Hepatitis A virus vaccination strategy and pre-immunization screening of Bangladeshi children

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Abstract:
Background: HAV infection is endemic in many developing countries like India, Pakistan, Nepal etc. Several seroprevalence studies show high rates of sero-positivity among children by sub-clinical infection. Therefore mass vaccination against HAV has not been recommended in endemic countries. Objective: To determine whether routine hepatitis A vaccination is indicated for all Bangladeshi children & also to know whether pre-vaccination screening is necessary. Materials & Methods: Serum samples from 254 children aged between 1-15 years were tested for antibody (IgM & IgG) against hepatitis A virus (HAV) to determine the seroprevalence of HAV antibody and do a cost-benefit analysis for decision making about vaccination against HAV among the children of Bangladesh. Results: Hepatitis A virus antibody was positive in 141 (55.5%) of 254 children. Age-specific sero-prevalence was 13 (23.2%) of 56 in 1-3 year, 64 (55.2%) of 116 in 3-5 year, 39 (70.9%) of 55 in 5-10 year & 25 (92.6%) of 27 in 10-15 year age group. Cost benefit analysis showed that the total cost of screening followed by vaccination was almost 1.8 times less than the total cost of vaccination of all children without screening. Conclusions: Majority of the children were found sero-positive against HAV around 15 year of age. Therefore mass vaccination against HAV may not be required for Bangladeshi children.

Key words: Hepatitis A virus (HAV); HAV seroprevalence; HAV vaccine

Introduction
Hepatitis A virus (HAV) infection occurs throughout the world but most common in developing countries. In these countries with high endemicity, 90% of the population is infected by 10 years of age. Here children are continuously exposed to the virus, which confers lifelong immunity. In many developing countries like India, Pakistan, Nepal several sero-prevalence studies have shown high rates of sero-positivity among child by sub-clinical infection. Therefore, mass vaccination against HAV has not been recommended in endemic countries. Furthermore, Hepatitis-A vaccine is expensive. In Bangladeshi children, limited data are available regarding the sero-prevalence of HAV antibody. In this context, the present study was designed to see the prevalence of HAV antibody (IgG & IgM) among children of different age group and to perform a cost benefit analysis study before formulating a vaccination strategy for the children of Bangladesh.

Materials & Methods
A cross sectional observational study was conducted from July 2008 to June 2009. Blood was collected at blood collection centers of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital & Dhaka Shishu (Children) Hospital (DSH). A total of

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254 children aged 1-15 years (boys=139 & girls=115), who had no previous history of jaundice or hepatitis or Hepatitis A vaccination but attended OPD of these two hospitals for other illnesses were included in this study. The sample size was determined by the prevalence rates of neighbouring countries with a similar socioeconomic condition (e.g., India & Pakistan) as there are no previous data on HAV prevalence particularly in the children of Bangladesh. With prior written consent, clinical history and relevant data were recorded and 2 ml of blood was collected from each of the study cases. Serum was separated, stored at -20°C and were tested for HAV antibody (IgG & IgM) by ELISA using the ELISA kit (DiaSorin Italy, ETI-AB-HAVK PLUS, no136, 01/2009) at the Department of Virology laboratory of BSMMU, Dhaka. The cut-off value was determined by the mean absorbance of the calibrator values. The presence or absence of anti-HAV was determined by comparing the absorbance values of unknown samples with the absorbance values below/above the cut-off values of the controls. For cost benefit analysis, pre-vaccination screening price was 2$ for each child & vaccine price along with vaccination charge was 15$ (Per dose).

A preformed semi structured data collecting form was used as a data collection instrument. Data were collected by researcher and analyzed by Statistical Package for social Science (SPSS) version 11.5 program. P value of <0.05 was considered as statistically significant.

**Results**

Hepatitis A virus antibody (total) was found positive in 141 (55.5%) of 254 children (Fig:1)

Fig: I Anti-HAV positivity among all children

![Graph showing Anti-HAV positivity among all children](image)

Table 1.1 Anti-HAV positivity with age

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>n</th>
<th>HAV antibody</th>
<th>$\chi^2$</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 5</td>
<td>172</td>
<td>Positive</td>
<td>11.397</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>95 (55.3)</td>
<td></td>
</tr>
<tr>
<td>5 – 10</td>
<td>55</td>
<td>Positive</td>
<td>4.970</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>16 (29.1)</td>
<td></td>
</tr>
<tr>
<td>10 – 15</td>
<td>27</td>
<td>Positive</td>
<td>1.129</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>25 (92.6)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.2 Seroprevalence of antibodies in children aged 1-5 year

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>n</th>
<th>HAV antibody</th>
<th>$\chi^2$</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 2</td>
<td>37</td>
<td>Positive</td>
<td>1.129</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>30 (81.1)</td>
<td></td>
</tr>
<tr>
<td>2 – 3</td>
<td>19</td>
<td>Positive</td>
<td>2.536</td>
<td>0.111</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>13 (68.4)</td>
<td></td>
</tr>
<tr>
<td>3 – 4</td>
<td>49</td>
<td>Positive</td>
<td>0.153</td>
<td>0.696</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>23 (46.9)</td>
<td></td>
</tr>
<tr>
<td>4 – 5</td>
<td>67</td>
<td>Positive</td>
<td>0.153</td>
<td>0.696</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>29 (43.3)</td>
<td></td>
</tr>
</tbody>
</table>

# Data were analysed using Chi-square ($X^2$) Test

Figures in the parentheses denote corresponding percentage

Table 1.2 shows anti-HAV positivity in children aged 1-5 year. Anti-HAV was found 18.9% in 1-2 year age group, 31.6% in 2-3 year age group, 53.1% in 3-4 year age group & 56.7% in 4-5 year age group.
Table 1.3 shows, total number of subjects were 254. Current cost of 2 doses of vaccine is $15 \times 2 = 30$. Anti-HAV assay by ELISA costs $2$ per test. Total cost of vaccination of all the 254 children without screening is $(30 \times 254) = 7620$. On the other hand total cost of screening all the children is $(2 \times 254) = 508$. After screening of all the 254 children, 113 were found anti-HAV negative, who needed vaccination. Cost of vaccination of these 113 children is $(30 \times 113) = 3390$. Thus, total cost of vaccination after prior screening is $(508 + 3390) = 3898$. Therefore the cost of vaccination without screening is almost 2 (1.95) times more than the cost of vaccination after screening (Table 1.3). Therefore, it is worthwhile to screen the individuals before recommending hepatitis A vaccine.

### Table 1.3: The cost benefit analysis of hepatitis A virus vaccination strategies

<table>
<thead>
<tr>
<th>Vaccine strategy</th>
<th>Total 254 children</th>
<th>Number of ELISA tests</th>
<th>Cost of ELISA 2$ per test</th>
<th>Number of vaccinees</th>
<th>Cost of vaccine 15$ per dose $ \times 2$</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without screening</td>
<td>254</td>
<td>0</td>
<td>0</td>
<td>254</td>
<td>7620$</td>
<td>7620$</td>
</tr>
<tr>
<td>With screening</td>
<td>254</td>
<td>254</td>
<td>508$</td>
<td>*113</td>
<td>3390$</td>
<td>3898$</td>
</tr>
</tbody>
</table>

*113 were found negative for anti-HAV

**Discussion**

Acute viral hepatitis caused by HAV is an acute, self-limiting infection. Hepatitis A virus infection is very common in early childhood and most of the infections are asymptomatic or mildly symptomatic. Immunity that develops following natural infection is stronger and persists longer than that develops following vaccination. Three epidemiological patterns of endemicity (low, intermediate and high) are observed worldwide. Each pattern has a different rate of infection, prevailing age of infection, and transmission model. HAV epidemiological pattern are highly dependent on age and level of hygiene. The distribution of HAV seroprevalence by age group may reflect current hepatitis A endemicity in countries and regions. The countries with low endemicity include Japan, Singapore, Hongkong and Taiwan whereas those with moderate endemicity include Thailand, Malaysia and Sri Lanka. Countries with high endemicity for HAV infections include India, China, Nepal, Bangladesh, Pakistan, Myanmar and Philippines. In many developing countries of Africa, Asia and Latin America, most infections occur by 5 years of age where seroprevalence approach 90-100% by 10-15 years of age. In Africa, Hendricks et al. showed anti-HAV positivity of >90% among the 5-10 year age group among lower class black children. India, China, Nepal, Pakistan and Bangladesh are included in high endemic zone and a large number of populations acquire immunity through subclinical infections in early life. During the last 5 years several reports from countries in southern Asia, Latin America and Europe showed a decreasing seroprevalence of protective antibody against hepatitis A virus.
tries. Mall et al.\textsuperscript{2} from India (Calcutta) reported 40% anti-HAV positivity in 1-5 year age group and through gradual increase in age the prevalence reached to 97% in the >16 year age group.

A recent study by Kamath et al.\textsuperscript{5} reported anti-HAV positivity of 61.6% in 5-10 year age group and 97% in 11-15 year age group in Chennai, India. Agboatwalla et al.\textsuperscript{8} & Sawayama et al.\textsuperscript{21} also reported similar results from Pakistan (94.1% seropositive by the age of 5 years) and Nepal (91.1% seropositive) respectively. Anti-HAV positivity was found 94.1% in 1-5 year age group at Rawalpindi and 99% in two rural villages in Nepal. In Africa, Raharimanga et al.\textsuperscript{14} reported that the overall seroprevalence of anti-HAV was 92.2%. In 8-10 year age group it was 83.7% and in 10-24 year age group it was 95.5%.

In the present study, it was evident that the cost of vaccination with screening is more than 2 times cheaper (3898$) than the cost of vaccination without screening (7620$). As such, these findings suggest to screen the individuals before recommending hepatitis A vaccination. Ahmed et al.\textsuperscript{19} also observed that the cost of vaccination with screening was almost three times cheaper (US$3418) than the cost of vaccination without screening (US$8928). It is to be economically worthwhile, the cost of vaccinating a group of people must be equal to or less than the cost of testing the entire group plus the cost of vaccinating the non-immune group.\textsuperscript{22} In India also reported that, if anti-HAV positivity is >50% in a particular age group, then it is advisable to screen the individual before HAV vaccination. On the other hand, when the chance of positivity is <50% in a particular age group, then vaccination can be offered without screening for antibodies.\textsuperscript{13} It is evaluated that in India, selective vaccination of high risk populations, based on their serological evidence of HAV antibody, could be a rational and cost effective approach.\textsuperscript{23} In a developed country like Argentina reported that universal vaccination against HAV was cost effective.\textsuperscript{24}

**Conclusions**

In the studied children anti-HAV positivity was more than 50% after 3 years of age and finally increased to more than 90% after 10 years of age. So, high proportion of children in the present study acquired HAV antibody since early childhood and anti HAV positivity increased with increase in age. On cost benefit analysis, the cost of vaccination with screening was almost 2 times cheaper than the cost of vaccination without screening. Therefore mass vaccination or vaccination without prior knowledge regarding the serostatus could be an unnecessary immunological assault & may not be a suitable strategy for Bangladesh in lieu of the present socioeconomic condition. Assult

**Recommendations**

Based on the present study, it may be recommended that in children less than 3 years of age vaccination without prior screening can be done. However in children of >3 years of age, pre-vaccination screening should be done prior to vaccination as this is cost effective, safe and more rational.

Further community based studies with larger sample size are required before giving a final recommendation for routine HAV vaccine to children of Bangladesh.

**Limitations of study**

Small sample size, selection biasness and absence of socio-economic status are the three limitations of this study.

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Reference:


