Tackling the Hepatitis B Disease Burden in India

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Globally, approximately 240 people have been infected worldwide with hepatitis B Virus (HBV). India has approximately HBV carrier rate of 3.0% with a high prevalence rate in the tribal population. With a population of more than 1.25 billion, India has more than 37 million HBV carriers and contributes a large proportion of this HBV burden. While horizontal transmission in childhood appears to be a major route of transmission, the role of vertical transmission is probably underestimated. Blood transfusion and unsafe therapeutic injections continue to be important modes of transmission of HBV. There is a need for large field studies to better understand HBV epidemiology and identify high prevalence areas, and public health measures to prevent disease transmission and decrease the burden of the disease. (J Clin Exp Hepatol 2014;4:312–319)

Hepatitis B virus (HBV) infection continues to remain a significant global health problem. Estimates of the World Health Organization (WHO) suggest that more than 2 billion people worldwide have been infected with HBV. Of these, approximately 240 million individuals have chronic (long-term) liver infections and at risk of serious illness and death, mainly from liver cirrhosis and hepatocellular carcinoma (HCC). More than 780 000 people die every year due to the acute or chronic consequences of hepatitis B.[1–4]

Based on the prevalence of Hepatitis B surface Antigen (HBsAg), different areas of the world are classified as having high (≥8%), intermediate (2–7%) or low (<2%) HBV endemicity. Countries which have high endemicity (where ≥8% of the population is HBsAg-positive) include South-East Asia, China, most of Africa, most of Pacific Islands, the Amazon basin and parts of the Middle East. Countries with intermediate endemicity (2–7%) include South Asia, Eastern and Southern Europe, Russia and Central and South America. The areas with low endemicity (<2%) include United States, Western Europe and Australia.[5]

Since India has one-fifth of the world's population, it accounts for a large proportion of the worldwide HBV burden. India harbors 10–15% of the entire pool of HBV carriers of the world.[6] It has been estimated that India has around 40 million HBV carriers. About 15–25% of HBsAg carriers are likely to suffer from cirrhosis and liver cancer and may die prematurely. Infections occurring during infancy and childhood have the greatest risk of becoming chronic. Of the 2.6 Crore (26 million) infants born every year in India, approximately 10 Lakhs (1 million) run the life-time risk of developing chronic HBV infection.[7]

Epidemiological data on HBV infection is therefore important for strategies to tackle the spread of the disease. It is imperative to reliably determine the burden of HBV disease in India, to identify any areas with higher endemicity than the rest of the country and to understand the risk factors associated with transmission of HBV. As a result, focused efforts can be made to prevent the spread of HBV, and thereby reduce the burden of HBV related chronic liver disease in the country.

EPIDEMIOLOGY OF HEPATITIS B VIRUS IN INDIA

There is a lack of large-scale population studies of the prevalence of HBV in India. Most of the available data is based on blood bank screening which can have its inherent biases and may not truly reflect the national prevalence.

The overall rate of HBsAg positivity has been reported to range between 2% and 8% in most studies.[8–10] The widely quoted figure of a carrier rate in India of 4.7% with an estimated carrier population of 56.5 million[9] may be an exacerbation. This estimate, which was based on the results of 19 studies, has some flaws that may result in overestimation. Many of these studies were based on data from blood bank donors, including professional blood donors who are known to have a higher prevalence of HBV infection. Moreover, the average prevalence of

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Abbreviations: HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HBV-DNA: hepatitis B virus deoxyribonucleic acid; HCWs: health care workers; HIV: human immunodeficiency virus; IVDU: intravenous/injecting drug user
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4.7% has been arrived at not as a weighted average but by calculating the simple average of the numbers in the individual studies.[11] Lodha et al[12] did a systemic review of literature of prevalence of hepatitis B in India and concluded that the true prevalence of hepatitis B in India was 1–2%. However, no statistical tool was used in the systemic review to synthesize the results of the different studies.

A meta-analysis found the point-prevalence of HBV to be 2.4% in non-tribal populations and 15.9% among tribal populations.[13] However, a disproportionately high amount of data is from a few areas. In a repeat calculation of the prevalence of HBV in India using population-weights, it was estimated that the point-prevalence of hepatitis B among non-tribal and tribal populations was 3.07% [95% CI: 2.5–3.64] and 11.85% (CI 10.76–12.93) respectively and the overall prevalence was 3.70% (CI: 3.17–4.24) (corresponding to a chronic carrier rate of 2.96%).[14] India has a population of more than 1.25 billion, and with an estimated prevalence of 3% HBV carrier rate, India is likely to have more than 37 million HBV carriers.

The data from various studies show wide geographic variations, which may represent differences in socio-economic status or cultural practices in different regions.

Population Studies

There is a paucity of population-based epidemiological information regarding hepatitis B virus (HBV) infection in India. According to the WHO report on prevention of HBV in India,[10] HBsAg prevalence among general population ranges from 0.1% to 11.7%, being between 2% and 8% in most studies.[15–25]

In the first large general population-based epidemiological study of HBV infection from India, Chowdhury et al[26] assessed the prevalence of serological markers of HBV infection in 19 villages in Birbhum district of West Bengal in Eastern India. Of the 7653 individuals who were included in the study, 227 (2.9%) tested positive for hepatitis B surface antigen (HBsAg), of whom 204 (90%) were HBeAg-negative and hepatitis B e antibody (anti-HBe)-positive, and 78% had normal alanine aminotransferase levels. HBV-DNA could be detected by polymerase chain reaction in only 32% of people.

Studies in Tribal Populations

A very high prevalence of HBV has been reported from the tribal population. The point-prevalence of HBsAg in the Idu Mishmi tribe of Arunachal Pradesh, which has common ancestral roots with the Lhoba tribe of Tibet, was found to be 21.2%.[27] Very high levels of HBsAg positivity have also been reported in the tribes of Andaman and Nicobar Islands (Nicobarese tribe—23.3%, Shompen tribe—37.8%, Jarawa tribe—65%).[28,29] The prevalence of HBsAg in Baiga tribal population of Madhya Pradesh was 4.4%.[30] Joshi et al[31] studied 11 different tribal populations of five districts of Madhya Pradesh and found HBsAg carrier rate of 2.99–21.54% among the various tribes. The prevalence of HBsAg was seen in 5.16% in Lambada tribes in the state of Andhra Pradesh, South India.[32]

The high endemicity of HBV infection in the tribal populations has been attributed to inbreeding, poor hygienic living conditions, close person-to-person contact and certain socio-culture practices that may facilitate transmission of HBV.[33]

Blood Bank Data

Blood bank data can have its inherent biases. On the one hand replacement donors have been seen to have a higher prevalence of HBV infection. On the other hand, persons with history of liver disease, known HBV infection, or even risk factors for HBV infection may either not volunteer for blood donation or may fail the strict prescreening by blood banks.

Notwithstanding this, blood bank data cannot be ignored as with the scarcity of large population studies, much of the data on prevalence of HBV in India is based on blood bank data.

Many of the blood banks show HBsAg prevalence was 0.2–4%, most of which have prevalence much lower than that of the commonly quoted prevalence data.[34–48]

Pregnant Women

Earlier studies have shown a prevalence of HBsAg positivity of 2.3–6.3% in pregnant women.[49–52] A large study involving 8575 pregnant women from Northern India, documented HBsAg carrier rate in antenatal mothers to be 3.7%, HBeAg carrier rate 7.8% and vertical transmission was observed in 18.6%.[53] However, a recent study by Dwivedi et al[54] has shown a lower prevalence rate of 0.9%. Moreover, unlike most studies showing lower levels of HBeAg positivity in HBV infected pregnant women,[8,53] Dwivedi et al[54] reported a high replicative rate, with 56.8% of the patients being HBeAg positive.

RISK FACTORS AND TRANSMISSION IN HIGH-RISK PERSONS

In comparison to these relatively lower prevalence rates of HBV in South Asia, the South-East Asian countries in general have a higher prevalence with the highest rates in Taiwan (>10%) and Thailand (>8%).[55] Despite the lower socio-economic status, illiteracy, low immunization rates, regional conflict and high-risk tribal populations, the prevalence of HBV is lower in India and the rest of South Asia as compared to South-East Asia.[56] Despite all the odds, this lower prevalence of HBV in South Asia may be due to the fact that unlike the vertical transmission of HBV in South-East Asia, the predominant mode of transmission is horizontally in South Asia.[57,58] Chronic HBV infection

in India is acquired in childhood, presumably before 5 years of age, through horizontal transmission.

This difference in transmission of HBV in South-East Asia and South Asia may be related to variations in genotype distribution and mutations in the HBV genome. Different genotypes may be preferentially transmitted by different modes.[59] In highly endemic areas where vertical transmission is the primary mode of transmission, Genotypes B and C are most prevalent. In contrast, in areas where horizontal or sexual transmission is more common, HBV genotypes A, D, E, F and G are commonly found. Pockets of high prevalence of genotype C in Arunachal Pradesh also have a high prevalence of HBV. Infection with HBV genotype A is associated with increased replication and high concentration of HBV-DNA in body fluids of HBV carriers, which may lead to an increased risk of horizontal transmission.[60,61] HBV genomic heterogeneity may also play an important role in HBV intrauterine infection and certain mutations in preS1 region, preS2 region and S region might infect fetuses more readily.[62]

In south Asia, the horizontal transmission is likely occurring at a younger age group. The exact mode of horizontal transmission is not defined but it may be due to contact of non-intact skin or mucous membranes with tears, saliva or blood containing secretions or through sharing of toothbrushes. The age of acquisition of HBV is an important determinant of outcome; the earlier the age, the higher the likelihood of chronicity. The risk of chronicity in HBV infection acquired at different ages ranges from >90% in newborns, 30% in children aged 2–5 years and <5% in adults. Neonates with vertically acquired HBV infection have a higher chance of chronicity and serve as a reservoir of the infection. On the other hand, infection acquired in adulthood is more likely to present as acute hepatitis B and contribute less to the burden of chronic HBV.

Parenteral transmission is also an important route of transmission of HBV and occurs through transfusion of infected blood or blood products, intravenous drug use, unsafe therapeutic injections, occupational injuries or nosocomial transmission during healthcare related procedures such as surgery, hemodialysis and organ transplantation. Injection drug use is not as widespread in India being encountered in only a few limited pockets.

Occupational Exposure in Health Care Workers (HCWs)

The risk of contracting HBV by HCWs is four-times greater than that of general adult population.[63] While earlier studies had shown a high prevalence of HBsAg positivity in HCW (2.21–10%),[64,65] recent studies have shown a relatively low prevalence (0.4–1.4%).[66–69]

Needle-stick injuries are commonly reported among nurses and lab technicians and commonly take place in ICU.[70] Shriyan et al[71] in a 2 year surveillance study have reported that 59/255 (23.13%) of HCW had needle-stick exposure. The highest rates are seen among dentists, physicians, laboratory workers, dialysis workers, cleaning service employees, and nurses.[72] Khakhkhar et al[73] found that HBsAg positivity was highest among laboratory technicians (4.1%) followed by nurses (1.7%). However, the positive rates of HBsAg were the highest for the HCWs with greater than thirty years in job, with overall positivity of 2.4%, suggesting greater exposure to blood and other recognized risk factors.

Transfusion of Blood and Blood Products

Transfusion-transmitted infection is a major challenge to the transfusion services. The prevalence of HBV infection reported by various authors from India ranges from 2 to 69.2%.[74–77] An earlier report of 1995 had shown that 69.2% of thalassemic patients had HBV infection.[74] However, subsequent reports have however shown a lower prevalence of HBV infection in thalassemics. Vidja et al[77] in 2011 have shown that only 2% of 200 multi-transfused patients of beta thalassemic major had HBV infection. The decrease in seropositivity may be because of implementation of measures such as (1) donor education, (2) strict standards for donor selection criteria, (3) improved serological screening protocols and (4) improved blood collection and transfusion techniques.

Unsafe Injection Practices

It is estimated that about 16 billion injections are administered each year worldwide and at least half of them are unsafe. India contributes to 25%–30% of the global injection load.[78] In India, injections overprescribed and unsafe injection practices are common.[79,80] Injections are often used unnecessarily for common self-limiting illnesses, with illiterate patients often demanding injections believing these to be more efficacious than the oral route. The annual frequency of injections is estimated as 2.9 per person, almost double of that in developed countries.[78]

Of the nearly 3.0 billion injections are administered annually in India, 1.89 billion are estimated to be unsafe due to inadequate sterilization, use of faulty techniques or unsatisfactory injection waste disposal.[78]

Unsafe therapeutic injections are an important method of transmission of the disease. Outbreaks of viral hepatitis B have been linked to inadequately sterilized needles and syringes.[81–83] The estimated median population attributable fraction for chronic hepatitis B linked to injections in India was 46% while that for hepatitis C and HIV was 38% and 12% respectively.[84]

Transmission by Intravenous Drug Abuse

India has an estimated 1.1 million injection drug users (IVDUs).[85] The prevalence of HBsAg positivity was seen in 2.7–10.8% of IVDUs.[86–88] In high-risk populations

including IVDUs, truckers and attendees of sexually transmitted disease clinic in Amritsar, the prevalence of HBV infection was seen in 17.8%.[89]

Human Immunodeficiency Virus Infection

The prevalence of HBV infection in HIV-infected persons has ranged between 2.25 and 29.7%.[90–95]

Perinatal Transmission

It has been estimated that HBV infection is largely acquired by horizontal transmission in childhood and perinatal transmission plays a less important role.[53] However the knowledge of dynamics of HBV transmission is imprecise and the role of perinatal transmission and horizontal transmission of this disease among children is based on inadequate evidence. The contribution by vertical transmission may be underestimated if we look at the high prevalence of replicative markers in HBsAg-positive pregnant women as reported by Dwivedi et al.[54,96]

Sexual Transmission

HBV can be transmitted through sexual intercourse. Sexual transmission adds less to the chronicity burden but can result in acute hepatitis B. Occult HBV infection has been observed in 12.2% of HIV patients infected through sexual transmission.[97]

Dialysis and Renal Transplantation

The prevalence of HBV infection amongst dialysis patients in India varies from 5 to 13%.[98,99]

TACKLING THE BURDEN OF HEPATITIS B VIRUS INFECTION IN INDIA

The first step in tackling the HBV disease burden in India is to have a more accurate assessment of the burden of the disease. This is possible with multi-centric population-based studies. It is likely that such an effort would show a lower prevalence of HBV than oft quoted. However, despite this the large population of the country would still contribute to a large chunk of the HBV infected population of the world.

There is also is a need to map out areas of high endemicity levels within each States in greater detail. These areas of high endemicity should be the focus of intensive screening and protective measures.

There should be a focus on screening of high-risk individuals including IVDUs, persons who receive blood transfusions, acupuncture, tattooing, unsafe injection practices, HCWs at risk of occupational exposure, etc. Identification and if necessary treatment of the HBV infected persons would play a role in decreasing the spread of the disease. Screening of pregnant women is already in place at most centers.

And most important would be the role of health education not only of the population in general and the high-risk population in particular but also the HCWs to prevent spread of disease following blood transfusions, medical procedures and unsafe medical practices.

Vaccination

Hepatitis B vaccine is effective, safe and provides long lasting immunity. Since 1992, WHO has recommended global vaccination against HBV, and by 2009, 177 countries had already incorporated this vaccine in their national immunization program.[100] In countries that have implemented universal childhood hepatitis B immunization, this has resulted in a decline HBV carrier rates and long-term consequences including hepatocellular cancer. Since the institution of Taiwan's program of universal hepatitis B vaccination, the incidence of hepatocellular carcinoma in children has declined.[101]

However, for a long time, HBV vaccination was not being universally carried out in India for perceived economic regions. Various cost effectiveness and cost-utility studies had been carried out which show that inclusion of the HBV vaccine in the national immunization will be cost effective.[10] Aggarwal et al[102] used a decision analysis approach and Markov modeling to compare the costs and health effects in two single-year birth cohorts, one of these received hepatitis B vaccination and the other did not. The study showed that inclusion of hepatitis B vaccine in India's national immunization program would lead to a reduction in HBV carrier rate from 4.0% to 1.15%.

Introduction of HBV vaccine was pilot-tested in 14 cities and 33 Districts in 2002–03; extended to 10 States in 2007–08 and the immunization was expanded to the entire country in 2011–12.[103] Government of India has included HBV vaccine in the National universal immunization program in the entire country in 2011–12.[104] The pentavalent vaccine that included hepatitis B and Haemophilus influenzae in addition to diphtheria, pertussis, and tetanus was initially tried in a pilot study (in Kerala and Tamil Nadu). After encouraging results, the program was extended to the states of Goa, Gujarat, Haryana, Jammu and Kashmir, Karnataka, Kerala, Puducherry, and Tamil Nadu.[105] However, there are concerns regarding the safety and tolerance of the pentavalent vaccine.[106]

However, the coverage with three doses of HBV vaccine was found to be lower than similarly timed three doses of DPT vaccine. There may be several causes of the poor uptake of hepatitis B vaccine in India. These include poor management of vaccine stocks, poor record keeping, lack of staff training, and use of multi-dose vials were among the main reasons for low coverage of the hepatitis B vaccine. HCWs were often reluctant to open 10-dose vials of vaccine if only one or two children were available for vaccinations, because they were concerned about wastage.[104]

A recent study has evaluated the effect of inclusion of HBV vaccine in universal immunization program in India. The study was conducted in 5–11 year-old rural children in five districts in Andhra Pradesh where childhood HBV immunization began in 2003. The authors compared markers for HBV in HBV-vaccinated (born in 2003/2004; n = 2674) and HBV-unvaccinated (born in 2001/2002; n = 2350) children. The authors found evidence that supported the efficacy of HBV immunization program in an Indian field setting, justifying the decision to include it in the universal immunization program.[107] However, a critical look at the study shows that the immunological benefits of HBV vaccination leave a lot to be desired. The authors found that vaccination did not reduce hepatitis B carrier rate, which is the primary aim of the immunization program. HBsAg positivity was seen in was 0.15% among the vaccinated compared to 0.17% in those not vaccinated (P = 0.855). While anti-HBc, a marker of exposure to HBV infection (but not to hepatitis B vaccine), was higher than among unimmunized children (1.79%), it was also present in 1.05% of the immunized children. At 6 years of age, protective levels of anti-HBs antibody (10 mIU/mL) were present only in about 59% of those immunized. By 11 years, only 13% had protective levels. For a vaccine that results in protective antibody levels in 95% of vaccinated persons, these are disappointing results suggesting that there is a need to critically examine the HBV vaccination schedule and delivery of the program.[108] It is also of note that these were results of a stand-alone Hepatitis B vaccine, and the results of the pentavalent vaccine may even be lower.[109]

Avoiding Unsafe Injection Practices

There is a need to educate HCWs regarding the need to avoid unnecessary injections and to adopt safe injection practices to prevent the spread of HBV and other bloodborne infections. Safe injection practices include the use of aseptic technique, not to reuse syringes or fluid infusion sets for multiple patients, and use of proper precautions when multiple-dose vials are used.

The auto-disable syringe has been shown to be a cost-effective alternative to the reuse of syringes in India.[84]

Provision of Safe Blood and Blood Products

A survey of blood transfusion practices in India showed that screening for transfusion-transmitted infections is unsatisfactory, often poorly regulated, and enforcement of existing guidelines is poor.[110] A strict audit of blood banking practices is required to prevent transmission of the disease.

Use of nucleic acid testing (NAT) has been proposed for preventing transmission of HBV as well as other bloodborne pathogens in Indian blood donors.[111,112] While such a strategy would make the blood transfusions safer, this would add to the cost of blood screening and is therefore not routinely recommended.

Other Preventive Measures

There should be a greater stress on health education not only for HCWs and high-risk groups like IVDUs but also in the general public about modes of transmission of the disease and the preventive methods. Spread of HBV through body piercing, acupuncture and tattooing, etc. needs to be addressed by health education about preventive measures. Following universal precautions can reduce transmission of HBV infection in healthcare settings. The unnecessary use of blood transfusions, where these are not clearly indicated, should be curbed. Care to prevent needle-stick injuries and post-exposure prophylaxis in HCWs needs to be emphasized. IVDUs need to be educated about transmission of infection and to avoid sharing of needles and syringes.

CONCLUSIONS

India has approximately HBV carrier rate of 3.0% with a high prevalence rate in the tribal population. With a population of more than 1.25 billion, India has more than 37 million HBV carriers and contributes a large proportion to the worldwide pool of HBV carriers. It is important to carry out larger studies to better elucidate the epidemiology of HBV and identify high prevalence areas and simultaneously focus on improving public health measures to prevent disease transmission and decrease the burden of the disease.

CONFLICTS OF INTEREST

The author has none to declare.

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