

Comparison of Seroepidemiology and Transmission Modes of Viral Hepatitis B in Iran and Pakistan

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Hepatitis B virus (HBV) infection is endemic in the Middle East region and is associated with significant morbidity and mortality. Strict strategies are needed for prevention, diagnosis and management of HBV infection. Reviewing literature about seroepidemiology and modes of infection transmission in Iran and Pakistan performed. Iran is in low endemicity and Pakistan in intermediate endemicity of HBV infection, now. Therapeutic injections, vertical transmission, transfusion, cultural and special traditions like ear, nose piercing, and high risk groups are important risk factors in Pakistan. Prevalence of HBV infection is still significant in children. High risk behaviors, including injection drug use (IDU) and sexual contact are main routes of HBV transmission in Iran. Intensifying vaccination of high risk groups and control on interfamily transmission in both countries is necessary. Effective coverage of HBV vaccination, has more control on therapeutic injections, screening pregnant women for HBV infection, and follow-up of babies of the HBsAg positive mothers in Pakistan is recommended. Regional collaboration of the two countries may overcome the spread of infection by promoting universal vaccination in all provinces of Pakistan, screening of hepatitis B, education, and surveillance in high risk groups of Iran. To implicate effective vaccination by regional and international health units, and addiction control in neighboring countries is necessary.

Keywords: Hepatitis B, Seroprevalence, Modes of Transmission, Regional Strategy, Prevention, Iran, Pakistan

Introduction

It is estimated 2 billion people are infected with hepatitis B virus (HBV) worldwide, among them 350 million are chronic carriers (hepatitis B surface antigen (HBsAg) positive) ⁽¹⁾. The prevalence of HBV infection has been reported to be different in various parts of the developed and developing world ⁽²⁻⁸⁾. Pakistan in some references has low and in others intermediate prevalence of HBV. The prevalence of HBV infection is endemic and high in the Far East, parts of the Middle East and sub-Saharan Africa, and low (<2% HBsAg positive) in the United States, Northern Europe and Australia. Bahrain, Iran, and Kuwait are areas of low endemicity for hepatitis B infection. Cyprus, Iraq, Egypt, Jordan, Oman, Palestine, Yemen, and Saudi Arabia have high endemicity. Intermediate prevalence of HBV infection (2% to 7% HBsAg positive) is reported from Japan, the Indian

subcontinent, parts of central Asia, and the United Arab Emirates ⁽²⁾. This article reviews the available literature so far on the epidemiology and potential risks of transmission of HBV in Iran and Pakistan, compares the programs of the two countries and makes recommendations for the prevention of such transmission.

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Received: 23 Nov 2007

Revised: 5 Jan 2008

Accepted: 12 Jan 2008

Hep Mon 2007; 7 (4): 233-238

Seroprevalence of Hepatitis B in Iran and Pakistan

Pakistan

The national estimates for prevalence and/or incidence of HBV infection in Pakistan are unknown. With an HBsAg carrier rate of 2.16 percent in apparently healthy individuals, Pakistan can be categorized as an intermediate HBV prevalence region according to WHO classification⁽⁹⁾. Pakistan remains in the intermediate HBV prevalence areas while few population-based studies are available, the estimate is 4.5 million carriers, with a carrier rate of 3-4% for HBV⁽¹⁰⁾. In a study in Karachi, during an 8-year period ending 2006, 4.92% were HBsAg positive and the majority of carriers (78.9%) were aged 16-49 years, and 70.8% of those were male. HBsAg positivity in Karachi has steadily increased in frequency in our hands from 2.84% in 1998 to currently 4.92%. That a significant majority of those positive in all age groups were male warrants deliberation on the credible modes of infection, including homosexuality⁽¹¹⁾. Pre-employment screening revealed 2.6% HBsAg positivity among the healthy individuals in northern Pakistan⁽¹²⁾, 7% in health professionals⁽¹³⁾, and 2-14% in blood donors⁽¹⁴⁻¹⁷⁾. A study reviewed the frequency of serologic evidence of hepatitis B in volunteer and replacement blood donors in Lahore, Pakistan between the years 1996-2005 and reported that the frequency was declining gradually⁽¹⁸⁾. Moreover, some hospital-based studies have revealed that 30-42% of the cases of chronic liver disease^(2, 19) and 78% of the cases of hepatocellular carcinoma⁽²⁰⁾ were positive for HBsAg. The pattern of the liver disease may vary in different geographical locations. These variations are attributable to the differences in environmental factors, eating habits, socioeconomic factors and other reasons⁽²¹⁾. A study from Ayub teaching hospital, Pakistan shows viral hepatitis was more common, followed by enteric hepatitis, drug induced liver injury, biliary atresia and Criglar-Najjar Syndrome⁽²²⁾.

Iran

It was estimated that over 35% of Iranians have been exposed to the HBV and about 3% were chronic carriers⁽²³⁾. In 1979, the prevalence of HBsAg in Iran ranged between 2.5% and 7.2%⁽²³⁾. In a study performed on 250,000 healthy volunteer blood donors in Tehran, 3.6% of male and 1.6% of female donors were HBsAg carriers⁽²⁴⁾. The prevalence rate of HBsAg positivity is low now, with HBsAg carrier rate of less than 2%⁽²⁵⁾. In general

population, this prevalence was 1.7% and 2.49%⁽²⁶⁾ in 1992 and 1993, respectively. Another study showed that HBV prevalence is 1.07% in blood donors in Shiraz in 2000⁽²⁷⁾. The reported prevalence, ranging from 1.7% in Fars Province to over 5% in Sistan & Balouchestan⁽²⁸⁾. Fifty-one to 56% of Iranian cirrhotic patients were HBsAg positive^(29, 30). A recent study showed that the rate of hepatitis B carriers varied between zero and 3.9% with an average of 1.7%⁽³¹⁾. HBV prevalence has decreased dramatically in Iranian population during the last decade. Improvement of the people's knowledge about HBV risk factors, national vaccination program since 1993 for all neonates, vaccination of high risk groups such as healthcare workers and the introduction of disposable syringes for use in vaccinations, hospitals and clinics might justify this decrease⁽³²⁾.

HBV Vaccination in Iran and Pakistan

In 2001-2002 Pakistan received a grant from the Global Alliance for Vaccines and Immunization (GAVI) that has enabled the introduction of hepatitis B vaccination in routine Expanded Program on Immunization (EPI). Vaccination for HBV as part of EPI was launched in a nationwide vaccination campaign in 2004. It started the first phase of the program last year by vaccinating children less than a year old in just 11 of Pakistan's 100 districts. In a trial in urban areas of Karachi and Lahore concluded that it is feasible to improve the cost-benefit ratio and compliance of hepatitis B vaccination by means of a two-shots of the vaccine employed in the trial⁽³³⁾. Recently, in Pakistan, hepatitis B vaccine has been integrated in routine immunization schedule of neonates, with estimated hepatitis B immunization coverage of 65 percent in 2004. There has also been large-scale hepatitis B vaccination in Armed Forces personnel in the past 10 years (unpublished observation) and among health care professionals, with vaccination status of 86 to 98 percent⁽³⁴⁾.

In Iran, the HBV vaccination was done in 2 provinces in 1989, and in 1993 the vaccination was included in the Expanded Program on Immunization (EPI) countrywide with the aim of eradication of the infection. It was recommended for all infants, and high risk groups. After 13 years of implementation, the coverage has reached an appropriate level from 62% in 1993 to 94% in 2005. Evaluation of risk factors in HBV infected people is important for designing the strategies to control the disease⁽³²⁾. The overall seropositivity

rates between 1991 and 1999 in the age group 2-14 years reduced significantly. A significantly higher decline in HBV carrier rate in rural than urban areas was observed ⁽³¹⁾.

Why Hepatitis B Still is Common in Children of Pakistan?

In a study in Pakistan, hepatitis B was the leading cause of chronic liver disease in children followed by Wilson's disease and autoimmune liver disease ⁽³⁵⁾. Hepatitis B is still common in children in Pakistan, but not in Iran. Pakistan lies between middle to low income countries. Zuberi reported an 8% prevalence of HBsAg in pregnant women. Among them, 21% were HBeAg positive ⁽³⁶⁾ suggesting possible early childhood transmission of hepatitis B infection in the country. In low socio-economic settings, horizontal transmissions of HBV through contact with infected family member have also been reported ⁽³⁷⁾, but these findings are yet to be verified.

In a study ⁽³⁸⁾ in children that were screened for HBsAg, the infection was more prevalent in subjects who received therapeutic injections and the odd of a positive test for HBsAg was 2.2 in those receiving therapeutic injection as compared to those who did not. It is imperative for eradication of HBV infection that universal vaccination of all newborns be carried out together with education of the public to limit injections to those who are safe and clinically indicated. A number of HBV positive children received therapeutic injections from local general practitioners not using a new syringe. However, children receiving therapeutic injections with new needles and syringes also demonstrated a high prevalence of HBV. This could be explained by unlawful practices in the country of used syringes being washed and packaged for re-sale. It is estimated that about half of all injections administered in Pakistan involve re-used syringes ⁽³⁹⁾.

In Pakistani children, 22.4% of acute hepatitis is due to HBV infection ⁽⁴⁰⁾. Zuberi *et al.* described HBsAg prevalence of 2.5% in pregnant women and out of these 17% HBeAg and 61% anti-HBe positive. Low frequency of HBsAg and HBeAg in pregnant women makes vertical transmission a less important cause of transmission ⁽¹⁰⁾. To reveal the efficacy of passive and active immunoprophylaxis in preventing perinatal transmission of HBV in Iran, 823 children born to the HBsAg positive mothers received HBIG in addition to recombinant vaccine, which significantly increased the protection against HBV infection ⁽⁴¹⁾. In 1824 subjects in Nahavand, Iran HBsAg was positive in 2.3%. The most

frequent relatives of index cases infected were sons and daughters (32.2% and 23.5%, respectively) ⁽⁴²⁾. Pre-marriage prevention of HBV transmission seems cost saving ⁽⁴³⁾.

Risk Factors of Hepatitis B in Iran and Pakistan

Some traditions especially in male gender such as undertaking circumcision or regular shaves by street or saloon barbers who re-use fixed blades or razors, contamination of skin abrasions during self-flagellation in religious rites, and anal or oral homosexual contact are important in HBV transmission in Pakistan ⁽¹¹⁾. In a study in Iranian gypsies, the prevalence of HBsAg positive was 18% ⁽⁴⁴⁾. Facial shaving by barbers may be a risk factor in adults in Pakistan ⁽⁴⁵⁾. Reused syringes have been identified as a major risk factor for hepatitis B and C in Pakistan, a country facing a growing epidemic of these infections ⁽⁴⁶⁾. Interventions to limit injections to those who are safe and clinically indicated are needed to prevent injection-associated infections in Pakistan ⁽³⁹⁾. The use of glass syringes in administering therapeutic injections was common in the past, and is still in practice in most of the low socioeconomic settings in developing countries. The "boiling method" employed to sterilize glass syringes in most of the health facilities is inadequate for complete sterilization. Therefore, these glass syringes act as a source for transmitting HBV and other blood borne pathogens ⁽⁴⁷⁾.

Pakistan has one of the highest frequencies of injections in the world ⁽⁴⁸⁾. In a study, the seroprevalence of HBsAg and HBcAb positive in 1824 subjects of Nahavand of Iran in 2002 was 2.3% and 7.8%, respectively. History of surgery and imprisonment were the major risk factors for HBV infection ⁽⁴⁹⁾. Blood transfusion may be a risk factor for HBV transmission in Pakistan. According to one estimate, more than 1.5 million units of blood are transfused annually in Pakistan. It is also known that HBV may be present in blood donations derived from blood donors who are HBsAg negative and anti-hepatitis B core antigen positive ⁽⁵⁰⁾. The risk, though small, still needs to be taken into account especially in areas with high HBV prevalence. Anti-HBc screening of blood donations is not mandatory in Pakistan. The majority of blood donors (99%) are replacement donors, who come to donate for their relatives or friends. Volunteer donors (6.98% of all donors) had the lowest seroprevalence for the diseases. In asymptomatic volunteer male blood donors in Karachi, Pakistan, HBsAg prevalence in the male volunteer blood donors was 2%

(7048/351309).

On univariate analyses, death of a family member due to liver disease, dental treatment received from a unqualified provider, therapeutic injections received in the past, type of syringe used for therapeutic injections, intravenous infusions received in the past, bleeding during shaving at barber's and sexual intercourse with multiple partners were significantly associated with HBsAg positivity. Multivariate logistic regression analysis showed that after adjusting for age and ethnicity, cases were significantly more likely than controls to have received dental treatment from unqualified dental care provider, have received 1-5 injections, more than 5 injections during the last five years or have received injection by a glass syringe. Injury resulted in bleeding during shaving at barber's was also significant predictor of HBsAg positivity⁽⁵¹⁾. Further complicating the situation, 50% of blood bank facilities in Karachi regularly use paid blood donors. During pre-donation interviews, only a small minority of donors were asked their history of high-risk behaviors. Of particular note is that voluntary donors form the minority of donors in Pakistan in this study, and commercial selling of blood is possible.

In Iran, all blood donors are volunteers. In a study from Karaj, Iran a cohort study in 2001 to 2003, with historical controls, the prevalence of HBV infection increased after 16 years old. In Karaj, the risk factors for chronic hepatitis B were older age, male gender, being married, history of contact with hepatitis, extramarital sexual activity, intravenous drug use, major surgery, experimental dentist visit, and some jobs (police, barber and driver)⁽⁵²⁾. In a study, 2447 HBsAg positive blood donors from 1997 to 2000, were compared with 2425 HBsAg negative donors in Tehran. Factors predicting HBV infection included family history of hepatitis B infection, history of blood transfusion, hospitalization, unsafe sex, male gender, and living in city area⁽⁵³⁾. Another study in blood donors in Ghazvin revealed that close contact with an HBV infected person, extramarital sexual contact, history of sexually transmitted diseases and high risk jobs were independent risk factors for prediction of hepatitis B infection. Horizontal mode is more important than vertical transmission in this region of Iran⁽⁵⁴⁾.

Summary

Routes of HBV transmission in Pakistan include unsafe injections, blood, sex and transmission from

infected mothers to their babies. Widespread practices such as unsafe injections, improper disposal of hazardous waste, recycling of used syringes without proper sterilization, sharing needles by injecting drug users and unsafe sex are believed to facilitate the transmission of these infections, resulting in high prevalence rates in the country^(39, 55). The ideal public health approach to disease prevention and control is to use routine population-based surveillance data to monitor the magnitude and distribution of the disease, identify high-risk subgroups, guide national strategic plans for prevention and control, and evaluate intervention efforts. While population-based surveillance may not always be feasible, sentinel surveillance of selected subgroups can serve as a cost-effective and viable alternative. For bloodborne pathogens such as HCV, HBV and HIV sentinel groups often include blood donors, antenatal clinic attendees, commercial sex workers and military recruits. Continued education of the public and healthcare professionals will play an important part in control of this problem since injections in the healthcare setting in Pakistan are reported as a risk factor for acquisition of hepatitis B and C in adults as well as children⁽³⁸⁾.

Family physicians can play an important role in educating people about the prevention of these diseases⁽⁵⁶⁾. The objective to educate people and test them for hepatitis was successful through utilizing ethnic community leaders, religious organizations, health care professionals, and a collaborative health fair⁽⁵⁶⁾. Education of the public and health care providers regarding hepatitis and the importance of supportive relationships to clients seeking and receiving hepatitis screening and vaccination is recommended⁽⁵⁷⁾. Development of a broad based mechanism to develop a consensus on national policy positions, incorporation of appropriate guidance from the provinces, giving provinces an active participatory role in decision-making, garnering their support and clearly demarcating roles is suggested⁽⁵⁸⁾.

Conclusions

Health providers and policy makers should collaborate for risk factors of HBV infection transmission in this area and design effective preventive programs. Additional and better control on health state of refugees in Iran is recommended. Large-scale surveillance data for this disease to estimate prevalence variations in each area, vaccination, safe injection, education, better control

on transfusion are recommended in Pakistan. Infection control measures in health-care settings including safe injection practices and proper sterilization techniques of medical instruments and education of barbers about the significance of sterilization of their instruments may reduce the burden of HBV infection in this and similar settings. Proper disposal of infected materials, use of disposable syringes, screening of blood and blood products, use of disposable syringes and razors, sterilization of surgical and dental instruments should be carried out.

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