Hepatitis A in Saudi Arabia: A comparative sero-epidemiological study


ABSTRACT

Objectives: To determine the prevalence of Hepatitis A Virus infection among Saudi children (1-12 years) in 1997. To compare the results with our previous study in 1989.

Methods: This is a randomized community-based study involving all of the regions of Saudi Arabia. All children were tested for antibody Hepatitis A Virus immunoglobulin (IgG) class.

Results: The prevalence of anti-Hepatitis A Virus IgG among 5355 Saudi children tested ranged from 10% in Taif to 82% in Giza regions with an overall prevalence of 25%. There is a reduction of the overall prevalence from 50.5% in 1989 to 25% in 1997.

Conclusion: This study shows a marked decline in Hepatitis A Virus infection in Saudi children 8 years after the first study. There is an almost 50% reduction of the overall Hepatitis A Virus prevalence. This dramatic decline in Hepatitis A Virus infection among the Saudi children will lead to a later exposure of elderly population groups to the Hepatitis A Virus infection and a new preventive strategy needing to be adopted.

Keywords: Hepatitis A, community-based.

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Hepatitis A has a worldwide distribution and, like other enteric infectious diseases, it is classically an infection of childhood and is related to conditions of sanitation and hygiene.1-3 Due to improved sanitation and living standards in many areas of the world, the epidemiology of hepatitis A is rapidly changing in these areas and the incidence and prevalence data that is a few years old may not be valid today.4-5 Moreover, as living conditions improve, more clinical cases are being diagnosed owing to the increased age of those susceptible,6-8 a paradoxical situation to infection in children where the majority of infections are subclinical. The recent availability of vaccines against hepatitis A7-9 and its safety and efficacy has made it increasingly important to understand the epidemiology of hepatitis A virus (HAV) in a given area before a strategy for the use of the vaccine is devised or implemented.

In 1989, a community-based study of all viral Hepatitises namely Hepatitis B Virus (HBV), Hepatitis A Virus (HAV), Hepatitis C Virus (HCV) was conducted before the mass HBV vaccine program.10 In that study, we determined the age-related prevalence of antibody to HAV (anti-HAV) among 4375 Saudi children (1-10 years) and an overall prevalence of 52% was found.11 This relatively high prevalence rate in children and an...
The overall prevalence of >90% in Saudi adults confirmed the high endemicity pattern of HAV in Saudi Arabia. Since that study, acute hepatitis A cases have been documented in hospitalized Saudi adults and an outbreak of HAV among Saudi children was reported. These observations along with the fact that Saudi Arabia underwent a major socioeconomic development during the past 10-15 years prompted us to re-examine the prevalence of anti-HAV in Saudi children and see whether a significant change in the epidemiology of HAV has occurred.

**Methods.** In 1997, a second community-based randomized study was undertaken. In order to have an accurate comparison between the 1989 and 1997 studies, we used the same strategy methods and catchment areas. Currently Saudi Arabia has an estimated population of 12 million people, who are almost distributed as 25% in rural and 75% in urban areas with almost 1:1 ratio to male:female. The sample size was estimated to be within 4741 samples. This sample size was distributed proportionately according to the population of each of the 14 health regions into which the Kingdom of Saudi Arabia is divided. Each of the 14 regions were stratified into urban and rural areas and a list of Primary Health Care Centres (PHCC) in each area was selected for each urban and rural area. The catchment population of each selected PHCC was further sub-divided into clusters of households defined by visible land marks such as roads and mosques. A simple random sample of clusters was selected and the required numbers of households was visited. After informed consent 5-10cc of blood was obtained from every child. Along with each sample, a form was filled up indicating the age, sex, and exact region. The blood was allowed to clot and sera separated by centrifugation. Sera were kept at -20°C and after the required number of samples of the region was completed, the sera was sent to the Virology Laboratory of King Khalid University Hospital (KKUH) in Riyadh for analysis. A total number of 5255 children (2642 males and 2713 females) aged 1-12 years were investigated.

**Laboratory test.** All specimens were tested for antibody to HAV (anti-HAV) immunoglobulin G class using the commercially available enzyme immunoassay (EIA) kits from Abbott Laboratories, North Chicago, Ill.

**Statistical analysis.** We used Z-test to compare the percentages drawn from 2 different years. A p-value <0.05 was judged to reflect a significant difference; a p-value between 0.05 and 0.1 was judged to reflect a trend.

**Results.** The prevalence of anti-HAV IgG among 5255 Saudi children tested ranged from 10% in Taif to 82% in Gizar region with an overall prevalence of 25% (Table 1). There was a continuous increase of anti-HAV IgG with age starting with 13% in children one year of age and reaching 34.5% at 10 years of age. The prevalence in 11 year olds was 26% but peaked to 49% in 12 year old children (Table 2). The prevalence of anti-HAV IgG was almost the same in males (26%) and in females (24%), and there was a statistical significance between children in urban areas (21%) compared to those in rural areas (33%) (P<0.000001) (Table 3).

Table 1 shows the prevalence of anti-HAV IgG in the various regions in 1989 and in 1997. The reduction in the prevalence was noticed in each region and was significant in most of the regions (P<0.00001 except for the Gizar region where the prevalence was almost the same after 8 years (81.6% in 1989 vs 82.2% in 1997). The prevalence of anti-
Table 2 - Comparison of the prevalence of anti-HAV in Saudi children between the year 1989 and year 1997 according to their age group.

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>1989</th>
<th></th>
<th></th>
<th>1997</th>
<th></th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. studied</td>
<td>Positive No.</td>
<td>Positive %</td>
<td>No. studied</td>
<td>Positive No.</td>
<td>Positive %</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>588</td>
<td>185</td>
<td>31.0</td>
<td>913</td>
<td>148</td>
<td>16.0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>3-4</td>
<td>1091</td>
<td>465</td>
<td>43.0</td>
<td>1356</td>
<td>297</td>
<td>22.0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>5-6</td>
<td>1132</td>
<td>577</td>
<td>51.0</td>
<td>1307</td>
<td>329</td>
<td>25.0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>7-8</td>
<td>850</td>
<td>508</td>
<td>60.0</td>
<td>970</td>
<td>280</td>
<td>29.0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>9-10</td>
<td>704</td>
<td>47</td>
<td>68.0</td>
<td>579</td>
<td>195</td>
<td>34.0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>11-12</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>230</td>
<td>79</td>
<td>34.0</td>
<td>---</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4375</td>
<td>2211</td>
<td>51.0</td>
<td>5355</td>
<td>1331</td>
<td>25.0</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

ND = NOT DONE

Table 3 - Comparison of prevalence of anti-HAV in Saudi children between urban and rural areas in 1997.

<table>
<thead>
<tr>
<th>Area</th>
<th>No. investigated</th>
<th>No. positive</th>
<th>Percent</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>3636</td>
<td>763</td>
<td>21</td>
<td>0.0001</td>
</tr>
<tr>
<td>Rural</td>
<td>1719</td>
<td>568</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5355</td>
<td>1331</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

HAV IgG with respect to age in 1989 and in 1997 is shown in Table 2. The reduction was noted in each age group and was statistically significant (P<0.00001).

Discussion. The results of our 2nd community-based study clearly shows that there has been a dramatic decline in exposure to HAV among Saudi children during the past 8-10 years. The overall prevalence of 25% of anti-HAV IgG in Saudi children 1-12 years of age is close to the prevalence rates reported from Western Europe and North American children (0-20%) and undoubtedly reflects the remarkable improvement of hygiene and sanitary conditions that took place in the Kingdom during the past 10-15 years. The reduction in anti-HAV IgG was noted in all age groups and was dramatic in 9 regions (50%), significant but less dramatic in 4 regions (50%) (Al-Baha, Najran, Tabouk, and Al-Jouf), and no decline in one region (Gizan). It is of interest to mention that Gizan and Najran regions border neighboring Yemen to the South of the Kingdom which is highly endemic for HAV and there is a continuous movement of people across the border due to family relationship and proximity. The same situation applies to Tabouk and Al-Jouf at the North of the Kingdom which borders Southern Jordan, an area also known to be highly endemic for HAV.

The decline of anti-HAV prevalence has been a well-known epidemiological feature in other developing countries that underwent socioeconomic and hygienic improvements. This decline, however, is not without consequences. For example, the transition from high to low endemicity to HAV in developing countries has lead to explosive outbreaks due to viral cross-contamination from endemic to non-immune sectors of the population via food or water. An outbreak of HAV infection has been recently reported among Saudi children. Furthermore, this decline in exposure to HAV has led to acute HAV cases in adults working in pediatric wards, day-care centers, medical laboratories, and in travelers to less developed countries. It has been estimated that in unprotected European travelers to endemic countries the risk of hepatitis A is 3-20 per 1000 per month. For the Saudi population, travelers from low to high endemicity region will have a risk acquiring this infection.

Our study raises the question of whether wide-scale use of HAV vaccine should be recommended in Saudi Arabia at this stage or whether vaccination should start in some regions only. We believe at this stage that the cost of the vaccine and the duration of immunity are 2 factors that have to be carefully evaluated before a decision on wide-scale use of HAV vaccine can be taken. In the meantime, an effective nationwide surveillance program for monitoring acute hepatitis A cases in the country should be established to determine the extent of morbidity related to HAV infection.

References
Gastroenterol Hepatol 1996; 8: 300-305.