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A study of hepatitis A virus seropositivity among children aged between 1 and 5 years of age: Implications for universal immunization

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ABSTRACT

Background: Hepatitis A virus (HAV) causes an enterically transmitted viral disease mainly affecting children and endemic in many developing countries, including India. There is an epidemiological shift with an increased incidence of symptomatic cases among children. This study was conducted to assess the seroprevalence of HAV among young children aged below 5 years and the need for universal immunization.

Method: This cross-sectional study was conducted at two tertiary care hospitals in Northern India, from Apr 2014 to Jul 2015, among healthy children aged between 1 and 5 years. The sample size was calculated based on the prevalence of HAV seropositivity of 40% among children aged <10 years [16–60%] and alpha error of 5%. Analysis of serum IgG against HAV was performed by enzyme-linked immunosorbent assay method, and results were analyzed.

Results: A total of 1084 children aged between 12 and 60 months were enrolled, with male-to-female ratio of 1.86:1. A total of 471 children (43.5%) were found to be positive for IgG against HAV. The seroprevalence of HAV was lower among younger children aged 12–23 months (odds ratio [OR] = 0.73, 95% confidence interval [CI] = 0.52–0.87, $p = 0.03$), which was statistically significant. Seropositivity of HAV was lower among boys and families consuming safe drinking water and having improved sanitation facilities.

Conclusion: The study observed lower seropositivity against HAV among younger children, making them susceptible of contracting the disease. Possible underlying risk factors were younger age, unsafe drinking water, poor sanitation, and low education status of parents. Therefore, vaccination may be recommended as optional vaccine at one year of age, along with improved public health efforts for safe drinking water, hygiene practices, and food safety.

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Introduction

Viral hepatitis continues to be a major public health problem in developing and developed countries worldwide including India and is now equated as a threat comparable to the “big three” communicable diseases—HIV/AIDS, malaria, and tuberculosis. Since the first officially reported epidemic of viral hepatitis in 1955 in Delhi, many outbreaks of hepatitis have occurred in different parts of the country.^{1–3} In a recent study by Rakesh et al³ from Kerala, Hepatitis A virus (HAV) was identified as the etiology for an outbreak of acute viral hepatitis at Mylapore village of Kollam district, and they noted a high attack rate in subjects aged 15–24 years (4.6%) when compared to subjects aged 5–14 years (3.1%). The seroprevalence of HAV is also changing over a period due to changes in socioeconomic and hygiene status, as well as living conditions. In India, seroprevalence of antibody to HAV exceed 90% in adults; however, limited epidemiological data are available on anti-HAV among children.^{4–12} The present study was designed to assess the seroprevalence of anti-HAV antibody in children of age group 1–5 years, determine the HAV susceptibility in this age group, and assess the need for universal immunization against HAV.

Material and methods

A cross-sectional study was carried out in two tertiary care service hospitals in Northern India from Apr 2014 to Jul 2015 among healthy children of age group 1–5 years to find out the seroprevalence of hepatitis A. The healthy children enrolled were those reporting to the immunization clinic, preprimary school, and residential area of the community. A sample size of 500 children at each center was calculated, based on the prevalence of IgG HAV seropositivity of 40% among children younger than 10 years [16–60%] and alpha error of 5%. Children with preexisting chronic liver diseases and having other comorbidities were excluded. Ethical clearance was obtained from the institutional ethical committee. The purpose and methodology of the study was explained to the parents, and informed consent was obtained. Detailed history including various risk factors associated with HAV infection was obtained from parents as per proforma. Sanitation facilities and drinking water supply were assessed based on World Health Organisation guidelines. Blood was collected under aseptic conditions and analyzed for IgG HAV serology by enzyme-linked immunosorbent assay method. During the study period, all patients admitted with jaundice were investigated to find out the etiology of hepatitis. The data were analyzed using multivariate logistic regression analysis to find out significant factors associated with the seroprevalence of HAV. The odds ratio (OR) and its 95% confidence interval were calculated. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

Results

A total of 1084 children were included in this study. Of the total study participants, 344 (31.7%) were aged between 48 and

60 months, 277 (25.6%) between 24 and 35 months, 251 (23.2%) between 36 and 49 months, and 212 (19.6%) between 12 and 23 months. There were 705 boys (65%) with male-to-female ratio of 1.86:1.

The seropositivity of Hepatitis A was found in 471 participants (43.5%), and remaining 613 (56.5%) children were found to be susceptible to Hepatitis A. The seroprevalence of HAV was found to be lower among males than females; however, the association between the two was not statistically significant ($p > 0.05$). The prevalence of HAV seropositivity between the age group of 1–5 years varied from 39% to 47% and was lower among the children aged 12–23 months than among children in the age group of 48–60 months (OR = 0.73, 95% CI = 0.52–0.87, $p = 0.03$). Thus, susceptibility was 60.4% (maximum) in children aged between 12 and 23 months as against 52.9% in those aged between 48 and 60 months as shown in Table 1.

Various factors associated with the HAV seroprevalence such as education of parents, drinking water supply, hygiene and sanitation facilities, past history of jaundice, jaundice in other family members, and hepatitis vaccination status were examined as shown in Table 2.

The method of purification of drinking water was candle filtration in 447 (41.2%) followed by reverse osmosis in 282 (26%) cases. Most families, 1061 (97.9%), had improved sanitation facilities. HAV seroprevalence was found to be significantly lower among those children who had improved drinking water and sanitation facility (43.4%) than children of families having poor drinking water and sanitation facility (47.8%). Past history of jaundice was found only in 30 (2.8%) children. The HAV seroprevalence was found to be significantly ($p = 0.0001$) higher (90%) among those children in whom past history of jaundice was present than who had no history of jaundice (42.1%). Family history of jaundice was observed in 34 (3.1%) children. Only 117 (10.8%) children had received hepatitis A vaccine. The seropositivity of IgG was found to be significantly ($p = 0.0001$) higher among those children who had received hepatitis A vaccine (82.1%) than who did not receive it (17.9%).

The significant factors associated with the HAV seroprevalence after multivariate logistic regression analysis showed that education of parents ($p = 0.01$), source of water supply ($p = 0.0001$), history of jaundice ($p = 0.013$), and hepatitis A vaccination ($p = 0.0001$) were significantly associated with the seroprevalence of HAV.

The possible etiologies of jaundice among the children who reported with jaundice were HAV infection in 37 (74%) (detected to have IgM HAV), followed by Hepatitis E Virus (HEV) in 7 (14%) and hepatitis B infection in 2 (4%) being positive for Hepatitis B surface antigen (HBsAg), and no definite cause was detected in 4 children.

Discussion

In the present study, hepatitis A seroprevalence was assessed among 1084 children aged between 1 and 5 years, and 471 children (43.5%) were found to have seropositivity for HAV. The study by Arankalle et al⁴ conducted in 2011–12 among 928 children (aged 18 months to 10 years) found that 348

Table 1 – HAV seroprevalence according to the age of study participants (n = 1084).

Age in months	No. of children (%)	HAV seropositivity (Serum IgG HAV)		OR (95%CI), p-value ¹
		Positive (Immune) No. (%)	Negative (Susceptible) No. (%)	
12–23	212 (19.6)	84 (39.6)	128 (60.4)	0.73 (0.52–0.87), 0.03*
24–35	277 (25.6)	116 (41.9)	161 (58.1)	0.80 (0.58–1.11), 0.19
36–47	251 (23.2)	109 (43.4)	142 (56.6)	0.86 (0.62–1.19), 0.37
48–60	344 (31.7)	162 (47.1)	182 (52.9)	1.00

HAV, hepatitis A virus.

(37.5%) children were seropositive for anti-HAV antibodies. Seroprevalence of HAV in the 6- to 10-year age group (50.3%) was higher ($P = 0.000$) than in the 18-month to 6-year age group (30.3%). Sabir et al.¹³ reported the seroprevalence of IgG antibodies to HAV being 33.1%, Mohammad et al.,¹⁴ 17.8%, and Baliga et al.,¹⁵ 19.31%. This difference in seroprevalence may be attributed to different endemicity of HAV in sociodemographically different study populations.

In the present study, the seroprevalence of HAV was significantly lower among the children aged 12–23 months than among those aged 48–60 months (OR = 0.73, 95% CI = 0.52–0.87, $p = 0.03$). In a similar study conducted by Mall et al.,⁵ seropositivity increased with age from 52.2% in the 1- to 5-year age group to 80.8% in those aged 16 years or more. A similar Indian study conducted in Hyderabad by Joshi et al.⁹ revealed that the seroprevalence was 31.8% (17/54) in children (<12 years) and 94.4% (34/36) in adults ($p < 0.001$). A study conducted by Dutta et al.¹⁰ among 420 healthy infants and children observed seropositivity for hepatitis A to be 60.0% (age 0–0.5 yr), 16.7% (age 0.5–1 yr), 16.7% (age 1–1.5 yr), 30.0% (age 1.5–2 yr), 46.7% (age 2–3 yr), 70.0% (age 3–4 yr), and 80.0% (age 4–5 yr). The higher rate of seropositivity of 60% in infants younger than 6 months could be due to maternal transfer of

antibodies in utero.¹⁰ Our study findings were not surprising given the fact that most of the study participants have grown up in environments where they had access to clean water and improved sanitation facilities, 1061/1084 (97.9%). Improvement in hygiene and socioeconomic conditions has undoubtedly contributed to this epidemiologic shift. Therefore, vaccination in susceptible population at any time after 12 months completed can prevent serious infections and epidemics at a later age.

The seropositivity of IgG test was found to be significantly ($p = 0.0001$) higher among those children who had received hepatitis A vaccination (82.1%) than who did not receive it (17.9%), thus confirming high seroconversion rates with available HAV vaccines. Only 117 (10.8%) children had received hepatitis A vaccine in our study as it was an expensive vaccine. In a similar study by Yun et al.,¹⁶ the vaccination rate of children was about 50% and the seroconversion rates after the 1st and 2nd vaccinations were 85%, and 96%, respectively. Another study by Hyun et al.¹⁷ showed the seroconversion rate of 86.17% after 2-dose vaccination, which was in consonance with our study. Regarding administration of hepatitis A vaccine, the Advisory Committee for Immunization Practices, CDC, recommends that all children be vaccinated against hepatitis A at the age 1 year. In India, as the living conditions are improving, the authors feel that the vaccine should be recommended to be given to all children below 2 years of age. The routine immunization has been recommended by various studies, and the Indian Academy of Pediatrics recommends two doses for any of the licensed vaccines that have to be given six months apart to children aged one year or older.^{18,19}

Table 2 – Factors associated with the HAV seroprevalence.

Factors for HAV	Adjusted OR	95% CI for OR		p-value
		Lower	Upper	
Education of mother				
Illiterate				1.00
High school and below	0.56	0.26	1.38	0.13
Below graduate	0.53	0.24	1.33	0.09
Above graduation	0.22	0.11	0.78	0.01*
Source of water supply				
No filtration being used				1.00 (Ref.)
Candle filter	0.31	0.21	0.44	0.0001*
UV filter	0.48	0.13	1.86	0.284
Boiling	0.18	0.07	0.56	0.003*
Reverse osmosis	0.23	0.16	0.37	0.0001*
Past history of jaundice				
Present	0.22	0.09	0.73	0.013*
Absent				1.00 (Ref.)
Hepatitis A vaccine				
Received	3.44	1.30	5.14	0.0001*
Not received				1.00 (Ref.)

OR, odds ratio; CI, confidence interval; HAV, hepatitis A virus; *, significant.

Conclusion

The present study observed a transition in the seroprevalence of HAV, with a lower seropositivity in younger children, making them susceptible of contracting the infection with HAV. Possible underlying risk factors were younger age, source of drinking water, and education status of parents. Effective vaccination against HAV infection is available, which will prevent the disease incidence in the community and reduce the impact of disease in terms of morbidity and school absenteeism. It may prove to be a cost-effective measure to introduce hepatitis A vaccination at the age of 1 year and introduced as optional vaccine. Vaccination efforts should be supplemented by public health efforts to improve sanitation, hygiene practices, and food safety.

Limitation of the study

This was a hospital-based study and may not give representative data for the community at large, and the sample size was small. A larger sample size would give more information on the project, which can be replicated to larger population.

Conflicts of interest

The authors have none to declare.

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