Prevalence of hepatitis A IgG in individuals with chronic hepatitis B infection in Babol

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معدل انتشار الغلوبولين المناعي IgG للالتهاب الكبدي "أ" لدى مرضى الالتهاب الكبدي "بي" المزمن في بابول

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الخلاصة: هدفت هذه الدراسة إلى التعرُّف على معدل الانتشار السابق لفيروس الالتهاب الكبدي "أ" لدى المصابين بعدوى التهاب الكبدي "بي" المزمن. وقد قيَّم الباحثون معدل انتشار الغلوبولين المناعي IgG للالتهاب الكبدي "أ" لدى 392 مريضاً، وأجريَت الدراسة في بابول في شمال جمهورية إيران الإسلامية في الفترة بين أيلول/سبتمبر 2004 وآذار/مارس 2005. واتَّضح أن معدل الانتشار في الشريحة العمرية 10– 19 سنة 59.4٪، وهو أقل، بدرجة يُعْتَدُّ بها إحصائياً، من معدلات الانتشار في الشريحة العمرية 20 – 29 سنة (89.8٪)، وفي الأعمار التي تزيد على 29 عاماً (97.5٪). ولم يكن هناك فرق يُعْتَدُّ به إحصائياً في معدل الانتشار بحسب الجنس أو مكان الإقامة. ووفقاً لهذه النتائج فإن نسبة كبيرة من المراهقين الإيرانيِّين وصغار البالغين المصابين بالالتهاب الكبدي "بي" المزمن معرَّضون لخطر العدوى بفيروس الالتهاب الكبدي "أ".

ABSTRACT To determine the prevalence of previous hepatitis A virus (HAV) infection in people chronically infected with hepatitis B virus (HBV), we assessed the prevalence of anti-HAV IgG in 392 patients. The study was carried out in Babol, northern Islamic Republic of Iran from September 2004 to March 2005. Prevalence in those aged 10–19 years was 59.4% and was significantly lower than that in those aged 20–29 years (89.8%) and those over 29 years (97.5%). There was no significant difference in prevalence according to sex or place of residence. A significant proportion of Iranian adolescents and young adults with chronic HBV infection are at risk of contracting HAV infection.

Prévalence des IgG anti-hépatite A chez les sujets atteints d'hépatite B chronique à Babol

RÉSUMÉ Afin de déterminer la prévalence d'une infection antérieure par le virus de l'hépatite A (VHA) chez des sujets atteints d'une hépatite B chronique, nous avons évalué la prévalence des IgG anti-VHA chez 392 patients. Cette étude a été menée entre septembre 2004 et mars 2005 à Babol, dans la partie septentrionale de la République islamique d'Iran. Nous avons constaté une prévalence de 59,4 % dans la tranche d'âge 10-19 ans, significativement inférieure à celle enregistrée chez les 20-29 ans (89,8 %) et les plus de 29 ans (97,5 %). Cette prévalence n'a laissé apparaître aucune différence significative en fonction du sexe ou du lieu de résidence. Un pourcentage significatif d'adolescents iraniens et de jeunes adultes atteints d'hépatite B chronique sont exposés au risque de contracter une infection due au VHA.

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Introduction

Hepatitis A has a worldwide distribution and is typically an infection of childhood that is more common under conditions of crowding and poor hygiene [*1*]. Virtually all adults living in certain areas of the Mediterranean basin, Africa and many parts of Asia or other parts of the developing world show evidence of past infection [*1,2*]. The severity of clinical symptoms following hepatitis A virus (HAV) infection is age-dependent: hepatitis A in children is mostly an asymptomatic disease, while adolescents and adults usually show symptoms of clinical hepatitis. There is conflicting evidence from a growing number of studies indicating that hepatitis A infection may have a more severe course and a higher fatality rate when superimposed on patients with underlying liver disease, including hepatitis B virus (HBV) infection, than patients having acute hepatitis A alone [*3–6*]. During a hepatitis A epidemic in Shanghai in 1988, the mortality rate from acute hepatitis A in carriers of hepatitis B surface antigen (HBsAg) was 5.6 times greater than that in non-carriers [*7*].

Although the age of exposure to hepatitis A has been increasing in the Islamic Republic of Iran, children and young adults remain the primary target. The seroprevalence of hepatitis A in children younger than 15 years has been reported as 22.3% [*8*].

Hepatitis A infection may have a more severe course and a higher fatality rate when superimposed on patients with chronic HBV infection. The purpose of this study was, therefore, to assess the seroprevalence of previous HAV infection (anti-HAV IgG) in HBV-infected individuals in our region.

Methods

This study was carried out at the Department of Infectious Diseases at Yahyanejad Teaching Hospital, Babol Medical University. This department serves > 1.5 million people living the cities of Babol and Amol and the surrounding villages. During the period September 2004–March 2005 we recruited into the study HBsAg positive individuals ≥ 10 years of age, who were attending the department. The hepatitis B section of the department monitors more than 3000 cases of chronic HBV-infected individuals. Follow-up includes testing for HBsAg, HBe antigen (HBeAg), aspartame aminotransferase, alanine aminotransferase and α-fetoprotein, which are performed at 6-month intervals.

Sample size was estimated as 384, based on 80% mean prevalence of anti-HAV IgG in the general population reported in many developing countries [*9–12*] and allowing for 4% maximum error. We increased this to 392 to allow for possible cases of anti-HAV IgM positive individuals and maintain the sample size. HBsAg positive individuals are followed up at 6-month intervals to check their chronic HBV infection status. We selected all consecutive cases ≥ 10 years old who were referred for monitoring of their condition until the sample size was reached.

The university ethics committee approved the study and all the patients gave their informed consent. There were no refusals to participate.

A 3 mL blood sample was taken from each participant. Sera were obtained by centrifuging all blood samples (Sigma Laborzentrifugen, Osterode, Germany) with relative centrifugal force 1122 g. The sera were stored at –20 °C in a refrigerator.

When all serum samples were collected, they were tested using enzyme-linked immunosorbent assay (ELISA) for anti-HAV IgG (DiaSorin, Vercelli, Italy). Estimation of anti-HAV IgM and total antibodies to hepatitis A were done in all cases. Sera

testing positive for total anti-HAV and IgM were excluded from the study. Samples testing negative for anti-HAV IgM and positive for total anti-HAV were considered anti-HAV IgG-positive. Cut-off levels for the 5 ELISA kits used for testing the 392 samples (~90 samples tested for each kit) for total anti-HAV were calculated as 0.438, 0.564, 0.697, 0.686 and 0.700, respectively.

Data were analysed with *SPSS*, version 13. Chi-squared and Fisher exact tests were used to compare data.

Results

The sample comprised 392 patients. Mean age was 29.0 (standard deviation 11.6) years (range 10–70 years). There were 158 (40.3%) patients aged > 29 years (Table 1). About one third of the participants were from urban areas (Table 1).

All samples were negative for anti-HAV IgM; 332 (84.7%) were HBsAg and anti-HBe positive and 60 (15.3%) were HBeAg positive.

Overall prevalence of anti-HAV IgG was 82.1%. Prevalence was greatest in those aged > 29 years, 97.5%. Seroprevalence in those aged 10–19 years was significantly lower than in the other 2 age groups ($P < 0.0001$) (Table 1).

Seropositivity was similar in males and females and for urban and rural residence.

Table 1 **Seroprevalence of anti-HAV IgG in patients with hepatitis B infection in Babol**

Characteristic	No. of cases		%
	Total	IgG+[a]	
Age group (years)			
10–19	106	63	59.4
20–29	128	115	89.8
> 29	158	154	97.5
Sex			
Male	231	192	83.1
Female	161	130	80.7
Residence			
Urban	134	110	82.1
Rural	258	212	82.2

[a]*Anti-HAV IgG positive.*
HAV = hepatitis A virus.

Discussion

In this study, the pattern of infection with regard to age was comparable with previous reports of past HAV infection in other developing countries [*9,10,13,14*]. The low prevalence of HAV infection in patients younger than 20 years in our region shows that changes in the epidemiology of infection have occurred in recent years. According to a study which was performed in 1997 in our region, seroprevalence was 85% in children under 15 years [*15*]. In a study conducted in Zabol province in the same year on individuals aged 10–19 years, prevalence of anti-HAV was 95% [*16*]. In another 1997 study, seroprevalence of anti-HAV in children under 14 years was 81% [*17*].

In developed countries in recent years, there has been a shift in the prevalence pattern of hepatitis A virus (HAV) infection from a younger to an older age group. This has been attributed to improvements in socioeconomic conditions and hygiene [*18–24*].

Hong Kong, Malaysia, Singapore, Taiwan and Thailand have also experienced a decline in childhood and adolescent HAV seroprevalence typical of countries which have undergone socioeconomic development. In the Philippines and Vietnam, age-related seroprevalence patterns are typical of high to moderate endemicity [*25*].

Data on the endemicity of HAV infection in Africa and the Middle East are scant, but most of the African countries appear to have high endemicity, with the exception

of subpopulations in certain areas. In Saudi Arabia, shifting HAV epidemiology has been documented in recent years. Similar findings have been reported from other countries in the Region [*26*]. In Turkey, the seroprevalence was 37.3% in 11–14-year olds and 43.2% in 15–19-year olds and seropositivity increased with age [*27–29*]. Data from 6 countries in South America showed that the epidemiology is shifting from high to intermediate endemicity, with the population susceptible to HAV infection shifting from children to adolescents and adults [*10*]. Some developing countries have high endemicity for HAV: seroprevalence has been reported at > 95% in people younger than 20 years [*12,30*].

Hepatitis A, an enterically transmitted disease, shows distinct association with socioeconomic status, populations with improved socioeconomic status experiencing lower exposure to the virus. With the varied epidemiological patterns and economical constraints in different countries, however, it does not seem to be possible to evolve a universal policy for immunization.

It has been proposed that, irrespective of endemicity of hepatitis A, high-risk groups such as HBV infected individuals should be immunized with hepatitis A vaccine [*5,6,31*]. Approximately, 5% of the world's population has chronic HBV infection, and most of these live in developing countries [*32*]. Vaccination of these patients against HAV is necessary and is related to HAV seroprevalence in each country. In regions with intermediate HAV prevalence, testing for previous HAV infection is not necessary and there is no cost-benefit in HBV-infected individuals aged ≥ 20 years. Testing should be limited to patients < 20 years, and those testing negative should be given HAV vaccine.

Our findings indicate that a significant proportion of the Iranian adolescent and adult population with HBV infection may be at risk of HAV infection. Thus, HAV prevaccination screening in our region must be limited to people younger than 20 years.

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