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Original Article

Seropositivity for Hepatitis A IgG Antibodies in the Cord Blood. Is The Prevalence Trend Changing?

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ABSTRACT

Background: The prevalence of Hepatitis A can be studied in an easy and non-invasive way by studying the immunoglobulin G (IgG) levels in the cord blood which is representative of adult population protected against Hepatitis A, either through vaccination or previous exposure. An epidemiological shift from high to intermediate endemicity of HAV is now being observed worldwide.

Aim: To find if improved health care, sanitation and socio-economic status have changed the previously documented seropositivity patterns in Delhi.

Design: An observational analytical cross sectional study was done in the Department of Paediatrics of a tertiary referral centre in Delhi from July 2011 to July 2013.

Method: 285 consecutive admissions in reproductive age group attending the family welfare services at the TirathRam Shah Hospital for the purpose of antenatal care and childbirth were recruited and their cord blood samples were analysed for the presence of anti HAV IgG antibodies.

Results: Out of 285 recruited subjects, a very high proportion i.e. 260 tested positive for Hepatitis A Virus IgG antibodies, showing 91.2 % seropositivity.

Conclusions: Hepatitis A seroprevalence continues to be high in the adult population from urban high socioeconomic strata of Delhi. The seroprevalence of anti-Hepatitis A antibodies is similar across various age groups in women of child bearing age irrespective of socio-economic status, geographical area, source of water supply or profession.

KEYWORDS: Hepatitis A; Anti HAV antibodies; Cord blood; Hepatitis A endemicity.

Introduction

The term Hepatitis refers to inflammation of the liver, which could be a result of many infectious or non-infectious insults. Hepatitis caused by infection with Hepatitis A virus (HAV) is the commonest variety of infectious hepatitis in childhood.[1] The prevalence of Hepatitis A can be studied in an easy and non-invasive way by studying

the IgG levels in the cord blood which is representative of adult population protected against Hepatitis A, either through vaccination or previous exposure.[2,3]

An epidemiological shift from high to intermediate endemicity of HAV is now being observed worldwide.[4] As a result, more adults in such areas of transition escape exposure to HAV in early childhood but become susceptible to infection during outbreaks. This reducing endemicity often results in a paradoxical increase in disease incidence rates and severity amidst improved socioeconomic and sanitary conditions.

India has conventionally been considered as an area of high endemicity, but many seroprevalence studies have shown declining seropositivity across all age groups and the probable trend is towards medium endemicity.[5,6] As per WHO guidelines, countries moving from high to intermediate endemicity should consider including Hepatitis A vaccine in their national immunisation program.[7] To be able to recommend optimal preventive vaccination strategy for India, it is essential to have an idea of recent seroprevalence pattern across all socioeconomic strata. However, there is paucity of such data in recent times, especially from higher socio-economic groups. No published seroprevalence study is available after introduction of Hepatitis A vaccine in India. The objective of this study was to find if improved health care, sanitation and socio-economic status have changed the previously documented seropositivity patterns.

Methods

This observational analytical cross sectional study was conducted in Department of Paediatrics of the Tirath Ram Shah Hospital, Delhi (July 2011 to July 2013). A total of 285 consecutive admissions (prospective mothers) in reproductive age group were enrolled in the study, after obtaining informed consent. These were segregated into four age groups ≤ 25 years, 26-30 years, 31-35 years and ≥ 36 years. Clinical details and relevant social history like the source of water supply, use of water purifier, residential area, educational level, occupation, monthly income, job profile and type of room taken during hospital stay were recorded as per predesigned, preset proforma. Based on above details, patients were divided into different socioeconomic grades as per modified Kuppuswamy's classification.[8]

Exclusion criteria

Enrolled mothers were checked for exclusion criteria, which included past history of vaccination against HAV, chronic steroid therapy, immunocompromised and malnourished state. Any subject found to be positive for above parameters was excluded from the study. Incidentally, Out of 316 successive admissions for child birth, 5 were excluded because of history of documented hepatitis A in the past and 26 for having received Hepatitis A vaccination.

Sampling method

2-3 ml of Cord blood sample was collected in a plain vial, under full aseptic precautions, and transferred immediately to the lab. Serum collected after centrifugation was transferred to 96 well microplate coated with HAV antigen forqualitative estimation of HAV IgG level using Engwell and Perlman ELISA kit (DSI Italy) and the result was read by ELISA reader after 30 minutes. Data were recorded in predesigned proforma and managed in excel spread sheet. Results were recorded as positive/negative for HAV IgG antibodies and compared after assigning them to various groups (age of the mother, socio economic grade and room category, job profile and source of water supply).

Outcome Measures:

1) Estimation of Anti Hepatitis A antibodies of IgG subtype in the cord blood.

2) To compare seroprevalence of Hepatitis A IgG antibodies in the cord blood of mothers from different socio- economic status.

Ethical considerations

Ethical clearance was obtained from the Institutional Ethical Committee prior to start of the study. Informed written consent was taken from all study participants. No pressure/coercion was exerted on the subjects for participation in the study. Confidentiality of information was assured to all the participants.

Analysis and statistical tools

Data was entered in Excel sheet and to analyse the data SPSS version 22 was used (Chicago, IL, USA). Means

and Standard Deviations (SD) were calculated for continuous variables while proportions and frequencies were calculated for categorical variables. It is also pertinent to mention here that because of small number of subjects in each subgroup, statistical significance of results is difficult to be well elucidated.

Results

A total of 285 women between the ages of 19 - 40 years were recruited in the study. Mean age of the study group was 27.5 years with standard deviation of 3.9 years. **Table 1** shows socio-economic and demographic profile of study subjects. Maximum women (49.8%) belonged to age group of 26- 30 yrs. 73% women were of upper class (grade 1) and remaining 27% were of upper middle and lower middle class (grade 2). 98.2% women were residents of Delhi. 78.9% had MCD tap as a source of water supply and were using reverse osmosis water purifiers.

Among 285 study subjects 260 were found to be positive for HAV IgG antibodies (91.2%) and remaining 25 women were found to be seronegative.

Table 2 shows relation of socio demographic and economic factors with seropositivity of the subjects. In the age group of <25 years 90.6% women were seropositive. 91.5% in age group of 26-30 years, 93.8% in age group of 31-35 and 80% women in age group > 35 years were seropositive respectively.

In the women belonging to socioeconomic status grade 1 seroprevalence was 92.3 % and in women of socioeconomic grade 2, it was 88.3 %, difference being statistically insignificant (p value > 0.05).Majority of women (280) were from Delhi and seropositivityrate was 91.1 % while all the 5 women from outside Delhi tested positive. Among the subjects whose main earning member of the family was in government job seropositivity rate was 90.9 % and for those who were not, it was 91.3 %. In the subjects who were using Municipal supply (MCD) water with purifier, cord blood positivity was 92.4 %, among those using MCD supply directly it was 86.4 % and in those using non-MCD (Bore well) water it was 100%.

Mothers getting admitted in deluxe room showed 94.6 % seropositivity, it was 93.1 % in women opting for

Table 1: Socio-demografic profile of study subjects.

Socio-demographic-economic parameters	Classification	Frequency	Percentage (%)
Age	< 25	85	29.8
	26 - 30	142	49.8
	31 - 35	48	16.8
	> 35	10	3.4
Kuppuswamys SES grade	Grade 1	208	73.0
	Grade 2	77	27.0
Area of residence	Delhi	280	98.2
	Outside Delhi	5	1.8
Source of water supply	MCD supply with purifier	225	78.9
	MCD supply withoutpurifier	59	20.7
	Non MCD supply	1	0.4
Job profile	Govt.	66	23.2
	Non govt.	219	76.8
Type of room taken during hospital stay	Deluxe	56	19.6
	Double sharing	29	10.2
	Triple sharing	86	30.2
	General ward	114	40.0

Table 2: Association between seroprevalnce and various socio- economicparameters.

Socioeconomic parameters	Classification	Seropositive women	Seronegative women	Seroprevalence (%)	Chi square, 'p' value
Age	< 25	77	8	90.6	2.019, 0.569
	26 - 30	130	12	91.5	
	31 - 35	45	3	93.8	
	> 35	8	2	80.0	
Kuppuswamy SES grade	Grade 1	192	16	92.3	1.121, 0.290
	Grade 2	68	9	88.3	
Area of residence	Delhi	255	25	91.1	0.489, 0.484
	Outside Delhi	5	0	100	
Source of water supply	MCD supply with Purifier	208	17	92.4	2.202, 0.333
	MCD supply without purifier	51	8	86.4	
	Non MCD supply	1	0	100	
Job profile	Govt.	60	6	90.9	0.11, 0.917
	Non govt.	200	19	91.3	
Type of room taken during hospital stay	Deluxe	53	3	94.6	1.412, 0.703
	Double sharing	27	2	93.1	
	Triple sharing	78	8	90.7	
	General ward	102	12	89.5	

P value > 0.05 for all factors studied

double sharing accommodation, 90.7 % in subjects of triple sharing room category and 89.5 % in patients getting admitted to general category ward. The differences were statistically not significant with respect to all the tested parameters by applying chi square test (**Table 2**)

Discussion

Hepatitis A virus (HAV) infection in early childhood is mostly asymptomatic or mildly symptomatic.[1] In the absence of specific anti-viral drugs, it requires only supportive management, with usually favourable outcome. However, it can at times lead to significant morbidity, prolonged hospitalisation and/or fulminant liver failure. The World Health Organization recommends universal Hepatitis A vaccination in intermediate endemic areas; however, there is no need of mass vaccination in high and low endemicity regions. Most of the countries are using a vaccination policy according to the endemicity characteristic representing the whole of the country. Therefore, to plan effective vaccination strategy, it is of paramount importance to keep following the seroprevalence patterns across various population groups.

Hepatitis A cannot be differentiated from other types of viral hepatitis on the basis of clinical or epidemiologic features alone. Serologic testing to detect immunoglobulin M antibody to the capsid proteins of HAV (IgM anti-HAV) is required to confirm a diagnosis of acute HAV infection.[9] Immunoglobulin G (IgG) anti-HAV, remains detectable for the person's lifetime and provides lifelong protection against the disease and is considered a dependable marker for studying prevalence of HAV.[10] Testing for IgG antibodies against Hepatitis A virus in the cord blood is a convenient and non-invasive

way to study the prevalence of HAV in adult population besides helping in formulating immunization strategy with respect to need and appropriate age for HAV vaccination.

In Central Asia, proportion of susceptible young/ adolescent children to Hepatitis A has been found to be increasing.[11] East Asian countries like China and Thailand have reported large outbreaks of hepatitis A, in recent times.[12,13] The seroprevalence has shown a declining trend in recent times in Singapore and Taiwan, which have seen marked improvement in level of sanitation and economic development.[14,15] This suggests changing trend in Asian countries, forming the basis of the present study.

In South Asian countries like Pakistan, Nepal and Bangladesh, nearly all adults and adolescents are seropositive, indicating very high chances of exposure to HAV in childhood.[16] Studies in Nepal have shown universal immunity by the age of 15 years.[17] Since India more closely resembles these countries, similar trend is expected to be prevailing here. Improvement in general sanitation in Delhi and higher awareness of our study group(comprising urban population of higher socio economic status) about preventive strategies like using purified water and vaccination, was expected to have a bearing on the demonstrated prevalence rates . But, we found a very high seroprevalence in cord blood, even 3 decades after the study by Tandon *et al* in 1984, where the cord blood seroprevalence was found to be 100 %.[18] Aggarwal *et al* in 1999 showed that infection by HAV occurred at an earlier age, and by adulthood most of the population was protected.[19] High seropositivity to the tune of 95% have been demonstrated in school children in previous studies from north and south India in the past.[20-22]

The seroprevalence in our study did not vary with socio-economic grade. Arankalle *et al* from Pune found significant decline in the positivity of HAV antibodies in children between 6-10 (85 to 30%) and 11-15 (92 to 45%) years of age, belonging to the higher income class in the urban areas, between 1982 and 1998 respectively.[23] Dhawan *et al* in 1998, from Mumbai found significantly lower seropositivity among children and adults from high socio-economic group (64.5%) compared to 85.3 per cent in individuals from low socio-economic class.[24] Similarly, Prakash *et al* in 1998, showed that younger children belonging to high socio-economic class in Indore, had increased frequency of acute hepatitis A.[25]

Jindal *et al* in 2002 reported that one third of the medical students in Delhi were still negative for anti-HAV IgG and hence at the increased risk of HAV infection, probably because most medical students belonged to relatively higher socio- economic strata.[26] Recent study by Hussain *et al* in Delhi done over a period of 5 years showed rise in incidence of symptomatic HAV infection from 10-22 % in children.[27]

Seroprevalence of HAV in a study population from Bijapur, in India is lower than other studies conducted in different parts of India. It has been proposed that the seroprevalence might have declined with improved sanitation and improved socioeconomic status or it may be a low endemic area.[28]

Most of the studies from India show high endemicity against Hepatitis A, with few susceptible adults, constituting only small proportion of total population. When we consider our results, we also notice that most of the women in reproductive age group from Delhi and adjoining states, belonging to higher socio-economic strata had already had exposure to HAV, despite considerable improvement in healthcare and sanitation facilities and overall socio economic development.

Differences between our data and those of others may relate to differences in HAV epidemiology in different population groups. Our hospital, being a paying hospital, caters primarily to population belonging to middle and higher socioeconomic classes. A high anti-HAV prevalence rate in this group is therefore unlikely to be related to socioeconomic factors. This may be related to differences in water supply systems, population densities, playing and mixing habits of children, educational status of parents, within the city. On the other hand, it is possible that, prevalence of anti-HAV antibodies in different regions of the country is different. Larger epidemiologic studies are necessary to elucidate the true reason for differences in prevalence of anti-HAV in different studies from our country.

Conclusion

As per our study, India is still a high endemic country for Hepatitis A and routine vaccination strategy against

Hepatitis A may still not be recommended, as per WHO guidelines. The thrust presently should be on improving standards of sanitation and hygiene. Further large population based seroprevalence studies may be necessary to devise the optimal vaccination strategy for Indian children.

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