

Asian Pacific Journal of Tropical Disease

journal homepage: <http://www.apjtc.com>



Infectious disease research <https://doi.org/10.12980/apjtd.7.2017D6-331> ©2017 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

Magnitude of hepatitis B infection in pregnant women and in clinically suspected infectious hepatitis at a tertiary care hospital in Ghaziabad

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ARTICLE INFO

Article history:

Received 18 Sep 2016

Received in revised form 29 Sep, 2nd revised form 8 Oct, 3rd revised form 12 Oct 2016

Accepted 30 Oct 2016

Available online 16 Nov 2016

Keywords:

Prevalence

Hepatitis B virus

Hepatitis B surface antigen

Hepatitis B e antigen

Pregnant women

India

ABSTRACT

Objective: To determine the magnitude of hepatitis B virus infection in pregnant women and in clinically suspected infectious hepatitis at a tertiary care hospital in Ghaziabad.

Methods: This prospective study was conducted on 327 patients in the age of 18–65 years in Department of Microbiology at Santosh Medical College, Ghaziabad between December 2014 to June 2016. Five milliliter blood samples taken from each suspected patient with acute infectious hepatitis were analyzed. The sera were separated and screened for hepatitis B surface antigen (HBsAg) by immune-chromatographic card test then HBsAg positive serum samples were tested again for HBsAg using ELISA kit. Positive samples for HBsAg in pregnant women were tested for hepatitis B e antigen (HBeAg) by ELISA test.

Results: HBsAg was identified in 18 (5.50%) samples, including 7 (2.14%) males and 11 (3.36%) females. Among these 18 samples, 55.56% were from age group of 21–35 years, which was statistically significant ($P < 0.05$) as compared to the other age groups. Among 11 HBsAg positive females, six of them were pregnant and the prevalence of HBsAg positive pregnant female was 1.83%. Four females were positive for HBeAg and the prevalence of HBeAg positive pregnant female was 1.22%. A total of 50% ($n = 3$) HBeAg positive cases were found in age group of 21–35 years, which was statistically significant ($P < 0.05$) as compared to the other age groups.

Conclusions: Study showed that hepatitis B virus is prevalent in general population and in pregnant women. Screening and vaccination should be considered by health policy makers to prevent the transmission of hepatitis B virus.

1. Introduction

Hepatitis B virus (HBV) is a small-enveloped partially double stranded DNA virus causing acute and chronic hepatitis in humans. Despite the availability of a safe and effective vaccine, HBV infection still represents a major global health problem, around 240 million people chronically infected worldwide and approximately 600000 deaths per year due to HBV[1].

In India, the situation is that nearly 3%–4% of the population was infected by HBV, and chronic hepatitis B constituting more than

50% of the chronic hepatitis cases. Because of a vast populace of India and lacking of a national vaccination program would spell off an anticipated expanding weight of contamination and liver infections because of HBV in this nation. In this perspective, the HBV epidemiology in India has become relevant because of the possibility that India may soon have the largest HBV infection pool in the world[2]. In India, the prevalence of chronic HBV infection in pregnant females is 0.82% and during pregnancy, HBV infection presents the risk of vertical transmission[3].

Chronic HBV infection represents the main risk factor for the development of hepatocellular carcinoma. Chronicity is approximately 5% in adult infections, but it reaches 90% in neonatal infections. Though HBV does not induce direct cytopathic effects under normal conditions of infection. The ongoing immune reaction and a consistent inflammation of the liver are believed to produce liver damage (fibrosis, cirrhosis and eventually hepatocellular carcinoma)[4].

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The study protocol was performed according to the Helsinki declaration and approved by Santosh Medical College and Hospital. Informed written consent was obtained from patients.

The journal implements double-blind peer review practiced by specially invited international editorial board members.

HBV is easily transmitted through contacting with infected body fluids (blood, saliva, semen, vaginal secretions and menstrual blood) of infected individuals[5]. Perinatal vertical transmission is the most common mode of transmission worldwide. In households with a chronically infected individual, HBV infection can occur via person-to-person, nonsexual contact[6].

The neonates have 90% risk who born from mother infected with chronic hepatitis B due to the acquiring of chronic HBV infection and its persistence from mother. In contrast, when HBV is acquired during adulthood, only 5%–10% of adults develop persistent chronic HBV infection[6]. Most of the developed countries screen all pregnant women for HBV infection. However, in the developing countries, it depends upon the risk factors. In India, there is no consistent policy of screening the pregnant women across the country. A meta-analysis of the prevalence of hepatitis B in India showed 2.4% prevalence in general population. However, the prevalence rate of hepatitis B surface antigen (HBsAg) in pregnant women varied from 1%–9% in different parts of the country and the prevalence of e antigen among them varied from 4.8%–68.7%[7].

A large single centre study from North India on 20104 pregnant women showed a chronic HBsAg positivity rate of 1.1%[3]. Majority of the pregnant women with viral hepatitis B are considered as chronic hepatitis B but a few may develop acute hepatitis in the third trimester of pregnancy resulting in 1% fulminant hepatitis[8,9]. During pregnancy, acute viral hepatitis involves a particular risk both for the mother and the baby.

Of the two secretory proteins, namely, HBsAg and hepatitis B e antigen (HBeAg), HBsAg does not usually cross the placenta. However, small sized HBeAg passes through the placental barrier even with low maternal viral load titre[10]. In newborn, transplacental HBeAg can be detected at one month of age but it would disappear before 4 months of age. However, in a few infected newborns with HBV viral titres, persistent detection of HBeAg for more than 4 months strongly indicates HBV chronicity[11].

HBeAg spillage through placenta induces HBV specific T cell tolerance in utero and intrauterine infection could be the main cause of the failure of immunoprophylaxis[12]. However, there are several evidences showed that the incidence of intrauterine transmission is rare and only happens in case of placental leakage.

Infants, which born from HBeAg positive mothers are likely to be infected and progress to chronicity. However, infants born from HBsAg positive mothers develop acute hepatitis and less likely to progress to chronicity[10]. In North India, HBeAg positivity rate was 7.8%, and risk of perinatal transmission was 18.6% from HBsAg positive mothers vs. 3% among infants of HBsAg-negative mothers[13].

1.1. Effect of HBsAg and HBeAg on pregnancy

HBV infection does certainly affect the outcome of pregnancy and

influence spontaneous abortion, stillbirth or prematurity. Increased frequencies of reproductive casualties were reported in pregnant women with acute or chronic hepatitis B infection. With HBV infection, the incidence of preterm birth observed was quite high around 21.9% vs. 12.1% in healthy controls[14].

The gestational diabetes and antepartum haemorrhage were also associated with chronic hepatitis B infection[15]. In a case-control study, HBeAg positivity was proved to be more important with high HBV DNA levels in transmission of HBV to infants[16].

HBeAg positivity is the marker of replicative form of HBV which may cross the placenta and play a role in the immunotolerance in utero[17]. In HBV genotype C, HBeAg seroconversion is longer, which may be the reason for higher perinatal transmissions in this genotype[18]. Therefore, in prenatal screening of pregnant women, it is important to check the HBeAg status along with HBsAg.

The aim of present study was to assess seroprevalence of HBV in this area and the presence of HBsAg and HBeAg in pregnant and non-pregnant women as the HBV is increasing in India.

2. Materials and methods

2.1. Study background and subjects

This was a prospective study conducted on 327 patients with clinically suspected acute infectious hepatitis, attending out-patients and in-patients Departments of Santosh Medical College and Teaching Hospital, Ghaziabad, India, between the periods of December 2014 to June 2016.

Inclusion criteria: patients aged between 18–65 years with suspected HBV infections and its sequelae. Patients are pregnant women who have the ability to provide written informed consent.

Exclusion criteria: patients received any immunization for HBV and suffered co-infections such as HBV-hepatitis C virus, HBV-HIV, HBV-hepatitis delta virus. Patients with liver disease are due to other viruses, alcohols and diabetics.

2.2. Sample collection and processing

Five milliliter blood samples received in the Serology Section of Department of Microbiology from patients suspected of acute infectious hepatitis were analyzed. The sera were separated and screened for HBsAg by Hepa Card (J. Mitra & Co. Pvt. Ltd. New Delhi, India) and positive serum was stored in frozen (20 °C) until tested for the viral markers. The positive serum samples for HBsAg by Hepa Card were tested again for HBsAg using commercially available ELISA kit (ERBA Transasia Bio-medicals Ltd. Daman, India). Serum samples tested positive for HBsAg in pregnant were tested for HBeAg (ELISA; Beijing Kewei Clinical Diagnostic Reagent Inc. Beijing, China).

2.3. Statistical analysis

Obtained data were analyzed by using the SPSS software for windows version 18. The comparison of data in respect of age groups and gender were performed by *Chi-square*. $P < 0.05$ was considered to be statistically significant.

3. Results

Of the 327 serum samples, 139 (42.51%) males and 188 (57.49%) females were screened for HBsAg (Table 1). HBsAg were identified in 18 (5.50%) samples, including 7 (2.14%) males and 11 (3.36%) females (Table 2). HBsAg were tested in the patients with an age of 18–65 years. Of these, 55.56% ($n = 10$) were from 21–35 years age groups, this was statistically significant ($P < 0.05$) in comparison to the other age groups. However, there was no significant difference based on sex ($P > 0.05$).

Table 1

Age distribution among patients with clinically suspected infectious hepatitis.

| Age group (years) | Males | Females | Total |
|-------------------|-------|---------|-------|
| < 20 | 22 | 23 | 45 |
| 21–35 | 89 | 124 | 213 |
| 36–50 | 24 | 34 | 58 |
| 51–65 | 4 | 7 | 11 |

Table 2

Sex and age distribution among HBsAg positive patients.

| Age group (years) | Males | Females | Total |
|-------------------|-------|---------|-------------|
| < 20 | 2 | 3 | 5 (27.77%) |
| 21–35 | 3 | 7 | 10 (55.56%) |
| 36–50 | 1 | 1 | 2 (11.11%) |
| 51–65 | 1 | - | 1 (5.56%) |

Of the 11 HBsAg positive females, six were pregnant and the prevalence of HBsAg positive pregnant females was 1.83% (Table 3). Four females were positive for HBeAg and two females were negative for HBeAg and the prevalence of HBeAg positive pregnant female was 1.22%. A total of 50% ($n = 3$) HBeAg positive cases were found in the age group of 21–35 years, which was statistically significant ($P < 0.05$) in comparison to the other age groups (Table 4).

Table 3

Distribution of HBsAg positive in pregnant ($n = 6$) and non-pregnant ($n = 5$) women.

| Age group (years) | Non-pregnant women | Pregnant women | Total |
|-------------------|--------------------|----------------|------------|
| < 20 | 1 | 2 | 3 (27.27%) |
| 21–35 | 3 | 4 | 7 (63.64%) |
| 36–50 | 1 | - | 1 (9.09%) |
| 51–65 | - | - | - |

Table 4

Distribution of HBeAg in pregnant women.

| Age group (years) | Positive | Negative | Total |
|-------------------|----------|----------|------------|
| < 20 | 1 | 1 | 2 (33.33%) |
| 21–35 | 3 | 1 | 4 (66.67%) |
| 36–50 | - | - | - |
| 51–65 | - | - | - |

4. Discussion

Hepatitis B occurs throughout the world and there is no seasonal variation. We have observed in developed countries, the incidence is more in adults than in children and more in urban than in rural areas. However, in Africa and the Far East, it is more common in infants and children where it is transmitted vertically or through close personal contact. The carrier rates are more than 5%. In endemic areas, the most individuals are infected perinatally, by vertical transmission, or in early childhood[19]. The carrier rate is lower in the temperate regions than in the tropical area, more in males than in females.

In this study 139 (42.51%) males and 188 (57.49%) females were tested for HBsAg with the age of 18–65 years. The present study shows 5.50% seroprevalence of HBsAg among clinically suspected infectious hepatitis patients which is similar to the studies (5%) conducted by Rajani and Jais[20]. The frequency of seropositivity was found to be higher than that reported in other studies (9.5%) conducted by Bart *et al.*[21], and the seroprevalence of HBsAg was found to be lower than that reported in other studies (1.2%) conducted by Giri *et al.*[22]. Variable results are found 1.55%, 1.43% and 1.09% in different studies in India[22–24]. The seroprevalence was higher (3.06%) in age group of 21–35 years. A study conducted by Rajani and Jais[20] also showed higher seroprevalence (7.6%) in age group of 20–30 years.

The seroprevalence of HBsAg in pregnant females was 1.83% which was similar to studies (2.37%) conducted by Bansal *et al.*[25] and the seroprevalence of HBsAg in pregnant females was found higher (7.30%) which was reported by Adegbesan-Omilabu *et al.*[26] and the seropositivity of HBeAg (66.67%) in pregnant females was dissimilar to which was reported by Adegbesan-Omilabu *et al.*(36.40%)[26].

With respect to gender-related prevalence, this study showed 2.14% prevalence in males and 3.36% prevalence in females where in other study conducted by Sonth *et al.*[27], higher prevalence was observed (0.73%) in males than females (0.27%). The high prevalence of HBsAg in females was responsible for the overall high prevalence in clinically suspected infectious hepatitis patients.

The present study revealed the trend of HBV seropositive with relation to age. The positivity for HBsAg in pregnant women was also higher. A higher prevalence of HBsAg detected in the present study was presumptively due to the lack of immunization against the virus. The higher levels are also related to the existence of uneducated population and unlicensed practitioners in developing countries like India that had taken advantage of a lack of consumer information in the medical services market and urged patients to take unnecessary injections for several decades. This is truly iatrogenic transmission of the disease.

The study showed that hepatitis B is prevalent in pregnant women and in general population, so special intervention programs should

be planned to aware and prevent vertical transmission in pregnant women and also awareness about highly infectious nature of HBeAg and its transmission from mother to fetus by placenta in pregnant. However, there is a clear need for close monitoring of both pregnant women with hepatitis B infection and their infants, both during and after the pregnancy. A special programme should be implemented for the general public, which is about to tell the mode of transmission of HBV. National immunization programme should implement immediately to curb this virus.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The authors are grateful to Dr. Ritu Agarwal, Associate Professor of Microbiology, Dr. Dakshina Bisht, Professor and Head of Department of Microbiology of Santosh Medical College, Ghaziabad, India and Dr. (Professor) Yogesh Tripathi, Dean of Santosh University Ghaziabad, India for their support.

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