Seroprevalence of hepatitis A virus antibodies among a sample of Egyptian children

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معدل الانتشار المصلي لأضداد فيروس الالتهاب الكبدي A ضمن عينة من الأطفال المصريين

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الخلاصة: قامت الباحثتان بالتعرف على معدل الانتشار المصلي لأضداد فيروس الالتهاب الكبدي A بين 269 طفلاً مصرياً تتراوح أعمارهم بين 2.5 و18 عاماً وينتمون إلى مختلف الطبقات الاجتماعية، للتأكُّد فيما إذا كان ينبغي إعطاء لقاح الالتهاب الكبدي A في وقت مبكر من الحياة أو أن من الممكن ترك الأطفال يكتسبون مناعة طبيعية ضده. ومن بين جميع الأطفال المشمولين بالدراسة كان لدى 61.4٪ منهم إيجابيةٌ لأضداد فيروس الالتهاب الكبدي A، وكان هناك زيادة ملحوظة في معدَّل الانتشار المصلي لتلك الأضداد مع تقدُّم العمر ومع انخفاض الطبقة الاجتماعية؛ ففي الأطفال دون سن السادسة كان 72.7٪ من الأطفال من الطبقات الاجتماعية العليا و19.0٪ من الأطفال من الطبقات الاجتماعية المنخفضة سلبيين لأضداد فيروس الالتهاب الكبدي ، ومن هنا استنتجت الباحثتان أن البرنامج الوطني للتمنيع ضد فيروس الالتهاب الكبدي A لا يحظى بالأولوية، وأوصت الباحثتان بالتلقيح لدى أطفال الطبقة الاجتماعية العليا في المرحلة قبل المدرسية دونما حاجة لاختبار أضداد فيروس الالتهاب الكبدي A، أما تلقيح أطفال الطبقة الاجتماعية المنخفضة والوسطى فلا يجرى إلا بعد اختبار لكشف تلك الأضداد.

ABSTRACT We determined the seroprevalence of hepatitis A virus antibodies (HAV Ab) among 296 Egyptian children aged 2.5–18 years of different social classes to ascertain whether to give HAV vaccine early in life or to leave children to acquire natural immunity. Overall 61.4% were seropositive for HAV Ab. There was a significant increase in the seroprevalence of HAV Ab with higher age and lower social class; in children aged < 6 years, 72.7% of high and 19.0% of low social class were seronegative for HAV Ab. A national vaccination programme for HAV is not a priority. We recommend vaccination against hepatitis A for high social class children at the preschool period without testing for HAV. Vaccination for middle social class children can be done, but only after testing for HAV.

Séroprévalence des anticorps contre le virus de l'hépatite A dans un échantillon d'enfants égyptiens

RÉSUMÉ Nous avons établi la séroprévalence des anticorps contre le virus de l'hépatite A (Ac anti-VHA) parmi 296 enfants égyptiens âgés de 2,5 à 18 ans de classes sociales différentes, afin de déterminer s'il fallait administrer le vaccin contre l'hépatite A pendant les premières années de la vie ou laisser les enfants s'immuniser naturellement. Globalement, 61,4 % étaient séropositifs aux Ac anti-VHA. L'augmentation de la séroprévalence des Ac anti-VHA était significative plus l'âge était élevé et la catégorie sociale basse ; chez les enfants âgés de moins de 6 ans, 72,7 % des enfants appartenant à une catégorie sociale supérieure étaient séronégatifs aux Ac anti-VHA, contre 19,0 % de ceux appartenant à une catégorie sociale inférieure. Le lancement d'un programme national de vaccination contre l'hépatite A n'est pas une priorité. Nous recommandons de vacciner les enfants d'âge préscolaire appartenant aux catégories sociales élevées sans dépistage du VHA. Les enfants appartenant aux catégories sociales moyennes peuvent être vaccinés, mais uniquement après dépistage du VHA.

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Introduction

Infection with hepatitis A virus (HAV) occurs worldwide and is the most common cause of acute viral hepatitis [*1*]. The prevalence of HAV infection closely correlates with the degree of environmental sanitation and the prevailing socioeconomic and hygienic conditions [*2*]. The most common mode of transmission of hepatitis A is via the faecal–oral route [*3*].

The highest prevalence of this infection is seen in developing countries, where low standards of sanitation promote the transmission of the virus [*1*]. In areas of high endemicity, most people become infected in early childhood. In this age group, the infection is usually mild, nonspecific or asymptomatic and induces anti-HAV antibodies that confer to life-long immunity against reinfection [*4*]. In areas of low endemicity (mostly developed countries), the incidence of HAV infection among young children is low, and the proportion of susceptible individuals, especially young adults, is high [*3*]. In older children and adults, infection is usually symptomatic [*5*].

An effective vaccine for hepatitis A virus is now available and provides consistent long-lasting protection [*6*]. It is highly immunogenic, with more than 97% of people developing a protective level of antibodies by 4 weeks after the 1st dose. The 2nd dose, given after 6 months for long-term protection, is expensive and the public health recommendations in most countries are fairly restrictive [*5*].

The low prevalence of hepatitis A in industrialized countries had resulted in an overall decrease in population immunity. This has guided recommendations for routine hepatitis A vaccination of children nation wide in the USA [*7*]. In contrast, the populations of developing countries naturally acquire life-long immunity against reinfection, and vaccination against HAV may have little role to play in these areas [*4*]. A rational vaccination policy in developing countries therefore requires information about the prevalence of immunity in the population.

In the past, Egypt was considered to be an area of high endemicity for HAV infection, with the highest prevalence of infection in early childhood [*8*]. Darwish et al. recorded a prevalence of 100% in 1996 [*9*]. However, there have been marked improvements in the economic, hygienic and sanitary conditions of the country in recent years, especially in urban areas [*10*]. Salama et al. recorded a HAV prevalence of 86.2% in 2004 [*11*]. This may have public health implications as it indicates that a proportion of the adolescent and adult population may be at risk of HAV infection. Hepatitis A is not a part of the standard vaccination programme in Egypt.

The aim of this study was to determine the seroprevalence of HAV antibodies (HAV Ab) among a group of Egyptian children aged 2.5–18 years of different social classes to ascertain if it is better to give hepatitis A vaccine early in life or to leave children to acquire their natural immunity, which is more economic and beneficial. We also aimed to ascertain what would be the most appropriate age for hepatitis A vaccination.

Methods

Sample

The study group was 220 children aged 2.5–18 years who attended paediatric clinics at the Medical Service Unit of the National Research Centre (NRC) in Cairo, Egypt, for minor illnesses from September 2002 to November 2003. A group of children of the same age group belonging to doctors (*n*

= 47) and nurses (n = 29) working in NRC clinics were also included in the study. The total number of children studied was 296. A simple random sampling method was used to select the children attending the paediatric clinics and the children of NRC staff (many doctors working at the unit wanted to participate in the study to know the immune status of their children). The study was approved by the ethical committee of the NRC.

Data collection

After informed consent was obtained from their guardians, all children were subjected to complete history-taking, including age, sex and educational status. In addition, information about the occupation and educational qualification of parents or guardians was obtained. Social class was classified as high, middle or low according to Fahmy and Sherbini [*12*]. Children were given a thorough medical examination to exclude the presence of any current liver disease. Any child with suspected liver disease or previous infection by HAV or vaccination by HAV vaccine was excluded from the study. Previous HAV infection was determined from a history of clinical illness (jaundice, changing colour of urine, isolation in fever hospital, vomiting, previous abnormal liver function tests). Previous vaccination was also determined from history.

About 5–10 mL of blood were obtained by venesection from each child. Serum samples were separated by centrifugation, coded and stored at –20 ºC until testing. Anti-HAV antibodies were detected in serum in a competitive binding assay based on ELISA techniques (DiaSorin, Italy). Tests for total anti-HAV antibodies do not discriminate between different antibody classes. Although the presence of total anti-HAV is a signal of exposure to the virus, it does not distinguish between present and past infection and therefore is mainly useful for epidemiological surveys [*13*].

Statistical analysis

SPSS, version 7.0 was used for statistical analysis. Comparisons between percentages were done using the chi-squared test. A P-value < 0.05 was considered statistically significant.

Results

The study included 296 children, of whom 157 (53.0%) were males. The mean age was 7.83 years (standard deviation 3.66), range 2.5–18 years. All children were classified into 3 age groups: 2.5–< 6 years (33.4%), 6 –< 9 years (31.8%) and 10–18 years (34.8%) (Table 1). The social classification was 43.9% high, 34.4 % middle and 21.8% low social class.

The laboratory analysis showed that 61.4% of the children were seropositive for HAV antibodies (HAV Ab) (missing data for 1 case). Table 2 shows the seroprevalence of HAV Ab in relation to sex, age group and social class. No statistically significant difference was found between seropositivity in males and females (P = 0.750). There was a statistically significant increase in the seroprevalence of HAV Ab with increasing age (P = 0.005). The seropositivity of HAV Ab significantly increased with decreasing social class level: 87.5% in the low social class compared with 43.0% in the high social class children (P < 0.001).

The difference in the seropositivity of HAV Ab with regards to the 3 age groups within each social class are summarized in Table 3. In the high social class group, 72.7% of age 2.5–< 6 years, 70.5% of age 6–< 9 years and 35.3% of age 9–18 years were seronegative for HAV Ab (i.e. non-immune). The difference was statistically

Table 1 **Descriptive data for all children tested for hepatitis A virus antibodies (HAV Ab) (*n* = 296)**

Variable	No.	%
Sex		
Male	157	53.0
Female	139	47.0
Age (years)		
2.5–< 6	99	33.4
6–< 9	94	31.8
9–18	103	34.8
Social class		
High	129	43.9
Middle	101	34.4
Low	64	21.8
Missing data	2	–
HAV Ab		
–ve	114	38.6
+ve	181	61.4
Missing data	1	–

significant ($P < 0.001$). This was not the case in the low social class group, where 19.0% of age 2.5–< 6 years, 9.5% of age 6–< 9 years and 9.1% of age 9–18 years were nonimmune. In the middle social class group, 40.9% of age 2.5–< 6, 27.6% of age 6–< 9 years and 21.4% of age 9–18 years were nonimmune.

Discussion

The overall seropositivity of HAV Ab among all our cases was 61.4%. Another Egyptian study in 2004 recorded a higher prevalence of HAV Ab (86.2%) in children aged 3–18 years [*11*]. Other, older, Egyptian studies also recorded a higher prevalence than ours [*9,14*]. The difference between the previous results and ours may be due to variability in sampling from different areas with different sanitation facilities, as children classified as high social class represented 43.9% of our sample. Other endemic countries have reported variable results. A study in Saudi Arabia recorded 52.4% prevalence in children aged 1–10 years [*15*]. Higher prevalence was recorded in Turkish children, with 95% positivity in the age group 1–15 years [*16*]. Aggarwal et al. found that 84% of Indian children aged 6 months to 18 years

Table 2 **Seroprevalence of hepatitis A virus antibodies (HAV Ab) by sex, age and social class**

Variable	HAV Ab					
	–ve		+ve		Total	
	No.	%	No.	%	No.	*P*-value
Sex						0.750
Male	62	39.5	95	60.5	157	
Female	52	37.7	86	62.3	138	
Age (years)						0.005
2.5–< 6	46	46.9	52	53.1	98	
6–< 9	41	43.6	53	56.4	94	
9–18	27	26.2	76	73.8	103	
Social class						< 0.001
High	73	57.0	55	43.0	128	
Middle	32	31.7	69	68.3	101	
Low	8	12.5	56	87.5	64	

Table 3 **Seropositivity of hepatitis A virus antibodies (HAV Ab) by age group and social class**

Social class	2.5–< 6 years				6–< 9 years				9–18 years				Total
	HAV Ab –ve		HAV Ab +ve		HAV Ab –ve		HAV Ab +ve		HAV Ab –ve		HAV Ab +ve		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
High*	24	72.7	9	27.3	31	70.5	13	29.5	18	35.3	33	64.7	128
Middle	18	40.9	26	59.1	8	27.6	21	72.4	6	21.4	22	78.6	101
Low	4	19.0	17	81.0	2	9.5	19	90.5	2	9.1	20	90.9	64

*P ***< 0.001.***

were positive for HAV antibodies [*4*]. Studies in Malaysia and Senegal recorded 40.9% and 93.1% seroprevalence respectively [*17*]. Lower prevalence was recorded in Poland, where anti-HAV antibodies in children and adolescents were 9.3% [*18*]. A Canadian study reported a seroprevalence of 2% of unvaccinated children aged 8–13 years [*6*]. The prevalence of HAV antibodies in the population < age 20 years was found to be 0% in Japan, and in Sweden it was higher among immigrants [*16*]. The low prevalence of HAV reported in Toronto, Canada, has raised concerns about the potential for a large-scale outbreak of HAV infection in these areas [*19*].

Hepatitis A virus infection in some regions has been changing, mainly in Western Europe but also in India and Korea [*20,21*]. This may also be the case in our country in areas with improved sanitation and hygiene. These changes suggest that immunity against HAV has generally decreasing in developing counties and large outbreaks could be expected, particularly in adults. As a consequence, there is a possibility in the future for older children and young adults to be at high risk for more severe course of the clinical disease [*22*]. Because of that routine vaccination may be recommended in such areas.

Our study showed no statistically significant difference between males and females as regard seropositivity. This finding agrees with Al Rashed [*15*], Aggarwal et al. [*4*] and Turk Aribas et al. [*16*]. In contrast Duval et al. in a Canadian study reported that HAV Ab seroprevalence was significantly associated with female sex [*6*].

In our work, there was statistically significant increase of HAV Ab with increasing age from 53.1% in age group 2.5–< 6 to 73.8% by age 9–18 years. This is presumably due to increased likelihood of exposure to HAV with advancing age. This result agrees with authors in different countries, in Saudi Arabia [*15*], Turkey [*16*], India [*4*], Brazil [*23*] and Cyprus [*24*].

The prevalence of HAV infection closely correlates with environmental sanitation and the prevailing socioeconomic and hygienic condition [*25*]. In developing countries, inadequate sanitation results in continuous transmission of HAV especially to children and young adults. Our study showed that the seropositivity of HAV Ab increased significantly with decreasing social class from 43.0% among children in the high social class to 87.5% in the low social class. This agrees with Al-Rashed [*15*] who reported a prevalence of anti-HAV of 35%, 48.5% and 90% among high, middle and low classes respectively. Also Das et al. in India reported a prevalence of 30.8% and 51.2% in persons with higher and lower socioeconomic status respectively [*26*]. This was also shown by Dhawan et al. [*27*] and Akbul et al. [*17*]. The level of education of parents (included in the social class classification) was very important in our study.

This agreed with Al-Rashed [*15*], Junquera et al. [*28*] and Salama et al. [*11*]. The overall high prevalence of HAV Ab in high social classes in Egypt may not be because they are exposed to poor sanitation but because this group included 33 children aged 9–18 years with prevalence of HAV of 64.7% who have more exposure to HAV at this stage through eating outside the home.

It is possible that the prevalence of anti-HAV Ab varies in different regions of the country, which may be related to differences in HAV epidemiology in different population groups [*4*]. This may explain the difference between our result (61.4%) and other Egyptian studies (ranging from 86.2%–89.4% up to 100%) [*9,11,14*]. This was also the case in Brazil, which is an endemic area for HAV where anti-HAV prevalence was 71.4% and 31.5% in children under the age of 5 years in 2 urban areas with different environmental hygiene and sanitary conditions [*29*]. The same was reported in India [*4,24*].

Three epidemiologic patterns of HAV infection are found around the world [1]. The 1st is in the developing world where HAV is highly endemic. Most children therefore become infected early in life and by the age of 10 years most of the population is immune [30]. Vaccination has no role in these areas. The 3rd is where HAV has almost been eradicated because of high standards of hygiene and sanitation, as in developed countries. HAV infection is thus uncommon in the young, and is generally only acquired during travel to endemic areas [30]. Here the chance of an epidemic is high and vaccination is recommended. The 2nd pattern is in countries where standards of hygiene have been steadily improving so that prevalence has declined to below 10%. In this case there is an increased proportion of infection occurring later, in adolescence or early adult life [30]. This may be the case in certain areas within developing countries, where the high social classes have improved sanitation and standards of living. In certain areas within developing countries where the high social classes have improved sanitation and standards of living the prevalence may have declined considerably.

In our study 72.7% of children aged 2.5–< 6 years and 70.5% aged 6–< 9 years within the high social class were seronegative for HAV Ab, i.e. by the age of 9 years most of this class were not immune and will be at risk of infection in case of contact with HAV. By the age of 18 years, still 35.3% were not immune. Improvements in general standards of sanitation have a paradoxical effect of greatly increasing the number of susceptible adults and creating the potential for large-scale epidemics [*30*]. In this situation, prophylaxis against hepatitis A has become increasingly important for this high-risk group. In contrast only 19.0% of age group 2.5–< 6 years and 9.5% aged 6–< 9 years within the low social class were seronegative for HAV, i.e. by the age of 9 years most of these children were immune to HAV (90.5% seropositive). Vaccination of this group is not recommended. As regard the middle social class, 40.9% of age group 2.5–< 6 years and 27.6% of age 6–< 9 years were seronegative, so by age of 9 years 72.4% of this social class were immune to HAV. So vaccination for this group may not be mandatory now.

Conclusions

The overall seroprevalence of anti-HAV Ab in our sample was 61.4%. Since more than half of population are immune to hepatitis A due to subclinical infection, a national vaccination programme may not be a priority now. Anti-HAV Ab prevalence was statistically significantly higher with higher age

and lower social class. Higher social class is the group at risk for infection occurring later in adolescence or early adult life with more severe symptoms in the case of contact with HAV. While our sample cannot claim to be representative of the Egyptian population it may be representative of the Cairo area as the children were living in different areas of urban Cairo.

Recommendations

Vaccination against HAV in Egypt should be a priority for children of high social class at the preschool period without pre-testing for HAV Ab. Children of low social class still acquire their immunity early in life, so there is currently no requirement to give the vaccine. We can also recommend vaccination for middle social class children at the preschool period and for high social class children aged 9–18 years but after testing for HAV Ab.

Well-planned population based epidemiologic studies in different areas of the country will allow formulation of cost-effective strategies for the use of hepatitis A vaccine.

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