming committees, with objectives derived from experiences from the baseline cross-sectional study. This introductory phase of the programme was launched in June 2006 in the seaside region of Guilan province, and completed in March 2009, with application in a comparison community in Mazandaran province. The implementation phase in the resident population was effected simultaneously in both provinces by the Caspian Sea coastline. Public health and safety issues were addressed in accordance with the intervention during the years 2006 to 2009.

#### Interventions

#### Residential areas near the Caspian Sea coastline

Elements of the plan in the intervention strategies in rural settings by the Caspian Sea coastline included environment modifications:

 modification of environmental change through, for example, the elimination of certain water reservoirs);

and raising community awareness via:

 information programmes for health care workers (behvarz), who were employed to educate clients about drowning risk factors, with a specific emphasis on training high-risk populations in basic resuscitation techniques; and

• integration of public health messages into local television and radio news, such as the *Darya* TV programme broadcast in Guilan province during the summer season (2 hours per day over the 3-month summer season).

## Water-recreation areas at the Caspian Sea

The intervention strategies in the Caspian seaside region included 2 initiatives to increase supervision by:

- extension of lifeguard services throughout the beach regions of the Caspian Sea (1 lifeguard for every 1500 m of beach, equivalent to 180 lifeguards, compared with 15 lifeguards before the intervention); and
- expansion of the number and scale of rescue service stations in the beach areas where the intervention was to be established (1 rescue service station for every 4500 m of beach, equivalent to 60 rescue service stations, compared with 8 rescue service stations before the intervention).

#### In both study areas

In both study areas, intervention programmes designed to effect recreational behaviour changes were implemented through public health educational campaigns, utilizing posters, pamphlets and notices at the sites of previous drownings. Their purpose was to inform the local community about circumstances related to drowning incidents in the country, to educate people about various means of preventing drowning and to gather data to facilitate the determination of causes of drowning. In both study areas, active interventions were implemented during 2006.

#### **Data sources**

Drowning data can be obtained from 2 sources in Islamic Republic of Iran—the death registry system and

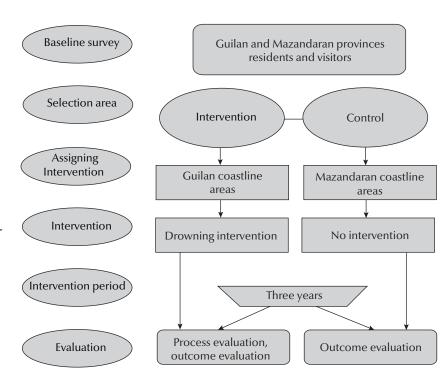


Figure 1 Model for implementation of a drowning prevention programme in the resident and visitor population in Guilan and Mazandaran provinces using a quasi-experimental study design

the forensic medicine system—both of which are based on death certificates. Also, weekly reports were used, which are based on case reports from

ambulance excursions, thus including cases that are not usually registered in hospitals [5]. Drowning fatality data were extracted from the forensic

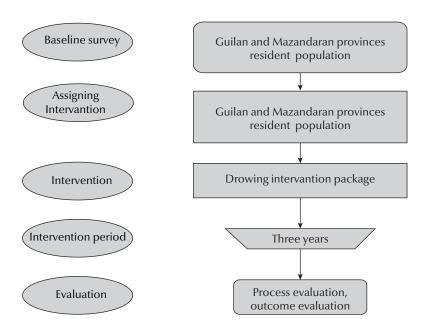


Figure 2 Model for understanding implementation of a drowning prevention programme in the resident population of Guilan and Mazandaran provinces, using a before and after study design

medicine system and the death registry, and near-drowning data were extracted only from the weekly reports. In calculating the denominators for the incidence of drowning, population statistics for 2005, for both before and after the implementation, were used. Both populations were obtained from Islamic Republic of Iran's official statistics registry [6], with exclusion of the tourist population due to a lack of reliable data for this group.

Additional data were obtained through household surveys of the family members of victims of unintentional drowning whose deaths occurred during the study period when the victims were residents in the study areas.

Health care workers (behvarz) were recruited to rural areas to work with health education staff on a programme of workshop training sessions related to drowning hazard identification. The programme entailed home visits by health personnel to the population in their service areas, and focused on enabling people to identify the risks related to drowning and on providing instructions about common, appropriate safety and prevention measures. These included ensuring adult supervision and the erection of fencing on the canal waterways and/or around open water reservoirs.

#### Definition of drowning

The World Congress of Drowning definition of drowning from 2002 was used: "Drowning is the process of experiencing respiratory impairment from submersion/immersion in liquid. Furthermore, drowning outcomes should be classified as: death, morbidity, and no morbidity" [7]. Immersion is the involuntary entry of a person into a body of water while submersion occurs if the person comes to lie under the water surface [8]. Near-drowning is when the person recovers after submersion in water [9].

#### Data analysis

We conducted our analysis using 2 approaches.

#### Residential areas near the Caspian Sea coastline

To assess any change in outcome in relation to unintentional cases of fatal drowning in the resident population, outcome measures were taken 3 years after implementation of the intervention package near the Caspian Sea coastline (March 2005–06 to March 2008-09). Population-based rates and relative risks (RR) were calculated using the most recent census data for Islamic Republic of Iran [6]. We examined the trend in the unintentional drowning rate in the area over time. Chi-squared tests for trend were used to test for differences over time in unintentional drowning rates between the sexes and between places of drowning.

## Water-recreation areas at the Caspian Sea

Odds ratios (OR) were used to compare drowning risks between the 2 time periods in both the intervention and control areas along the beaches of the Caspian Sea. For individuals with more than 1 case of near-drowning, only the first episode was included in the data set. Unconditional logistic regression was used, and the interaction parameters for the population ORs within different seasons were compared using the Wald test. A 5% significance level was used to reject all null hypotheses. The method used to calculate confidence intervals (CI) for proportions was the Wilson score method without continuity correction. CI for the ORs were calculated using the methods described by Armitage and Berry. The method used to calculate CI for differences between 2 proportions was the Newcombe-Wilson method without continuity correction. The CI for a relative-risk reduction is 1 minus the CI for the relative risk [10].

#### Results

#### **Programme process**

Information about the drowning prevention programme was broadcast every day on local TV between 14.00 and 18.00 hours during the summer seasons. More than 100 000 pamphlets related to the drowning prevention programme were distributed in the study areas among the visitor and resident populations.

Drowning prevention package materials were incorporated into the Red Crescent Society's cardiopulmonary resuscitation courses and health workers' education planning. More than 360 community volunteers were trained in first response, including cardiopulmonary resuscitation, and about 2100 health workers were educated in accordance with the drowning prevention package.

The initial response of the community was gauged after piloting and implementing the intervention package in a small district within the study area. All the FGD groups were aware that drowning is a health problem. Most groups reported that, due to a lack of supervision by parents, most drowning cases among children happened during daylight hours. The participants suggested some prevention measures. For example, male children should be trained in basic swimming, and additional rescue stations were needed along the Caspian Sea coastline. Integrating public health messages into local TV, such as the Darya programme, and lake and canal/waterways fencing in rural settings would prevent drowning events.

In partnership with local government bodies, 31 protected areas for swimming on the beaches of the Caspian Sea were established, and more than 200 hazards were identified.

#### Overall programme outcomes

Overall, there were 1294 drowning deaths among the resident and visitor

Table 1 Number of cases of unintentional fatal drownings between 2005–06 and 2008–09, before and after the programme intervention, in the resident population around the

rs)	No.	2005_06							norsal period			
ears)	No.	2007			2006-07			2007-08			2008-09	
Total Age (years) 0-9	191	ь <b>%</b>	/100 000b	No	e%	/100 000b	No.	e%	/100 000b	No.	%a	/100 000b
Age (years) 0–9		100.0	4.24	154	100.0	3.07	204	100.0	4.04	160	100.0	3.04
6-0												
	27	14.1	2.75	21	13.6	2.61	20	8.6	2.47	17	10.7	2.08
10–19	19	31.9	6.12	52	33.8	5.40	57	28.0	5.40	21	13.1	2.10
20-65	93	48.8	4.08	70	45.5	2.40	117	57.3	4.00	112	70.0	3.80
65+	10	5.2	3.90	=	Ε.	3.07	10	4.9	2.82	10	6.2	2.80
Sex												
Male	164	82.8	ı	139	90.2	I	159	77.9	I	147	91.8	ī
Female	27	14.1	I	15	9.7	I	45	22.0	I	13	8.1	Ĩ
Location												
Sea, unprotected	89	46.5	I	06	58.0	I	96	47.0	I	22	34.5	Ĩ
Sea, protected	_	0.5	I	2	1.2	ı	9	2.9	ı	2	6.0	Ī
River	75	39.0	I	52	33.7	ı	80	39.2	ı	78	49.0	Ī
Lake	10	5.2	I	8	5.1	I	12	5.8	I	23	14.5	Ĩ
Canal	10	5.2	I	0	0.0	ı	2	2.4	ı	0	0.0	Ī
Other	9	3.1	I	2	1.2	I	2	2.4	I	2	6.0	Ĭ

«Percentage of cases; "Rate per 100 000 resident population.

populations in northern Islamic Republic of Iran between March 2005 and March 2009. During the 4-year time period covered by the study, the average annual number of drowning deaths in Guilan province was 124, ranging from 91 cases during March 2008-09 to 193 cases during March 2007-08, while drowning deaths in Mazandaran province ranged from 176 cases during March 2007–08 to 232 cases during March 2005–06. Drowning death rates for tourists could not be computed since denominator data were incomplete [6].

#### Residential areas near the Caspian Sea coastline

Evaluation of the impact of the drowning prevention programme on the resident population around the Caspian Sea coastline showed favourable changes in the overall risk associated with drowning in the resident population of both study groups within the time frame of the study (Table 1). During the 4-year period (2005–06 to 2008-09), 709 fatal cases of unintentional drowning occurred in the resident population in the study area. The incidence fell from 4.24 per 100 000 residents at baseline in 2005-06 to 3.16 per 100 000 at endline in 2008-09, although no consistent trend was detectable in the intervening periods (Table 1).

On average, 86% of the victims were male and only 14% female, and more men than women drowned in every year of the study. The relative risk of drowning for males versus females in the resident population was highest in 2008-09 (RR = 10.9) but there was no consistent trend in other years (RR = 5.84 in 2005-06, RR = 8.96 in 2006-07, RR = 3.40 in2007-08).

All the age groups identified within the study period showed consistently decreasing numbers of drowning fatalities, except for the 20-65 year age group, for whom the fatality rate

Table 2 Distributions of annual rates of unintentional fatal and non-fatal drownings between 2005/06 and 2008/09 in residents and tourists of water-recreation areas at the Caspian Sea in northern Islamic Republic of Iran: comparison of the intervention area (Guilan province) and control area (Mazandaran province)

Variable		Ye	ars	
	Baseline	e period	Interventi	on period
	2005-06	2006-07	2007-08	2008-09
Total no. of cases				
Intervention area	76	126	218	161
Control area	183	207	206	290
No. of drownings (fatal)				
Intervention area	49	67	101	32
Control area	112	132	115	148
No. of near-drownings (non-fatal)				
Intervention area	27	59	117	129
Control area	71	75	91	142
Estimated population proportion fatal cases) (%) (95% CI)				
Intervention area	0.64 (0.53-0.74)	0.53 (0.49-0.62)	0.46 (0.40-0.53)	0.20 (0.14-0.27)
Control area	0.62 (0.54-0.68)	0.64 (0.57-0.70)	0.56 (0.49-0.62)	0.51 (0.45-0.57)
Estimated population OR (95% CI)				
Intervention area	1.81 (1.14-2.89)	1.14 (0.80-1.61)	0.86 (0.66-1.13)	0.25 (0.17-0.36)
Control area	1.58 (1.17-2.12)	1.76 (1.33-2.33)	1.26 (0.96-1.66)	1.04 (0.83-1.31)
Population OR (95% CI) comparing intervention and control areas				
Intervention area	1.15 (0.66-2.01)	0.65 (0.41-1.01)	0.68 (0.47-1.00)	0.24 (0.15-0.37)
Control area	ref	ref	ref	ref
RR (95% CI), comparing intervention and control areas				
Intervention area	1.05 (0.86-1.29)	0.83 (0.69-1.01)	0.88 (0.73-1.06)	0.39 (0.28-0.54)
Control area	ref	ref	ref	ref
RR (95% CI) reduction (%) comparing intervention and control areas				
Intervention area	-0.05 (-0.25-0.16)	0.17 (-0.00-0.33)	0.12 (-0.06-0.29)	0.61 (0.44-0.76)
Control area	ref	ref	ref	ref

OR = odds ratio; RR = relative risk; CI = confidence interval.

fluctuated. The highest annual rates were in the 10–19 year age group, which ranged from 6.12 per 100 000 at baseline to 2.08 per 100 000 at endline.

A chi-squared test for trend between the sexes found that the decline in the incidence of drowning was significantly greater in females when looking at age groups (P = 0.001); the highest rate was observed among 10-19-year-olds, with an annual rate of between 2.1 and 6.1 per  $100\,000$  resident population during the period 2005-09.

The majority of drowning fatalities occurred in unprotected areas along the Caspian Sea coastline and in rural settings, where rivers were the most high-risk environment (Table 1).

## Water-recreation areas at the Caspian Sea

In the evaluation of the interventions in the Caspian seaside region, 756 cases of drowning deaths and 711 cases of near-drowning were identified during the study period in the beach areas of the Caspian Sea in the resident and tourist populations. In the intervention area, Guilan province, the risk of drowning decreased from baseline in 2005-06 (OR = 1.81, 95% CI: 1.14-2.89) to endline in 2008-09 (OR = 0.25, 95% CI: 0.17-0.36), and the probability of a case of death decreased from 64% to 20% (Table 2). In the control area, Mazandaran province the risk of drowning decreased only slightly from 2005-06 (OR = 1.58, 95% CI: 1.17-2.12) to 2008-09 (OR = 1.04, 95% CI: 0.83-1.31) and the probability of drowning decreased from 62% to 51% (Table 2).

Comparing risks in Guilan province and Mazandaran province showed a significant decrease over time from OR = 1.15 (95% CI: 0.66– 2.01) at the beginning of the study to OR = 0.24 (95% CI: 0.15-0.37) at the end. Comparing the population probabilities for risk of drowning between the provinces, we can see that the decreasing trend over time was more pronounced in the intervention area (Guilan province) than in the control area (Mazandaran province). Also the comparison confirmed by the logistic regression showed a significant difference in ORs both within and between the groups over time. The observed results revealed significant effects of time and group, and also a time and group interaction. Furthermore, we can see that swimming in the intervention area showed a slightly greater relative risk of drowning than swimming in the intervention area at the beginning of the study (RR = 1.05), whereas by the end of the study this had fallen considerably (RR = 0.39) (Table 2, Figure 3).

#### Discussion

Drowning prevention programmes have not been consistently implemented in low- and middle-income countries. This is the first study to evaluate a drowning prevention programme in a contemporary environment in such countries. The study was designed to determine the feasibility of implementation of a drowning prevention programme in northern Islamic Republic of Iran. Our baseline study showed that the drowning rate in the area investigated was similar to those reported in known high-risk populations, such as in Alaska, lower- and middle-income countries in the Americas and other low- and middle-income countries in the eastern Mediterranean [11,12].

When looking at the unintentional drowning rates in the resident population by age, the highest annual rates were in the 10–19 year age group, which ranged from 6.12 per 100 000 at baseline to 2.08 per 100 000 at endline. A large number of studies have shown that more than half of all drowning deaths

are of children below the age of 15 years [13]; one reason for this is that older children (10 –19 years old) overestimate their physical ability. Younger children (< 10 years old) are at risk due to immature skills in swimming and lack of parental supervision. All the age groups showed consistently decreasing numbers of drowning fatalities over the study period, except for the 20–65 year age group, for whom the fatality rate fluctuated.

With regard to place of occurrence in the resident population, our research found that standing bodies of water, such as lakes, were a potentially hazardous environment for young children [5], and unintentional falls into rivers and canals was a common cause of drowning in older children. These findings are consistent with those of previous studies [14].

The data revealed a male-to-female relative risk of 5.84 in the resident population during the first year of measurement, which rose to 10.9 during the final year of the study period. This means that, in every year, males drowned more frequently than females. Males in Islamic Republic of Iran are more likely to engage in various water activities during all seasons of the year and at any time of the day or night, but females are more likely to engage in recreational activities in or near their home in shallow water, and also while they are on holiday; cases of drowning among females tended to occur during daytime [5].

This study also identified a significantly greater decline (by the end-year of the intervention) in the frequency of drowning fatalities on the beaches of the Caspian Sea in the intervention area (Guilan province), where the prevention programme had been adopted, compared with the control area (Mazandaran province), which did not adopt the drowning prevention programme. This means that supervision by a lifeguard or lifesaver of the people who venture into the sea was a positive factor in the reduction of drowning



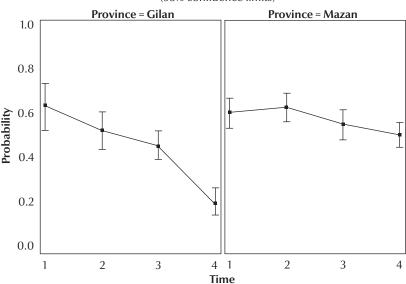


Figure 3 Comparing the population probabilities of the risk of unintentional fatal and non-fatal drownings between the intervention area (Guilan province) and control area (Mazandaran province) after the intervention package in water-recreation areas by the Caspian Sea

along Caspian Sea beaches. This finding is consistent with the falls in the rate of drowning found in high-income countries [15]. A previous study found that the Caspian Sea Liefguard Service, supported by the government, accounted for more than 90% of the medical costs of drowning, where the drowning cost per person was over 17 times the country's gross domestic product per capital [16]. It is suggested that interventions to drowning prevention have been highly cost-effective during the study period.

The effectiveness of intervention programmes and educational campaigns regarding drowning prevention vary according to their design, intensity and objectives [17,18]. In this study, we utilized a comprehensive community-based quasi-experimental design to assess the feasibility of the intervention package. It was difficult to measure the effectiveness of the individual intervention components separately [19]. Therefore, the evaluation was performed with respect to the effect of the whole package. The results appear to suggest that, during the study period, the drowning fatality rate decreased more in the intervention area than in the control area. This could indicate a significant effect of the local intervention. However, it is possible that other factors might have affected the frequency of drowning in the study areas during the study period. Although the reduction in drowning fatality rates in the control area was not statistically significant, it suggested a generally decreasing temporal trend in injury rates. The findings showed that drowning prevention measures—comprising in this study lifeguard services and lake, pond and canal/waterway fencing are effective, which is in accordance with the findings of other studies [20]. Interestingly, a systematic review of primary prevention strategies found that fencing, a strategy that specifically targets toddlers and young children, is the only effective intervention [21]. Fencing has been successfully

implemented in and around canals and other water bodies in rural areas in China and Bangladesh [8,22]. The Islamic Republic of Iran has not passed legislation in this respect, so the drowning prevention programme policy-makers did not make a specific effort in this regard during the programme phase.

Three main types of biases might have affected the validity of the study: selection bias, misclassification and confounding. To minimize selection bias, we included only unintentional drowning victims in our findings. Thus, the main potential sources of bias in our study are likely to be data misclassification and confounding. We have demonstrated some shortfalls in the reporting of drowning events, owing to the fact that information on drowning deaths in a number of cases was incomplete or lacking, perhaps at least partially due to misclassification of the cause of death [23]. Under-reporting may also have influenced reliability, despite the fact that data were gathered from multiple reporting systems. Additional studies involving the capture-recapture of data may prompt improvements in the injury registry systems for similar study populations [23]. Bias in selection effects refers to differences between intervention and comparison groups in before-after studies. Any 2 communities labelled as similar in our research are unlikely to be identical in all the respects that might have affected the impact of the intervention. The choice to conduct a before-after study is usually determined by whether resources for carrying out that study are an issue, and might involve confounding factors that are difficult to control for, whereas the use of quasi-experimental designs, which are easier to interpret, can facilitate the determination of at least a few potential confounding factors.

Regarding external validity, given that the study was population-based, its findings should be applicable to all individuals in the catchment areas that meet the inclusion criteria. Since the results presented in this study were largely based on registry systems that essentially comprise all the regions of Islamic Republic of Iran, our results are likely to be applicable to the whole population. Also, the data collected for this study were used within a health system framework in a rural setting similar to those existing in more developed countries.

Like other population-based programme evaluations [24,25], our evaluation had a number of limitations. Inadequate budgets limit evaluation design and activities, but the most significant limitation here lies in a lack of comparison data [16], constraining conclusions about associations between the programme and the changes observed on the impact and outcome measures. Because of defects in estimating the tourist population, the rate of drowning was not calculated for this group. Finally, trend analysis was not possible since it was constrained by the number of observations.

#### Conclusions

The study shows that reducing the risk of drowning is possible by raising community awareness, in partnership with relevant organizations. Since the programme was designed to involve the community, it was expected to be feasible and accepted by that community. To determine the effectiveness of the intervention package, we need to increase efforts to develop its evidence base, e.g. by expanding the time intervals of analysis to evaluate long-term impacts and to consider seasonal variations. The lifeguard service provided by trained professionals (lifeguards) and community volunteers (lifesavers) was a vital tool in implementing the prevention programme and presumably a major influence on the drowning rate in the coastal areas of the Caspian Sea. The Islamic Republic of Iran health care

delivery system is ideally positioned to provide support for complementary drowning prevention strategies, employing education as an essential element in rural settings around the Caspian Sea.

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## Contraceptive use by Iranian women with hypertension, diabetes or obesity

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## استخدام موانع الحمل لدى الإيرانيات المصابات بارتفاع ضغط الدم أو بالسكّري أو بالسّمنة مرضية نجومي، نكار مروت دار، فرنوش داودي، سحر حسيني

الخلاصة: تحتاج النساء المصابات بحالات طبية مزمنة إلى المعالجة بحذر بموانع الحمل. وتهدف هذه الدراسة المستعرضة التي أجريت في طهران إلى التعرف على أنهاط استخدام المصابات بارتفاع ضغط الدم أو بالسكّري أو بالسّمنة لموانع الحمل. وقد شملت الدراسة 264 امرأة تتراوح أعهار هن بين 18 و 52 عاماً، وكان 18 منهن (30.7) مصابات بالسكّري من النمط الثاني، وكان 100 منهن (37.9) مصابات بالسّمنة أو بزيادة الوزن (منسب كتلة الجسم أكثر من 25 كغ/ م²) وكان 83 منهن (31.5) مصابات بارتفاع ضغط الدم. وفي المجموعات الثلاث، كان معدل استخدام طرق منع الحمل مختلفاً بقدر يُعتَدُّ به إحصائياً قبل التشخيص عها هو عليه بعد التشخيص. فقبل التشخيص كانت الطريقة الأكثر شيوعاً لمنع الحمل هي الهرمونات التي كانت تعطى لـ 55٪ من المصابات بالسكّري و 71.6٪ من المصابات بازدياد الوزن، و 78.3٪ من المصابات بارتفاع ضغط الدم. أما بعد التشخيص فقد أصبح سحب العضو أثناء الجهاع هو الطريقة الأكثر شيوعاً لدى المصابات بالسكّري (35.4٪ ولدى السمينات والمصابات بزيادة الوزن 28٪، وكادت تكون الطريقة الأكثر شيوعاً لدى المصابات بارتفاع ضغط الدم (35.4٪). وانتهت الدراسة إلى أن مستوى استخدام طرق آمنة وحديثة لمنع الحمل لدى المصابات ببعض الحالات الطبية المزمنة هو مستوى منخفض وينبغي إيلاء المزيد من الاهتهام لذلك.

ABSTRACT Women with chronic medical conditions require careful contraceptive management. The aim of this cross-sectional study in Tehran was to determine the pattern of contraception use by women with diabetes, hypertension or obesity. A sample of 264 women aged 18–53 years old was recruited; 81 (30.7%) had diabetes type 2, 100 (37.9%) were obese/overweight (BMI > 25 kg/m²) and 83 (31.5%) had hypertension. Across all 3 groups, the rate of use of contraceptive methods was significantly different before and after diagnosis. Before diagnosis of disease the most common method was hormonal contraception in all women (55.0%, 71.6% and 78.3% of diabetic, overweight and hypertensive women respectively), whereas after diagnosis coital withdrawal was the most common method in diabetic and obese/overweight women (41.2% and 28.0% respectively) and almost the most common method for hypertensive women (35.4%). Use of safe and modern methods of contraception in women with certain chronic medical conditions was low and needs more attention.

#### Utilisation de la contraception chez des femmes iraniennes hypertendues, diabétiques ou obèses

RÉSUMÉ Les femmes atteintes d'affections médicales chroniques ont besoin d'une prise en charge prudente de leur contraception. L'objectif de la présente étude transversale menée à Téhéran était de déterminer les tendances dans l'utilisation de la contraception chez des femmes diabétiques, hypertendues ou obèses. Un échantillon de 264 femmes âgées de 18 à 53 ans a été recruté ; 81 femmes (30,7 %) étaient atteintes d'un diabète de type 2 tandis que 100 femmes (37,9 %) étaient obèses/en surpoids (IMC > 25 kg/m²) et 83 (31,5 %) souffraient d'hypertension. Dans l'ensemble des trois groupes, le pourcentage de recours à des méthodes contraceptives après la pose du diagnostic a considérablement changé par rapport au pourcentage relevé avant. Avant le diagnostic de l'affection, la méthode la plus fréquente était hormonale chez l'ensemble des femmes interrogées (55,0 %, 71,6 % et 78,3 % des femmes diabétiques, en surpoids et hypertendues, respectivement), alors qu'après la pose du diagnostic, le retrait coïtal était la méthode la plus fréquente chez les femmes atteintes diabétiques et obèses/en surpoids (41,2 % et 28,0 % respectivement) et presque la méthode la plus fréquente chez les femmes hypertendues (35,4 %). L'utilisation de méthodes de contraception sûres et modernes chez les femmes atteintes de certaines affections chroniques était faible. Le sujet mérite que l'on y accorde davantage d'attention.

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#### Introduction

Women of reproductive age (15–44 years) are affected by many chronic medical conditions that have important effects on the preconception health of the woman and on pregnancy outcomes [1,2]. Chronic conditions such as asthma, hypertension and diabetes may limit the activities of women or lead to them being hospitalized [3]. Obesity is also an increasing health problem. Based on a data from the United States (US), obesity affects 13% of women aged 18-24 years and 19% of women aged 24–44 years [4]. Obesity increases the risk of certain morbidities during pregnancy, such as macrosomia, gestational diabetes and pregnancy-induced hypertension [5]. Chronic illness can also affect women's contraceptive choices. Chuang et al. in a qualitative study of women with diabetes, obesity or hypertension aged 18–45 years in the US reported knowledge deficits about pregnancy-related risks in women with these disorders [6]. They also found that these women were less likely to engage in preconception health promotion and family planning.

A high proportion of eligible women in the Islamic Republic of Iran (78.5%) use modern contraception [7]. Nevertheless, more than 10% of married women aged 14-49 years use coital withdrawal as a method of contraception [8] and this rate has been reported to be as high as 17.8% to 22% [7,8]. Compared with the world average (3%), it is a high rate of use of the method [8]. It seems that women with chronic medical conditions may select withdrawal as a method of contraception due to fear of side-effects of hormonal contraceptives. Because of the importance of maternal and fetal morbidity and mortality in these women after unwanted pregnancy as a sequence of using an unsafe method of contraception, the current study was carried out to determine the pattern of contraception by diabetic, hypertensive or obese women.

#### Methods

#### Study sample

In a hospital-based, cross-sectional survey, 300 women with diabetes type 2, hypertension or overweight/obesity were invited to participate in the study. During 2010, 300 women aged 18-53 years old (reproductive age) attending the teaching hospitals of Tehran University of Medical Sciences were assessed during their visit for selected outpatient diseases. They were selected by a sequential sampling method during the study period. Women were eligible for the present study if they were of reproductive age (18-53 years), had indications for contraceptive use, were sexually active, not pregnant and had a diagnosis of diabetes, hypertension or overweight/obesity. Sexually active women were defined as having a husband in the past 12 months. We defined overweight as body mass index (BMI) between 25-30 kg/m<sup>2</sup>, and obesity as BMI  $\geq$  30 kg/m<sup>2</sup>. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mmHg or diastolic BP ≥ 90 mmHg [9]. Diabetes was defined as history of taking insulin or any oral drugs for control of diabetes. A woman was considered as having diabetes if she replied positively to the 2 following questions: "Have you ever been told by your physician that you have diabetes?" Subjects who responded "yes" were then asked: "Do you use any prescription for controlling your diabetes?" We excluded women who refused to participate in the study, illiterate women and subjects with severe physical or mental illnesses. Of the 300 consecutive eligible women, 264 agreed to participate in the study and completed checklists.

#### **Data collection**

The method of collecting data was interview using a structured checklist which had been developed by an extensive literature search and a panel of experts. Pilot interviews were conducted on 15 subjects. Based on the result of

these interviews, the checklist was revised. All interviews were conducted in the waiting room of outpatient clinics. All interviewers were medical students who underwent standardized training. The aim of the study was explained to the women. All survey participants were asked about demographic data, medical history and method of contraception used. Demographic variables included age, weight, height, literacy and the number of children. We also asked about the number of abortions and unwanted pregnancies. We asked about recent use of contraceptives and type of contraceptive used before the diagnosis of their disorder. Age was classified into 3 groups for analysis: 18-34 years, 35-44 years and 45-54 years.

#### Statistical analyses

All statistical analyses were performed using *SPSS*, version 16. We used frequency tables and percentages for frequency of contraceptive use by type of diseases. The chi-squared test was used for assessing association between contraceptive use, other characteristics of women and type of diseases. Wilcoxon signed ranks test was used to compare frequency of recent and pre-diagnosis type of contraceptive use by women. The significance level was P < 0.05.

#### Results

The characteristics of the study sample of 264 women are illustrated in Table 1. Most women had less than highschool education (46.4%) and were housewives (84.7%). They were equally distributed across the 3 age groups (range 33.0% to 33.7%). A majority of women had 2–3 children (57.2%). Almost one-third of the women (81, 30.7%) had diabetes, 83 (31.5%) were hypertensive and 100 (37.9%) were obese/overweight. The median BMI in obese/overweight women was 28.5 kg/m². The most common recently used

Table 1 Baseline characteristics of the study	women (n = 264)	
Variable	No.	%
Type of disease		
Diabetes	81	30.7
Hypertensive	83	31.5
Obese/ overweight	100	37.9
Education		
Less than high school	122	46.4
High school graduated	103	39.2
Academic	38	14.4
Occupation		
Housewife	222	84.7
Worker/clerk	40	15.3
Age (years)		
18–34	88	33.3
35–44	89	33.7
45-55	87	33.0
No. of children		
< 2	64	24.2
2–3	151	57.2
4+	49	18.2
Type of contraception (recent)		
Withdrawal	90	34.4
Hormonal	23	8.8
IUD	34	13.0
Condom	43	16.4
Tubal ligation/vasectomy	72	27.5

IUD = intrauterine device.

contraceptive method was withdrawal (34.4%).

Table 2 describes the characteristics of the women by type of disease. The rate of hypertension was greater in women aged 45–54 years (57.8%) than younger women (34.9% and 7.2% in women aged 35-44 and 18-34 years respectively). The highest rate of obesity was among 18–34-year-olds (59.0%). These differences were statistically significant (P < 0.001). The type of contraception use was also significantly different between groups. Withdrawal was the most common method in obese/overweight and diabetic women. Hypertensive women had used a permanent contraceptive method (37.8%) more than other methods. The second most common method in

diabetic women were tubal ligation/vasectomy (33.8%) and in obese/overweight women was condoms (23%). Withdrawal was the second most common method (35.4%) in hypertensive women (P < 0.001).

To investigate whether chronic medical conditions may have affected choice of contraceptives, we compared the pattern of contraception use by women before and after diagnosis of their disease. As we can see in Figure 1, across all 3 groups, the frequency of use of contraceptive methods were significantly different before and after diagnosis (P < 0.01). The most common method was hormonal in all women before diagnosis of disease (55.0%, 71.6% and 78.3% of diabetic, overweight and hypertensive women

respectively), whereas after diagnosis of disease coital withdrawal was the most common method in diabetic and obese/overweight women (41.2% and 28.0% respectively) and almost the most common method for hypertensive women (35.4%). The second most common method of contraception was withdrawal (14.8% and 8.4%) even before diagnosis of disease in diabetes and hypertensive women. Thus, overall, 11.8% (31/263) of women were using a traditional method of contraceptive (withdrawal) before diagnosis of their disease compared with 34.2% after diagnosis.

There were significant associations of literacy and number of children with using coitus withdrawal/no method. Women with higher education used withdrawal/no method less than women of other educational levels (13.2% versus almost 38.0%), but women with higher ( $\geq$  4) and lower (< 2) numbers of children used the withdrawal method more than women with 2–3 children (almost 38.0% versus 30.0%). We could not find any association between selection of contraception method and other variables.

#### Discussion

In this study of women with hypertension, diabetes or obesity/overweight, our findings showed that the most common contraceptive method used was coitus withdrawal (34.4%). There was a significant difference in the frequency of use of contraceptive methods before and after diagnosis of chronic disease in these women.

A majority of women were house-wives and were less than high-school graduated. Women with diabetes were less educated and the most common method of contraception was withdrawal. Women with hypertensive were more likely to be older, have more children and use tubal ligation/vasectomy. Obese women were more

Table 2 Characteristics of women by type of chronic disease suffered

Variable		betes = 81)		overweight 100)		tension = 83)	<i>P</i> -value
	No.	%	No.	%	No.	%	
Education							< 0.001
Less than high school	47	58.8	28	28.0	47	56.6	
High-school graduated	27	33.8	46	46.0	30	36.1	
Academic	6	7.5	26	26.0	6	7.2	
Occupation							0.059
Housewife	70	88.6	78	78.0	74	89.2	
Worker/clerk	9	11.4	22	22.0	9	10.8	
Age (years)							< 0.001
18–34	23	28.4	59	59.0	6	7.2	
35-44	27	33.3	33	33.0	29	34.9	
45–54	31	38.3	8	8.0	48	57.8	
No. of children							< 0.001
< 2	17	21.0	41	41.0	6	7.2	
2–3	44	54.3	54	54.0	53	63.9	
4+	20	24.7	5	5.0	24	28.9	
Type of contraception (recent)							< 0.001
Withdrawal	33	41.2	28	28.0	29	35.4	
Hormonal	3	3.8	15	15.0	5	6.1	
Condom	12	15.0	23	23.0	8	9.8	
IUD	5	6.2	20	20.0	9	11.0	
Tubal ligation/vasectomy	27	33.8	14	14.0	31	37.8	

IUD = intrauterine device.

educated, had jobs and the most common method of contraception was withdrawal.

In the current study 11.8% of women reported using a traditional method of contraceptive (withdrawal) before diagnosis of their disease. This rate increased to 34.2% after diagnosis. We also found that the rate of using the withdrawal method ranged from 28.0% in overweight to 41.2% diabetic women. The same rate in another study, performed in the US, was 25.8% of diabetic women and 20.0% to 23.4% of overweight and obese women respectively [10]. These percentages are high and highlight the risks of unwanted pregnancy that these women face due to their contraceptive choices.

This high rate of obese/overweight women (28.0%) who did not use any modern method of contraception is

concerning. The rate of obesity worldwide is increasing and has more than doubled since 1980. In 2008, 1.5 billion adults aged 20 years and older were overweight, and of these nearly 300 million women were obese [11]. Obesity is known to be an important risk factor for maternal and fetal morbidity and mortality and increased rates of obesity and diabetes in offspring [12–14]. It has been shown that obese women are less likely to use a contraceptive method as compared with women with normal BMI [10,15]. Reasons for this are unclear; there may be an assumption that fertility is impaired among obese women or that using certain contraceptives could be dangerous. Nevertheless, it seems contraceptive counselling to assist these women to choose a safe, modern method of contraception is necessary.

Our findings showed that 41.2% of women with diabetes did not use any modern method of contraception. This rate was 14.8% before diagnosis of their disease. In the study of Chuang et al. in the US, the rate of contraceptive nonuse was 25.8% in diabetic women [10]. In another study of diabetic women, the rate of non-use of any contraceptive method was 10.7% [16] and use of "barrier/natural" methods was 47%. In some studies, it has been shown that overall use of contraceptive methods in diabetic women is similar to that of a comparison group (without diabetes) [16]. The prevalence of diabetes mellitus type 2 is increasing worldwide [17] and three-quarters of people affected by diabetes in developing countries are under 65 years old [18]. Therefore more women of reproductive age have diabetes, with all the accompanying risks

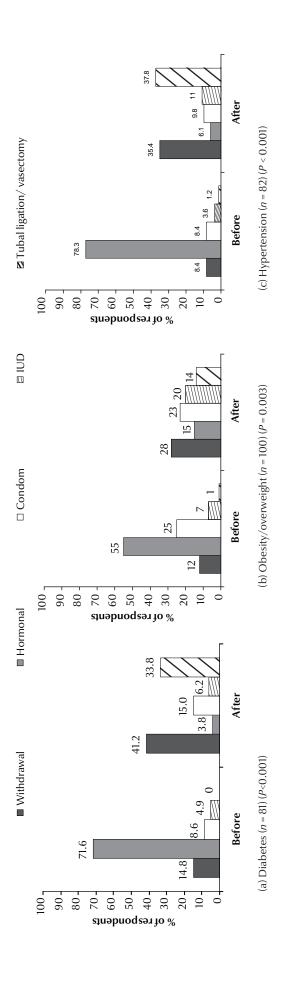


Figure 1 Frequency of contraceptive use before and after diagnosis of chronic disease in the 3 groups of women

of maternal and fetal mortality and morbidity. As in obese women, there may be many reasons why women with diabetes are less likely to use a safe contraceptive method. Having negative attitudes about contraception, perception of impairment of fertility and lack of proper counselling of diabetic women to choose a safe method of contraception are possible explanations of the high rate of non-use of modern contraception in these women.

We showed that 35.4% of women with hypertensive disorder did not use any modern method of contraception. Women with chronic medical conditions such as hypertension are of particular concern because of the increased risk for pregnancy-related morbidity and adverse pregnancy outcomes. Our study showed that these women are at increased risk for unintended pregnancy too. To assess how chronic medical conditions influence the intent for pregnancy and family planning behaviours in women, Chuang et al. performed a qualitative study on women ages 18–45 years with diabetes, obesity or hypertension [6]. They reported knowledge deficits about pregnancy-related risks in women with all 3 chronic diseases. They also found these women were less likely to engage in preconception health promotion and family planning.

One weakness of our study was the possibility of recall limitations. We asked about the use of contraceptives before the diagnosis of women's medical conditions and therefore recall bias may have influenced the reliability of data about methods used in the past. On the other hand, our findings showed a clear pattern of changes overall between before and after diagnosis of disorders and a great majority of women had shifted to less risky methods after diagnosis. Another limitation was the small sample size in each group, and we suggest future studies with higher sample sizes. We also suggest future studies on women with medical conditions about types of contraception used, along with assessment of their knowledge and attitudes related to pregnancy, preconception health and family planning. Our work is the first study with this topic in the Islamic Republic of Iran and this is one of the strengths of the current study.

In conclusion, our study showed that use of a safe and modern method of contraception in women with chronic medical condition such as diabetes, hypertension and obesity was low and needed more attention. Since new and safe contraceptive methods are now available, physicians and other health staff should consider women with chronic medical diseases by educating, counselling and suggesting a proper method by each woman's diseases. Through counselling of these women, we can predict lower morbidity and mortality of mothers and improve overall health and quality of life of women with chronic medical condition of reproductive age.

We also suggest doing such studies in future with larger sample size and focusing on the psychological aspects of using withdrawal as a contraceptive method by couples.

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## Knowledge of diabetes among type 2 diabetes patients attending a primary health care clinic in Sri Lanka

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المعارف عن السكّري لدى مرضى السكّري من النمط الثاني الذين يراجعون عيادة للرعاية الصحية الأولية في سيريلانكا دنوشة بريادرشني بريره، رسني اريندي ايديويرادي دي سيلفا، وغاواتي لييانغي بادمني بريره

الخلاصة: تعتبر معارف المرضى حول أمراضهم بالغة الأهمية في مكافحة السكّري والوقاية من مضاعفاته. وقد أجرى الباحثون دراسة وصفية مستعرضة شمر واحد شملت المرضى الذين يراجعون إحدى عيادات السكّري في مستشفى في مستوى الرعاية الصحية الأولية في موراتوا، سيريلانكا. فخلال فترة شهر واحد من عام 2009، أدرج الباحثون في الدراسة جميع المرضى الذين شُخّصَ لديهم السكّري من النمط الثاني والذين راجعوا العيادة لفترة تزيد على ثلاثة أشهر، وقد استخدم الباحثون استبياناً مهيكلاً يديره القائم على المقابلة لدى 150 مريضاً (135 مريضة و 15 مريضاً) أجابوا على 25 سؤالاً عن معارفهم حول السكّري، ثم ضَرَبَ الباحثون درجة كل سؤال بالرقم 4 للحصول على سلم قياس يتراوح بين 0 و100. وقد أحرز معظم المرضى (70.0٪) درجات جيدة (تزيد على 65) حول اختبار المعارف، مع ظهور فجوات بالغة الأهمية في معارفهم، ولاسيًا ما يتعلق منها بمعارفهم عن أعراض سوء التحكّم بالمرض وعن أهمية المنتقل من سواهم في المتوسط، فقد كان لديهم مستويات أعلى من غلوكوز الدم على الريق. وخلص الباحثون إلى أن برامج التثقيف ضرورية لرأب الفجوات البالغة الأهمية في معارف المرضى.

ABSTRACT Patients' knowledge about their illness is considered important in controlling diabetes and preventing complications. A descriptive, cross-sectional study was conducted among patients attending the diabetes clinic of a primary care level hospital in Moratuwa, Sri Lanka. During a 1-month period in 2009 all consenting patients diagnosed with type 2 diabetes who had been attending the clinic for more than 3 months were included in the study. Using an interviewer administered, structured questionnaire 150 patients (135 females, 15 males) answered 25 questions about diabetes knowledge (scored ×4 to give score range 0–100). A majority of patients (70.0%) had a good score (> 65) on the knowledge test but critical gaps in knowledge were revealed, especially regarding knowledge about symptoms of poor control and importance of regular follow-up. Although patients with longer duration of diabetes had higher mean knowledge scores, they also had higher fasting blood glucose levels. Education programmes are needed to address critical gaps in patients' knowledge.

## Connaissances sur le diabète chez des patients diabétiques de type 2 consultant dans un centre de soins de santé primaires au Ski Lanka

RÉSUMÉ On considère que les connaissances des patients sur leur maladie sont importantes pour le contrôle du diabète et la prévention des complications. Une étude descriptive transversale a été menée auprès de patients consultant dans le service de prise en charge du diabète de l'hôpital de soins de santé primaires de Moratuwa (Sri Lanka). Pendant un mois en 2009, tous les patients consentants, à qui l'on avait diagnostiqué un diabète de type 2, et qui consultaient dans ce service depuis plus de trois mois, ont été recrutés dans l'étude. À l'aide d'un questionnaire structuré administré par un professionnel, 150 patients (135 femmes, 15 hommes) ont répondu à 25 questions sur leurs connaissances en matière de diabète (les scores ont été multipliés par quatre pour obtenir une échelle allant de 0 à 100). La majorité des patients (70,0 %) ont obtenu un bon score (> 65) au questionnaire, mais des lacunes majeures ont été constatées au niveau des connaissances, en particulier sur les symptômes d'un mauvais contrôle et l'importance d'un suivi régulier. Si les patients diabétiques depuis plus longtemps ont obtenu en moyenne de meilleurs scores de connaissances, leur glycémie à jeun était aussi plus élevée. Des programmes éducatifs sont requis pour s'attaquer aux importantes lacunes des patients au niveau des connaissances dans ce domaine.

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#### Introduction

The rapid increase in the prevalence of diabetes mellitus is a major public health concern worldwide. Elevated blood glucose levels and microvascular and cardiovascular complications substantially increase the morbidity and mortality associated with the disease [1]. The World Health Organization projects that by 2030 more than half of diabetics in the world will live in Asia, thereby creating a strain on the financial and medical resources of those countries [2]. The prevalence of diabetes is especially high in South Asia. A national survey in Sri Lanka in 2008 found that the prevalence of diabetes was 10.3% [3].

The importance of self-management skills in diabetes care has been stressed by the American Diabetes Association (ADA) [4]. Patients with diabetes, however, often lack sufficient knowledge about their disease and thus frequently have poor self-management skills [5,6]. Studies have indicated that poor health literacy may be a particularly important barrier to chronic disease care and good health outcomes [7]. It is imperative that the patients and key members of their families understand the basic facts about diabetes, such as the importance of maintaining good glycaemic control and the individual treatment schedules and preventive measures in the control of diabetes mellitus. This study attempted to assess the knowledge of diabetes and its complications among patients attending a primary care diabetes clinic in Sri Lanka.

#### Methods

#### Study design and setting

This was a descriptive, cross-sectional study conducted in the outpatient diabetes clinics of Moratuwa district hospital, a primary health care hospital in Moratuwa city, in the Western province of Sri Lanka. This hospital

provides services free of charge, and the target patient population includes people living in close proximity to the hospital. Patients usually attend the clinic once a month. All patients with diabetes are treated by the primary care medical practitioners of the hospital. The usual care consists of starting with oral hypoglycaemic agents with assessment of control and combining oral hypoglycaemics as necessary. Insulin may be added as necessary for adequate control. Patients attend the clinic once a month and drugs are issued free of charge as available. Patients have to buy unavailable drugs at their own cost. Fasting blood sugar is determined once a month at the hospital laboratory.

#### Sample and setting

During the 1-month period 1 July 2009 to 1 August 2009 all consenting patients aged 18+ years diagnosed with type 2 diabetes who had been attending the clinic for more than 3 months were included in the study. Diabetes was defined as fasting plasma glucose (FPG) >7 mmol/L or random plasma glucose >11.1 mmol/L, once if symptomatic or repeated if asymptomatic A single month was selected as the study period as the same patients come to the clinic once a month for their follow-up visits and to obtain their medication. A total of 150 patients with type 2 diabetes were entered in the study. All patients were provided with an information sheet, given a verbal explanation of the nature of the study by the researchers and their verbal consent was obtained prior to enrolment.

#### **Data collection**

Participants were interviewed by the researchers using a validated, structured questionnaire. An extensive literature search was conducted in formulating the questionnaire and a number of studies based on questionnaires with similar questions were used [8–10]. The questionnaire was first drafted by

the 3 investigators, 2 family physicians and a community physician. The subject content was scrutinized and approved by a specialist in endocrinology. The questionnaire was finalized after engaging in several focus group discussions utilizing a Delphi technique among the researchers, doctors and nurses caring for the patients and a sample of the pilot group of patients. The questionnaire was piloted on 20 patients who regularly attended the diabetic clinic and attended the hospital primary care unit for health care visits other than to attend the diabetic clinic. These 20 patients were excluded from the study.

The questionnaire was formulated in all 3 official languages Sinhala, Tamil and English, checked by a professional translator, and was administered by the principal investigator. The questionnaire consisted of 2 sections: demographic details and diabetes knowledge assessment. The section on diabetes knowledge consisted of 25 questions about the symptoms of diabetes, symptoms of hypoglycaemia and hyperglycaemia, optimal control targets, micro- and macrovascular complications and lifestyle modifications. Each item had yes/no/don't know response key. A scoring system was developed, whereby the total number of correct responses for the knowledge section was calculated for each respondent and multiplied by 4 to give a score out of 100. Each correct answer was given a mark and the total mark calculated out of 100. Knowledge was graded as very good (score > 75), good (65–75), average (50–65), poor (40-50) or very poor (< 40). Each questionnaire took approximately 5–8 minutes to administer. Data were also obtained regarding recent glycaemic control as part of the routine screening at the clinic.

#### **Data analysis**

The data were analysed using SPSS, version 16 statistical package and Student *t*-test was used to compare group means.

#### Results

#### Demographic data

The mean age of the participants was 56.3 years (SD 10.1), range 30–71 years. The majority of the 150 respondents were married (96.0%), dependent on others for their income (94.0%), female (90.0%) and living within 5 km of the hospital (98.0%). The illiteracy rate was 8.0%, while 42.6% had received primary education and 49.3% secondary education. A majority of respondents (83.3%) had a family income below rupees (Rs) 10 000 per month (US\$ 90 approximately) (Table 1).

#### Clinical data

Almost half of the participants (49.3%) had been diagnosed with type 2 diabetes for > 5 years, 36.7% for 1–5 years and 14.0% for < 1 year. The mean value of the latest fasting blood sugar (FBS) test was 163 mg/dL.

#### **Knowledge about diabetes**

The overall mean knowledge score of the participants was 68.1% (SD 9.0%). A majority of participants (70.0%) had a good or very good score (> 65) on the knowledge test, while 26.76% had a very good score (> 75) (Table 2). A high proportion of the participants (44.0%) believed that diabetes could be cured (Table 3). More than 90% of patients could not recognize the symptoms of hypo/hyperglycaemia and only around 60% knew the normal range of fasting blood sugar, that blood sugar should be measured regularly to assess control, that regular exercise is helpful to control diabetes and that it is important to control the diet in addition to taking medication in the management of diabetes. Only twothirds of the sample (68.0%) knew that feet should be examined regularly for any lesions and even fewer (50.0%) knew the importance of assessing vision annually.

Table 1 Demographic profile of the study group of patients with diabetes attending a primary care clinic at Moratuwa district hospital

Variable	No. of patients	% (n = 150)
Age (years)		
< 40	15	10.0
40-60	71	47.3
> 60	64	42.6
Sex		
Male	15	10.0
Female	135	90.0
Education level		
Illiterate	12	8.0
Primary	64	42.7
Secondary	74	49.3
Occupation		
Employed	9	6.0
Not employed	141	94.0
Marital status		
Single	6	4.0
Married	144	96.0
Income per month (Rs)		
< 5000	47	31.3
5000-10 000	78	52.0
10 000–25 000	23	15.3
> 25 000	2	1.3
Own income		
Have an own income	9	6.0
No own income (dependant)	141	94.0
Family		
Living alone	14	9.3
Living with family	136	90.6

The mean knowledge scores among those who had had the disease for a longer duration was higher than those who had the disease for a shorter duration of time and this difference was statistically significant (Student t-test, P < 0.001) (Table 4). However, this did not translate into better control of their blood sugar levels, as those who had had diabetes for the longest also had the highest mean FBS level. There was no significant difference in mean knowledge score among those with illiterate or primary level of education [1.57 (SD 0.72)] compared with those with secondary education [1.53 (SD 0.86)].

#### Discussion

It is essential that diabetic patients should possess good knowledge about their illness in order to improve their self-management skills and thereby prevent complications. Research has found that less frequent self-care behaviours were evident among particularly high-risk diabetic patients with lower educational levels [11]. Another study revealed that among primary care patients with type 2 diabetes, poor health literacy was independently associated with worse glycaemic control and higher rates of retinopathy [12,13].

Table 2 Diabetes knowledge scores at different cut-offs among the study group of patients

Knowledge score	Grade	No.	%
≥ 75	Very good	40	26.7
65–74	Good	65	43.3
50-64	Average	33	22.0
40-49	Poor	12	8.0
< 40	Very poor	0	0.0

There is growing evidence highlighting the importance of self-management skills in diabetes, and the ADA has endorsed self-management education as the process of providing the person with diabetes with the knowledge and skills that are necessary for self-care, management of crises and implementation of lifestyle changes [14].

It was encouraging that in our study a majority of participants (70.0%) had good or very good scores (> 65) on the knowledge test. A similar study carried out in Pakistan revealed that only 13.6% of the participants had a good knowledge score (> 60) [15].

Many of our findings in the various knowledge areas were consistent with the findings of other studies, such as the knowledge that diabetes can be inherited. Even in other studies, in which the overall diabetes knowledge did not appear to be adequate, participants had stated that diabetes was an inheritable disease [16]. Despite the fact that the majority of patients had had diabetes for more than 5 years a major proportion (44.0%) of the participants thought that diabetes could be cured. This agrees with evidence from other studies which indicated that a high proportion of patients in a study in Gujarat state in India (38.2%) believed that diabetes could be cured [17].

Although the overall mean knowledge score (68.1%) was satisfactory, it is noteworthy that only 58.0% knew the normal range of fasting blood sugar and 60.7% knew that blood sugar should be measured regularly to assess control. This is also consistent with other studies done in the South Asian region where the majority of patients did not know the ideal blood glucose target

levels [10,15,18]. A high proportion of our participants (40.0%) did not know that regular exercise is helpful to control type 2 diabetes. It is also noteworthy that only 60.0% knew that it is important to control the diet in addition to taking medication for diabetes. In a similar study conducted in Pakistan it was reported that only 28% of diabetic thought dietary modification was important while only 6% believed that weight loss was important in the management of diabetes [16].

It is alarming to note that although the great majority of patients knew that chronic complications do occur (90.0%), most patients were unaware of the symptoms of hyperglycaemia or hypoglycaemia (90.0%). Only 68.0% of patients knew that feet should be examined regularly for any lesions. A study carried out in Pakistan found that knowledge about diabetic foot care was poor in 30.7% of diabetics [19]. Also concerning is that, even though diabetes is currently the leading cause of new cases of blindness in adults in many industrialized countries and an increasingly more frequent cause of blindness elsewhere [20], only half of our study participants knew the importance of assessing vision annually to prevent diabetic retinopathy. Patients' knowledge about diabetic eye disease was also poor in other studies carried out in the South Asian region. Hoque et al. in Bangladesh, for example, found that only 4.9% of their study participants were aware about diabetic eye disease [9].

There were some limitations to our study that should be noted. The percentage of female patients was 90.0%. This is probably due to the fact that the clinic was conducted on weekdays when more male patients might be at work compared with the female participants who were mostly dependent, married females. This study was a small study conducted at a diabetes clinic caring for approximately 300 patients per month. Therefore the good knowledge reported here may not be

Table 3 Knowledge of diabetes among the study group of patients (n = 150)

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Item	% correct			
Know that diabetes could be inherited	92.7			
Know that chronic complications could occur	90.0			
Know that diabetes is associated with a lack of effective insulin in the body	90.0			
Know that regular examination of feet should be done	68.0			
Know that blood sugar should be measured regularly to assess control	60.7			
Know that regular exercise is helpful to control diabetes	60.0			
Know the importance of dietary regulation in addition to medication	60.0			
Aware of normal range of fasting blood sugar	58.0			
Know that diabetes cannot be cured	56.0			
Know that annual eye examination should be done	50.0			
Able to recognize symptoms of hypoglycaemia	8.0			
Able to recognize symptoms of hyperglycaemia	9.3			

 $\begin{tabular}{l} Table 4 Knowledge scores and current blood sugar control among the study group of patients by duration of diabetes from time of diagnosis \\ \end{tabular}$ 

<b>Duration of diabetes (years)</b>	No. of patients	%	Overall knowledge score	Fasting blood sugar level (mg/dL)
			Mean (SD)	Mean (SD)
<1	21	14.0	58.0 (2.3)	110 (12.2)
1–5	55	36.7	62.6 (6.8)	164 (7.5)
> 5	74	49.3	75.0 (5.3)	176 (7.6)
Total	150	100.0	68.1 (9.0)	163 (23.6)

SD = standard deviation.

representative of the community as there may be diabetics who do not visit the hospital.

#### Conclusion

In conclusion, although overall knowledge about diabetes among

our patients was adequate there were critical gaps in knowledge. In particular, knowledge about the management of diabetes and diabetic complications was poor. This study has helped identify areas where there were gaps in patient knowledge. The findings could be used in an integrated programme to improve patient self-management. Since this

study was conducted at a single community health care centre the results do not reflect the knowledge of the general population and further studies are required particularly in different settings to identify patient educational needs and methods to improve self-management of diabetes.

Competing interests: None declared

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### Prévalence du surpoids et de l'obésité chez des enfants scolarisés à Tébessa (Est algérien) entre 1995 et 2007

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#### معدّل انتشار السّمنة وازدياد الوزن بين أطفال المدارس في تبسة (شرق الجزائر) في الفترة من 1995 إلى 2007 سليمة طالب، حياة اولعهارة، عبد الناصر عقلي

الخلاصة: تقيِّم هذه الدراسة معدل انتشار ازدياد الوزن والسِّمنة بين أطفال المدارس في القطاع العام عن تتراوح أعهارهم بين 4 سنوات و13 تبسة، شرقي الجزائر، على مدى 12 عاماً. وقد حصل الباحثون على أوزان وأطوال الطلاب من البطاقات الصحية، وبلغ عدد أولئك الطلاب 12618 طالباً في الفترة من 1995 حتى 2007، منهم 49.4٪ من الفتيات و 50.6٪ من الفتيان. واتضح للباحثين أن معدل انتشار ازدياد الوزن والسِّمنة خلال الفترة بين 2005 و2007 أصبح 8.49٪ بعد ما كان 17.39 في الفترة 1995–1998. وقد نقص معدل انتشار ازدياد الوزن من 12.55٪ ليصل إلى 8.36٪ الفترة وقد نقص معدل انتشار الرين الأطفال في أعهار تتراوح بين 10 و10 سنة؛ هم وحدهم الذين ظهرت عليهم التغيرات خلال هذه الفترة. وقد كان عدد الفتيات السمينات (3.2٪) أكثر من عدد الفتيان السِّمان السِّمان ورغم نقص معدلات الوزن والسِّمنة خلال 10-12 عاماً، فإن هذه المعدلات تشير إلى الحاجة إلى إجراء ترضُّد وبائي وإعداد استراتيجية ذات توجه صحي للوقاية ازدياد الوزن والسِّمنة لدى الأطفال.

RÉSUMÉ La présente étude a pour but de déterminé la prévalence du surpoids et de l'obésité chez les enfants âgés de 4 à 13 ans et scolarisés dans les établissements publics de Tébessa (Est algérien) sur une période de 10-12 ans. Les mesures du poids et de la taille de 21 618 enfants (49,4 % de filles et 50,6 % de garçons) ont été obtenues à partir de leurs carnets de santé de 1995 à 2007. La prévalence du surpoids et de l'obésité est passée de 17,39 % en 1995-1998 à 8,49 % en 2005-2007. Le surpoids passe de 12,55 % à 6,38 % (p = 0,0001) et l'obésité de 4,48 % à 1,80 % (p = 0,0001) sur la même période. Les enfants âgés de 10 à 13 ans sont les seuls qui présentent une évolution durant cette période. Les filles sont plus touchées par l'obésité que les garçons (3,2 % contre 2,82 % ; p = 0,033). Les garçons sont plus en surpoids (8,73 % contre 7,94 % ; p = 0,034). Si les taux de surpoids et de l'obésité ont diminué sur les 10-12 années, il demeure nécessaire de procéder à une surveillance épidémiologique et de mettre au point une stratégie de promotion de la santé orientée vers la prévention de l'obésité infantile.

#### Prevalence of overweight and obesity in schoolchildren in Tebessa (eastern Algeria) between 1995 and 2007

ABSTRACT This study assessed the prevalence of overweight and obesity among public-school children aged 4 to 13 years in Tebessa, eastern Algeria over 10/12 years. Weight and height measurements of 21 618 schoolchildren were obtained from their health cards for 1995 to 2007 (49.4% girls and 50.6% boys). The prevalence of overweight and obesity in 2005/2007 was 8.49%, down from 17.39% in 1995/1998. Overweight decreased from 12.55% to 6.38% (P = 0.0001) and obesity from 4.48% to 1.80% (P = 0.0001) over the same time period. Children aged 10 to 13 years were the only ones who showed changes during this period. More girls were obese than boys (3.20% versus 2.82%, P = 0.033), while more boys were overweight (8.73% versus 7.94%, P = 0.034). While the rates of overweight and obesity have decreased over 10/12 years, the rates still suggest the need for epidemiological surveillance and the development of a health-oriented strategy for prevention of childhood obesity.

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#### Introduction

La prévalence de l'obésité de l'enfant est en augmentation aussi bien dans les pays industrialisés que dans les pays en développement. L'accroissement de la prévalence de l'obésité pédiatrique et ses conséquences morbides ainsi que la tendance de cette obésité à persister à l'âge adulte représentent un problème de santé publique important et justifient la mise en place de stratégies préventives et thérapeutiques efficaces [1].

Chez l'enfant, l'obésité a des retentissements psychologiques et psychiatriques: troubles de l'image corporelle, dépression, agressivité [2,3]. Un enfant obèse le reste souvent à l'âge adulte [4,5]. Une revue récente de la littérature montre que 26 à 41% des enfants obèses à l'âge préscolaire et 42 à 63% des enfants obèses à l'âge de scolarisation le restent à l'âge adulte [6]. Selon Gortmaker et al, 30 à 40% des adultes obèses l'étaient déjà à l'adolescence [7]. L'obésité est un facteur de risque important pour d'autres pathologies se développant tout au long de la vie [8]. Les coûts de santé liés à l'obésité représentent environ 10% des dépenses de santé dans les pays industrialisés [9].

Les méthodes employées pour définir l'obésité étant différentes selon les auteurs, il est difficile de comparer, d'une étude à l'autre, la prévalence de l'obésité infantile dont l'estimation peut varier considérablement, de 1 à 25% [10]. En 10 ans, elle aurait augmenté de 53% au Japon [11], de 21 à 65% en Grande-Bretagne [12], de 60% aux États-Unis [13] et de 75% à Singapour [14]. Afin de pouvoir estimer la prévalence et l'évolution de cette épidémie, une étude épidémiologique a été mise en place en vue de déterminer la prévalence de la surcharge pondérale et de l'obésité chez des élèves scolarisés dans les établissements publics de la ville de Tébessa (Algérie) et de suivre l'évolution du surpoids et de l'obésité durant la période allant de 1995-2007.

#### Méthodes

Cette étude concerne l'estimation de la prévalence de la surcharge pondérale (surpoids, obésité) et de son évolution fondée sur des données consignées sur les carnets de santé des enfants pendant la visite annuelle des Unités de Dépistage et de Suivi (UDS). L'indicateur utilisé pour évaluer la corpulence est l'indice de masse corporelle (IMC) qui correspond au rapport poids/taille2 (exprimé en kg/ m2). L'objectif de l'étude est de déterminer la prévalence de la surcharge pondérale (surpoids, obésité) chez des enfants et adolescents âgés de 4 à 13 ans et scolarisés au niveau de la commune de Tébessa. Cette tranche d'âge a été choisie pour des raisons pratiques et physiologiques. En effet, après 6 ans, l'obésité a une meilleure valeur prédictive du statut adipeux de l'adulte [15]. De plus, cette tranche d'âge pourrait être une période favorable pour des stratégies de prévention et mérite donc un intérêt particulier. En 2006, le taux de scolarisation à Tébessa était de 96 % (Communiqué du Conseil du Gouvernement algérien du 27 février 2007).

#### Population et lieu d'étude

La circulaire interministérielle n° 1 du 6 avril 1994 portant sur le plan de réorganisation de la santé scolaire a permis la création des Unités de Dépistage et de Suivi (UDS) dépendantes à la fois du Ministère de la Santé et de la Population, du Ministère de l'Éducation nationale et du Ministère de l'Intérieur et des Collectivités locales. Il s'agit de mettre en œuvre « un plan de redressement basé sur l'amélioration de la qualité des prestations et du niveau de couverture sanitaire en milieu scolaire... ». Ces unités sont situées au niveau des établissements scolaires et comprennent un cabinet médical et du personnel médical (médecin, dentiste) et paramédical. Les élèves suivis par les UDS appartiennent en principe aux classes cibles: 1ère AF (Année fondamentale), 2º AF, 7º AF et 1ère AS (Année secondaire); actuellement 1ère AP (Année primaire), 2º AP, 1ère AM (Année moyenne), 1ère AS. Ils font l'objet d'un interrogatoire, d'un examen clinique, visuel et dentaire et de mesures anthropométriques.

Pour pouvoir étudier l'évolution de l'obésité et du surpoids des enfants par sexe et par tranche d'âge, nous avons relevé les mesures anthropométriques (poids et taille) de l'enfant inscrites sur son carnet de santé pendant la visite annuelle aux UDS de la commune de Tébessa, de 1995 à 2007. Au total, 16 écoles primaires, 10 collèges d'enseignement moyen et 8 lycées ont été concernés par cette étude, qui a porté sur une population de 21 618 enfants et adolescents, dont 10 691 filles (49,4 %) et 10 927 garçons (50,6 %), âgés de 4 à 13 ans.

#### Mesures anthropométriques

Les mesures anthropométriques que nous avons recueillies concernent le poids et la taille. Ces mesures permettent de calculer l'indice de masse corporelle (IMC). L'Organisation mondiale de la Santé a fait de l'IMC (rapport du poids sur le carré de la taille) l'instrument privilégié pour l'étude de la corpulence au niveau mondial. Cet indice ne s'est imposé que récemment pour saisir et mesurer le sous-poids, le surpoids et l'obésité sur de larges populations [16]. Ces mesures sont prises par le personnel médical des UDS pendant la visite annuelle des enfants scolarisés à ces structures.

## Seuil définissant les limites de l'obésité et du surpoids

Les seuils retenus dans cette étude sont ceux définis par Cole et al en 2000 [17]. Les courbes de référence sont établies à partir des données recueillies dans différents pays. Les seuils définissant des degrés 1 et 2 de surpoids chez l'enfant sont constitués par les courbes de centiles de l'IMC atteignant respectivement

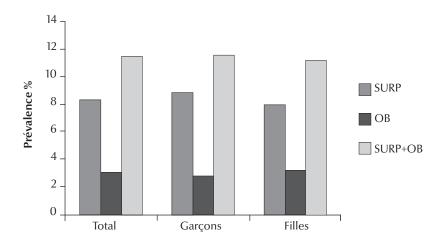


Figure 1 Prévalence globale de l'obésité et du surpoids par sexe (SURP : surpoids ; OB : obésité ; SURP+OB : surpoids + obésité)

les valeurs 25 et 30 kg/m² à 18 ans. Ces valeurs correspondent aux seuils définissant le surpoids et l'obésité chez l'adulte [18]. L'intérêt majeur de cette définition internationale est la possibilité de comparer les enfants du monde entier entre eux, selon une méthode et des indicateurs uniques.

Les centiles IOTF C-25 (centile atteignant  $25 \text{ kg/m}^2$  à 18 ans) et IOTF C-30 (centile atteignant  $30 \text{ kg/m}^2$  à 18 ans) définissent respectivement le surpoids et l'obésité [17].

#### **Statistiques**

Les logiciels utilisés pour la saisie et le traitement des données sont Excel 2000 et Minitab version 13. Le test du  $\chi^2$  a été utilisé pour les comparaisons de fréquences. Le seuil de significativité est fixé à 0.05.

#### Résultats

#### Prévalence globale du surpoids et de l'obésité par sexe

La figure 1 présente la prévalence globale du surpoids et de l'obésité de 1995 à 2007 par sexe. La prévalence globale du surpoids incluant l'obésité durant les 10 ans de 1995 à 2007 est de 11,37 %. La prévalence de l'obésité seule est de 3,0 %, celle du surpoids seul

est de 8,34 % La prévalence du surpoids incluant l'obésité est de 11,55 % chez les garçons contre 11,14 % chez les filles (p = 0,333). La prévalence de l'obésité seule est plus élevée chez les filles que chez les garçons (3,2 % contre 2,82 % ; p = 0,033). La prévalence du surpoids seul est plus élevée chez les garçons que chez les filles (8,73 % contre 7,94 % chez les filles ; p = 0,034).

## Prévalence de l'obésité et du surpoids entre 1995 et 2007

La prévalence du surpoids tend à diminuer depuis 1995 (Figure 2). Elle passe de 12,55 % en 1995-1998 à 6,38 % en 2005-2007 (p = 0,0001). On observe également une diminution dans la prévalence de l'obésité. Elle passe de 4,84 % en 1995-1998 à 1,8 % en 2005-2007 (p = 0,0001). La prévalence du surpoids incluant l'obésité est également en diminution. Elle passe de 17,39 % en 1995-1998 à 8,49 % en 2005-2007 (p = 0,0001).

#### Prévalence du surpoids, de l'obésité et du surpoids incluant l'obésité par sexe de 1995 à 2007

Durant toute cette période de 1995 à 2007, les filles semblent plus obèses que les garçons, mais la différence n'est pas significative (Figure 3). La prévalence de l'obésité chez les filles passe de

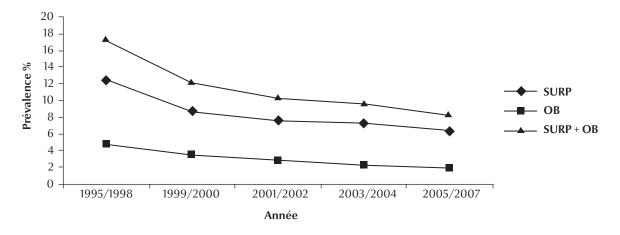


Figure 2 Évolution de la prévalence de l'obésité et du surpoids de 1995 à 2007 (SURP : surpoids ; OB : obésité ; SURP+OB : surpoids + obésité)

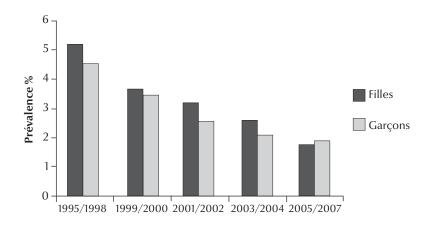


Figure 3 Évolution de la prévalence de l'obésité par sexe de 1995 à 2007

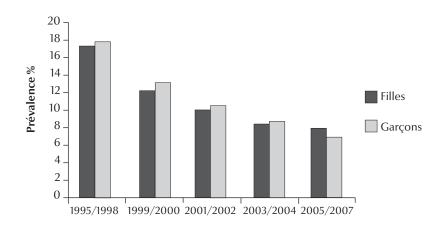


Figure 4 Évolution de la prévalence du surpoids incluant l'obésité par sexe de 1995 à 2007

5,2 % en 1995-1998 à 1,78 % en 2005-2007 (p = 0,0001). Le pic de prévalence de l'obésité est observé en 1995-1998. Chez les garçons, la prévalence de l'obésité passe de 4,5 % en 1995-1998 à 1,83 % en 2005-2007 (p = 0,0001).

La prévalence maximale est observée également en 1995-1998.

La prévalence du surpoids incluant l'obésité passe chez les filles de 17,13 % en 1995-1998 à 8,84 % en 2005-2007 (p = 0,0001). Chez les garçons, cette prévalence passe de 17,62 % en 1995-1998 à 7,55 % en 2005-2007 (p = 0,0001). Aucune différence significative n'a été trouvée entre filles et garçons (Figure 4).

#### Prévalence globale du surpoids et de l'obésité par âge

La prévalence du surpoids et de l'obésité par âge et par sexe est présentée dans la figure 5. La prévalence du surpoids seul (≥ C-25 et < C-30) est comprise entre 10,93 % et 8,62 %. La prévalence de l'obésité seule (≤ C-30) est située entre 6,91 % et 2,32 % La prévalence du surpoids incluant l'obésité (≥ C-25) varie entre 17,84 % et 10,94 %.

Les prévalences maximales du surpoids et de l'obésité sont observées dans la tranche d'âge de 4 à 5 ans. La prévalence minimale du surpoids est observée à l'âge de 7 ans (7,03 %) alors que les révalences minimales de l'obésité seule (2,27 %) ainsi que celle du surpoids incluant l'obésité (9,46 %) sont observées dans la tranche d'âge 8-9 ans.

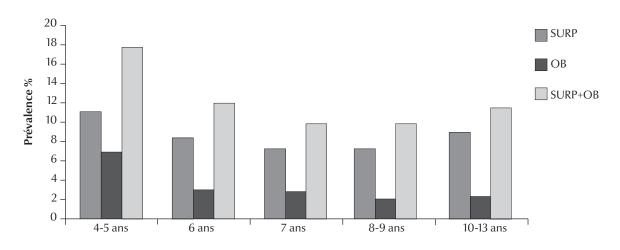


Figure 5 Prévalence globale de l'obésité et du surpoids par âge (SURP : surpoids ; OB : obésité ; SURP+tOB : surpoids + obésité)

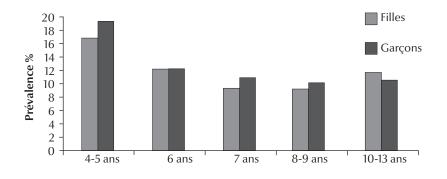


Figure 6 Prévalence du surpoids incluant l'obésité par âge et par sexe

#### Prévalence globale de l'obésité et du surpoids par âge et par sexe

La prévalence du surpoids incluant l'obésité par âge et par sexe est présentée dans la figure 6. Pour les catégories d'âge 4-5 ans, 7 ans et 8-9 ans, la prévalence du surpoids, obésité incluse, est plus élevée chez les garçons mais la différence n'est significative que pour le groupe d'âge de 7 ans (p = 0,037). Pour la tranche d'âge 10-13 ans, la prévalence est plus importante chez les filles, mais la différence n'est pas statistiquement significative. Chez les enfants âgés de 6 ans, la prévalence est similaire entre filles et garçons. Le pic de prévalence est observé à l'âge de 4-5 ans. Il est de 19,01 % chez les garçons et de 16,69 % chez les filles.

La prévalence de l'obésité est plus élevée chez les garçons pour les tranches d'âges 4 -5 ans et 10-13 ans, mais la différence n'est significative que pour le groupe d'âge 4-5 ans (p = 0,028). Chez les filles, la prévalence de l'obésité est plus élevée que chez les garçons pour les tranches d'âge de 6 ans (p = 0,0001) et 8-9 ans (p = 0,037). Pour la catégorie d'âge de 7 ans, la prévalence de l'obésité est similaire entre les deux groupes (Figure 7).

#### Discussion

Dans notre étude, la prévalence du surpoids incluant l'obésité entre 1995 et 2007 est de 11,37 %, celle de l'obésité seule est de 3,0 % et celle du surpoids seul est de 8,34 %. Nous avons observé que les filles sont plus touchées par l'obésité que les garçons (3,2 % contre 2,82 %; p = 0,033). Cette prédominance de l'obésité chez les filles s'explique par le fait qu'à Tébessa, les garçons s'adonnent plus aux jeux actifs que les filles. En plus, dans la région de Tébessa, dès que les filles atteignent l'âge de la puberté, elles n'ont plus droit

aux jeux d'extérieur (marelle, saut à la corde, course, etc.).

En Tunisie, Bedoui et al. cité par Blouza S [19], dans une étude portant sur 5000 enfants de 7 à 14 ans en 1997-1998, ont montré une prévalence de l'obésité de 2,6 % ; ces données semblent inférieures à nos résultats. Également en Tunisie, l'équipe du laboratoire de recherche « Épidémiologie et Prévention des Maladies cardio-vasculaires » a réalisé en 2005 une enquête sur l'obésité auprès de 3199 enfants d'âge scolaire dans la région de l'Ariana et a montré que la prévalence de l'obésité était de 7,4 %, avec 8,6 % chez les garçons et 6,1 % chez les filles [20]. Au Maroc, selon une étude réalisée auprès de 274 mères, 37,1 % des nourrissons âgés de 0 à 2 ans avaient une surcharge pondérale ou étaient obèses [21]. En 1993, dans une étude récente effectuée en milieu scolaire en Arabie saoudite, les garçons âgés de 6 à 18 ans ont montré une prévalence de l'obésité de 15,8 % [22]. Par rapport à ces dernières études réalisées dans le monde arabe, nos données restent inférieures.

En comparant nos résultats à ceux de l'Europe, nous pouvons situer l'Algérie à des valeurs proches de celle de la Grande-Bretagne en 1994 [23] et du Nord de l'Europe où la prévalence du surpoids est de 10-20 % [24]. Nos valeurs sont aussi proches de celles observées en Allemagne chez des enfants âgés de 5 à 6 ans [25]. En revanche, nos valeurs sont très inférieures à celles du Sud de l'Europe [24,25] et des États-Unis où la prévalence de l'obésité dépasse 30 %. Aux États-Unis, la prévalence de l'obésité chez l'enfant était estimée en 1998 à 21,5 % chez les Afroaméricains, 21,8 % chez les Hispaniques et 12,3 % chez les blancs non hispaniques [26]. Parmi la communauté des Indiens d'Amérique, la prévalence varie entre 25 % et 46 % [27]. En Europe, les taux les plus élevés de surcharge pondérale chez les enfants d'âge scolaire (enseignement primaire) des deux sexes

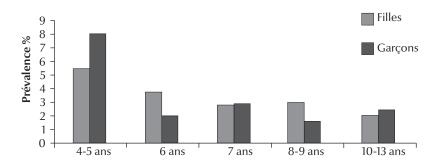


Figure 7 Prévalence de l'obésité par âge et par sexe [p = 0,028 (4-5 ans), p = 0,0001(6 ans), p = 0,037 (8-9 ans)]

sont enregistrés au Portugal (32 % chez les 7-9 ans), en Espagne (31 % chez les 2-9 ans) et en Italie (27 % chez les 6-11 ans) [25].

Il existe peu d'études de prévalence de l'obésité chez les enfants scolarisés algériens. Selon les références de l'IOTF, une étude réalisée en 2005 sur des enfants de 5 à 18 ans dans la région Ouest du pays (El Bayed et Teniat El Had) a montré une prévalence du surpoids incluant l'obésité de 12 % et une prévalence de l'obésité de 2 %. À la même période, dans l'Est du pays dans la ville de Jijel, la prévalence du surpoids incluant l'obésité est estimée à 14,5 % et la prévalence de l'obésité est de 1,2 % [28]. Une étude sur des enfants et adolescents de 6 à 16 ans dans la région du Khroub en 2001-2002 indique une prévalence du surpoids et de l'obésité de 12,8 % et 6,4 % respectivement [29]. À Constantine, la prévalence du surpoids, obésité incluse, chez 5101 élèves âgés de 6 ans était de 10,2 % [30]. Également à Constantine, en 2004 [31], la prévalence du surpoids chez 810 enfants âgés de 7 à 13 ans était de 10,5 %, celle de l'obésité était de 7,4 %. Le même auteur a montré chez des enfants et adolescents scolarisés à Constantine en 2006 une prévalence de surpoids, obésité incluse, de 9,92% [28]. Dans la commune de Tébessa, dans une étude sur des enfants et adolescents âgés de 4 à 18 ans, la prévalence du surpoids, obésité incluse, a été estimée à 10,54 % ; la prévalence de l'obésité seule est de 3,36 % [32].

Dans notre étude, la prévalence du surpoids incluant l'obésité est passée de 17,39 % en 1995-1998 à 8,49 % en 2005-2007 (p = 0,0001). La prévalence de l'obésité est passée de 4,48 % en 1995-1998 à 1,80 % en 2005-2007 (p = 0,0001). Les enfants âgés de 10 à 13 ans sont les seuls qui présentent une évolution durant cette période. Chez ces enfants, la prévalence du surpoids incluant l'obésité a augmenté, passant de 6,0 % en 1995-1998 à

10,47 % en 2005-2007. Nous pensons qu'à l'âge de la puberté, les enfants sont plus touchés par le surpoids et l'obésité.

Malgré la diminution de la prévalence du surpoids et de l'obésité à Tébessa, la situation est préoccupante. En effet, les enfants âgés de 10-13 ans présentent une augmentation d'environ 4 % entre 1995-1998 et 2005-2007. Même si les résultats ne sont pas toujours strictement comparables (population de référence distincte, critère de définition de l'obésité différent), nous pouvons constater que nos résultats sont plus faibles que ceux observés dans d'autres pays. Dans une étude comparative, on trouve que le pourcentage d'enfants obèses de la ville de Tunis est passé de 1,7 % en 1996 à 16,0 % en 2004, et que la prévalence de la surcharge pondérale est passée de 7,1 % à 8,5 % durant la même période [33]. Des études statistiques réalisées en Tunisie montrent qu'en 1995, la surcharge pondérale et l'obésité touchent respectivement 41,3 % et 13,2 % de la population urbaine contre 30,4 % et 7,8 % de la population rurale.

En Europe, on enregistre des chiffres plus élevés. La hausse annuelle de la prévalence de la surcharge pondérale dans les pays européens était en moyenne de 0,1 point de pourcentage au cours des années 1970 ; elle est passée à 0,4 point de pourcentage dans les années 1980, à 0,8 point de pourcentage au début des années 1990, pour finalement atteindre 2,0 points de pourcentage dans certains pays dans les années 2000. En Suisse, la surcharge pondérale chez l'enfant s'est accrue, passant de 4 % en 1960 à 18 % en 2003. Au Royaume-Uni (Angleterre), ces chiffres ont augmenté de 8 à 20 % entre 1974 et 2003. Dans plusieurs régions d'Espagne, la prévalence de la surcharge pondérale a plus que doublé de 1985 à 2002. La seule baisse de prévalence a été observée en Fédération de Russie durant la crise économique qui a suivi la dissolution

de l'Union des républiques socialistes soviétiques (URSS). La prévalence de l'obésité des enfants de 5-12 ans a été multipliée par quatre en France entre les années 1960 et 2000, alors qu'entre 1971-1974 et 1999, elle a triplé aux États-Unis chez les enfants de 6-11 ans [34]. Au Canada, la prévalence de l'obésité infantile a triplé entre 1981 et 1996 [35]. Également au Canada en 2004, le taux combiné d'embonpoint et d'obésité était supérieur d'environ 70 % à ce qu'il était en 1978-1979 tant chez les garçons que chez les filles, alors que le taux d'obésité était 2,5 fois plus élevé [36].

En Algérie, dans une étude menée à Tébessa auprès de 3396 enfants âgés de 5 à 8 ans, la diminution de la prévalence du surpoids et de l'obésité était moins importante que celle du présent travail. La prévalence de l'obésité est passée de 1,06 % en 1998 à 0,72 % en 2005, la prévalence du surpoids est passée de 6,38 % en 1998 à 5,08 % en 2005 [37]. En revanche, selon une étude réalisée à Constantine chez des enfants âgés de 5 à 18 ans, la prévalence du surpoids incluant l'obésité est passée de 8,27 % en 1996-1998 à 10,12 % en 2004 ; la prévalence de l'obésité est passée de 1,26 % à 1,88 % [28]. Ceci peut s'expliquer par le fait que la ville de Constantine est une grande agglomération plus urbanisée que Tébessa.

Vu que le pays fait face actuellement à des difficultés socio-économiques et politiques, les structures de santé scolaire en place doivent permettre une analyse régulière des données de surveillance de la croissance effectuée en routine dans tous les établissements scolaires en Algérie, et par conséquent les mesures anthropométriques doivent être relevées systématiquement. Les données épidémiologiques de l'obésité infantile dans notre pays sont mal connues jusqu'à nos jours, mais leur existence dans plusieurs régions du territoire national impose un dépistage précoce pour une meilleure prise en charge et une politique de prévention dès l'enfance permettant de réduire la charge de morbidité à l'âge adulte.

#### Conclusion

L'obésité, facteur de risque important de nombreuses pathologies, pose un problème de santé publique. En Algérie, il existe peu de données statistiques dans ce domaine. La présente étude avait pour objectif de déterminer la prévalence et l'évolution de la surcharge pondérale et de l'obésité chez des élèves scolarisés à Tébessa durant la période allant de 1995 à 2007. La prévalence du surpoids, obésité incluse, était de 11,37 %. Cette prévalence est passée

de 17,39 % en 1995-1998 à 8,49 % en 2005-2007. Les enfants âgés de 10 à 13 ans sont les seuls qui ont présenté une évolution durant cette période. Les filles sont plus touchées par l'obésité que les garçons. Inversement, les garçons sont légèrement plus touchés par le surpoids que les filles. Rappelons que l'obésité est directement responsable de l'apparition d'une longue série de complications médicales et psychologiques qui justifient une politique de prévention active, précoce et ciblée. Ainsi une surveillance annuelle de l'évolution de l'indice de masse corporelle par rapport à la courbe de corpulence du carnet de santé, et tout particulièrement avant 6 ans pour repérer l'apparition du rebond d'adiposité, est une tâche urgente à mettre en place.

#### Remerciements

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Conflit d'intérêt : aucun.

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## Dietary behaviours and dental fluorosis among Gaza Strip children

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# السلوكيات من حيث النُظُم الغذائية وتسمُّم الأسنان بالفلور لدى الأطفال في قطاع غزة ليس محمد عرفة أبو حلوب، يحيى عوض عابد

الخلاصة: لوحظ وجود معدل انتشار مرتفع لتسمُّم الأسنان بالفلور لدى الأطفال في قطاع غزة. وقد هدفت هذه الدراسة إلى التعرف على تاريخ الإرضاع من الثدي، والسلوكيات من حيث النُظُم الغذائية لدى الأطفال في قطاع غزة، وإلى دراسة الترابط المحتمل مع شدة ومعدل انتشار تسمُّم الأسنان بالفلور. فأجرى الباحثان دراسة مستعرضة شملت عينة عشوائية عنقودية مطبَّقة تضم 350 طفلاً تتراوح أعهارهم بين 12 و18 عاماً مع أمهاتهم. وجمع الباحثان المعطيات حول السلوكيات من حيث النُظُم الغذائية خلال الأعوام السبعة الأولى من العمر من خلال استبيان يستكمل أثناء المقابلة؛ وكان تسمُّم الأسنان بالفلور يحدَّد باستخدام مَنْسَب ثيلسترب – فيرسكوف. واتضح للباحثيْن أن معظم الأطفال (82.9٪) كانون يقتصرون على الرضاعة من الثدي خلال الأشهر الستة الأولى من حياتهم، ولو أن 98.1٪ منهم قد تناولوا الشاي خلال السنة الأولى من العمر. وكان معدل انتشار سممُّم الأسنان بالفلور ومع شدته. ويوصي الباحثان بإجراء المزيد من الدراسات حول مدخول الفلوريد في الغذاء من أجل وضع الخطط للتدخلات تسمُّم الأسنان بالفلور ومع شدته. ويوصي الباحثان بإجراء المزيد من الدراسات حول مدخول الفلوريد في الغذاء من أجل وضع الخطط للتدخلات الوقائية.

ABSTRACT A high prevalence of dental fluorosis has been identified among children in the Gaza Strip. This study aimed to determine the history of breastfeeding and dietary behaviours among children in the Gaza Strip and to examine potential associations with the prevalence and severity of dental fluorosis. A cross-sectional study recruited a stratified cluster random sample of 350 children aged 12–18 years and their mothers. Data about dietary behaviours in the first 7 years of life were collected by interview questionnaire. Dental fluorosis was determined using the Thyllstrup-Fejerskov index. A majority of children were breastfed exclusively in the first 6 months (82.9%) but 98.1% were given tea in the first year of life. The prevalence of dental fluorosis was 78.0%. Both intake of animal proteins and plant proteins were negatively associated with the prevalence and severity of dental fluorosis. Further studies to investigate fluoride intake is required to plan preventive interventions.

#### Comportements alimentaires et fluorose dentaire chez des enfants de la Bande de Gaza

RÉSUMÉ Une prévalence élevée de fluorose dentaire a été observée chez des enfants de la Bande de Gaza. La présente étude visait à déterminer les antécédents d'allaitement au sein et les comportements alimentaires chez des enfants de la Bande de Gaza puis à examiner les associations possibles avec la prévalence et la sévérité de la fluorose dentaire. Une étude transversale a recruté 350 enfants âgés de 12 à 18 ans et leurs mères, formaient un échantillon randomisé et stratifié en grappes. Les données sur les comportements alimentaires au cours des sept premières années de vie ont été recueillies par questionnaire lors d'un entretien. La fluorose dentaire a été déterminée à l'aide de l'indice Thylstrup-Fejerskov. Une majorité des enfants avait été nourrie exclusivement au sein au cours des six premiers mois de vie (82,9 %) mais 98,1 % avaient consommé du thé pendant leur première année. La prévalence de la fluorose dentaire était de 78,0 %. Les apports en protéines animales et végétales étaient négativement associés à la prévalence et la sévérité de la fluorose dentaire. Des études supplémentaires évaluant l'apport en fluor sont requises pour prévoir des interventions préventives.

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#### Introduction

Dental fluorosis is an enamel defect of the teeth caused by hypomineralization due to excessive fluoride intake during the period of enamel formation [1]. This period lasts from birth to 5 years old for anterior permanent teeth and to 13 years old for all permanent teeth [2].

Children in the Gaza Strip have suffered from the problem of dental fluorosis for decades. In 1991, Sansur first identified this problem and emphasized its seriousness [3]. In 1999, the prevalence of dental fluorosis in 7th grade (12-year-old children) in Rafah (60.0%) was the highest, followed by Khan Younis (50.5%), while in North Gaza, where the fluoride concentration was very low in drinking water, it did not exceed 7.1% [4]. Recently, a high prevalence of dental fluorosis (60%) was detected among children of school age in the Gaza Strip [5].

Severe dental fluorosis in the Gaza Strip is multi-factorial. A World Health Organization report stated that drinking water, foods, fluoridated toothpaste and air pollution with fluoride are sources of fluoride exposure [6]. It was pointed out that there is a potential association between breastfeeding and a lower risk of dental fluorosis [7-10]. Previous studies suggested that malnutrition could be a risk factor that increases the prevalence and severity of dental fluorosis [6,8–11]. In the Islamic Republic of Iran a studies found that foods had a considerable contribution (up to 22%) to the total dietary fluoride intake among children [12], and in Brazil foods were identified one of the main sources of fluoride along with water to the total dietary fluoride intake of preschool children [13]. It has also been found that drinking tea and eating fish may increase the risk of dental fluorosis [14].

There are no studies investigating the relationship between nutrition and

oral and dental disorders in Palestine. Thus, the objectives of this paper were to investigate the history of breastfeeding during early childhood and the history of nutrition behaviours during the first 7 years of age, to estimate the prevalence and severity of dental fluorosis and to examine the potential associations between prevalence and severity of dental fluorosis and breastfeeding practices and nutrient consumption among 12–18-year-old children in the Gaza Strip.

#### **Methods**

#### Study design and sample

This was a community-based, crosssectional study of school-age children. The sample size, according to Epi Info, version 6 statistical program, was 350 children. The anticipated prevalence of dental fluorosis used for sample size estimation was 60% with confidence interval 5%. A proportional, stratified cluster random sample of children were selected from home settings in the 5 Gaza governorates (North Gaza, Gaza City, Midzone, Khan-Younis, and Rafah). Each selected cluster was served by water supplies of known wells and the fluoride concentration of municipal well supplying tap water for each child's home was known from the governorate municipality. Children aged 12-18 years old who were born and had spent their first 7 years of life in the same house at the time of the study and who were drinking from the municipal drinking water supply were recruited.

#### **Data collection**

Children were interviewed with their mothers. The researcher used a questionnaire to collect data on the history of breastfeeding, baby formula usage during child infancy and frequency of child's consumption of different foods and milk and tea during the first 7 years of life. Consumption of animal proteins (e.g. meat, chicken, fish, cheese), plant

proteins (e.g. nuts, peas, beans, rice, wheat, maize), calcium-rich foods (e.g. milk, yogurt, cheese) and vitamin C from fruits (e.g. oranges) and vegetables (e.g. spinach, chilli) were determined based on mothers' estimation of the children's intake. Consumption was classified as high (> 3 times/week), moderate (2–3 times/week) or low  $(\leq 1 \text{ time/week})$ . In some cases the data were analysed in 2 groups, age 1-3 years, when most children are still at home, and 4-7 years, the age when children in Gaza Strip start to attend nurseries and kindergartens and when a change in eating behaviours would be expected.

The prevalence and severity of dental fluorosis was determined using the Thyllstrup-Fejerskov index (TFI) of dental fluorosis [15]. The researcher asked the child to brush his/her teeth, and then examined the teeth in normal daylight and recorded the TFI score of the buccal surfaces of all permanent teeth, including the permanent molars.

The study questionnaire was revised and validated by 12 experts in psychology, environment, nutrition, public health, dentistry, and dental public health. Then the questionnaire was piloted among 10 children with their mothers from different areas in all Gaza governorates. The pilot sample was excluded from the study.

Approval for the study was obtained from the Helsinki ethics committee in the Gaza Strip and the Palestinian Ministry of Health. Informed consent was obtained from the children and their families, after complete explanation of the purpose of the research, reassurances about confidentiality and that participation in the study was optional.

#### **Analysis**

SPSS, version 14.0 for used data coding, entry and analysis. Cross-tabulations between dental fluorosis and each of the potential risk factors were developed.

The relationship between variables was examined using the chi-squared test or Fisher test. Results were considered statistically significant at *P*-value < 0.05.

#### Results

# Baby formula usage and breastfeeding during infancy

The majority (82.9%) of the mothers practised exclusive breastfeeding at least in the first 6 months of the child's life (Table 1). Among mothers who started giving formula milk to the child 61.9% started it in the first 1–2 months; 61 (96.8%) of these mothers used tap water to reconstitute infant formula milk and the rests used mineral water.

#### Milk consumption

The percentage of the children who started to milk drinking at age 16+ months was 51.1%. Of these children 51.6% had 3+ cups of milk per day between 1–3 years of age and 92.7% had 1 cup of milk per day between 4–7 years old. Only artificial milk was consumed by 80.8% of these children, and of those who had artificial milk it was reconstituted in tap water for 99.4%.

#### Tea consumption

Many children (44.1%) started to drink tea early, as young as 1 year old. At ages 1–3 years a majority (98.1%) drank only 1 cup of tea per day while at ages 4–7 years 58.1% drank 1–2 cups of tea per day. Tea was prepared with tap water for 98.6% of these children (Table 1).

#### **Food consumption**

Just over half of children (52.4%) ate fish < 3 times per month (Table 2). Consumption of animal proteins was moderate for 48.6% and consumption of plant proteins was moderate for 44.3%. The study found that 78.9% of children had high consumption of calcium-rich foods. A high consumption of vitamin C from fruits was reported (80.3%) whereas only 55.7%

Table 1 Breastfeeding, milk and tea drinking of children aged 12-18 years in Gaza Strip during their first 7 years of life

Strip during their first 7 years of life		
Variable	No.	%
Exclusively breastfed for first 6 months		
Yes	290	82.9
No	60	17.1
Total	350	100.0
Month when formula was started		
1–2	39	61.9
3+	24	38.1
Total	63ª	100.0
Month when milk drinking was started		
1–15	89	48.9
16+	93	51.1
Total	182	100.0
No. of cups of milk drunk per day age 1-3 years		
1-2	88	48.4
3+	94	51.6
Total	182	100.0
No. of cups of milk drunk per day age 4-7 years		
1	114	92.7
2	9	7.3
Total	123	100.0
Type of milk drunk		
Artificial milk	147	80.8
Animal milk	26	14.3
Artificial and animal milk	9	4.9
Total	182	100.0
If artificial milk, type of water used to reconstitute		
Tap water	155	99.4
Mineral water	1	0.6
Total	156	100.0
Year in which tea drinking was started		
1	124	44.1
2+	157	55.9
Total	281	100.0
No. of cups of tea drunk per day age 1-3 years		
1	259	98.1
2+	5	1.9
Total	264	100.0
No. of cups of tea drunk per day age 4-7 years		
1–2	155	58.1
3+	112	41.9
Total	267	100.0
Type of water used to prepare tea		
Tap water	277	98.6
Mineral water	4	1.4
Total	281	100.0

°In addition to the 60 mothers who used formula in the child's first 6 months, 3 mothers started to use formula during the 7th to 9th months.

Table 2 Food consumption of children aged 12-18 years in Gaza Strip during their first 7 years of life

Variable	No.	%
No. of times fish consumed per month		
1–2	150	52.4
3+	136	47.6
Total	286	100.0
Consumption of animal proteins (e.g. meat, chicken, fish, cheese)		
High	100	28.6
Moderate	170	48.6
Low	80	22.9
Total	350	100.0
Consumption of plant proteins (e.g. nuts, peas, beans, rice, wheat. maize)		
High	107	30.6
Moderate	155	44.3
Low	88	25.1
Total	350	100.0
Consumption of calcium-rich foods (e.g. milk, yogurt, cheese)		
High	276	78.9
Moderate	47	13.4
Low	27	7.7
Total	350	100.0
Consumption of vitamin C from fruits (e.g. oranges)		
High	281	80.3
Moderate	54	15.4
Low	15	4.3
Total	350	100.0
Consumption of vitamin C from vegetables (e.g. spinach, chilli)		
High	195	55.7
Moderate	34	9.7
Low	121	34.6
Total	350	100.0

had high consumption of vitamin C from vegetables.

# Prevalence and severity of dental fluorosis

According to the TFI scores, 273 children had signs of dental fluorosis, giving a prevalence of dental fluorosis among this sample of Palestinian children in Gaza Strip of 78.0%. TFI scores were 1–4 (moderate fluorosis) for 63.4% and 5–8 (severe fluorosis) for 14.6%.

The highest prevalence was TFI score 5 (7.4%) while the lowest was for TFI score 8 (0.3%) (Figure 1).

#### Relationship between dietary behaviours and dental fluorosis

Table 3 shows that there were no statistical significant differences in the rate of dental fluorosis whether the child had exclusive breastfeeding during the first 6 months of life or not; whether the child drank formula milk in age 1–2 months

or after that; and whether mineral or tap water was used to reconstitute infant formula. There were also no statistical significant differences in the rate of dental fluorosis for children's consumption habits during the first 7 years of life whether: drinking < 2 or 2+ cups of milk during; starting to drink tea at age year 1 or after year 2; eating fish < 3 or 3+ times per month; consuming low or high amounts of calcium-rich foods; consuming low or high amounts vitamin C as fruits; and consuming low or high amounts of vitamin C as vegetables a during the first 7 years of life.

In contrast, there were negative high statistical significant associations between dental fluorosis level and consumption of animal proteins and plant proteins. In other words, a higher consumption of animal proteins or plant proteins during the first 7 years of the child's life significantly decreased dental fluorosis prevalence and severity (P = 0.005 and P = 0.026 respectively) (Table 3).

#### Discussion

Formula milk consumption during first 6 months of infancy could increase the risk of dental fluorosis [10,16]. In a non-fluoridated rural area of Ontario, Canada, a study found that when the breastfeeding period increased from < 6 months, 6-12 months, to > 12 months, the dental fluorosis prevalence among 752 children decreased significantly from 27.2%, 19.6% to 13.8% respectively. Dental fluorosis prevalence was 87% among children having formula reconstituted with tap water [8]. Marshall et al. determined that using formula reconstituted with fluoridated water and lower intake of human milk and cow's milk which have low fluoride concentrations (0.005–0.010 ppm fluoride and 0.03–0.06 ppm fluoride respectively) increased the risk of dental fluorosis among children at the early ages [9]. Buzalaf et al. advised avoiding excessive

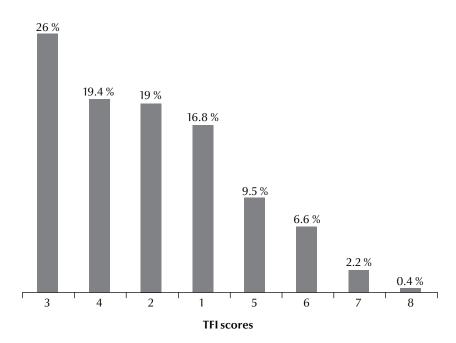


Figure 1 Prevalence and severity of dental fluorosis among children aged 12-18 years in Gaza Strip (TFI = Thyllstrup-Fejerskov index)

fluoride intake by using fluoridated water with ≥ 1 ppm fluoride concentration to dilute powdered infant formulas [17]. In Poland, it was found that the fluoride concentration in 29 brands of powdered formulas was low (mean 29.0 μg/100 g) but that the fluoride intake would exceed the recommended daily intake for infants when reconstituting the formula milk with water having > 0.5 ppm of fluoride [18]. Moynihan et al. estimated the fluoride concentration of infant milk formula available in the United Kingdom to be between 0.03 and 1.32 mg/g in non-reconstituted formula powders [19]. This fluoride concentration slightly increases to 0.13-1.19 mg/L in infant formula reconstituted with water of 0.1 mg/L fluoride concentration, while a remarkable rise in fluoride concentration to about 1.48–5.22 mg/L was observed when formula was reconstituted with water of 1 ppm fluoride concentration. As a result, infant fluoride intake from formula prepared with low and optimally fluoridated water was approximately 0.01-0.08 and 0.13-0.58 mg/kg body weight/day respectively. However, the

present study did not find any statistical significant differences between children who were breastfed during the first 6 month of age or not, children who were provided formula milk from month 1 or 2 of age or after that and children who had a formula reconstituted with mineral water or home tap water.

Previous studies found that the incidence of dental fluorosis among non-milk-consuming children (37.4%) was higher than that of milk-consuming children (7.1%) in 2 areas affected with dental fluorosis in the Province of Jiangxi in China [20] and that fluoride concentrations in milk are low [21]. Nevertheless, we found no significant differences in the prevalence of dental fluorosis between children drinking < 2 and children drinking 2+ cups of milk during the first 7 years of life.

It has been reported that fish and tea are rich in fluoride [14]. Gikunju et al. illustrated that high fluoride content of fish muscle may be the cause of high fluoride intake and the development of dental fluorosis among people living in Lake Naivasha in Kenya [22], while in the Rift Valley area fluoride content of

fish fillets did not appear to be responsible for the prevalence and severity of dental fluorosis among residents [22]. The later findings of Gikunju et al. may support the findings of the current study in which we found that eating fish < 3 or 3+ times per month did not indicate significant differences in the risk of dental fluorosis [22].

A study by Sansur among UN-RWA schoolchildren in the Gaza Strip showed that schoolchildren in all regions drank approximately 3 cups of tea per day on average [3]. The highest (3.19 cups) was in Rafah and the lowest (2.4 cups) was in Bani Suhila. Consistent with our results. Shomer et al. demonstrated that children in Gaza Strip were consuming tea in an early age [5]. We found that 44.1% of children were given tea since the first year of age. However, there were no statistically significant differences in the prevalence of dental fluorosis between children receiving tea before year 2 of life and who received it after that. This contrasts with the suggestion that tea could be a source of high fluoride intake [14], as illustrated in a study showing that brick tea was one of the factors responsible for dental fluorosis in Tibetan children in the natural reserve of Mount Qomolangma [23].

Whitford has argued that fluoride absorption is inversely related to dietary calcium intake, because dietary calcium at high concentrations may cause net fluoride secretion into the gastrointestinal tract [24]. In the present study, however, consuming more foods rich in calcium (e.g. milk, yogurt, cheese) was not a protective factor for dental fluorosis.

In the current study, there was a negative highly statistically significant association between the level of consumption each of animal proteins or plant proteins during the first 7 years and dental fluorosis prevalence and severity. In North Tanzania, a study of 165 schoolchildren (aged 6–18 years) found that the prevalences of moderate

Table 3 Associations between dietary behaviours and dental fluorosis of children aged 12–18 years in Gaza Strip during the first 7 years of age based on Thyllstrup-Fejerskov index (TFI) scores

Variable	Total		TFI	score of d	lental fluor	osis		<i>P</i> -value
			0		-4	5	5-8	
	No.	No.	%	No.	%	No.	%	
Total	350	77	22.0	222	63.4	51	14.6	
Exclusively breastfed for first 6 month								0.220
Yes	290	64	22.1	188	64.8	38	13.1	
No	60	13	21.7	34	56.7	13	21.7	
Month when formula was started								0.678
1–2	39	9	23.1	22	56.4	8	20.5	
3+	24	4	16.7	13	54.2	7	29.2	
Type of water used to reconstitute formula								0.373
Tap water	61	12	19.7	0	0	49	80.3	
Minimal water	2	1	50.0	0	0	1	50.0	
No. of cups of milk drunk/day age 1-3 years								0.791
1–2	88	20	22.7	56	63.6	12	13.6	
3+	94	22	23.4	56	59.6	16	17.0	
No. of cups of milk drunk/day age 4-7 years								0.228
1	114	27	23.7	0	0	87	76.3	
2	9	4	44.4	0	0	5	55.6	
Year in which tea drinking was started								0.099
1	124	20	16.1	78	62.9	26	21.0	
2+	157	34	21.7	104	66.2	19	12.1	
No. of times fish consumed per month								0.240
1–2	150	34	22.7	90	60.0	26	17.3	
3+	136	26	19.1	94	69.1	16	11.8	
Consumption of animal proteins								0.00
High	100	31	31.0	56	56.0	13	13.0	
Moderate	170	23	13.5	122	71.8	25	14.7	
Low	80	23	28.8	44	55.0	13	16.3	
Consumption of plant proteins								0.026
High	107	35	32.7	60	56.1	12	11.2	
Moderate	155	27	17.4	105	67.7	23	14.8	
Low	88	15	17.0	57	64.8	16	18.2	
Consumption of calcium-rich foods								0.482
High	276	63	22.8	175	63.4	38	13.8	
Moderate	47	7	14.9	33	70.2	7	14.9	
Low	27	7	25.9	14	51.9	6	22.2	
Total	350	77	22.0	222	63.4	51	14.6	
Consumption of vitamin C from fruits								0.110
High	281	67	23.8	175	62.3	39	13.9	
Moderate	54	5	9.3	40	74.1	9	16.7	
Low	15	5	33.3	7	46.7	3	20.0	
Consumption of vitamin C from vegetables								0.45
High	195	43	22.1	121	62.1	31	15.9	
Moderate	34	4	11.8	26	76.5	4	11.8	
Low	121	30	24.8	75	62.0	16	13.2	

(TFI score 1–4 score) and severe (TFI score 5–9) dental fluorosis were 67%, and 21% respectively among vegetarian children, and were lower than the prevalences of moderate and severe dental fluorosis among non-vegetarian children (95% and 35% respectively) [25]. This could explain the negative significant associations between the level of consuming plant protein and dental fluorosis in the current study. As a result

it could be argued that some dietary behaviours could be associated with dental fluorosis in addition to the existence of excessive fluoride in drinking water and they should be considered when investigating the associated risk factors to dental fluorosis in developing and undeveloped courtiers and developing interventions for prevention of fluorosis.

In conclusion, it is important to have information on the intake of

fluoride by children living in the Gaza Strip and to identify the children at higher risk of dental fluorosis at the ages of tooth development. Such information will enable the development of an appropriate preventive strategy to reduce the fluoride intake to a suitable level in order to prevent dental fluorosis and other potential health hazards.

Competing interests: None declared.

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# Saudi Arabian expatriate worker fitness-screening programme: a review of 14 years of data

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# برنامج تحرّي لياقة العاملين المغتربين في المملكة العربية السعودية: مراجعة لمعطيات 14 عاماً فهد محمد السويدي، زياد أحمد ميمش، رأفت فيصل الحكيم، سمير عبد المحيد عتلم

الخلاصة: ينبغي أن يخضع العاملون الوافدون لفحص طبي في بلدانهم الأصلية ضمن مراكز معتمدة قبل وصولهم إلى بلدان مجلس التعاون الخليجي. وتستطلع هذه المراجعة ملامح المرتسم الوبائي للعاملين الوافدين المسجلين في المملكة العربية السعودية والذين وجد أنهم لائقين طبياً للعمل. والدراسة هي تحليل وصفي شمل 480 272 480 بطاقة موجودة ضمن قاعدة المعطيات لوزارة الصحة تعود للفترة من 1997 حتى 2010؛ وقد كان معظم العاملين قادمين من إندونيسيا (34.3٪)، وكانت النسبة الإجمالية للعاملين الوافدين غير اللائقين منخفضة (77.0٪)، وكان أعلى معدل لعدم اللياقة هو بين العاملين القادمين من إثيوبيا (4.06٪)، يتلوهم القادمون من الصومال (4.41٪). وقد كان أكثر الأسباب شيوعاً هو التهاب الكبد "بي" (57.5٪)، تتلوه الأمراض غير السارية (21.2٪)، ثم العدوى بفيروس الالتهاب الكبدي "سي" (17.4٪). وتشير مراجعة النشريّات الطبية أن مجمل عدد العاملين المسجلين في وزارة الصحة السعودية أقل من التقديرات الفعلية، وأن معدل العاملين غير اللائقين أقل مما هو عليه لدى بقية بلدان مجلس التعاون الخليجي، مما يشير إلى أن المعايير وضان الجودة في مختبرات المملكة العربية السعودية تحتاج لمزيد من المراجعات.

ABSTRACT Expatriate workers must be medically examined in their country of origin at accredited centres prior to their arrival in any Gulf Cooperation Council (GCC) country and are reexamined when they enter the country. This review investigated the epidemiological profile of registered expatriate workers in Saudi Arabia who were found medically unfit to work. A descriptive analysis was performed on 4 272 480 records of a Ministry of Health database from 1997 to 2010. The greatest proportion of workers was from Indonesia (34.3%). The total proportion of unfit expatriate workers was low (0.71%). The highest rate of unfitness was among workers from Ethiopia (4.06%), followed by Somalia (2.41%). Hepatitis B infection was the most common cause (57.5%), followed by noncommunicable diseases (21.2%) and hepatitis C infection (17.4%). This review suggests that the total number of workers registered in the Saudi Ministry of Health was underestimated, and the rate of unfit workers was lower than for other GCC countries, suggesting that standards and quality assurance in Saudi laboratories require revision.

### Programme saoudien d'évaluation des aptitudes physiques des travailleurs expatriés : examen de 14 années de données

RÉSUMÉ Les travailleurs expatriés doivent passer une visite médicale dans leur pays d'origine, dans un centre accrédité avant leur arrivée dans un pays du Conseil de coopération du Golfe, et sont ensuite réexaminés sur place. Le présent examen portait sur le profil épidémiologique des travailleurs expatriés enregistrés en Arabie saoudite qui avaient été déclarés médicalement inaptes au travail. Une analyse descriptive de 4 272 480 dossiers, issus d'une base de données du ministère de la Santé, entre 1997 et 2010 a été réalisée. La plus importante part des travailleurs venait d'Indonésie (34,3 %). La proportion totale de travailleurs expatriés inaptes était faible (0,71 %). Le taux d'inaptitude le plus élevé a été observé chez les travailleurs éthiopiens (4,06 %), et somaliens (2,41 %). L'infection par le virus de l'hépatite B était la cause la plus fréquente (57,5 %), suivie par les maladies non transmissibles (21,2 %) et l'infection par le virus de l'hépatite C (17,4 %). Cette analyse semble indiquer que le nombre total de travailleurs enregistrés au ministère de la Santé saoudien était sous-estimé et que le taux de travailleurs inaptes est inférieur à celui des autres pays du Conseil de coopération du Golfe, ce qui donne à penser qu'une révision des normes et de l'assurance qualité des laboratoires saoudiens est nécessaire.

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#### Introduction

With the globalization of the oil and gas industries in the late 1970s, Saudi Arabia became an important destination for many expatriate workers from many nations [1,2]. In 1983 the health authorities in Saudi Arabia, in compliance with the regulations and recommendations of the World Health Organization (WHO), started to perform mandatory medical screening on all expatriate workers. In Saudi Arabia this screening programme is seen an important strategy for preventing the spread of communicable diseases due to the higher numbers of expatriate workers and their dependants (31.1% of the total population in Saudi Arabia) [3]; the high rates of communicable diseases in many of the countries of origin; and the nature of the work of some expatriates (e.g. housemaids, health workers, private drivers and food handlers), which brings them into direct contact with Saudi citizens [4].

In 1995, the executive board of health ministers for the Gulf Cooperation Council (GCC) took responsibility for publicizing and implementing the rules and regulations for medical examinations of expatriate workers in all GCC countries [3,5]. Under the scheme expatriate workers must be medically examined and tested in their country of origin at accredited centres, prior to their arrival in a GCC country. All expatriate workers are reexamined on arrival in Saudi Arabia. This is a prerequisite to issue their stay permits. Their health screening results are compared with the medical certificates issued in their country of origin. The executive board of health ministers for GCC countries arranges for annual (unannounced) visits to accredited centres to ensure implementation of unified standards. Violations within a centre may result in penalties, including the withdrawal of accreditation or fines if an expatriate worker who holds

a fitness certificate from one of these centres is subsequently identified as unfit in the Saudi fitness-screening programme [6].

There are important epidemiological indicators among expatriate workers in Saudi Arabia, e.g. their nationality distribution, the magnitude, distribution and causes of their medical unfitness and the trends of disease among them. This review was made to investigate the epidemiological profile of registered expatriate workers in Saudi Arabia who were found to be medically unfit for work.

#### Methods

A systematic review was conducted in the Ministry of Health (MOH) electronic database of the available and accessible data for the Saudi expatriate worker fitness-screening programme. Data from each year of a 14-year period (1997–2010) were compared with paper records. Incomplete data were requested from the regional coordinators. Microsoft *Excel* software was used to pool data for all years and for the subsequent analysis. A descriptive

analysis was carried out and the results presented in distribution tables and graphs.

A literature search of the screening of expatriates was limited to the early 1980s and 2000s, when screening began in Saudi Arabia. The review included published books, reports and articles on the web or in print.

#### Results

#### **Background data**

In this review, the total number of registered expatriate workers re-examined in Saudi Arabia was 4 272 480. The average number examined each year was 305 177. The number of workers tested over the study period varied in each year, but generally increased slightly over time. The highest number of examinations took place in 2010, and the lowest in 2007 (Figure 1). The majority of workers examined (3 970 875, 93.1%) were men, and the male to female ratio was nearly 13:1 (Table 1). The highest proportion of expatriates came from Indonesia (34.2%), with the smallest proportion from Somalia (0.08%). The highest proportion of

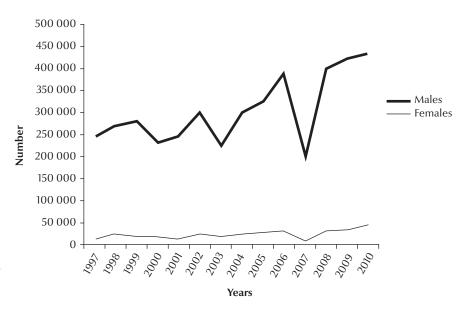


Figure 1 Annual number of expatriate workers examined in Saudi Arabia over the period 1997–2010

1.88 4.06 0.16 0.02 1.46 0.54 0.27 1.61 1542 30 230 **Total** 2587 323 209 233 661 176 707 38 908 20884 1.29 0.76 Table 1 Distribution of nationality, sex and medical unfitness among expatriate workers in Saudi Arabia examined in 1997-2010 1.21 Unfit **Females** 2 516 248 50 64 125 32 769 3878 5367 8 598 6 290 2 972 1890 2 690 0.50 0.25 1.63 1.99 4.04 1.44 Males 2 339 143 938 73 633 6 685 258 900 390 615 33 541 17 912 6 630 314 611 227 371 14 677 3 970 875 All other countries that have political ties with Saudi Arabia. Syrian Arab Republic **3angladesh** Philippines ndonesia Sri Lanka Pakistan Ethiopia remen somalia Nepal

women came from Somalia (35.8%), and the lowest from Egypt and Pakistan (2.7% each).

#### **Prevalence of unfitness**

Over the study period, a total of 30 230 workers (0.71%) were found to be unfit to work. Most of them (27 714, 91.7%) were men. The highest rate of unfitness was among Ethiopian workers (4.06%), followed by those from Somalia (2.42%) and Nepal (1.88%), with the lowest rate found in workers from Turkey (0.02%) (Table 1). Throughout the first 10 years of the period studied, there was little variation in the numbers of unfit workers. In 2007 there was a sudden decrease, and this was followed by a significant increase in 2008, which peaked in 2010 (Figures 1 and 2).

#### Causes of unfitness

Among the total 30 230 unfit workers hepatitis B virus (HBV) infection was the most common cause of unfitness (17 371 cases, 57.5%), followed by chronic (noncommunicable) diseases (pooled data) (6581, 21.8%), hepatitis C virus (HCV) infection (5265, 17.4%) and human immunodeficiency virus (HIV) infection (413, 1.4%). The numbers of workers with infection and chronic diseases during the period studied are shown in Figure 2.

#### Infectious diseases

The total number of workers with infectious diseases was 23 649 and 21 665 (91.7%) were men (Table 2). The average annual number of workers with HBV was 1150, followed by 500 cases of HCV, 86 of TB and 35 of HIV. The highest rates of HBV were in workers from Indonesia (29.9%) and the Philippines (13.0%); the lowest rate was among Turkish expatriates (0.01%) (Table 2). The highest rates of HCV were also found in workers from Indonesia (7.22%) and the Philippines (3.32%). There were no cases from Turkey. The highest rates of HIV infection were in workers from Indonesia

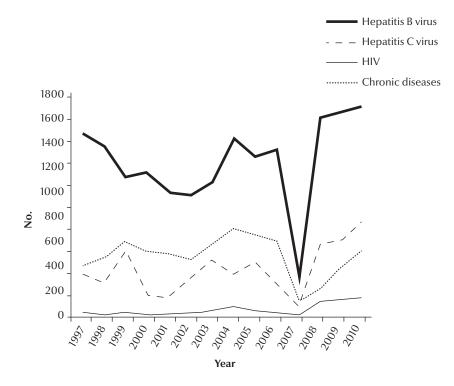


Figure 2 Main causes of unfitness (diseases) among expatriate workers examined in Saudi Arabia over the period 1997-2010

(0.78%) and the Philippines (0.32%) (Table 2).

#### Noncommunicable diseases

Among the 6581 expatriates who were unfit to work due to chronic (noncommunicable) diseases, 6049 (91.9%) were men (Table 3). Diabetes mellitus and hypertension were the most common problems (95.7%). The highest rates of these diseases were found in workers from Indonesia (36.4%) and India (17.6%). The occurrence of neoplastic and neuropsychiatric diseases was very low in workers from Indonesia. Among the women registering pregnancy as their cause of medical unfitness, the greatest number were from the Philippines (1.79%) (Table 3).

#### Discussion

The data for this review were obtained from records over a 14-year period from 1997, when electronic data collection started in Saudi Arabia, to 2010. This long time period allowed a reasonable assessment of the time trends to be made. The increase in the number of expatriate workers arriving in Saudi Arabia from 2005 onwards may be due the influx of workers from new sources, such as China, Nepal, Viet Nam, Ethiopia and Eritrea, which were added to the programme around 2005. The sudden and transient decrease observed in worker numbers in 2007 may relate to the start of the online registration process. The staff responsible for online registration may not have been adequately prepared or trained, and the online facilities may have been insufficient at that time. Thereafter, the numbers registered returned to preonline levels. Workers from Indonesia represented the majority of expatriates, probably because families in Saudi Arabia prefer to employ Indonesian workers as housemaids and private drivers [7-10].

Most expatriate workers were men. Women, who accounted for 7% of the total, are usually employed as housemaids or health-care workers [11,12].

Approximately one-third of workers from Somalia were females; this is the country from which the highest proportion of women come, and may be a result of the ongoing conflict in Somalia that has forced many families to leave the country.

Ideally, there should be no unfit cases at the time of re-screening in Saudi Arabia. The data showed this was not the case. Although the rate of unfitness was only 0.71% this represents a total of 30 230 workers who were unfit to work. This discrepancy raises issues regarding the accuracy and quality of testing in the countries of origin. In general, the highest specific unfitness rates were found among workers from Africa. This was expected because of the limited medical care available in African countries [13]. Recent WHO reports show that some of the highest prevalence rates of HIV infection, HBV, HCV and TB are in Horn of Africa countries [14–16]. These countries would benefit from efforts directed at ensuring the quality and accuracy of their medical testing procedures.

The average annual number of expatriates who were unfit to work due to infectious diseases was found to be lower in this study than in the official MOH statistics, especially for HIV (413 cases), HCV (5265 cases) and TB (257 cases) [17,18]. However, the non-Saudi individuals included in the MOH statistics may have lived in Saudi Arabia for many years and may have acquired their infection after arriving in the country. Therefore, these data cannot be compared with data from the expatriate screening programme. For the same reason, the figures regarding non-infectious diseases cannot be compared. Data on the regional distribution of unfit workers was not available because of technical problems in the computerized reporting system.

HBV was the most common cause of unfitness among all the workers in this study. This was followed by chronic diseases and HCV. The pattern of these

0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.02 0.00 0.65 0.01 Leprosy Venereal diseases 0.00 0.00 0.09 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.03 0.01 0 0 0 0 0 0 21 Malaria & filarial 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.01 0 64 Cause of unfitness 0.00 0.00 0.03 90.0 0.03 0.00 0.00 0.12 Table 2 Distribution of infectious diseases among unfit expatriate workers by nationality in Saudi Arabia, 1997-2010 TB 34  $\infty$ 15 9 28 0 27 0.08 0.00 0.04 0.07 0.00 Η 9 0 1.80 90.0 90.0 1.09 92.0 0.97 0.00 1.26 1.95 0.14 HCV 5 265 1707 229 426 299 32 6.83 0.52 0.47 1.43 HBV 615 122 339 17371 infections cases of diseases 4 032 2 266 1373 1378 2 139 379 190 22 23 649 Syrian Arab Republic Bangladesh Philippines Indonesia Sri Lanka Pakistan Ethiopia Country Somalia Othersa Sudan Turkey Nepal Yemen India Egypt Total

"All other countries that have political ties with Saudi-Arabia.

HBV = hepatitis B virus; HCV= hepatitis C virus; HIV = human immunodeficiency virus; TB = tuberculosis.

Table 3 Distribution of noncommunicable diseases among unfit expatriate workers in Saudi Arabia in 1997-2010

Country	Total cases of non- communicable disease	Chronic diseaseª		Neop	Cause o olasms		s sychiatric sases	Pre	gnancy
	No.	No.	%	No.	%	No.	%	No.	%
Indonesia	2 417	2 397	36.40	0	0.00	18	0.27	2	0.03
Philippines	193	61	0.93	3	0.05	11	0.17	118	1.79
India	1177	1 156	17.60	0	0.00	0	0.00	21	0.32
Bangladesh	548	528	8.02	0	0.00	0	0.00	20	0.30
Pakistan	654	640	9.72	1	0.02	0	0.00	13	0.20
Egypt	2	0	0.00	2	0.03	0	0.00	0	0.00
Sri Lanka	448	405	6.15	0	0.00	4	0.06	39	0.59
Sudan	183	183	2.78	0	0.00	0	0.00	0	0.00
Nepal	354	339	5.15	0	0.00	1	0.02	14	0.21
Ethiopia	429	429	6.52	0	0.00	0	0.00	0	0.00
Yemen	109	109	1.66	0	0.00	0	0.00	0	0.00
Syrian Arab Republic	5	4	0.06	1	0.02	0	0.00	0	0.00
Turkey	0	0	0.00	0	0.00	0	0.00	0	0.00
Somalia	39	39	0.59	0	0.00	0	0.00	0	0.00
Others	23	6	0.09	0	0.00	9	0.14	8	0.12
Total	6 581	6296	95.70	7	0.11	43	0.65	235	3.57

<sup>&</sup>lt;sup>a</sup>Mainly diabetes mellitus, hypertension, other liver and kidney diseases.

diseases among workers is consistent with the pattern of disease in most Asian and African countries where infectious diseases are more common [13]. Workers from Indonesia and the Philippines had the highest specific rate of unfitness due to HIV, HBV and HCV and chronic diseases. Although the prevalence of HIV and hepatitis infections is high in South-East Asia [19–21] the rate of HIV cases among Africans was higher than that for South-East Asians in our study.

The rates of unfit expatriate workers in other GCC countries, namely United Arab Emirates and Kuwait, have been reported as 3.2% and 4.1% respectively [22,23]. These are considerably higher than that in our review of Saudi Arabia (0.71%). One reason for this difference might be that the quality of re-examinations in the other GCC countries is better than that in Saudi Arabia. An investigation into the technical quality standards and procedures of the designated Saudi

laboratories might be warranted on this basis. Despite the relatively low rate of unfit workers identified in our study and throughout GCC countries, there is a sound rationale to revise and supervise the accredited testing centres in the countries of origin.

The total number of registered expatriate workers in this worker fitnessscreening programme (3 970 875) is an underestimate, presumably because of limitations in the reporting system. There were lower annual numbers of expatriate workers in this review than those recorded in other official sources. Data from the Ministry of Labour state the total number of workers coming to Saudi Arabia was approximately 1.2 million in 2008 and 1.12 million in 2009 [11]. It is understood that not all expatriate workers are registered in MOH records, and about one-third are examined in other governmental health sectors [11]. However, as we showed here, the registered number of expatriate workers in the MOH was still low. There are several reasons for this. First, not all the health regions are connected to the computerized reporting network (some still send faxed reports because the necessary infrastructure is lacking). Secondly, not all private authorized testing centres are yet connected to the network. Thirdly, there is limited coordination among other governmental health sectors and partners, such as the Ministry of Interior and Ministry of Labour. All these factors make it difficult for the MOH to accurately identify expatriate workers in Saudi Arabia.

The greatest drawback of the screening programme was that some of the data of unfit workers reported to the MOH were incomplete (e.g. missing worker code numbers and names of the external centres issuing the fitness certificates). These insufficiencies led to delays in identifying the external centres that had violated the rules, which meant that they were able to issue even greater numbers of inaccurate certificates.

Among the limitations of this study is that the data review was based on the electronic records of the MOH database. This was insufficient in terms of providing certain variables, e.g. on the distribution of noncommunicable diseases by type. The paper records obtained from the MOH headquarters and regions were disorganized and difficult to review. There were few references in the literature to expatriate workers in Saudi Arabia, and those that were found were not recent.

#### **Conclusions**

Expatriate workers in Saudi Arabia originate from many countries, mostly in South-East Asia, and the highest rate of unfitness was found among workers from African countries. HBV was the main cause of unfitness, followed by noncommunicable diseases such as diabetes mellitus and hypertension. The lower rate of unfit workers found at the time of re-examination

in Saudi Arabia compared with other GCC countries requires investigation and revision of the test standards and quality assurance processes in the Saudi-designated laboratories. The lower than expected numbers of registered expatriate workers in this worker fitness-screening programme suggest that reporting system for data from all authorized centres to the MOH must be improved.

Competing interests: None declared.

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# Study of operated primary and secondary (recurrence) hydatidosis in hospitals of Kermanshah, west of Islamic Republic of Iran

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دراسة حول الكيسات العدارية الأولية أو الثانوية (الناكسة) التي أجريت لها عمليات جراحية في مستشفيات كرمان شاه، غربيّ جمهورية إيران الإسلامية

مهدي وجداني، سينا وجداني، سارة لطفي، فريد نجفي، نصر نزاري، يزدان حمزاوي

الخلاصة: إن داء الـمُشْوِكات الكيسي الذي تسببه المرحلة اليَرَقية من ديدان المشوكة الحبيبية يمثَّل أحد التهديدات للصحة العمومية العالمية. وتهدف هذه الدراسة إلى التعرُّف إلى السيات الديمغرافية والسريرية لحالات الكيسات العدارية الأولية والثانوية في غربي جمهورية إيران الإسلامية. وقد أجرى الباحثون استعراضاً استعادياً للسجلات في سبعة مستشفيات تابعة للقطاعَيْن العام والخاص في كرمان شاه في الفترة بين عامي 2004 و2009؛ وشملت الدراسة تحليل 529 ملفاً لحالات مشتبه بها، ووجدوا أن 291 حالة كيسة عدارية قد أجري لها عمليات جراحية وتم تأكيدها. وقد كان 51.5٪ من المرضى من الإناث، و57.7 منهم يعيشون في المدن أو الضواحي، وكانت أكبر المجموعات العمرية تشكيلاً لنسبة 75.5٪ من الحالات هي 31-40 عاماً. أما أكثر الأعضاء إصابة فكان الكبد 64.9٪ وقد تلقى معظم المرضى (79.4٪) وليس كلهم المعالجة بالألبندازول. والتهى الباحثون إلى وجوب اعتبار ولاية كرمان شاه منطقة موطونة بمرض الكيسات العدارية البشري، ووجوب بذل المزيد من الجهود الوقائية.

ABSTRACT Cystic echinococcosis, caused by the larval stage of *Echinoccocus granulosus*, is a global public health threat. The aim of this study was to determine the demographic and clinical characteristics of cases of primary and secondary hydatid cyst in the west of the Islamic Republic of Iran. A retrospective record review was made in 7 public and private hospitals in Kermanshah from 2004 to 2009. Of 526 files of suspected cases analysed, 291 cases of hydatid cyst had been operated upon and confirmed. Of the patients, 51.5% were females, 57.7% lived in urban and suburban areas and the largest age group (17.5%) was 31–40 years. The major organs involved were liver (64.9%) and lung (26.8%) and 18 cases (6.2%) were confirmed as secondary hydatidosis. Most patients (79.4%) had been treated with albendazole. Kermanshah province should be considered an endemic region for human hydatid cyst disease; greater efforts in prevention are needed.

# Étude de l'hydatidose primaire et secondaire (récidive) opérée dans des hôpitaux de Kermanshah, dans l'ouest de la République islamique d'Iran

RÉSUMÉ L'échinococcose cystique, causée par le stade larvaire d'*Echinoccous granulosus*, représente une menace pour la santé publique mondiale. L'objectif de la présente étude était de déterminer les caractéristiques démographiques et cliniques des cas de kyste hydatique primaire et secondaire dans l'ouest de la République islamiqued'Iran. Une revuer étrospective des dossiers aétémenée dans septhôpitaux publics et privés de Kermanshah entre 2004 et 2009. Sur un total de 526 dossiers de cas suspects analysés, 291 cas de kyste hydatique avaient été opér és et confirmés. Les patients étaient 51,5 % à être des exeféminin, 57,7 % vivaient dans des zones urbaines ous uburbaines et le groupe d'âge le plus nombreux (17,5 %) était celui des 31-40 ans. Les principaux organes touchés étaient le foie (64,9 %) et les poumons (26,8 %) et 18 cas (6,2 %) ont été confirmés comme hydatidose secondaire. La plupart des patients (79,4 %) avaient été traités par albendazole. La province de Kermanshah devrait être considérée comme une région d'endémie pour le kyste hydatique humain ; des actions de prévention renforcées sont nécessaires.

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#### Introduction

Cystic echinococcosis, caused by the larval stage of Echinoccocus granulosus, is a global public health threat. The embryos penetrate the wall of the intestine and are carried in the bloodstream to vital organs such as the liver, the lungs or the brain, where they can form into watery blisters called hydatid cysts [1,2]. The disease presents a substantial burden on the human population. Current estimates suggest that cystic hydatid disease caused by *E. granulosus* results in the loss of 1-3 million disability-adjusted life years per annum. The annual cost of treating cases and economic loss to the livestock industry approximately amounts to US\$ 2 billion. These diseases are perhaps some of the more important global parasitic diseases, with more than 1 million people affected at any time [3].

Hydatid disease is endemic in sheep-raising areas of Africa, the Mediterranean region of Europe, the Middle East, Greece, Asia, South America, Australia and New Zealand [4,5]. The parasite has a very wide geographical distribution [6] and there is evidence for the emergence or re-emergence of human cystic echinococcosis in parts of China, Central Asia, Eastern Europe and Israel. E. granulosus is endemic too in the Islamic Republic of Iran, with stray dogs acting as the final host of the disease and sheep as the intermediate hosts. Human infections are regularly observed in medical centres in different parts of Islamic Republic of Iran [7,8] but the western region of the country is more affected by this parasite than the other parts [9]. Some studies in single hospitals or isolated cases have been reported previously from other areas [10–12]. As there is limited information on the epidemiology of the disease in the west of the Islamic Republic of Iran, we aimed to study the demographic and clinical characteristics of cases of primary and secondary hydatid cyst in Kermanshah hospitals.

#### Methods

#### Study design and setting

A retrospective study from 2004–09 was performed in 7 private and public hospitals for tracking primary and secondary hydatid cyst in Kermanshah. The province of Kermanshah is located in the middle of the western part of the Islamic Republic of Iran, with a population of 1 900 831 in the last census in 2011. It is an agricultural and traditional livestock region of the country and women participate in the farming lifestyle as much as men. The province has a moderate mountainous climate and is suitable for husbandry of animals, particularly sheep. On the other hand, stray dogs, sheep and domestic herbivores in the mountain area and prairie have contributed to the existence of human and veterinary unilocular hydatid cyst.

#### **Data collection**

All documents were reviewed and files were analysed from all patients suspected to be infected with hydatid cyst who had been hospitalized and had undergone physical examination for clinical manifestations, computerized tomography scanning, magnetic resonance imaging, sonography and diagnostic laboratory testing by surgery specialists. Out of 526 files examined a total of 291 cases were reported to be infected with hydatid cyst. Data on age, sex, occupation, organs involved, primary or secondary recurrence of hydatid cyst and medication (albendazole-treated or not), were extracted from the hospital files. After surgery, oral albendazole 10 mg/kg or 400 mg twice daily for 4 weeks was administrated, and repeated as necessary for up to 12 cycles, each separated by an interval of 2 weeks, repeated after 3-6 months.

#### Data analysis

The data was analysed with *SPSS*, version 16, and simple descriptive statistics are reported.

#### Results

A total of 526 cases were studied in 7 hospitals during a 6-year period. Patients had undergone diagnosis based on clinical manifestations and 291 cases were operated on and verified with hydatid disease. Based on the most recent census data for the population of Kermanshah province (1 900 831) this was an annual rate of approximately 2.6 per 100 000.

The principal sites of infection were the liver (64.9%) and lung (26.8%); 3 cases (1.0%) were infected in both organs. Smaller numbers were infected in the pelvic area (5 cases, 1.7%), while the remaining case involved the kidney, omentum, spleen, pancreas, gallbladder, prostate, bladder (3 cases each) and the uterus, mesentery or vertebrate (1 case each) (Table 1). Among these cases liver and lung involvement were reported at the highest rates.

The sex distribution showed 51.5% females and 48.5% males (Table 1). Just over half of patients were from urban areas (57.7%) and 42.3% were from residential rural areas. The age distribution indicated 6.9% of people infected were between 1–10 years of age and the oldest person diagnosed was 80 years old. The most prevalent age group for hydatid cyst disease was 31–40 years (17.5%).

Out of 291 patients, 18 cases (6.2%) were confirmed as secondary (recurrence) human hydatid cyst and 93.8% as primary hydatid cyst. Nearly three-quarters of patients with hydatidosis (73.2%) underwent laparotomy and 26.8% underwent laparoscopy surgery. Albendazole was used after surgery on 231 cases (79.4%). Albendazole medication lasted approximately 3 months and rarely over 6 months to 2 years. The recovery rate of hydatid cyst disease was 79.4%.

#### Discussion

E. granulosus is a cosmopolitan parasite and endemic regions exist in each continent. Considerable public health

problems occur in many areas, including countries of Central America, South America, Western and Southern Europe, Middle East, North Africa, sub-Saharan countries, China and Russia. Generally the Islamic Republic of Iran is an endemic area of hydatidosis [13,14]. Based on our data we estimated an annual rate of human hydatid cyst of 2.6 cases per 100 000 people annually in hospitals in the province of Kermanshah. Another series reported the annual incidence of operated hydatidosis in Islamic Republic of Iran to be 4.8 per 100 000 people [15]. An overall rate of 1.45 cases per 100 000 people was reported in another study; the incidence was highest in Khorasan province (in the north-east of the country) with 4.45 cases per 100 000 people and the lowest in Hormozgan province (in the south of the country) with 1 case per 100 000 people [16]. The rate in other countries people were Greece (13 per 1 000 000), rural regions of Uruguay (75 per 1 000 000), rural regions of Argentina (143 per 1 000 000), Xinjiang in China (197 per 1 000 000) and Turkana in Kenya (220 per 1 000 000) [17]. Neighbouring Turkey had 18–20 cases per 1 000 000 people [18]. Stray dogs represent a major threat for transmission to humans [19]; in Kermanshah, the prevalence of *E. granulosus* in dogs and red foxes were reported as 16.7% and 7.1% respectively [20].

In this study it was found that females were more affected than males. The relationship between domestic sheep, dogs and humans is very close in the region, and women that have agricultural occupations and work as traditional livestock farmers are more directly exposed to these animals. On the other hand, women who are housekeepers in urban areas are mostly exposed to raw vegetables for daily diet consumption and may consume E. granulosus eggs. Studies elsewhere in the country found that the rate of infection in urban areas was greater than rural areas [21], but our findings contradicted

Table 1 Demographic and clinical characteristics of 291 cases of human hydatidosis in hospitals of Kermanshah, Islamic Republic of Iran from 2004–2009

hydatidosis in hospitals of Kermans	shah, Islamic Republic of I	ran from 2004-2009
Variable	No. of cases	%
Total	291	100.0
Sex		
Male	141	48.5
Female	150	51.5
Age (years)		
1–10	7	7
11–20	7	7
21-30	13	13
31–40	18	18
41–50	14	14
51-60	16	16
61–70	8	8
71-80	16	16
80+	2	2
Residence		
Urban	168	57.7
Rural	123	42.3
Site		
Liver <sup>a</sup>	189	64.9
Lung <sup>a</sup>	78	26.8
Pelvic area	5	1.7
Kidney	2	0.7
Omentum	2	0.7
Spleen	2	0.7
Pancreas	2	0.7
Adrenal gland	2	0.7
Gallbladder	2	0.7
Prostate	2	0.7
Bladder	2	0.7
Uterus	1	0.3
Mesentery	1	0.3
Vertebrate	1	0.3
Туре		
Primary hydatid cyst	273	93.8
Secondary hydatid cyst	18	6.2
Treatment		
Albendazole	231	79.4
No albendazole	60	20.6

<sup>a</sup>Both liver and lung: 3 cases (1.0%).

that. Other studies also showed that patients with hydatid cyst disease were mostly females [16,17,22–25].

In our study, the youngest age of patients with hydatid cyst disease was between 1-10 (6.9%) years of age and the

2 oldest cases were over 80 years of age (2.1%), but the highest rate of hydatid cyst was between 31–40 years of age (17.5%). A study in Iraq found that the mean age of patients with hydatidosis was 31 years of age [26]. Other studies

observed the highest number of infected cases in north-west Islamic Republic of Iran were in the age group 20–40 years [1], and in the northern region of the country in the ages 21–30 years [23]. The highest rate of hydatidosis cases throughout the country were between ages 20–29 years.

Most hydatid cyst organ operations are done on the liver and the rate of liver operations is higher than any other organs [23]. Our study recognized the rate of organ operations on pelvic area, kidney omentum, spleen, pancreas, adrenal glands, gallbladder, uterus, mesenteric area, prostate and bladder were lower than the lung and liver. Recent surgeries reported a rare case of perianal hydatid cyst in Kermanshah province from a rural area [27]. Other investigations identified an infrequent hydatid cyst in the thyroid [28]. Generally, hydatid cysts can be found in the liver and the lungs of infected adults; however, the lungs were more affected than the liver in paediatric groups [29]. Our study showed that only 1.0% of cases had simultaneously infection of the lungs and liver. Nevertheless, other studies showed that the rate of simultaneous liver and lung cysts to be as high as 26% [30] and 12.1% [16].

In this study, most patients had primary hydatid cyst (93.8%), whereas 6.2% with hydatid cyst recurrence were referred to as having secondary hydatid cyst. Another study reported recurrences in only 2% of cases [31]. Some studies indicated the recurrence rate to be variable and commonly ranged from 1.5%–2.5% [32]. In addition, a study in 2010 observed the recurrence of hydatid disease to be 8% during a median follow-up period of 33 months. Other studies indicated a reported incidence

between 1.1%-25%, which may be caused by spilling of the cyst's contents during a previous operation [4]. In Iraq, in which 14.5% of patients had cystic lesions in the liver or other abdominal organs, no recurrences of hydatidosis were observed, except in 1 patient who was referred to a surgery department as a case of pleural effusion drainage despite albendazole therapy [26]. In contrast, some countries reported no recurrences among 65 patients who had undergone surgical hydatid cyst removal in the liver [22]. Other research groups suggested chemotherapy was needed for recurrence of the disease [33]. Some studies reported secondary ovarian hydatid cyst after a 15-year hepatic involvement and recurrence after 30 months [34]. One case study reported a 34-year-old woman who had a 4-time resection of a hydatid cyst from her abdomen. She later developed respiratory symptoms and more than 800 secondary cysts were removed [35].

In our research, laparotomy removal of hydatid cyst, aspiration, reaspiration of fluid cyst with scolicidal agents, skin resection surgery and pre- and postoperative use of albendazole therapy from 12 weeks to 6 months had been prescribed; 20.6% of patients did not take albendazole therapy after surgical removal of hydatid cysts. Other studies recommended that preoperative treatment with albendazole is effective in reducing the rate of recurrence [12]. Other surgeons recommended albendazole for 3 21-day courses with 10day rest periods between courses and only 1 recurrence was reported from month 1-72 [26]. Some suggested that the frozen-seal technique is safe and effective for the surgical treatment of hydatid disease in non-endemic areas

and results showed the recurrence rates and mortality rates were lower [4]. In our study, surgical methods and the use of chemotherapeutic agents such as albendazole were employed, even though the secondary or recurrence rates were higher than in other studies (6.2%). However, prior to the operation in some cases, albendazole was administered and continued for 6 months after surgery. A review article suggested that albendazole use postoperatively may be necessary, especially for bone treatment for a period of 2 years with praziquantel. This regimen can be employed for multiple recurrences [36]. Other researchers suggest that especially in cases of recurrent intra-abdominal extra-hepatic hydatid cyst without concomitant hepatic cyst(s) presence, treatment with albendazole may lead to disappearance of the recurrent cyst and therefore should constitute a first-line therapeutic option prior to any planned reoperation [37].

In the present study, female housekeepers in urban and suburban areas, aged between 30-50 years old, with liver and lung involvement were the groups most commonly infected with epidemiological hydatid cyst in Kermanshah province. The recurrence rate of secondary primary cyst in all patients was 6.2%. As these results suggest, Kermanshah province should be considered as an endemic region in the medical geography zone. Regions near western Islamic Republic of Iran, including neighbouring countries, should be considered as endemic regions for hydatid cyst disease. Better efforts at prevention of hydatid cyst disease are needed in the area including reducing the secondary rate of hydatid cyst.

Competing interests: None declared.

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# Study of host immunity in patients with *Helicobacter pylori*-related idiopathic thrombocytopenia

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#### دراسة مناعة النَّويّ لدى مرضى قلَّة الصفيحات المجهول السبب المتعلق بالـمُلْوِيّة البوابية سامر محمود زهران، نهلة عبد المنعم حامد، محمد محمود الدفراوي، حنان كهال عبد العزيز إبراهيم، منى جمال مرسى

الخلاصة: أجرى الباحثون هذه الدراسة لاختبار دور الخلايا التائية المساعدة Thl في المناعة، وقد شملت الدراسة 24 مريضاً بقلة الصفيحات المجهولة السبب المرتبطة بالإيجابية المصلية للملوية البوابية. وقسم الباحثون المرضى إلى مجموعتين؛ مجموعة تضم 12 مريضاً لديهم قلة الصفيحات المُتوَاسَطة بالمناعة (المجموعة 1)، ومجموعة تضم 12 مريضاً لديهم قلة الصفيحات غير الـمُتوَاسَطة بالمناعة (المجموعة 2). ثم أدرج الباحثون في دراستهم 10 أفراد سلبيين مصلياً للملوية البوابية (المجموعة 3) أو مجموعة الشواهد. واتضح للباحثين أن تعداد الصفيحات البدئي كان أخفض بمقدار يُعتَدُّ به إحصائياً لدى المجموعة 1 ما هو عليه لدى المجموعة 2؛ وقد استؤصلت الملوية البوابية في عشرة من المرضى الإثني عشر في المجموعة 1 وفي جميع مرضى المجموعة 2. وقد حصل تحسن عابر (لمدة تقل عن ثلاثة أشهر) في تعداد الصفيحات لدى مريضين اثنين من المجموعة 1، في حين لوحظ تحسن استمر لأكثر من ستة أشهر لدى جميع المرضى في المجموعة 2. وكان هناك ترابُط مباشر يُعتَدُّ به إحصائياً بين تعداد الصفيحات وبين مستويات كل من عامل النخر الورمي (٣-١٢٦) والانتر فيرون – (٣-١٤٦) في كلتا مجموعتي الدراسة، مع ترابُط لا يُعتدُّ به لدى المجموعة 3. وخلص الباحثون إلى أنه ينبغي اعتبار العدوى بالملوية البوابية ضمن التشخيص التفريقي في جميع حالات قلة الصفيحات، ويجب استئصال الملوية البوابية من جميع المصابين بقلة الصفيحات ممن لديهم الملوية البوابية ضمن التشخيص التفريقي في جميع حالات قلة الصفيحات، ويجب استئصال الملوية البوابية من جميع المصابين بقلة الصفيحات ممن لديهم الملوية البوابية أبيدة.

ABSTRACT To test the role of T helper cell Th1 immunity we recruited 24 patients with idiopathic thrombocytopenia associated with H. pylori seropositivity. They were divided into 2 groups: 12 with immune-mediated thrombocytopenia (Group 1) and 12 with non-immune mediated thrombocytopenia (Group 2). We also recruited 10 individuals seronegative for H. pylori (Group 3) as controls. Initial platelet count was significantly lower in Group 1 than Group 2. H. pylori was eradicated in 10 of 12 patients in Group 1 and in all patients in Group 2. Transient improvement (< 3 months) in the platelet count occurred in only 2 patients in Group 1 while improvement for > 6 months was observed in all patients in Group 2. There was a statistically significant direct correlation between platelet count and levels of TNF- and IFN- $\gamma$  in both study groups, while a non-significant correlation was seen in Group 3. Thus, H. pylori infection should be considered in the differential diagnosis of all cases of thrombocytopenia, and should be eradicated in all H. pylori-positive patients with thrombocytopenia.

# Étude de l'immunité de l'hôte chez des patients atteints d'une thrombocytopénie idiopathique liée à *Helicobacter pylori*

RÉSUMÉ Afin de tester le rôle de l'immunité des lymphocytes T auxiliaires de type Th1, nous avons recruté 24 patients atteints de thrombocytopénie idiopathique associée à une séropositivité pour  $Helicobacter\ pylori$ . Ils ont été répartis en deux groupes : 12 patients souffrant d'une thrombocytopénie à médiation immunitaire (groupe 1) et 12 patients atteints d'une thrombocytopénie à médiation non immunitaire (groupe 2). Nous avons aussi recruté 10 personnes séronégatives pour H. pylori (groupe 3) comme témoins. La numération plaquettaire initiale était nettement plus faible dans le groupe 1 que dans le groupe 2. H. pylori a été éradiqué chez 10 patients sur 12 dans le groupe 1 et chez tous les patients du groupe 2. Une amélioration transitoire (< 3 mois) de la numération plaquettaire a été observée chez seulement deux patients du groupe 1 tandis qu'une amélioration de plus de six mois a été enregistrée chez tous les patients du groupe 2. Une corrélation directe statistiquement significative a été constatée entre la numération plaquettaire et les taux de TNF- $\alpha$  et d'IFN- $\gamma$  dans les deux groupes étudiés, alors qu'une corrélation non significative a été observée dans le groupe 3. Par conséquent, l'infection à H. pylori doit être envisagée dans le diagnostic différentiel pour tous les cas de thrombocytopénie et doit être éradiquée chez tous les patients atteints de thrombocytopénie positifs pour H. pylori.

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#### Introduction

Helicobacter pylori is a Gram-negative bacterium that colonizes the mucous layer of the human stomach [1]. It causes gastritis and is an important risk factor for gastric ulcer, duodenal ulcer, gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma. In addition to its role in gastroduodenal diseases, *H. pylori* infection has been associated with a number of non-digestive system diseases including chronic thyroiditis, rheumatoid arthritis, Sjögren syndrome and immune thrombocytopenic purpura (ITP) [1].

According to the Maastricht III consensus conference, ITP along with unexplained iron deficiency anaemia are extra-intestinal diseases for which H. pylori infection detection and eradication are indicated [2]. The role of *H. pylori* in the pathogenesis of ITP is still controversial. Several mechanisms have been proposed to explain the association. The first is molecular mimicry, i.e. the presence of cross reaction between antibodies against the cytotoxinassociated gene (CagA) of H. pylori, and platelet antigens causing accelerated platelet clearance [3]. Another proposed mechanism is modulation of host immunity following colonization by *H. pylori* to favour the emergence of autoreactive B-1 cells and the enhancement of phagocytic capacity of monocytes together with low levels of the inhibitory Fcy receptor IIB [4].

The aim of this work was to test the role of T helper cell Th1 immunity by correlating tumour necrosis factor alpha and gamma interferon (Th1 cytokines) to platelet count in *H. pylori*-infected idiopathic thrombocytopenic patients. Adding *H. pylori* eradication therapy to standard therapy for thrombocytopenia may result in better response.

#### Methods

The study was carried out on 24 randomly selected patients (17 females and 7 males) seropositive for *H. pylori*, who had chronic ITP and had presented to Alexandria Main University Hospital during the period March-December 2010. The age range of the patients was 14–34 [mean 24.83; standard deviation (SD) 5.26] years. They presented with purpura or bleeding from different sites but without dyspeptic symptoms (nausea, vomiting, epigastric pain). Patients with hepatic, pulmonary, renal, cardiac diseases, overt autoimmune disease, malignancy, human immunodeficiency virus (HIV) infection, and hepatitis C virus infection as well as those who had previously undergone H. pylori eradication therapy were excluded from the study.

Informed, written consent was obtained from all participants or a parent for those who were under the age of consent. The study was approved by the ethics committee of Alexandria University.

According to the aetiology of thrombocytopenia, the 24 participants were divided into 2 main groups. Group 1 consisted of 12 patients with immune thrombocytopenia [9 newly diagnosed, 3 refractory to steroid, i.e. patients with persistent symptomatic and severe thrombocytopenia < 10 000/μL after 2 weeks of prednisone (1 mg/kg/ day)]. Group 2 consisted of 12 newly diagnosed patients with non-immune thrombocytopenia. Splenectomy had not been performed in any patient in Group l at presentation. We also recruited 10 healthy persons from among the relatives of the patients (Group 3, control group). These were matched for age and sex and they were all seronegative for *H. pylori*.

ITP was defined as isolated thrombocytopenia with no clinically apparent associated conditions or other causes of thrombocytopenia according to the American Society of Hematology guidelines [5]. *H. pylori* eradication therapy regimen consisted of amoxicillin (1000 mg twice daily), clarithromycin (500 mg twice daily) and omeprazole (20 mg twice daily) for 1 week. To assess the response to eradication therapy, the *H. pylori* antigen stool test was repeated 4 weeks after the completion of eradication therapy.

The platelet count was determined in each participant in Groups 1 and 2 immediately before eradication therapy was initiated, and counts were monitored for at least 6 months after completion of eradication therapy, being measured every 4 weeks. Those who did not attend on a regular basis were excluded from the study. Response to treatment was defined as complete if the platelet count was above  $150 \times 10^9/L$ , and partial if the platelet count increased by more than  $50 \times 10^9/L$  6 months after the eradication therapy [6].

All participants in this study were subjected to:

- thorough history-taking and clinical examination with special stress on duration of ITP before eradication treatment, previous and concomitant treatment for ITP and history of any eradication regimen administered;
- complete blood picture;
- bone marrow aspiration (for patients only) to exclude secondary causes for thrombocytopenia;
- hepatic and renal function tests;
- serum enzyme-linked immunosorbent assay (ELISA) testing for *H. pylori* IgG [7];
- stool antigen assay (HpSA) [8];
- antiplatelet platelet antibody detection (for patients only) by modified antigen-capture enzyme immuno-assay (MACE):Antibodies against platelet glycoprotein (GP) GPIb/IX, GPIIb/IIIa, and other platelet antigens were detected using monoclonal antibody-specific immobilization of platelet antigens (MAIPA) [9];

 quantitative measurement of serum tumour necrosis factor alpha (TNF-α) and gamma interferon (IFN-γ) using the ELISA kit (RayBio, United States of America) [10,11].

A 5-mL sample of blood was collected for the detection of H. pylori antibodies just before the endoscopy. The samples were kept at room temperature for 1 hour, followed by centrifugation at 1500 rpm for 10 min. The serum was aliquoted into cryovials and stored at -70 °C.

Serum samples were tested for the presence of anti-*H. pylori* antibodies using EIAgen *H. pylori* IgG kit (Adaltis, Italy). This is based on a "sandwich" enzyme immunoassay, where samples and standards were incubated in microtitre plate wells coated with the first monoclonal anti-IgG antibody in the presence of a second anti-IgG monoclonal antibody linked to acetylcholinesterase (assay range: 5–1000 pg). All steps were carried out according to the manufacturer's instructions.

A stool sample was collected within 3 days of the endoscopy and before the initiation of any therapy against *H. pylori*. Samples were stored in a coolbox containing ice packs until they were transferred to the laboratory, where they were immediately transferred to cryovials and stored at –70 °C until tested.

Diluted stool samples were analysed using the HpSA enzyme immunoassay kit according to the manufacturer's instructions (Meridian Diagnostics, Inc., Cincinnati). The kit employs affinity-purified polyclonal anti-H. pylori rabbit antibodies adsorbed to microwell plates. Following addition

of peroxidase-coupled antibody and substrate, the colour reaction was read using quantitative spectrophotometric determination (450 nm). HpSA optical density values above 0.160 were considered positive; values between 0.140 and 0.159 indeterminate, and values below 0.140 negative.

Antibodies against platelet glycoprotein GPIb/IX, GPIIb/IIIa, and other platelet antigens were detected using monoclonal antibody-specific immobilization of platelet antigens (MAIPA), a novel antigen-specific capture assay for the detection of platelet antibodies (Geissen, Berlin, Germany).

Statistical analysis was done using SPSS, version 9.0.0. Results are expressed as mean and standard deviation. Chi-squared was used for analysis of categorical data. Analysis of variance (ANOVA) test was done for comparison of means of quantitative data between the 3 groups. Further analysis of the ANOVA test was done using least significant differences (LSD) to determine the difference between means. Pearson's correlation (r) was used to study the correlation between initial platelet count and different variables. Pvalue < 0.05 was considered statistically significant.

#### Results

Table 1 shows the age and sex of the 3 groups: age ranged from 14 to 34 years (mean 24.83; SD 5.26). There was no statistically significant age or sex difference between the control and patient groups.

There were statistically significant differences between the 3 groups as regards initial platelet count, TNF-α and IFN-γ (Table 2). Initial platelet count was lower in the immune mediated (Group I) than in the non-immune mediated (Group 2) H. pylori-seropositive patients. H. pylori was eradicated in 10 of 12 treated patients in group 1 and in all 12 patients in group 2. Transient improvement (< 3 months) in the platelet count occurred in only 2 patients in Group 1 while improvement of more than 6 months was observed in all patients in Group 2 (Table 2). Platelet recovery was observed as early as 1 week after H. pylori eradication in 4 patients, and 2 weeks after completion of eradication therapy in the rest of the Group 2 patients.

Table 3 shows the correlation between initial platelet count and age, TNF-α and IFN- $\gamma$  levels. There was highly significant direct correlation between platelet count and levels of TNF-α (r = 0.829, P = 0.001) and IFN- $\gamma$  (r = 0.812, P = 0.001) in Group 1, and a statistically significant direct correlation between initial platelet count and levels of TNF-α (r = 0.698, P = 0.012) and IFN- $\gamma$  (r = 0.579, P = 0.049) in Group 2. In Group 3, however, there was no statistically significant correlation between initial platelet count and TNF-α or IFN- $\gamma$  levels.

#### Discussion

No dyspeptic symptoms were present in any patient of both groups. A significant association between *H. pylori* 

Table 1 Demographic data of the thrombo	cytopenia patients and the control	group
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Parameter	Group 1 (n = 12)	Group 2 (n =12)	Group 3 ( <i>n</i> =10)	Statistics
Age (years), [mean (SD)]	25.41 (7.29)	24.25 (2.01)	25.2 (6.3)	F = 0.143; P = 0.867
Males	4	3	4	2 0 560 0 0 753
Females	8	9	6	$\chi^2 = 0.569; P = 0.752$

Group 1 = patients with immune thrombocytopenia; Group 2 = patients with non-immune thrombocytopenia; Group 3 = controls. SD = standard deviation.

Table 2 Clinical and laboratory data of the thrombocytopenia patients and the control group

Parameter	Group 1 (n = 12)	Group 2 (n = 12)	Group 3 ( <i>n</i> = 10)	Statistics
Initial platelet count (× 109/L) [mean (SD)]	16.9 (5.3)	82.7 (13.8)	325.6 (60.7)	F = 245.168; P < 0.001; LSD: (1,2)*, (1,3)*, (2,3)*
Platelet specific antibodies	Present	Absent	Absent	
Helicobacter pylori eradication	10 patients	12 patients	-	
No. of responders	2 patients	12 patients	-	
Time to response (weeks)	4	1 (4 patients); 2 (8 patients)	-	
Duration of response (months)	< 3	> 6	-	
TNF-α (pg/mL) [mean (SD)]	60.3 (18.1)	49.7 (8.5)	31.9 (28.6)	F = 14.873; P < 0.001; LSD: (1,2)*, (1,3)*, (2,3)*
IFN-γ (pg/mL) [mean (SD)]	69.9 (17.5)	53.8 (21.1)	36.9 (4.7)	F = 8.962; P < 0.001; LSD: (1,2)*, (1,3)*, (2,3)*

Group 1 = patients with immune thrombocytopenia; Group 2 = patients with non-immune thrombocytopenia; Group 3 = controls. F = a analysis of variance test, LSD = l least significant difference,

SD = standard deviation; TNF = tumour necrosis factor; IFN = interferon.

infection and the presence of dyspepsia has been reported by some researchers [12] but not by others [13].

Initial platelet count was lower in the immune mediated (Group 1) than in the non-immune mediated (Group 2) patients. Although *H. pylori* was eradicated in 10 of 12 treated patients in group I and in all patients in Group 2, transient improvement (< 3 months) in the platelet count occurred in only 2 patients in Group 1 while improvement over more than 6 months was observed in all patients in Group 2. The pretreatment factor that was more consistently associated with a platelet response to *H*. pylori eradication was a shorter ITP duration [6]. There are conflicting reports about the predictive value of age and baseline platelet count. The variability of *H. pylori* strains may be a contributing factor [14,15].

Platelet recovery was observed as early as 1 week after *H. pylori* eradication in 4 patients, and 2 weeks after completion of eradication therapy in the rest of the Group 2 patients. The observed low number of patients with platelet recovery in Group 1 may be attributed to initial low platelet count. Many study designs consider the first assessment of the platelet count 1 month after eradication therapy [16]. However, platelet

recovery was observed as early as 3 days after eradication in one report [17] and in another there was a rapid platelet increase within 1 week in roughly half of the responders [18]. Responses have also been observed several weeks after eradication [16]. The minimum duration of the platelet increase that defined a response was 1 month in one study [19] and 3 months in 2 other studies [20,21].

The improvement in platelet count following H. pylori eradication has been explained by 1) clarithromycin included in eradication regimens has anti-inflammatory properties which may improve platelet autoreactivity by blocking the production of proinflammatory cytokines, and 2) antimicrobials used for H. pylori treatment may eradicate other commensal bacteria that stimulate cross reactive platelet antibodies [4]. In support of these hypotheses, a 2009 meta-analysis showed an increase in platelet count following treatment in some patients with ITP regardless of the outcome of eradication therapy [4].

The increased platelet count in patients in whom *H. pylori* eradication failed or in those who received proton pump inhibitor monotherapy could be mediated through a reduction in the quantity of *H. pylori* and/or a bacteriostatic effect of the regimen [6].

In our study IFN- $\gamma$  and TNF- $\alpha$  levels were significantly higher in the study groups compared with the control. H. pylori infection and ITP are associated with a T helper 1 (Th1)—type immune response [6] characterized by increased levels of Th1 cytokines, such as IFN- $\gamma$  and TNF- $\alpha$ , which can increase the release of proinflammatory cytokines [22]. Overproduction of TNF- $\alpha$  can lead to autoimmune disease. Hence, H. pylori—induced alterations in cytokine profiles might promote development of immune thrombocytopenia [23].

In Group 1, there was highly significant direct correlation between platelet count and levels of TNF-α and IFN- $\gamma$ ; in Group 2 a statistically significant direct correlation was present between initial platelet counts and levels of TNF-α and IFN-γ. In Group 3, no statistically significant correlation was observed. IFN- $\gamma$  and TNF- $\alpha$  affect B-cell proliferation and differentiation into immunoglobulin secreting cells. In addition, IFN- $\gamma$  and TNF- $\alpha$  also enhance the function of macrophages, upregulating the expression of their IgG receptors. Abnormalities in the production of these cytokines may be involved in the clinical course of autoimmune thrombocytopenic purpura [24]. The absence of platelet-specific antibodies

Table 3 Correlation between initial platelet count and clinical and laboratory parameters in patients (Groups 1 and 2), and controls (Group 3)

Parameter	Age (years)	Platelet count (× 10°/L)	TNF-α (pg/mL)	IFN-γ (pg/mL)
		Group 1	(F3/ ···-/	(F8) ···-/
Age (years)				
r		0.23	0.30	0.19
Р		0.47	0.34	0.548
Platelet count (× 10°/L)				
r	0.23		0.829	0.81
Р	0.47		0.001	0.001*
TNF-a(pg/mL)				
r	0.30	0.829		0.797
Р	0.34	0.001*		0.002*
IFN-γ (pg/mL)				
r	0.19	0.81	0.797	
Р	0.548	0.001*	0.002*	
		Group 2		
Age (years)				
r	-	-0.395	-0.329	0.059
Р	-	0.204	NS	NS
Platelet count (× 10 <sup>9</sup> /L)				
r	-0.395	-	0.698*	0.579*
Р	0.204	-	0.012	0.049
TNF-a(pg/mL)				
r	-0.329	0.698*	-	0.432
Р	0.296	0.012	-	0.161
IFN-γ(pg/mL)				
r	0.059	0.579*	0.432	-
Р	0.856	0.049	0.161	-
		Group 3		
Age (years)				
r		-0.27	-0.15	0.14
Р		0.448	0.678	0.69
Platelet count (× 10°/L)				
r	-0.27		0.507	0.42
P	0.448		0.135	0.227
$TNF-\alpha (pg/mL)$	0.55	0.555		0.45
r	-0.15	0.507		-0.186
P	0.678	0.135		0.606
IFN-γ(pg/mL)	0.14	0.42	0.100	
ľ	0.14	0.42	-0.186	
Р	0.69	0.227	0.606	

\*Correlation is significant at the 0.05 level (2-tailed).

 $TNF = tumour\ necrosis\ factor;\ IFN = interferon;\ r = Pearson\ correlation.$ 

 $NS = not significant (P \ge 0.05).$ 

in Group 2 may be explained by the requirement for a certain level of Th1 cytokines to elicit antibody production or perhaps the antibody titre is below

the limit of detection. Further studies are needed to confirm this possibility because of the low number of patients in our study.

T-cells are generally hyporesponsive during *H. pylori* infection, and the response is polarized toward a T helper 1 (Th1) response. This type of response

may be induced by *H. pylori* neutrophilactivating protein and the cell wall lipopolysaccharide [6].

#### Conclusion

Despite the low number of the studied patients, we can suggest that even in the absence of antibodies against platelets, an immune process is still present; thus *H. pylori* infection should be considered in the differential diagnosis of all cases of thrombocytopenia (immune and non-immune) and should be routinely included in the initial work up of chronic thrombocytopenia. We also suggest that *H* 

.pylori should be eradicated in all *H. pylori*-positive patients with throm-bocytopenia. However, this research need to be repeated on a wider scale to confirm this finding.

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