Seroprevalence of hepatitis E virus in pregnant women in northern Lebanon

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Abstract

Background: Hepatitis E virus is the main cause of acute hepatitis globally. Infection is especially serious in pregnant women in whom the death rate can reach 25%. The prevalence of hepatitis E virus in pregnant women in Lebanon is not known.

Aims: This study aimed to investigate the seroprevalence of hepatitis E virus infection in a sample of pregnant women in northern Lebanon.

Methods: A total of 450 pregnant women from Tripoli, North Lebanon were enrolled in the study. Sera were tested for the presence of anti-hepatitis E virus IgG antibodies using an ELISA technique. Information was collected on the sociodemographic characteristics of the women and their risk factors for hepatitis E virus infection (drinking-water source, blood transfusion and contact with animals).

Results: Only one woman was positive for hepatitis E virus giving a prevalence of 0.22%. She had good living conditions, socioeconomic status and educational level and reported no exposure to any risk factors associated with hepatitis E virus infection. Most of the women (87.3%) had a medium or high income level, 47.1% had a university education and 64.9% drank bottled water. Only a small proportion were exposed to risk factors for hepatitis E virus infection: 14.7% had direct contact with animals and 3.8% had had a blood transfusion.

Conclusion: The prevalence of hepatitis E virus infection in the sample was low (0.22%). However, further epidemiological studies among other population groups are required to determine the national prevalence of hepatitis E virus in Lebanon.

Keywords: hepatitis E virus, prevalence, pregnancy, Lebanon

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Introduction

Five forms of human viral hepatitis are known. Among them, hepatitis E virus is the most common cause of acute viral hepatitis and jaundice worldwide *(1)*. Globally, it is estimated that about 20 million hepatitis E infections occur every year, with more than three million symptomatic cases and about 44 000 hepatitis E-related deaths *(2)*.

Hepatitis E virus belongs to the genus *Hepevirus* within the family Hepeviridae. A single hepatitis E virus serotype and four major genotypes (HEV1, HEV2, HEV3 and HEV4) have been described *(3,4)*. Although these four genotypes are able to infect humans, they show different epidemiological patterns depending on their geographical distribution *(1)*. In developing countries, HEV1 and HEV2, which are associated with faecal–oral transmission and waterborne spread, cause numerous sporadic cases and outbreaks. HEV3 and HEV4 are common in several animal reservoirs; they are transmitted to humans through zoonotic foodborne routes and cause sporadic cases of increasing importance *(1,5–7)*.

Unsafe water supplies, poor hygiene, overcrowded living conditions, young adult age and close contact with animals, especially pigs, are risk factors for hepatitis E infection. Hepatitis E infection is generally an acute, self-limiting disease; however, in some cases, it can cause acute liver failure or chronic liver disease *(8,9)*. In pregnant women, hepatitis E infection can cause serious illness characterized by frequent occurrence of fulminant hepatitis *(10,11)* with a high mortality rate, which is 10-fold higher than the mortality rate in men or non-pregnant women *(12)*.

Hepatitis E infection can be detected using serological assays of anti-hepatitis E virus immunoglobulin M (IgM) and IgG in patient sera, mostly by enzyme-linked immunosorbent assays (ELISA) *(11,13)*. IgM antibodies decrease in the weeks following infection and subsequently are rarely detectable and even absent in most studies of hepatitis E virus seroprevalence. In contrast, detectable levels of anti-hepatitis E virus IgG may persist for years after infection *(11,13)*. These antibodies are therefore widely used to evaluate the prevalence of the virus in various populations including asymptomatic pregnant women *(11)*.

In Lebanon, the prevalence of anti-hepatitis E virus IgG antibodies has been investigated in only one study of blood donors and the results showed 4% positivity *(14)*.

However, the prevalence in pregnant Lebanese women has never been studied. Therefore, the aim of our study was to investigate the prevalence of hepatitis E virus infection in pregnant women in Tripoli, the main city of the North Lebanon governorate.

Methods

Study design and participants

This was a cross-sectional study conducted during a 5-month period (April to August 2015) in Tripoli in northern Lebanon.

The sample size was determined using the single population proportion formula: $N = z^2p(1-p)/w^2$, where z = standard normal distribution value at 95% confidence level which is equal to 1.96, p = the expected prevalence of hepatitis E virus in pregnant women and w = the margin of error, taken as 4%. As the prevalence of hepatitis E virus in pregnant women in Lebanon was not known, we used the highest prevalence (12.7%) reported from Turkey, a neighbouring country (*15*). Based on these parameters, the calculated minimum sample size was 267. Tripoli was divided into four geographical regions. From each region, one health facility of 19 attended by pregnant women was randomly selected. A trained nurse of the antenatal unit of the facility explained the purpose of the study to the potential participant, obtained her consent, filled the questionnaire with the participant and then collected the blood sample. In total, 450 women were enrolled in this study, representing all the pregnant women attending the selected health facilities during the study period. Non-Lebanese pregnant women were excluded from the study.

Data collection

The women were surveyed using a questionnaire which included the known risk factors for hepatitis E virus infection (drinking water source, blood transfusion, sociodemographic and contact with animals), pregnancy stage, sociodemographic characteristics (age, education level and income level). The minimum wage (675 000 Lebanese pounds; US$ 450) was used to classify the income level. Families with a monthly income below the minimum wage were classified as low income. Families with a monthly income ranging from the minimum wage to twice the minimum wage were classified as middle income. Families with a monthly income more than twice the minimum wage were considered high income

Serological tests

Three millilitres (3 mL) of venous blood were collected into a clot activator tube by venepuncture. Sera were separated immediately and kept frozen at –20 °C until tested. The presence of anti-hepatitis E virus IgG antibodies was examined using an ELISA kit (Euroimmun, Lübeck, Germany) following the manufacturer's instructions. According to the manufacturer, tests performed with this assay have a specificity and sensitivity of 100%.

Data analysis

Data were analysed using GraphPad Prism 6 software. Quantitative data are presented as mean and standard deviation (SD); categorical data are presented as frequencies.

Ethical considerations

Ethical approval for the study was obtained from ethics committee of the Azm Center for Research in Biotechnology and Its Applications, Lebanese University. Informed consent was obtained from each participant included in the study. Written consent was obtained from each literate participant. In the case of illiterate participants, the nurse explained the purpose of the study to the woman and a literate witness (another health care worker or a person accompanying the woman). If the illiterate women agreed to participate by giving her verbal consent, the literate witness signed on her behalf.

Results

A total of 450 pregnant women participated in the study. The age range of the participants was 15–43 years, with a mean age of 28.33 (SD 5.82) years. None of the participants had clinical symptoms associated with hepatitis E virus infection at the time of sample collection. Anti-hepatitis E virus IgG antibodies were found in only one participant (0.2%). She had good living conditions, socioeconomic status and educational level and reported no exposure to any of the risk factors associated with hepatitis E virus infection. Most of the women in the study had a medium (46.4%) or high (40.9%) income level, about half (47.1%) had a university education and two thirds (64.9%) drank bottled water (Table 1). Only a small proportion were exposed to the risk factors associated with hepatitis E virus infection: 14.7% had direct contact with animals and 3.8% had had a blood transfusion.

Discussion

To the best of our knowledge, our study is the first to determine the seroprevalence of anti-hepatitis E virus IgG antibodies in pregnant women in Lebanon. Our results revealed a very low prevalence of hepatitis E virus (0.22%). This prevalence was the lowest reported in other Mediterranean countries for the same group (Table 2). These data may reflect limited circulation potential of this virus in Lebanese pregnant women.

The status of hepatitis E virus infection has been reported in several countries of the Eastern Mediterranean Region including Egypt, Islamic Republic of Iran, Iraq, Saudi Arabia, Tunisia and United Arab Emirates (*26*). In these countries, numerous studies have been performed in different populations including blood donors, pregnant women, hepatitis patients and haemodialysis patients. In contrast, the prevalence of hepatitis E virus and its associated disease in Lebanon is largely unknown and epidemiological data are limited to a single study of seroprevalence performed on 100 blood donors in 1998 which showed a low prevalence (4% of positivity) (*14*).

Table 1 Demographic characteristics of the sample of pregnant women in Tripoli, Lebanon and risk factors for hepatitis E virus infection

Variable	No. (*n* = 450)	%
Age group (years)		
≤ 25	158	35.1
26–34	212	47.1
≥ 35	80	17.8
Pregnancy trimester		
First	111	24.7
Second	145	32.2
Third	194	43.1
Educational level		
Illiterate	9	2
Primary school	41	9.1
Middle school	107	23.8
Secondary school	81	18
University	212	47.1
Income level		
Low	57	12.7
Medium	209	46.4
High	184	40.9
Contact with animals		
Yes	66	14.7
No	384	85.3
Blood transfusion		
Yes	17	3.8
No	433	96.2
Drinking water source		
Bottled water	292	64.9
Tap water	111	24.7
Spring and well water	47	10.4

Several studies have obtained similar results to ours showing a low prevalence of hepatitis E virus infection in pregnant women: 0.4% in El Paso, United States of America (*27*), 1% in Rio de Janeiro, Brazil (*28*), 1.6% in Ciudad Juarez, Mexico (*27*) and 1.6% in Caracas, Venezuela (*29*). Importantly, even in endemic countries with suspected outbreaks of hepatitis E virus infection such as the Islamic Republic of Iran, a relatively low prevalence of hepatitis E virus (3.6%) was reported in pregnant women (*30*). In Lebanon, no hepatitis E virus outbreaks have occurred and the country is not considered endemic for the disease. Our data differ from those of other studies that examined pregnant women which showed a high prevalence of hepatitis E virus: 58.6% in Dakahlya Governorate, Egypt (*21*) and 28.8% in Rajasthan, India (*31*). Such discrepancies in hepatitis E virus prevalence in pregnant women in different countries are not surprising because even in the same country, considerable epidemiological differences exist. For example, a study in France in pregnant women showed a higher seroprevalence of hepatitis E virus in the south (29.3%) than in the north of the country (3.6%) (*22*). Changes of hepatitis E virus prevalence in different regions and countries may be explained, in part, by sociodemographic and sanitation differences.

Our study in pregnant women showed an even lower prevalence of hepatitis E virus (0.22%) than in Lebanese blood donors (4%) (*14*). In addition to differences in geographical area and population group examined, this difference may, to some extent, be due to sanitation and hygiene improvements in the country between 1998 and 2015. Progressive improvements of sanitation conditions, provision and wide use of filtered and bottled water, and organization of effective food safety campaigns may effectively reduce the faecal–oral transmission and waterborne spread of hepatitis E virus, which are the main modes of transmission of this virus in developing regions. Such improvements are therefore important to

Table 2 Seroprevalence of anti-hepatitis E virus antibodies in pregnant women in Mediterranean countries

Country	Sample size	% positive	Kit manufacturer	Year (reference)
Turkey	245	12.6 (IgG); 0 (IgM)	Virotech GmbH, Germany	2004 (15)
	386	7 (IgG)	Globe Diagnostics, Italy	2006 (16)
Spain	424	0.94 (IgG)	Abbott Diagnostics, United States of America	2004 (17)
	1517	5.45 (IgG); 0 (IgM)	Biokit, Spain	2010 (18)
	1040	3.6 (IgG); 0.67 (IgM)	DiaPro Diagnostic Bioprobes, Italy	2010 (19)
Egypt	2428	84.3 (NS)	In-house enzyme immunoassay	2006 (20)
	116	58.6 (IgG)	Genelabs Diagnostics, Singapore	2011 (21)
France	315	7.74 (IgG); 0 (IgM)	Wantai, China	2014 (22)
	263[a]	5.6 (IgG and IgM)	Abbott Laboratories, United States of America	1993 (23)
Tunisia	404	12.1 (IgG); 0 (IgM)	Globe Diagnostics SRL, Italy	2011 (24)
Greece	98[b]	2 (NS)	Abbott Laboratories, United States of America	1996 (25)

NS: not specified.

[a] *Pregnant women born outside France.*

[b] *Pregnant Albanian refugees.*

public health measures for decreasing hepatitis E virus infections and related mortality and morbidity.

Good hygiene and sanitation conditions are important factors in maintaining the low prevalence rate of hepatitis E and must continue to improve. However, the Syrian conflict has displaced millions of Syrians from Syria to neighbouring countries, including Lebanon which hosts about 1.5 million Syrian refugees. Because of their unfavourable living conditions, displaced populations and refugees are at higher risk of hepatitis E virus infection and large outbreaks of this virus in such populations have been documented, for example in Darfur, Sudan (*32*). Maintaining the low prevalence hepatitis E virus in Lebanon in these new circumstances requires more vigilance and careful epidemiological monitoring of the refugee population at risk.

It is important to note that the different serological tests available for hepatitis E virus detection show considerable discrepancies in their results (*33–37*). Indeed, significantly different IgG seroprevalence values have been reported in the same populations from the same geographical areas using different serological assays (3.6% and 16.2% in United Kingdom blood donors and 10.9% and 31.3% in French kidney and liver transplant recipients) (*35,37*). We used only one commercially available assay to test sera. It is possible therefore that our results may not reflect the actual prevalence of anti-hepatitis E virus IgG antibodies in our sample of pregnant woman. In addition, we did not check anti-hepatitis E virus IgM antibodies or the serum levels of liver enzymes such as alanine aminotransferase and aspartate aminotransferase which are important markers of an acute recent hepatitis E virus infection (*11,13*). We may therefore have missed possible subclinical asymptomatic cases of ongoing acute hepatitis E virus infection.

Since our study included only pregnant women from four health facilities in Tripoli in the north of Lebanon, our results may not reflect the actual prevalence of hepatitis E virus in the North governorate or at the national level. Moreover, in Lebanon, pregnant women are not all covered by the health system; therefore, we may have missed poorer women who are usually at higher risk of hepatitis E virus infection but who never or rarely seek antenatal care. Future studies that sample a wider range of the population would be more helpful.

Our results suggest that hepatitis E virus does not need to be included in routine prenatal screening programmes. However, further studies among both pregnant women and other populations in different areas of the country are needed to clarify the prevalence and epidemiological trends of hepatitis E virus infection in Lebanon.

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Séroprévalence du virus de l'hépatite E chez les femmes enceintes au nord du Liban

Résumé

Contexte : Le virus de l'hépatite E constitue la principale cause d'hépatite aiguë dans le monde. L'infection est particulièrement grave pour les femmes enceintes, chez qui le taux de mortalité peut atteindre 25 %. La prévalence du virus de l'hépatite E chez les femmes enceintes au Liban n'est pas connue.

Objectifs : La présente étude visait à étudier la séroprévalence de l'infection par le virus de l'hépatite E dans un échantillon de femmes enceintes au nord du Liban.

Méthodes : Au total, 450 femmes enceintes de Tripoli, dans le nord du Liban, ont été incluses dans l'étude. Des prélèvements sériques ont été effectués à la recherche d'anticorps de la classe des IgG dirigés contre le virus de l'hépatite E en recourant à la méthode ELISA. Des informations ont été recueillies sur les caractéristiques sociodémographiques de ces femmes et leurs facteurs de risque d'infection par le virus de l'hépatite E (source d'eau de boisson, transfusion sanguine et contact avec les animaux).

Résultats : Une seule femme a été testée positive au virus de l'hépatite E, pour une prévalence de 0,22 %. Ses conditions de vie, son statut socio-économique et son niveau d'études étaient bons, et elle n'avait indiqué aucune exposition à aucun facteur de risque associé à l'infection par le virus de l'hépatite E. La plupart des femmes (87,3 %) avaient un niveau de revenu moyen à élevé, 47,1 % d'entre elles avaient reçues une formation universitaire et 64,9 % buvaient de l'eau en bouteille. Seule une faible proportion d'entre elles étaient exposées à des facteurs de risque d'infection par le virus de l'hépatite E : 14,7 % d'entre elles avaient un contact direct avec des animaux et 3,8 % avaient reçu une transfusion sanguine.

Conclusion : La prévalence de l'infection par le virus de l'hépatite E dans l'échantillon était faible (0,22 %). Cependant, d'autres études épidémiologiques au sein d'autres groupes de population sont nécessaires pour déterminer la prévalence du virus de l'hépatite E à l'échelle nationale au Liban.

الانتشار المصليّ لفيروس التهاب الكبد E بين الحوامل في شمال لبنان

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الخلاصة

الخلفية: فيروس التهاب الكبد E هو السبب الرئيسي لالتهاب الكبد الحاد على مستوى العالم. وتكون العدوى به خطيرة خصوصاً بالنسبة للحوامل اللاتي قد يصل معدل الوفيات بينهن إلى 25%. وليس معروفاً سبب انتشار التهاب الكبد E بين الحوامل في لبنان.

الأهداف: هدفت هذه الدراسة إلى استقصاء أسباب الانتشار المصلي للعدوى بفيروس التهاب الكبد E في عينة من الحوامل في شمال لبنان.

طرق البحث: بلغ مجموع الحوامل اللاتي شملتهن هذه الدراسة 450 سيدةً من طرابلس، شمال لبنان. وقد فُحصت الأمصال للتحقق من وجود الأجسام المضادة من مجموعة الجلوبيولين المناعي IgG لفيروس التهاب الكبد E باستخدام مقايسة المُمْتز المناعي المرتبط بالإنزيم. وجُمعت معلومات حول الخصائص الاجتماعية السكانية للنساء، وعوامل الخطر المرتبطة بتعرضهن للإصابة بعدوى فيروس التهاب الكبد E (مصدر مياه الشرب، ونقل الدم، ومخالطة الحيوانات).

النتائج: تبين إصابة امرأة واحدة فقط بفيروس التهاب الكبد E، مما يمثل الانتشار بنسبة 0.22% فقط. وتتمتع هذه السيدة بظروف معيشية جيدة، ووضع اجتماعي واقتصادي جيد، ومستوى تعليمي جيد، وأفادت بعدم تعرضها لأي من عوامل الخطر المرتبطة بالعدوى بفيروس التهاب الكبد E. وكان مستوى الدخل لمعظم النساء اللاتي شملتهن الدراسة (87.3%) متوسطاً أو مرتفعاً؛ و47.1% منهن حاصلات على شهادة جامعية؛ و64.9% منهن يشربن الماء المعبّأ في قوارير. وتعرضت نسبة ضئيلة منهن فقط لعوامل خطر الإصابة بعدوى فيروس التهاب الكبد E: منهن 14.7% خالطن الحيوانات بشكلٍ مباشر؛ و3.8% خضعن لعملية نقل دم.

الاستنتاج: كان معدل انتشار العدوى بفيروس التهاب الكبد E منخفضا في العينة (0.22%). ولكن يلزم إجراء مزيدٍ من الدراسات الوبائية على مستوى الفئات السكانية الأخرى لتحديد انتشار فيروس التهاب الكبد E على المستوى الوطني في لبنان.

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