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Hepatitis B Surface Antigen Carrier State among Asymptomatic Pregnant Women and Its Correlation with Vertical Transmission

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ABSTRACT

Hepatitis B virus (HBV) is a public health problem worldwide. It is highly endemic in Asia and Sub-Saharan Africa. Horizontal and perinatal transmissions are thought to be major modes of transmission in these countries. Therefore, the present study was carried out to assess the role of HBV in apparently healthy pregnant women and to assess the impact of replicating status of HBV in asymptomatic carrier mothers. Seroprevalence of Hepatitis B virus was determined among pregnant women attending antenatal clinic. Serum samples were collected and screened for HB_sAg, $HB_eAg$and anti-HB_e markers using Enzyme Linked Immunosorbent Assay (ELISA). The overall prevalence of hepatitis B surface antigen among pregnant women was 7.8%. The participant women were mostly of age group of 21-25 years. Infants born to asymptomatic HB_sAg carrier mothers were followed up for 3 months to determine the vertical transmission of HBV infection. The rate of transmission of infection from HB_sAg positive mothers to infants was 25% irrespective of HB_sAg status, whereas it was nearly 100% in case of HB_sAg positive mothers, supporting the conclusion that perinatal transmission is the major mode of transmission. The study revealed that prevalence of HB_sAg carrier state in the study area was significant enough to start routine antenatal screening for HB_sAg. Therefore, screening and immunization of pregnant women and infants should be made mandatory in the antenatal and postnatal programmes in hospitals, for the eradication of HBV infection.

Keywords: prevalence, HBV infection, HB_sAg, HB_eAg, anti-HB_e

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INTRODUCTION

Hepatitis B virus (HBV) occurs Worldwide and constitutes a serious public health concern. Globally, more than two billion people have been infected with HBV and 350 million people remain infected chronically and become carriers of the virus, and 1.5 million deaths occur from HBV related liver diseases, including end stage cirrhosis and hepatocellular carcinoma each year[1]. It has been estimated that up to 10% of the 350 million Hepatitis B chronic carriers arise in India. The carrier rate of Hepatitis B in India may vary in the different regions and is often quoted as being 4.7%[1-3]. In areas of intermediate prevalence like India[4-6] vertical transmission of infection from mother to infants is very important route of HBV[7-9]. It has been reported that 10-20% of women seropositive for HB_sAg transmit the virus to their neonates but the risk of acquiring infection for a neonate can be as high as 85-90%, if the mother is HB_eAg positive[10,11]. It is generally agreed that risk of chronic infection with HBV is inversely related to age of onset of infection. The probability of developing the carrier state following HBV infection is greatest in early life and decreases with increasing age. Up to 90% of babies born to carrier mothers become carriers and they are at a very high risk of developing chronic liver disease at a younger age[12] and represent the most important reservoir of infection in the community[13]. Thus prevention of transmission of infection in this group would be helpful to decrease overall carrier rate. Prevention of perinatal transmission is possible with immunoprophylaxis of risk babies shortly after birth[14]. Prenatal HB_sAg screening would identify infected mothers and thus allow immunization of their newborns with hepatitis B immune globulin (HBIG) and hepatitis B vaccine, a regimen that is 85-95% effective in preventing development of chronic HBV carrier state[15-17]. The present study was therefore carried out to assess the role of HBV in apparently healthy pregnant women and to study the impact of replicating status of HBV in asymptomatic carrier mothers in determining the vertical transmission of HBV to the children born to them.

MATERIALS AND METHODS

The study population consisted of 500 asymptomatic pregnant women attending antenatal clinics at the Institute of Obstetrics and Gynecology, Egmore, Chennai. The study was conducted for a period of 1 year. Pregnant women were informed about the study, potential benefits for their current and future pregnancies and verbal consent was obtained from them. Using a standard questionnaire, all subjects

were questioned for risk factors: history of abortion, caesarian, tattooing, blood/blood - product transfusion, surgical operation, and previous hepatitis of unclear etiology.

In all cases, maternal venous blood and cord blood samples were collected. After initial screening tests of maternal samples for HB_sAg, all sera were stored at -20˚C. the HB_sAg positive maternal samples were subsequently tested for HB_eAg, anti-HB_e. Cord sera from babies born to HB_sAg positive mothers were also tested for HB_sAg, HB_eAg. All positive test results were rechecked. Sera were tested for HB_sAg, HB_eAg, anti-HB_e with commercially available enzyme linked immunoassays (Organon Teknika, Netherlands). All laboratory tests were performed following the manufactures' instructions.

RESULTS

When the rate of HB_sAg positivity in the study group was analyzed, it showed that out of the 500 pregnant women tested, 39 were positive for HB_sAg giving an overall seroprevalence of 7.8%. The results of the seroprevalence study are presented in Table No.1. Most of the studied women (223, 44.6%) were in the 2nd trimester of gestation. This group also had the highest HB_sAg seropositivity of 11.65% (226/223), followed by those in the 3rd trimester of gestation with 9 (5.35%) of 168 screened while the 1st trimester had the least prevalence of 4 (3.66%) of the 109 screened (Table No. 2).

Table No. 1: Prevalence of HB_sAg in different study groups

S.No	Details	Number tested	HB_SAg positivity		95% CI
			Number	%	
1.	Asymptomatic pregnant women	500	39	7.8	(5.45-10.15)
2.	Children born to HB_SAg positive mothers	16	4	25	(3.78-46.22)

Table No. 2: Prevalence of HB_sAg based on trimester

Trimester	No. screened	No. positive	Prevalence (%)	95% CI
1st (1-3 months)	109	4	3.66	0.14-7.2
2nd (4-6 months)	223	26	11.65	7.45-15.87
3rd (7-9 months)	168	09	5.35	1.95-8.77
Total	500	39	7.8	5.45-10.15

On the basis of age groups, the highest prevalence rate (12%) was found among 21-25 years age group. The results show that there is increase in HB_sAg titers with increase in age up to 25 years followed by a decline. At least one seropositive case for HB_sAg was found in all age groups except in the age groups 41 – 45 association between age and seroprevalence of Hepatitis B infection ($p<0.05$) (Table No.3). None of the risk factors was significantly associated with detection of HB_sAg among the pregnant women. 85% of the HB_sAg positive subjects (33 of 39) had any one of the risk factors for hepatitis B infection, e.g., history of jaundice, surgery, or blood transfusion. The prevalence rate associated with predisposing factors showed that those who had previous history of abortion had the highest HB_sAg prevalence rate of 18%, followed by HB_sAg positive mothers (15%) with history of jaundice and those who had blood transfusion (12.8%). The results are shown in Table No. 4.

Table No. 3: Age specific seroprevalence of HB_sAg in asymptomatic pregnant women in Chennai (*n*=500)

Age group (years)	Number tested	No. of HB_sAg Positive	Prevalence (%)
16-20	59	2	3.38
21-25	121	15	12.4
26-30	119	13	10.92
31-35	97	8	8.24
36-40	61	1	1.63
41-45	43	0	0
Total	500	39	7.8

$X^2 = 19.42$, df = 5, $p<0.05$

Table No. 4: Assessment of risk of hepatitis B virus infection among HB_sAg positive and HB_sAg negative pregnant women

Risk factors		No. screened	HB_sAg positive (%)
Previous history of Jaundice	Yes	39	6 (15.3)
	No	461	33 (7.1)
Previous history of hepatitis	Yes	39	03 (7.7)
	No	461	36 (7.8)
History of blood transfusion	Yes	39	05 (12.8)
	No	461	34 (7.5)
Use of abortion	Yes	39	07 (18)
	No	461	32 (7)
Practice of tattooing	Yes	39	03 (7.7)
	No	461	36 (7.8)
History of surgery	Yes	39	03 (7.6)
	No	461	36 (7.8)
History of hospitalization	Yes	39	04 (10.2)
	No	461	36 (7.8)

In order to analyze the replicative status of the mother we did perform HB_eAg and anti- HB_e screening. Of the 39 HB_sAg positive samples, 16 (41.0%) were HB_eAg positive, 8 (20.5%) were anti- HB_e positive, 6 (15.33%) were HB_eAg and anti- HB_e positive and rest 9 (23.0%) were negative for both HB_eAg and anti- HB_e. Hence, 16 out of 500 (3.2%) of the study population were found to be infectious, with 70-90% chance of transmitting infection to their newborns. The 16 babies born to HB_sAg positive mothers, 4 had detectable HB_sAg in cord blood samples. Out of the 4 HB_sAg positive children, 3 children born to HB_eAg positive mother had acquired HB_sAg indicating the high rate of HBV transmission from HB_eAg positive mothers. Surprisingly, one anti- HB_e positive mother also transmitted HBV to her child. None of the 16 children born to HB_sAg positive mothers was HB_eAg positive (Table No.5)

Table No. 5: Relationship between maternal HB_eAg / Anti HB_e status and risk of perinatal HBV infection in infants.

S.No	Mothers HB_eAg/ anti- HB_e Status	No. positive (n = 39)	No. of infants (n = 16)	No. of infants infected with HB_sAg	No. of months followed up	Risk of transmission (%)
1	HB_eAg+ Anti- HB_e^-	16	3	3	5	100
2	HB_eAg– Anti- HB_e^+	8	4	1	5	25
3	HB_eAg+ Anti- HB_e^+	6	4	-	5	-
4	HB_eAg– Anti- HB_e -	9	5	-	5	-

DISCUSSION

India is an area of intermediate HBV endemicity, with the total number of HBV carriers in the general population estimated to be around 43 million[18]. The available data suggests that the majority of the carrier states occur in childhood[19]. The HB_sAg positivity in antenatal pregnant women in India ranges from 1-12.3% with a mean of 4.22 %[20]. In the present study, the prevalence of HB_sAg among the pregnant women was 7.8%, this is in accordance with reported average HB_sAg prevalence rate, which conforms to India's status as an endemicity area as reported previously.

In this study, women on their second trimester of pregnancy had the highest prevalence of 18.4%, contrary to observations of Lilavati *et al*[21] that the third trimester in pregnant women had the highest prevalence rate.The age of acquiring infection was found to be the major determinant of the incidence of HBV[22]. The greatest prevalence of infection occurs among individuals of reproductive age. This can be explained by the greater probability of exposure of these women to risk factors. When age specific prevalence was considered, age group 21-25 had a higher prevalence (12.4%). This finding is in contrast to HBV infection prevalence, which normally shows a linear rise with age reported by other investigators in pregnant women and in other studies[23-25]. This could be due to facts that we had a less number of subjects in the older age group. Such discrepancy could be due to the differences in study design, population and geographical distribution.

This study revealed an association between HB_sAg positivity and history of abortion. Having history of abortion increased the risk of having HBV infection compared with those who had not suffered such experience. As known, abortion is directly related to sexually active women, and one most important

mode of transmission for HBV is exposure to heterosexual partners[26]. Therefore, other reasons such as instrumentation during abortion and related activities may also serve as source of exposure.

Prevalence of HB_sAg positive mothers in our study was 41%. However the reported HB_eAg positive rates among HB_sAg positive pregnant women in India varies between 8% and 47%. Most studies show positive rates towards the lower end of this range[27-29]. Our results were in accordance with reported average HB_eAg prevalence rate, on comparison of our results with other studies from different countries on pregnant women showed variable results. This difference in hepatitis epidemiology in pregnant women in these countries could be of the regional variation, study population, traditional operation, sexual practices and medical exposure.

Maternal HB_eAg positivity in perinatal period is of great importance for the vertical transmission of HBV infection resulting in extremely higher rates of mother to infant transmission compared to infant born from HB_eAg negative mothers[30-32]. The transmission rate of HBV in HB_eAg positive mothers to their children is in the range of 58-90% with a mean of 73.76%. Transmission by mothers who are only HB_sAg positive (HB_eAg and anti- HB_e negative) ranges from 5.5-20% with a mean of 15.36%[33]. In our study, on analysis of impact of mothers, HB_eAg positivity on HBV transmission to their children revealed that 100% of HB_eAg positive mothers transmitted the virus to their children as reported earlier.

The study concludes that there is a significant HBV carrier problem in pregnant women in Tamilnadu. HB_eAg positive mothers transmit HBV to a higher degree to their children, anti- HB_e positivity does not rule out the possibility of HBV transmission. The study further confirms that HBV vaccination has to be given to all children born to HB_sAg carrier mothers.

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