Sero-epidemiology of hepatitis A in black South African children

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Abstract **A community-based sero-epidemiological survey was undertaken to determine the age-specific prevalence rates of hepatitis A virus (HAV) infection in a representative sample of 782 urban black children aged from newborn to 13 years. Among children aged 0 - 5 months, the prevalence of anti-HAV was 68,8% (95% confidence interval (CI) 60,6 - 77,0%); this fell to a low of 2,5% (CI 0,1 - 4,9%) in those aged 6 - 11 months, implying the presence of maternal antibody in the first few months of life. By the age of 2 years, 51,2% (CI 45,7 - 56,7%) had anti-HAV, by age 4 the prevalence had risen to 81,4% (CI 75,5 - 87,3%) and by age 6, the prevalence of anti-HAV was almost 100% (CI 90,5 - 96,7%), reflecting the poor socio-economic and environmental conditions these children live in. The lowest prevalence of HAV infection among urban black South African children was during infancy, before the age at which the incidence rate rose sharply; e.g. 1 out of 5 children was already infected with HAV by its 2nd birthday. Vaccination in infancy will therefore have the biggest impact on the spread of HAV. However, before HAV vaccination in infancy is advocated, vaccine immunogenicity in infancy and the possible detrimental effect of maternal antibodies on the immunogenicity of the vaccine need clarification.**

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Hepatitis A virus (HAV) is transmitted primarily via the faecal-oral route and outbreaks of the disease are therefore usually associated with poor socio-economic conditions.[1] In developing countries most children are infected at an early age,[2] while in developed countries outbreaks in crèches are an important source of HAV infection.[3]

In May 1969, viral hepatitis was declared notifiable throughout South Africa. In 1979 this proclamation was amended to include differentiation between HAV and hepatitis B virus (HBV) infections. South African notification data suggest that HAV infections have been increasing steadily since 1981.[4] Despite this, there has been a dearth of research on HAV infection in South Africa, apart from research on animal models[5,6] and laboratory diagnosis.[7] A possible explanation is that hepatitis A is regarded as a mild illness without serious sequelae.[8]

A recent article in the *SAMJ* highlighted this, stating that 'the epidemiology of hepatitis A infection in South Africa is uncertain, with very few sero-epidemiology studies having been undertaken'.[9] The scant available data suggest that HAV is very common among blacks in adolescence and adulthood; a study of black South African children failed to find a single subject over the age of 10 years who did not have anti-HAV.[10] In a select group of hepatitis patients in South Africa it was shown that anti-HAV was 100% prevalent in black patients whereas white patients had a substantially lower prevalence.[11] Neither of these two studies provides adequate data on age-specific prevalence rates of HAV infection.

In this sero-epidemiological study we report the age-specific prevalence rates of immunoglobulin G (IgG) antibodies to HAV in a representative sample of urban black children aged from newborn to 13 years. It is important to establish the age at which HAV infection becomes common so that the appropriate age for HAV vaccination can be determined and a rational HAV vaccination policy adopted.

Subjects and methods

The study was designed to provide a reliable representation of urban black children. The fieldwork was carried out in 1985 in Umlazi, a dormitory township south of metropolitan Durban. Running water is available in many of the established homes but not in the burgeoning squatter communities on the peripheries of the township. There is a clear lack of adequate solid waste disposal as evinced by a build-up of garbage in the general environment.

The method of sampling has already been described.[12] Altogether 805 children were selected. The sample was stratified into three age groups.

Group 1: 411 schoolchildren (205 boys; 206 girls) aged between 6 and 13 years were selected randomly from 10 schools in proportion to total school enrolment. School attendance in this age group is 93%.

Group 2: 343 children (163 boys; 180 girls) aged between 1 year and 6 years were randomly selected, viz. from every 17th household in 6 different sections of Umlazi.

Group 3: 51 infants (26 boys; 25 girls), ranging from newborn to 1 year of age, were randomly selected from the 7 Umlazi clinics, in proportion to clinic attendance.

The overall response rate was 83%. The mean age of the entire sample was 7 years and 3 months. After informed consent had been obtained, a questionnaire was completed by the parent and blood was drawn from the child.

All blood specimens were centrifuged on the day of collection and the separated sera stored at -20°C until tested in 1986 for IgG antibody to HAV (anti-HAV). Sera from 23 children were insufficient, therefore only 782 sera were tested for anti-HAV by means of radioimmunoassay with a commercially available test kit (Abbott Laboratories, North Chicago, USA).

Statistical analysis was undertaken with the Statistical Analysis System, release 6.03 edition, 1988 (SAS Institute Inc., Cary, NC, USA).

Results

Of the 782 children, 577 (74%) were positive for anti-HAV of the IgG class.

Among children aged 0 - 5 months, the prevalence of anti-HAV was 68,8% (95% confidence interval (CI)

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60,6 - 77%); this fell to a low of 2,5% (CI 0,1 - 4,9%) in the 6 - 11 month-old group, implying the presence of maternal antibody in the first few months of life (Fig. 1). By the age of 2 years, 51,2% (CI 45,7 - 56,7%) had anti-HAV and by age 4 years, prevalence of anti-HAV was 81,4% (CI 75,5 - 87,3%). Overall there were no significant differences in the prevalence of anti-HAV in boys and girls, therefore sex-specific data are not presented.

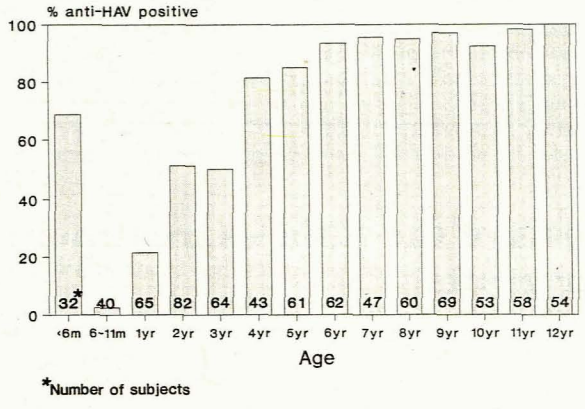

FIG. 1.
Age-specific prevalence of anti-HAV antibodies in Umlazi.

There was no association between anti-HAV and mother or father's educational level within the range of educational levels found in this township. After adjustment for age, the apparent association between anti-HAV and HBV markers was found to be spurious. A study from Hong Kong also showed that a correlation between anti-HAV and HBV markers could be created as a result of confounding by age.[13]

Discussion

HAV transmission is common in black children aged 1 - 5 years and continues to rise steadily until a prevalence of almost 100% is reached at the age of 6 years. This pattern of age-specific prevalence among black South African children mirrors that described in other developing countries.[2,14,15]

The rapid rise in the prevalence of HAV infection is a consequence of socio-economic and environmental factors which exert a striking influence on the transmission of HAV. Accordingly several studies have reported a declining transmission of HAV as socio-economic conditions improve.[16,17] This suggests the potential usefulness of periodic HAV seroprevalence surveys, in the absence of widespread vaccination, as measures of socio-economic and sanitary improvements in a particular community.

According to notification data, HAV infections have been increasing steadily since 1981, with a more rapid increase in the annual number notified since 1987. The 1990 notification data show that the incidence rate of HAV infection among blacks was a low 0,5/100 000 whereas among whites it was a high 15,8/100 000. This raises the question of whether the higher rates reported in whites reflect under-reporting among blacks or whether the majority of cases among black children are subclinical because of the early age of infection. The high prevalence of anti-HAV from a very early age which this survey demonstrated, suggests that the latter is likely to be the reason. Given this degree of differential under-reporting between the races, it is unfortunate that HAV notification data cannot be used to assess changes in environmental and sanitary conditions.

Following hepatitis A vaccine licensure in many European countries,[18] it is necessary to consider vaccine applicability in countries which have a typical developing country epidemiological profile for HAV infection. However, before advocating the widespread use of hepatitis A vaccine in childhood, certain issues such as the timing of vaccination and immunogenicity of the vaccine in infants need to be clarified.[19]

For groups which are at high risk of acquiring HAV infection, such as the staff at day-care centres and health care personnel, a clear case can be made for targeted immunisation. However, an attempt to control the spread of HAV in the general population will require widespread vaccination in the first year of life, well before the peak age of HAV infection. The prospect of including hepatitis A vaccine together with other common vaccines in the usual regimen given to infants is tempting but needs to be considered in the light of our findings that children up to the age of 5 months had a high prevalence of anti-HAV, which then decreased between the ages of 6 months and 1 year. If infancy is the appropriate age for vaccination, the currently unknown significance of the persistence of maternal anti-HAV antibodies in relation to its effect on hepatitis A vaccine immunogenicity needs to be elucidated. The importance of maternal antibody persistence for timing of other vaccinations has recently been highlighted.[20] The relevance of this point with regard to HAV vaccine is underscored by a study which showed that simultaneous administration of immunoglobulin with HAV vaccine resulted in a slight reduction in the immunogenicity of the vaccine.[23]

HAV infection is an indication of the extent of the public health problems in South Africa, since the early age of onset of HAV infection among black children reflects the poor environmental conditions in black townships in this country. Notwithstanding the prime role of socio-economic development strategies, vaccination presents a further opportunity to control the spread of HAV. However, before vaccination is advocated, age-specific prevalence rates of HAV infection and the possible detrimental effect of maternal antibodies on the immunogenicity of the vaccine must be considered when the most appropriate age for the administration of HAV vaccine is decided.

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