

Vaccination against hepatitis A virus may not be required for schoolchildren in northern India: results of a seroepidemiological survey

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Objectives To evaluate the current seroprevalence of antibodies against hepatitis A virus (HAV) in a sample of schoolchildren above 10 years of age and to determine the prevalence of HAV-induced hepatitis in adults at a tertiary care hospital in northern India between January 1992 and December 2000.

Methods Sera from 276 male and 224 female schoolchildren aged 10–17 years were tested for anti-HAV antibodies by enzyme-linked immunosorbent assay. Consecutive patients with a diagnosis of acute viral hepatitis who attended a liver clinic were tested for the serological markers of HAV, hepatitis B Virus, hepatitis C virus, hepatitis D virus, and hepatitis E virus.

Findings Of the male and female children, 96.3% and 98.2%, respectively had anti-HAV antibodies in their sera. The prevalence of these antibodies in the age groups 10–12, 13–14, and 15–17 years were 98.6%, 94.8%, and 98.3% respectively. The frequency of HAV-induced acute viral hepatitis (69/870, 8%) in adults did not show an increasing trend.

Conclusion Mass HAV vaccination may be unnecessary in northern India because the seroprevalence of protective antibodies against HAV in schoolchildren aged over 10 years remains above 95% and there has been no apparent increase in HAV-induced acute viral hepatitis in adults.

Keywords Hepatovirus/immunology; Hepatitis antibodies/immunology; Hepatitis B surface antigens; Hepatitis, Viral, Human/virology; Child; Adult; Seroepidemiologic studies; India (*source: MeSH, NLM*).

Mots clés Virus hépatite A/immunologie; Anticorps antivirus hépatite/immunologie; Antigène HBS; Hépatite virale humaine/virologie; Enfant; Adulte; Etude séro-épidémiologique; Inde (*source: MeSH, INSERM*).

Palabras clave Hepatovirus/inmunología; Anticuerpos antihepatitis/inmunología; Antígenos de superficie de la hepatitis B; Hepatitis viral humana/virología; Niño; Adulto; Estudios seroepidemiológicos; India (*fuentes: DeCS, BIREME*).

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Introduction

The hepatitis A virus (HAV) is an enterically transmitted hepatotropic virus and is the major cause of acute viral hepatitis (AVH) in children (1). In areas of high endemicity most children are exposed to the virus and the consequent acquisition of antibodies against the virus confers lifelong immunity (2).

During the last five years, several reports from countries in southern Asia, Latin America, and Europe have documented a decreasing seroprevalence of protective antibodies against HAV (3–8). This change has been brought about by improved hygiene and sanitation in these countries, where the decreased exposure of children to water and food contaminated with HAV has resulted in a higher incidence of HAV infection among adults. HAV infection in non-exposed adults causes

more severe and prolonged disease (9–12). Safe and highly immunogenic vaccines (13, 14) are now available and mass HAV vaccination of children is being recommended in regions of low endemicity (15).

In India the seroprevalence of HAV antibodies exceeds 90% in adults (16). However, there have been recent reports of a decreasing prevalence of HAV in this country, suggesting that the seroprevalence of HAV antibodies is becoming similar to that in the industrialized world (17, 18). Consequently, HAV vaccination has been recommended for schoolchildren and adults (19). The sample size of children in studies conducted in India has been small. The study from Mumbai (18) sampled children from a population who came to hospital for the treatment of non-gastrointestinal diseases. A study from Delhi (17) included a sample of the adult population only. Clearly, seroprevalence data relating to the healthy paediatric popula-

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tion are necessary in order to assess the need for routine or mass vaccination. The present study was therefore designed to evaluate the seroprevalence of HAV antibodies in an adequate sample of schoolchildren aged 10–17 years in two government schools in Delhi. We also evaluated the prevalence of HAV-induced hepatitis with onset in adulthood between January 1992 and December 2000 in a tertiary care referral centre for liver disease, with a view to determining whether any change had occurred in its incidence.

Methods

The two schools in Delhi were chosen because the subjects were the children or wards of central government employees from various regions of the country and belonged to a wide range of socioeconomic strata. The age range of the 276 boys and 224 girls was 10–17 years.

Departmental and institutional ethical clearance for the study was obtained. Permission was granted by the school authorities and consent for medical examination and blood sampling was obtained from the parents of all the children involved.

A history of any serious medical illness, including jaundice, was obtained and a thorough physical examination was performed. A sample of 5–7 ml of blood was drawn from every child and standard laboratory methods were employed to test for haemoglobin, total leukocytes, liver function, hepatitis B surface antigen (HBsAg), and total antibodies to HAV. The serological markers (HBsAg and anti-HAV antibodies) were investigated by enzyme-linked immunosorbent assay (ELISA) with commercially available kits (Organon Teknika, The Netherlands).

Assuming 90% seropositivity of anti-HAV antibody among children aged over 10 years, we calculated that a sample size of 144 children would be adequate with an α error of 5% (95% confidence) and a precision of 5% for the estimation of prevalence.

In order to evaluate the prevalence of HAV-induced acute viral hepatitis (AVH) among the adult population we analysed consecutive patients diagnosed as having AVH who attended the liver clinic between January 1992 and December 2000. The diagnosis of AVH was based on the clinical profile, biochemical tests, and serological tests for hepatotropic viral infections. Each patient diagnosed as having AVH was tested for HBsAg, IgM antibody to hepatitis B core antigen (IgM anti HBe), antibody to hepatitis C virus (anti HCV), IgM antibody to hepatitis E virus (IgM anti HEV), and antibody to hepatitis D virus (anti HDV) by ELISA. Those patients who were positive for IgM anti-HAV were diagnosed as cases of HAV-induced AVH.

Results

Anti-HAV antibodies were present in 486 of the 500 children (97.2%) (Table 1). Of the 500 children, 178 (35.6%) were aged 15–17 years, 174 (34.8%) were aged 13–14 years, and 148 (29.6%) were 10–12 years of age; seropositivity for anti-HAV antibodies was detected in 175 (98.31%), 165 (95%), and 146 (98.6%) of the children in the respective age groups ($P = 0.33$) (Table 1). In adults the incidence of AVH attributable to HAV did not increase (Table 2). Between January 1992 and December 2000, 870 diagnosed cases of AVH were registered in the liver clinic and 69 (8%) of them were attributable to HAV.

Discussion

The prevalence of protective antibodies against HAV among schoolchildren aged 10–17 years was 97.2%, and was similar in the age groups 10–12, 13–14, and 15–17 years and in boys and girls (Table 1). This indicated that, by the time they were 10 years of age, most of the children had acquired anti-HAV antibodies, in accordance with the expected pattern of HAV seroprevalence in a region of high endemicity (20). Similar results have been reported from Lucknow ($n = 73$), where the seroprevalence of anti-HAV antibodies was 91% in children aged 6–10 years and 96% in those aged 11–18 years (21). In Delhi the seroprevalence of anti-HAV antibodies was reported to be 80% by the age of 10 years ($n = 420$) (22). No change in the seroprevalence of anti-HAV antibodies was detected in Pune between 1982 and 1992 (23). Patterns of endemicity similar to that in the present study have been found in other developing countries, where, despite improvements in gross national product, the seroprevalence of anti-HAV antibodies remains high (24).

However, two recent Indian studies have indicated lower seroprevalences of anti-HAV antibodies in schoolchildren (17,

Table 1. Number and frequency of schoolchildren seropositive for anti-HAV^a antibodies by age and sex

Age in years /sex	No. of children seropositive for anti-HAV antibodies
10–12 ($n = 148$)	146 (98.6) ^b
Male ($n = 76$)	74 (97.3)
Female ($n = 72$)	72 (100)
13–14 ($n = 174$)	165 (94.8)
Male ($n = 94$)	89 (94.6)
Female ($n = 80$)	76 (95)
15–17 ($n = 178$)	175 (98.3)
Male ($n = 106$)	103 (97.1)
Female ($n = 72$)	72 (100)
Total ($n = 500$)	486 (97.2)
Male ($n = 276$)	266 (96.3)
Female ($n = 224$)	220 (98.2)

^a HAV = hepatitis A virus.

^b Figures in parentheses are percentages.

Table 2. Annual number and frequency of acute viral hepatitis (AVH) and HAV^a-induced AVH in adults, 1992–2000

Year	AVH	HAV-induced AVH
1992	24	3 (12.5) ^b
1993	91	10 (10.9)
1994	95	5 (5.26)
1995	94	11 (11.7)
1996	158	15 (9.4)
1997	116	11 (9.4)
1998	56	8 (14.2)
1999	120	5 (4.6)
2000	116	1 (8.0)
Total	870	69 (8.0)

^a HAV = hepatitis A virus.

^b Figures in parentheses are percentages.

18). In Delhi an anti-HAV antibody prevalence of 36.7% was reported among 500 adults (17). In a study involving 284 children and 386 adults in Mumbai it was found that 50% of children belonging to families of high socioeconomic status did not possess immunity against HAV infection (18). Both of these studies were hospital based and included subjects attending hospital for treatment of non-gastrointestinal diseases. Thus they were not representative of healthy schoolchildren, in whom the assessment of seroprevalence of anti-HAV antibodies would influence the strategy of mass HAV vaccination. The present study was based on a large sample and included children belonging to a wide range of socioeconomic strata. The results of the three Indian studies cited above (21–23) were similar to those of the present one. It appears that at least 90% of Indian children acquire protective antibodies against HAV by the age of 10 years.

Any reduction in the seroprevalence of anti-HAV antibodies among Indian schoolchildren during the last decade would be expected to have produced a rise in the annual incidence of HAV-induced AVH in the adult population, at least at the referral centres for liver disease in northern India. However, the etiological analysis of the AVH patients registered at our liver clinic between 1992 and 2000 did not reveal an increasing trend of HAV-induced AVH (Table 2). A multicentre study conducted in India during the late 1980s revealed that HAV was the etiological agent in 70 out of 1243 adult AVH patients (6%) (25). The present study indicated that HAV played the same role in 8% of cases of AVH in adults ($n = 870$) registered at our centre between 1992 and 2000.

Therefore, during the last two decades there has been evidently no change in the proportion of HAV-induced AVH among adults in India.

Further studies may be necessary in order to determine precisely when, between the ages of 1 and 9 years, children in northern India acquire anti-HAV antibodies. The study in Lucknow revealed the presence of these antibodies in about 90% of children aged 6–10 years (21). The present study was confined to two schools and was limited to the city of Delhi. Affluent subgroups of the population may benefit from HAV vaccination but the majority of the children in the present study had acquired protective antibodies against the virus by the time they went to school. In these circumstances, mass vaccination against HAV may not be cost-effective in a population where HAV is highly endemic. The general pattern seen in developing countries is that exposure to HAV is virtually universal before the age of 10 years (20). In rural Liberia an annual incidence of HAV seroconversion of 45% in infants aged 1–5 years was reported (26). In Indonesia, 95% of 9-year-old children were naturally immune to HAV infection (24). Therefore, in countries where HAV is highly endemic, mass vaccination against the virus may not be necessary, and large population-based studies involving adequate sampling are needed in order to assess whether it is appropriate. ■

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Conflicts of interest: none declared.

Résumé

Résultats d'une enquête séro-épidémiologique sur l'utilité de la vaccination anti-hépatite A des écoliers dans le nord de l'Inde

Objectif Evaluer le taux de séroprévalence actuel des anticorps dirigés contre le virus de l'hépatite A (HAV) chez un échantillon d'écoliers de plus de 10 ans et déterminer la prévalence de l'hépatite induite par le HAV chez l'adulte dans un établissement hospitalier de niveau tertiaire dans le nord de l'Inde entre janvier 1992 et décembre 2000.

Méthodes Le sérum de 276 écoliers et 224 écolières de 10 à 17 ans a été examiné à la recherche d'anticorps anti-HAV au moyen d'un test ELISA (*enzyme-linked immunosorbent assay* = titrage au moyen d'un immunoadsorbant lié à une enzyme). Les marqueurs sérologiques des HAV, HBV, HCV, HDV et HEV ont été recherchés chez les patients consécutifs ayant un diagnostic d'hépatite virale aiguë consultant dans un service d'hépatologie.

Résultats Les anticorps anti-HAV étaient présents dans le sérum de 96,3 % des garçons et 98,2 % des filles. La prévalence de ces anticorps dans les classes d'âge 10-12 ans, 13-14 ans et 15-17 ans était respectivement de 98,6 %, 94,8 % et 98,3 %. Aucune tendance à l'augmentation de la fréquence des hépatites virales aiguës induites par le HAV chez l'adulte n'a été notée (69/870, soit 8 %).

Conclusion La vaccination de masse contre le HAV pourrait être inutile dans le nord de l'Inde, dans la mesure où la séroprévalence des anticorps protecteurs anti-HAV reste supérieure à 95% chez les écoliers de plus de 10 ans et où aucune augmentation apparente des hépatites virales aiguës induites par le HAV n'est observé chez l'adulte.

Resumen

La vacunación contra la hepatitis A, tal vez innecesaria entre los escolares del norte de la India: resultados de una encuesta seroepidemiológica

Objetivo Evaluar la actual seroprevalencia de anticuerpos contra el virus de la hepatitis A (VHA) en una muestra de escolares de más de 10 años de edad, y determinar la prevalencia de hepatitis por VHA entre los adultos en un hospital de atención terciaria del norte de la India entre enero de 1992 y diciembre de 2000.

Métodos Se utilizó la prueba de inmunosorción enzimática para analizar los sueros de una muestra de escolares (276 varones y 224 mujeres) de 10-17 años a fin de determinar el nivel de

anticuerpos anti-VHA. Se analizó además el suero de una serie de pacientes consecutivos con diagnóstico de hepatitis vírica aguda que acudieron a un consultorio de atención hepática, para determinar los marcadores serológicos de los virus VHA, VHB, VHC, VHD y VHE.

Resultados Entre los escolares, el 96,3% y el 98,2% de los niños y las niñas, respectivamente, presentaban anticuerpos anti-VHA en el suero. La prevalencia de estos anticuerpos en los grupos de edad de 10-12, 13-14 y 15-17 años fue del 98,6%,

94,8% y 98,3%, respectivamente. La frecuencia de hepatitis vírica aguda por VHA (69/870, 8%) en los adultos no reveló una tendencia al aumento.

Conclusión Considerando que la seroprevalencia de anticuerpos protectores contra el VHA observada entre los escolares de más de

10 años permanece por encima del 95%, y que no se da un aumento claro de los casos de hepatitis vírica aguda por VHA en los adultos, es posible que la vacunación masiva contra el VHA sea innecesaria en el norte de la India.

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