Hepatitis B Prevalence during Pregnancy

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In order to determine the efficacy of a new hepatitis B immune globulin (HBIG), a phase 3, vertical transmission (mother to child) clinical interventional trial of hepatitis B virus (HBV) post exposure prophylaxis (PEP) was conducted at selected sites (*n*=15) throughout India. This required a large screening program for HBsAg positivity at prenatal clinics located in tertiary care hospitals. 36,379 pregnant women consented to be tested for Hepatitis B surface antigen (HBsAg) by Rapid Test and if positive-confirmed by ELISA. The weighted mean prevalence was 0.82% (95% CI, 0.72, 0.91). In conclusion, the prevalence of HBV carrier state during pregnancy in India in this study was low compared to previous reports.

Key Words: *Hepatitis B, India, Pregnancy, Prevalence.*

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The carrier rate of Hepatitis B in India may vary in the different regions and is often quoted as being 4.7%(1,2). This is a mean of means of various studies and includes high risk populations(2). In a systematic review and meta-analysis of the prevalence of HBV infection in India, Batham, *et al.*(3) found that the point prevalence among non-tribal populations is 2.4% (corresponding to a chronic carrier rate of 1.9%). A great majority of the transmission of Hepatitis B in India and other developing countries occurs by vertical transmission from an infected carrier mother to the neonate, intrapartum or antenatally. 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 may become carriers and they are at a very high risk of developing chronic liver disease at a younger age(4). It has been estimated that up to 10% of the 350 million Hepatitis B chronic carriers worldwide arise in India. The burden of disease globally by vertical transmission is significant and this has led to the development of prophylaxis protocols adopted by many countries to decrease the pool of chronic carriers worldwide.

We conducted this study in 15 centers all over India to assess the prevalence of hepatitis B in pregnant women, mainly from non-tribal urban regions. This was a part of a larger study to demonstrate the safety and efficacy of a new hepatitis B immune globulin (HepaGam^{TM} Cangene Corporation, Winnipeg, Manitoba, Canada) for post exposure prophylaxis.

METHODS

This study was conducted from November 2003 to July 2006. For the purpose of this short communication, the epidemiological data from the screening tests performed in 36,379 pregnant women at 15 centers will be reported. Study centers were selected for the study on the basis of expected screenings or enrolments into the study. All pregnant women attending the antenatal clinics of these centers were screened for HBsAg at 5-9 months of gestation after informed consent was obtained. We

used a rapid HBsAg test Kit (ACON Laboratories Inc, USA). A positive HBsAg test was confirmed by enzyme-linked immunosorbent assay (ELISA) after the pregnant woman signed the second part of an Informed Consent Form, consenting to her and her child's participation in the study. Bioelisa HBsAg ELISA kit (Biokit, Barcelona, Spain) were used according to the manufacturer's recommendations for HBsAg detection and absorbance was measured using an ELISA reader (MRX Microplate Reader, Dynatech, USA). The study was approved by DCGI (Permission No from DCGI: 12-51/2003-DC) and hospital ethics committees at each of the 15 institutions involved in this study, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and in accordance with the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, E6 Good Clinical Practices: Consolidated Guidelines, Food and Drug administration (FDA) regulations and IEC-required procedures.

This large scale screening program in 15 tertiary care hospitals throughout India identified 398 (***Table* I**) HBsAg positive women allowing some epidemiological data to be collected of the prevalence of HBV carrier state during pregnancy across all represented populations in India.

Statistical analysis: The number of patients in each study center varies so the mean might deliberately over-represent or under-represent certain segments of the population. To restore balance of the number of patients enrolled in each center, the prevalence of HBsAg positivity was estimated using a weighted pooled point estimate along with a 95% confidence interval(5). Using this method, less weight will be placed on the study center with smaller number of enrolled patients and greater weight on the study center with larger number of enrolled patients. All calculations were performed using SAS® version 8.2. RNTMC screened 472 subjects and 0 tested HBsAg positive by screening test kit, the prevalence rate at this center was corrected to read 0.001 in order to include this data into the formula for weighted prevalence rates (***Table* I**).

RESULTS

Out of 36,379 pregnant women screened, 406 were HBsAg positive by rapid screen Further testing of these 406 positive tests determined that 398 were positive by ELISA. Thus the false positivity rate of the rapid screen is 2%.

The range of prevalence of HBsAg positivity in pregnant women varied from 0.4% (VHBMC, Bangalore) to 4.6% (SJMCH, Bangalore) and the overall mean prevalence of HBsAg positivity was 1.09% (95% CI 0.99-1.21) and the overall weighted mean of the prevalence of HBsAg positivity was 0.82% (95% CI 0.72-0.91). It has been confirmed that the high prevalence of HBsAg positivity at SJMCH in Bangalore was due to pre-selection of the population at this hospital since it is a referral center for "infectious cases" for the area. The mean prevalence of HBsAg positivity and weighted mean of the prevalence of HBsAg positivity excluding SJMCH prevalence rate was calculated to be 1.05% (95% CI 0.95-1.16) and 0.81% (95% CI 0.72-0.90), respectively.

TABLE I PREVALENCE OF HBSAG AT PRENATAL SCREENING

Site Name	Screened	HBsAg Positive	Prevalence (%)
Pune	900	9	1
Chandigarh	2438	31	1.3
Panaji, Goa	1802	35	1.9
Bangalore*	1600	9	0.6
Bangalore+	2205	8	0.4
Hyderabad	3051	52	1.7
Nagpur	932	5	0.5
Baroda	4099	27	0.7
Udaipur	472	0	0
Bangalore	432	20	4.6
Lucknow	3403	42	1.2
Kolkata	5022	56	1.1
Mumbai	3180	25	0.8
Kolkata	4316	42	1.0
Pune	2527	37	1.5
Total	36379	398	Mean 1.09%
			Weighted Mean 0.82%

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WHAT THIS STUDY ADDS?

- The Hepatitis B carrier state prevalence in women attending antenatal clinics in tertiary hospitals in urban areas in India is less than 1%.

DISCUSSION

The prevalence of HBsAg positivity in pregnancy which was observed in this prospective, intervention study is less than 50% of previously reported non-tribal prevalence rates in systematic review of literature(2,3). The main limitation of the study is that the centers were located in urban areas and these centers were tertiary care referral centers. However, volunteer patients were not selected on the basis of referrals or walk-ins from the surrounding areas and not referrals except SJMCH, Bangalore. There is little change in weighted mean prevalence of HBsAg positivity excluding SJMCH (0.81%) compared to the overall weighted mean prevalence of HBsAg positivity including SJMCH (0.82%). This sample of patients screened and enrolled into the study may not be representative of the prevalence of hepatitis B infection in rural areas but is representative of the prevalence in urban areas.

The HBsAg rapid screen (Rapid Test Kit ACON Laboratories Inc, USA) was accurate in 98% of cases when used in a mass screening program of this nature and may be a cost effective means of screening pregnant women for HBsAg to identify at risk populations eligible for immunoprophylaxis of their neonates.

The weighted mean prevalence of HBsAg positivity in our multi-center prospective study was 0.82%, which is roughly less than one half of the previously reported point prevalence of HBsAg carrier state in non tribal populations in India(3). Consequently, the pharmaoeconomics of implementing an immuno-neprophylaxis program consisting of testing all pregnant mothers for HBsAg status and the administration of HBIG and recombinant hepatitis B vaccine within 12 hours of delivery to at risk neonates across the India may roughly be one half the previously estimated costs.

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Competing interests: Cangene Corporation provided study grant to the participating 15 tertiary care hospitals in India.

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Annexure

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