Hepatitis A virus (HAV) is a food and water-borne agent primarily transmitted by fecal-oral route and has worldwide distribution. Person to person spread from asymptomatic cases or during the incubation period of clinical cases represents an important transmission mechanism. The infection is usually self-limiting with occasional fulminant hepatic failure and mortality and does not lead to chronicity. The first killed vaccine was licensed in 1991. Fortunately, though there are several genotypes of HAV, a single serotype exists. Thus, vaccine produced using any of the strains would be useful worldwide.

An inverse relationship has been observed between prevalence of HAV infection and standards of hygiene and sanitation in a community. Childhood HAV infections predominantly represent subclinical infections. With rising living standards most children are not exposed to HAV and therefore clinical hepatitis A in adults has become an important public health problem for industrialized nations. Such countries are attempting to formulate economically viable policies for control of the disease through vaccination.

Developing countries and hepatitis A

In developing countries, hepatitis A is hyperendemic on account of almost universal exposure of children to the virus leading to predominant subclinical infections and life-long immunity. Use of vaccine for prevention of hepatitis A was obviously therefore not considered. However, changing epidemiology forces these countries to suitably modify the views in relation to use of hepatitis A vaccine.

Most of the developing countries are in different phases of transition as far as hepatitis A is concerned. Most African countries, Bhutan, Nepal, Pakistan, Palestine, Syria, and Vietnam continue to remain hyperendemic for hepatitis A and need to be monitored with periodic surveys. A distinct shift in the age for maximum HAV exposure was documented in South-East Asian countries and China, parts of the Middle East and White people in South Africa. An explosive outbreak of hepatitis A reporting over 300,000 cases (47 deaths) and associated with consumption of raw clams in Shanghai, China in 1988 represents an example of the magnitude of HAV infection in susceptible population. Importantly, a serosurvey conducted in Shanghai in 1984 showed a biphasic increase with age, approaching 100 per cent only above the age of 50 years.

Indian scenario

As far as India is concerned, with over one billion population, over-crowded living conditions and lack of proper sanitation and education, hepatitis A continues to be a very frequent infection. Based on recent studies conducted in different parts of India (Pune, Mumbai, Delhi, Chennai), it is apparent that children from low socio-economic category continue to be almost universally exposed to HAV. Thus, at present this population does not qualify for immunization with hepatitis A vaccine. Based on age-stratified population surveys conducted in Pune in 1982, 1992 and 1998, a distinct change in the degree of exposure to HAV was demonstrated only in population belonging to higher socio-economic status. In fact, lower socio-economic status was independently associated with a 23-fold higher risk of HAV infection. A very high exposure of children from lower-middle socio-economic status remained unchanged during the observation period of 16 yr. Based on a hospital-based survey a significantly lower exposure of higher socio-economic group (64.5%) compared with the lower socio-economic group (85%) was documented from Mumbai.

It is important to consider here studies reporting lower exposure of populations to HAV. A Delhi-based study reported a significantly lower anti-HAV positivity in subjects < 35 yr (57%) than > 35 yr (92.1%). Surprisingly, no difference with respect to socio-economic status was
noted. The same group recorded that 37.4 per cent of the first year medical students were anti-HAV negative. Whether the drastic differences in anti-HAV seropositivity reflect distinctly different populations screened by these investigators is not clear. There seems to be an urgent need to address this issue.

Based on limited samples (n=90, 2-64 yr), 69 per cent children below 10 yr and 25 per cent of children below 15 yr from Hyderabad were found to be anti-HAV negative. The anti HAV antibody positivity was similar in different income groups, probably because of small sample size.

Analysis of 1612 subjects representing 5 cities from different parts of India (Kolkata, Cochin, Indore, Jaipur and Patna) showed that anti-HAV positivity varied from 26.2 to 85.3 per cent. Almost 50 per cent children between the age of 1-5 yr were found to be susceptible to HAV. Interestingly, municipal water supply and not family income, was associated with exposure to HAV.

Based on the studies conducted so far, it is clear that in the recent past a substantial susceptible pool is generated in India along with majority of the population still in the hyperendemic state excreting the virus in feces. With contamination of water with HAV containing feces, which seems very likely on account of the prevalent system for sanitation and supply of drinking water, epidemics of hepatitis A seem a distinct possibility.

**Vaccination and long-term immunity**

Duration of immunity is an important concern for developing countries. If the policy of childhood immunization is adopted, in the absence of desired long-term immunity, exposure to HAV in adulthood would lead to severe clinical disease, especially because circulation of HAV continues in a substantial proportion of the population. The recent estimates predict protective immunity at least for 20 yr without additional boosters.

**Age of vaccination**

With the availability of hepatitis A vaccine in India, many pediatricians are immunizing infants with this vaccine. This is a serious issue. Interference of maternal antibodies with immune response to hepatitis A vaccine has been shown. With almost all the mothers from lower socio-economic status and most from higher socio-economic status being anti-HAV positive, early immunization of babies born to anti-HAV positive mothers may be futile and may lead to questioning of the efficacy of the vaccine. Based on a study of 499 children aged 3 days - 6 yr, concluded 9-10 months to be appropriate age for vaccination. However, it may be necessary to conduct a study on effect of maternal antibodies on the immune response in our settings before definite guidelines can be provided.

**Target populations for vaccination**

Though universal immunization of newborns/infants seems to be the best option for control/elimination of hepatitis A, the same does not seem to be practical even for developed nations. So far, Israel is the only country adopting the policy of universal immunization. Based on the prevalence patterns and financial constraints, each country needs to formulate its own immunization policy.

**Carriers for hepatitis B & C**

For countries with high HBV or HCV carrier rates, exposure to HAV later in life can lead to serious complications. During Shanghai epidemic in 1988 (carrier rate ~ 10%), an elevated mortality rate was observed in hepatitis B surface antigen (HBsAg)-positive patients (0.05%) in Thailand and Hong Kong, HBsAg-positive adolescents and young adults were particularly prone to severe hepatitis A infection. Immunization of such carriers yielded desired immune response. The tribal populations from Andaman & Nicobar islands with very high HBsAg carrier rate in both adults and children showed a decline in anti-HAV positivity in children aged 10 yr. Immunization of these tribes with declining numbers may be considered probably following pre-vaccination screening.

As far as adult chronic hepatitis patients are concerned, over 97 per cent anti-HAV positivity was shown among Indian patients excluding possibility of HAV infection being of any significance in this category and therefore not constituting target group for hepatitis A vaccination.
Day care centres

Day-care Centres have become mandatory for a modern society. Several countries including India have reported outbreaks of hepatitis A among children from such centres\(^27\). A community outbreak was associated with an original infection from a day care centre\(^28\).

Sewage workers/Food handlers

Considering the presence of HAV in the feces of infected persons, sewage workers and food handlers in low endemic areas could be important constituents in the transmission of the virus. Studies conducted in Singapore\(^29\) and Israel\(^30\) showed 2.2 fold and no risk respectively in the sewage workers. In Taiwan, 78 per cent of food-handlers younger than 30 yr were anti-HAV negative\(^31\) needing hepatitis A vaccine. In India, at present sewage workers do not need the vaccine. Data from food handlers from different settings are not available.

Travelers to endemic countries

Probability of risk of transmission of various pathogens including hepatitis A virus was recently considered during Hajj in Saudi Arabia\(^32\). A similar possibility during Kumbh Mela or similar gatherings needs to be considered. In Nepal, 91 per cent of the foreigners and 95 per cent Nepalese were diagnosed as hepatitis A and E cases respectively during the same period\(^33\) emphasizing the need for adequate protection of the travelers against hepatitis A.

Military troops

Studies from Israel\(^22\) have shown that increase in anti-HAV negative recruits poses greater risk both in personal morbidity and military operational ability. The need for vaccine in this category is therefore obvious.

Several countries are opting for immunization of school children. Usefulness of a primary dose of the vaccine followed by a second dose after 6, 12, 18 months was recently shown in Taiwan\(^34\) and such a flexible schedule may prove useful in other countries as well.

Recently we investigated an epidemic of viral hepatitis involving over 100 cases in children (Chadha \textit{et al}, unpublished observations) and the etiology was HAV. This seems to be the first example of large-scale outbreak of hepatitis A in India and sets an alarm for the possibility of such outbreaks in future.

Serosurveys reported so far provide ample evidence of changing epidemiology of HAV in India, especially with respect to socio-economic status. However, a multi-centric population-based study using uniform criteria for enrollment and same test for anti-HAV screening would prove extremely useful in providing nation-wide guidelines for hepatitis A vaccination and to avoid unnecessary vaccine usage as well as to ascertain the optimum benefit for those needing the vaccine.

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