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The Impact of Hepatitis A Vaccination

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Abstract: *Worldwide the prevalence of Hepatitis A virus in various countries are grouped into high, intermediate low and very low endemicity. Even in USA having very low endemicity have incidence of acute hepatitis A of 12.0 cases/100,000 persons in 1995.To prevent mortality and morbidity related with Hepatitis A virus infection, after implementation of routine childhood Hepatitis A vaccination in USA the incidence of acute Hepatitis A infection has declined by 92% in 2007. Routine childhood vaccination has produced similar results in Israel, Spain, Australia and selected region of Italy. But in countries of Asia, Latin America, Middle East and Eastern Europe having intermediate or low endemicity , implementation of routine childhood Hepatitis A vaccination has not been done. Although there is variation in HAV sero-prevalence rates in these country due to economic growth and improving hygiene conditions in these countries. In India there is heterogenous exposure of Hepatitis A virus in different region of the country. There is transition of anti-HAV prevalence from high to intermediate endemicity in urban population which has lead to increase in frequency of acute viral Hepatitis A infection from 10.6% to 22.0% in five years period (1999-2003). A extensive nationwide epidemiological evaluation of anti-HAV sero-prevalence, cost-benefit analysis for HAV infection with subsequent framing of guidelines for the same is urgently needed in our context.*

I. Introduction

Hepatitis A virus (HAV) infects more than 80% of the population in many developing countries by late adolescence [1]. Anti-HAV prevalence in population worldwide has grouped countries into high, intermediate low and very low endemicity. USA accounts for low endemicity while Sub-Sahara Africa and Mongolia accounts for the high endemicity of hepatitis A virus (HAV) infection. Even in low endemicity areas the incidence of acute hepatitis A in USA was 12.0 cases/100,000 persons in 1995 [2]. Even this incidence of hepatitis A infection in USA varies by race, ethnicity (highest among Native Americans and Alaskan Native), location (highest in Western United States) and with age (highest in people of 5 to 14 years of age) [3]. The sero-prevalence of anti-HAV IgG in a Alaskan Village after an epidemic in 1993 was 49% [4]. The sero-prevalence of HAV antibody in Brazil (Transitional endemicity) at public child care centre in 2006 was 89.5% [5]. While the sero-prevalence of anti HAV in Turkey (Intermediate endemicity) varies among its own geographical region. In southern and eastern region of Turkey anti HAV IgG prevalence was 80% (5-9 yrs of age) and >90% (after 14 yrs). In central and western region the anti-HAV prevalence was 50% (5-9 yrs of age) and <80% (other age group) [6]. A study in school children (4-18 yrs of age) from Delhi in 2003 indicated 93.2% sero-prevalence of anti HAV IgG [7]. Young children have highest rates of infection and after often source of infection for others as they mostly remain asymptomatic with low hygiene practice [8]. Hepatitis A infection results in substantial morbidity with significant cost caused by medical care and lost work time. Approximately 11% to 22% of people who develop hepatitis A require hospitalization.

Active immunization using heat inactivated hepatitis A vaccine (Hepatitis A antigen derived from HM175 viral strain grown in MRC-5 cell culture - Havrix) has been approved for use in United States and throughout much of the world [9]. This group of vaccines are highly immunogenic. Mathematical models using data from adults suggest that protective level of antibody following completion of vaccination series could persist for 20 yrs [10]. The efficacy of inactivated vaccine (HM175 strain) was 94% (95% confidence interval : 79% to 99%) in a large field trial in 40,000 (approx.) Thai children of 1 to 16 years of age after two doses (360 ELISA unit per dose) administered 1 month apart [11]. Considerably herd immunity is also achieved in mass vaccination. There was 94% declining in number of reported hepatitis A cases following vaccination of approximately two thirds of children in a California County [12].

In developed countries with low anti-HAV endemicity, routine childhood hepatitis A vaccination has resulted in fall of incidence of acute hepatitis A infection. In USA, after implementation of 1999 recommendations the incidence of acute hepatitis A has declined by 92% i.e. from 12.0 cases/100,000 population (1995) to 1.0 case/100,000 population in 2007. This rate is to be reduced further for routine hepatitis A vaccination in all children of United States aged 12-23 months since 2006(2). The impact of universal childhood vaccination of Hepatitis A in Alaska was very significant. HAV incidence in all age group declined from 60.0 cases/100,000 population (1972 to 1995) to 0.9 case/100,000 poipulation (2002-2007). The decrease of incidence was largest (99.8%) among children aged upto 14 years [13]. Routine childhood vaccination has produced similar results in Israel, Spain, Australia and selected region of Italy. Hepatitis A vaccination

programs (1998) in Netherlands for migrant children (Turkish and Moroccan children) have shown to reduce incidence of HAV from 70.3 cases/100,000 population (2000) to 13.5 cases/100,000 population in 2005 [14].Recently, a study in USA mentioned that universal childhood Hepatitis A vaccination led to significant reductions in Hepatitis A related mortality and morbidity. The universal vaccination programme has been cost saving compared with a regional vaccination policy. Also the herd protection effects of Hepatitis A vaccination programs had a significant impact on Hepatitis A mortality, morbidity, and cost-effectiveness ratios [30].

Anti-HAV prevalence estimate suggest that middle-income region countries of Asia, Latin America, Middle East and Eastern Europe have intermediate or low endemicity as their sero-prevalence rates are declining with economic program and improved hygiene standards [15]. The variation in HAV sero-positivity supports a universal HAV immunization policy for children in countries of intermediate endemicity [6]. In Argentina after June 2005, the universal immunization in infants was introduced into the national immunization calendar. A comparative study showed that total Hepatitis A related and unspecified hepatitis cases decreased from 157,871 in 2000-2004 to 17,784 in 2006-2010 [31].

In Bangkok prevalence of anti-HAV (2000-2002 period) in people younger than 25 years was low (1.95%) but high (90.92) in people older than 25 years. This was due to profound socio-economic developments and significant improvement in sanitation and hygiene in preceding decade. Hence, to reduce the incidence of symptomatic disease of HAV infection in these young age groups HAV vaccination policy was desired [16]. A study from Taiwan showed 15% anti HAV prevalence in 948 subjects (age 0.3 to 63 years). There was minimum sero-conversion at ages ranging from 1 to 30 years. It also demonstrated decline in prevalence of HAV infection among children, adolescents and young adults. It was due to improvement in socio-economic status and environmental sanitation. Hence the risk of sudden outbreak exist due to travel and migration in that area. The role of HAV vaccination is important to prevent an outbreak in the community [17].

Similarly sero-prevalence of anti-HAV among adolescents and young adults in Korea is 10%. The incidence rate of viral hepatitis A in the area is 20 cases/100,000 population. Due to which these population group are susceptible to HAV injection. Hence an urge to promote Hepatitis A vaccination in children and consider catch-up vaccination for adolescents and young adults was needed [18].

The sero-prevalence of anti-HAV in Saudi Arabia was 18.6% in 2008 among 1357 students (16-18 yrs) of Madi Neh, Al-Qaseem and Aseer region. Among them the anti-HAV IgG prevalence in lower economic class student was 36.6%, lower middle economic class 16.6%, upper middle economic class 9.6% and upper economic class 5.1%. These variation in sero-prevalence can be nullified using universal HAV vaccination program [19]. The study indicates that these countries may have increasing burden of disease from HAV infection in future. Hence, they may benefit from newer expanded vaccination program in different regions based on anti HAV sero-prevalence in that region.

In India the age of acquiring hepatitis A virus infection is shifting from early childhood to adolescence and adulthood. Occasional reported outbreaks of HAV from Pune (2004) and Shimla in 2007 was due to mixing of sewerage water in the town water supply system [20]. There is heterogenous exposure of hepatitis A virus in different region of the country. The sero-prevalence of anti-HAV among Delhi school children (4-18 years of age) was 93.2% [7]. While sero-prevalence was 62.6% among medical students (mean age 19.9 years) of Delhi [21]. This difference of sero-prevalence may be due to less exposure of HAV contaminated food or water and increase in hygiene standards among medical students. In another study on anti HAV sero-prevalence in Delhi in year 2000 showed overall prevalence of 71.2%. The prevalence in subjects more than 35 years was higher 92.1% (186/200 persons) than in subjects with 57% (170/298 persons) of less than 35 years [22]. Hence the need for anti HAV vaccination is based on anti HAV sero-prevalence for that population specially in context with socio-economic group. A study at Hyderabad on sero-prevalence of anti HAV in adults was 94.4% (total 36 adults). 69% of children (33/48 children) below 10 years were sero-negative. This indicated that children below 10 years of age were susceptible to HAV infection and HAV vaccination was needed [23]. In Eastern India cities (Kolkata, Cochin, Indore, Patna, Jaipur) the sero-prevalence for anti-HAV was 65.9% in 1998. Seropositivity in 1-5 years age group was 52.2% while it was higher (80.8%) in persons aged 16 years or more. This epidemiological pattern of HAV prevalence indicated of intermediate endemicity [24]. Sero-epidemiology anti HAV in voluntary donors from Pune in 2004-2005 was 97.4% (persons > 25 years) and 90.4% in 18-25 years of age group. Among them HAV positivity was remarkably low in high socio-economic group (88.9%) compared to middle socio-economic group (88.96%) compared to middle socio-economic group (95.86%) in the study [25]. The transition of anti-HAV prevalence to intermediate endemicity in urban population has lead to increase in frequency of acute viral hepatitis A infection from 10.6% to 22.0% in five years period (1999-2003). Similar increase was seen in adults from 3.4% to 12.3% during same period [26]. A cost benefit analysis for HAV vaccination among population (1-25 years) of high anti-HAV prevalence (74.8%) was studied in Bangladesh. It was found that cost for vaccination with screening for anti-HAV was almost three times cheaper than vaccination without screening. Hence a policy based on screening for HAV antibody before vaccination was recommended in Bangladesh [27].

Socio-economic improvement has impacted HAV infection to shift from high to intermediate endemicity in many part of China. Vaccination schedule at ages 12 and 18 months for all healthy children was used in 2005. A Markov model was used to predict hepatitis A outcomes and cost. Analysis was run in five regions with anti-HAV prevalence of 50%, 50-69%, 70-79%, 80-89% and 90% respectively. It was found vaccination could gain quality adjusted life years (QALYs) through the whole country. More cost-effective vaccination was found in lower infection regions. The study suggested that universal childhood hepatitis A vaccination should be first administered in province with lowest infection level with knowledge accumulation. Further evaluating the zone of immunization would be considered to be expanded gradually from provinces with lower infection level to those with higher infection level [28]. However, HAV vaccination and changing life styles associated with booming economy has contributed to rapid decline in risks to acquire hepatitis A virus infection in China during a study period between 1990 and 2006 [29].

In Indian scenario the HAV exposure profile in the population is heterogenous. The age of acquiring Hepatitis A virus infection is shifting from early childhood to adolescence. This may lead to increase in incidence of symptomatic viral hepatitis A infection with risks of liver failure in young adults. People in areas with improvement in living standards and hygiene are more susceptible to HAV infection. A study at superspeciality hospital in India showed that 17.1% children and 6.72% of adults were suffering from acute viral hepatitis A infection needing hospitalization [30] . A extensive nationwide epidemiological evaluation of anti-HAV sero-prevalence, cost-benefit analysis for HAV infection with subsequent framing of guidelines for the same is urgently needed in our context.

The impact of mass HAV vaccination in whole birth cohort in Israel, Bahrain and in sub-populations or regions of Australia, China, Italy, Argentina,Spain had spectacular results. The disease incidence in vaccinated cohorts and also in the whole population have plummeted within few years of the start of mass vaccination. It also confers herd immunity if the main spreaders of the virus are targeted for immunization. This may encourage other countries of low endemicity to start mass vaccination against HAV. However, global disease burden of HAV is generally thought not to be high enough to justify such moves. Countries of Sub-Saharan Africa and parts of South Asia with high endemicity for HAV have almost no susceptible adolescents and adults. Countries of Asia, Latin America, Eastern Europe and Middle East have intermediate or low level of endemicity for Hepatitis A virus infection. The countries of these regions may have an increasing burden of disease from Hepatitis. A virus infection. They may benefit by introducing new or expanded HAV vaccination program in their disease control strategy.

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