PREVALENCE IN NORTH INDIA OF HEPATITIS B CARRIER STATE AMONGST PREGNANT WOMEN

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Abstract. The study was undertaken to determine the hepatitis B carrier rate in North India along with the relative infectivity of the carriers. A total of 1,112 pregnant women were investigated for hepatitis B carrier state during their routine visits to antenatal clinics. All three tiers of the health care delivery system were included from four regions of North India. The sera were screened for the presence of hepatitis B surface antigen (HBsAg), hepatitis B "e" antigen (HBeAg), and antibody to hepatitis B "e" antigen (Anti-HBe) by third generation Macro ELISA tests. The average hepatitis B surface antigen carrier rate was 9.5%. The carriers were found to be of relatively low infectivity with HBeAg and Anti-HBe present in 12.0% and 25.3% of the HBsAg carriers respectively, and both these markers absent in 62.7%. It was concluded that in the past decade the hepatitis B endemicity in North India has probably increased, but the relative infectivity of the carriers remains the same.

INTRODUCTION

Hepatitis B is a disease of public health importance not only for its high prevalence and world wide distribution but also for its potential for chronicity leading to cirrhosis and hepatocellular carcinoma.

At present the number of persistent carriers of hepatitis B in the world are estimated to be more than 300 million (Maynard,1990). There is a wide variation in the prevalence of HBV infection and its sequelae in various population groups round the globe (Ramia *et al*, 1991; Sobeslavsky *et al*, 1980; Sung, 1990).

Both horizontal and vertical mechanisms are important in transmission of hepatitis B (Maynard *et al*, 1989; Sung, 1990) and their relative importance also varies geographically (Beasley *et al*, 1984; Francis *et al*, 1981; Ramia *et al*, 1991). Genetic determinants in various ethnic groups have been found to be responsible for the variation in incidence of infection and chronicity (Sung, 1990), and in the relative importance of perinatal or vertical transmission (Ghendon, 1990; Sung, 1990). Variation explained by genetic factors has been documented also for HBeAg-positivity in HBsAg carrier mothers (Beasley *et al*, 1977; Ramia *et al*, 1991). Studies have been undertaken by many scientific groups in India and the HBsAg carrier rate reported variably as 0.6% to 21.5%.

The present work was undertaken to determine the HBsAg carrier rate along with the relative infectivity in terms of HBeAg and Anti-HBe, amongst healthy pregnant women from antenatal clinics of all three tiers of the health care delivery system from four regions of North India.

MATERIAL AND METHODS

A total of 1,112 pregnant women were the subjects for this study and were sero-investigated during their routine visits to antenatal clinics. The sampling included antenatal clinics in district health centers, bigger hospitals and medical colleges in Delhi, Uttar Pradesh (North India), Rajasthan (North-west India), and Manipur (North-east India) : all three tiers of the health care delivery system were included from four States of India in the northern region.

Blood samples were collected observing usual precautions, serum separation was mostly performed in the Hepatitis Laboratory at the National Institute of Communicable Diseases (NICD). Samples from Manipur were transported as sera to the Laboratory, due to the greater distance between Manipur and Delhi. All the sera were stored at -20°C till tested.

The serum samples were screened for presence

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of hepatitis B surface antigen (HBsAg) by subjecting them to a third generation Macro ELISA (Bead ELISA) test (Auszyme Monoclonal from Abbott Laboratories). The sera tested as reactive for HBsAg were further screened for "e" antigen of the hepatitis B virus (HBeAg) and its specific antibody (Anti-HBe), using the Macro ELISA (Bead ELISA) test from Abbott Laboratories (HBe EIA).

RESULTS

Out of the 1,112 antenatal women serotested (598 from Delhi, 206 from Uttar Pradesh, 295 from Rajasthan, and 13 from Manipur), HBsAg was detected in 106 (67 from Delhi, 18 from Uttar Pradesh, 20 from Rajasthan, and 1 from Manipur) (Table 1). The average HBsAg carrier rate in antenatal women was thus computed as 9.5% for North India.

Sera from eighty-three of the HBsAg positive antenatal women were tested for HBeAg and Anti-HBe. Fifty-two sera (62.7%) were non-reactive for both the markers, 10 (12.0%) sera were reactive for HBeAg only, and 21 (25.3%) sera were reactive for Anti-HBe only (Table 2).

DISCUSSION

The present study was undertaken in order to find out the carriage rate for hepatitis B in North India and to assess whether perinatal or horizontal transmission is likely to be more important in building the carrier pool. This is significant at this point of time when India is considering its strategy for control of hepatitis B through immunoprophylaxis.

Endemicity patterns of HBV prevalence vary geographically (Maynard *et al*, 1989; Ramia *et al*, 1991). Classification of low, intermediate, and high endemicity depends on the HBsAg carrier rate being 0.2-0.5% (less than 2%), 2-7% and 8-20% (>7%), respectively (Maynard *et al*, 1989; Sung, 1990). The western world is reported to have low endemicity (Ramia *et al*, 1991; Sobeslavsky *et al*,

Table 1

Antenatal sero-screening for hepatitis B surface antigen (North India).

Name of region	Location of region	No. of antenatal women serotested	No. of samples positive for HBsAg
Delhi	National capital territory of India	598	67
Uttar Pradesh	a state in central North India	206	18
Rajasthan	a state in North-west India	295	20
Manipur	a state in North-east India	13	1
Total		1,112	106 (9.5%)

Table 2

Reactivity of HBsAg positive sera for HBeAg and Anti-HBe.

Total no. of HBsAg positive sera further tested = 83			
HBeAg+ Anti-HBe+	HBeAg+ Anti-HBe-	HBeAg- Anti-HBe+	HBeAg- Anti-HBe-
0 (0.0%)	10 (12.0%)	21 (25.3%)	52 (62.7%)

1980) whereas Africa, Asia, Middle East, South America and Eastern Europe have intermediate to high endemicity (Hsu-Mei *et al*, 1988; Maynard *et al*, 1989; Ramia *et al*, 1991). High risk or selective immunization is recommended for low endemicity areas and mass immunization for areas of intermediate and high endemicity (Maynard *et al*, 1989). For the Asian-Pacific region the endemicity has been reported as being from 0.1% to 26.0% depending on the ethnic groups (Sung, 1990), highlighting the need for actual determination of endemicity in any particular country rather than depending on any generalization.

Reports from Indian studies give the HBsAg carrier rate as 0.6% to 21.5% (Guha *et al*, 1988; Gupta *et al*, 1985; Jain, 1992; Joshi *et al*, 1990; Khatri *et al*, 1980; Nayak *et al*, 1987; Prasad *et al*, 1983; Shanmugam *et al*, 1978, 1982; Tandon *et al*; 1984) amongst different groups of healthy population (pregnant women, voluntary blood donors, staff and students of medical colleges, non-pregnant women, tribal populations, children, adults, etc) from urban and rural areas of various regions of India. These studies have used various technics from gel diffusion to radio-immunoassay, which makes the data non-comparable. The other drawback with these studies is that each sample population is small, patchy and institutional, and thus the results cannot be representative of India. A study was conducted in 1986 involving 8,575 pregnant women in two large hospitals in Delhi (Nayak *et al*, 1987), according to which the HBsAg carriage was reported as 3.7% (intermediate endemicity). The technic used for HBsAg screening was Micro ELISA (Organon, Netherlands) in that study.

In our study involving 1,112 pregnant women, the HBsAg carrier rate was found to be 9.5% (high endemicity). As compared to the study by Nayak *et al* (1987) we report a greater endemicity for HBsAg carriage in North India. This could be explained by our study coming almost a decade later and by our using Macro ELISA (Abbott) diagnostic kits which are perhaps of higher sensitivity.

Policy regarding hepatitis B immunization, *ie* the selective versus universal approach, is dependent also on assessment of the contribution of perinatal transmission to the overall rate of HBV carriage in the specific geographical area (Maynard *et al*, 1989).

The earlier in life the infection occurs, the greater the chance of becoming a chronic carrier (Nayak *et al*, 1987; Ramia *et al*, 1991; Sung, 1990). Thus an early age of infection substantially increases the burden of chronic carriage in endemic regions (Maynard, 1990). It may seem logical that in areas of high HBV endemicity, perinatal transmission must be high. But this is not always the case. The relative frequency of positivity of the "e" antigen (HBeAg) and "e" antibody (Anti-HBe) amongst hepatitis B carrier mothers (*ie* the infectivity status of carrier mothers) is an important factor that influences perinatal transmission (Maynard *et al*, 1989; Ramia *et al*, 1991; Sung, 1990) because the presence of HBeAg is indicative of active virus replication and high infectivity (Guha *et al*, 1988; Hsu-Mei *et al*, 1988; Nayak *et al*, 1987). Both Southeast Asia and Tropical Africa are high endemicity areas (HBsAg carrier rate 10%), but the HBeAg positivity is much higher (5%) in the former as compared to the latter (2%) and the perinatal transmission is 30-50% and 10-20% respectively (Maynard *et al*, 1989).

The HBeAg positivity in HBsAg carrier mothers has been documented as varying widely in various population groups (Ramia *et al*, 1991). This could be due to ethnic or environmentally related factors (Ramia *et al*, 1991). There is evidence that the expression of HBeAg seems to be genetically determined (Ghendon, 1990). Possibly the susceptibility to perinatal infection is also genetically determined because some studies indicate that there are differences in maturation of liver cells in new borns which can influence viral replication and thus the susceptibility to perinatal infection (Ghendon, 1990). Perinatal transmission is reported as more important in the Asian Pacific region, and horizontal transmission in Africa, Middle East and Latin America (Ghendon, 1990; Ramia *et al*, 1991; Sung 1990). Rates of HBeAg in HBsAg carrier mothers vary considerably from one population to another : 30-40% in Southeast Asia, 16-20% in Africa, 7-12% in Middle East (Ramia *et al*, 1991). Anti-HBe positivity has been reported in 18-36% of HBsAg carrier women amongst Asians and Africans in the USA and among the Japanese (Nayak *et al*, 1987).

Therefore, it is important to not only know the HBV endemicity in a specific population but also to know the relative prevalence of HBeAg and Anti-HBe amongst HBsAg carriers in that population.

In the present study it was observed that in HBsAg carrier antenatal women the positivity for

HBeAg and Anti-HBe was 12.0% and 25.3%, respectively, with 62.7% carriers being negative for both these markers. This compares well with data in a similar population group (antenatal women in Delhi) a decade ago where the rates for HBeAg and Anti-HBe were 7.8% and 30.1%, respectively, with 62.1% HBsAg carriers being negative for both these markers (Guha *et al*, 1988; Nayak *et al*, 1987).

In conclusion, we report a high endemicity of hepatitis B carrier state in North India based on our study of healthy antenatal women from all three tiers of the health care delivery system from four regions of North India. Considering the frequency of positivity of HBeAg and Anti-HBe amongst the HBsAg carrier women, the carriers have been found to be of low or intermediate infectivity thus decreasing the importance of perinatal transmission in constributing to the overall carrier pool. Our observations, when seen along with those of Nayak *et al* (1987) reveal that in the past decade the hepatitis B endemicity in North India has possibly increased, but the relative infectivity of the carriers has remained the same.

To the best of our knowledge this is the first study on such a large scale, spanning from the most peripheral health care point (district health center) to the most central (referral hospital), and covering the entire North India from east to west. But it suffers from the lacuna that it is not a field-based population study. This, coupled with the fact that it comments only on the situation in North India and not the entire country makes it inadequate for being the sole foundation for the decision regarding national HBV immunization policy for India.

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