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Research Article

Pattern of hepatitis B and C infection among gravid women and their newborns in a tertiary care infirmary in India

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ABSTRACT

Background: The objective is to determine the prevalence of the hepatitis B and C virus among pregnant women, to assess impact of maternal hepatitis B virus (HBV) or hepatitis C virus (HCV) carrier status on pregnancy outcomes and to gauge the risk factors associated with them. Antenatal clinic attenders and women undergoing termination of pregnancy over three years.

Methods: The study was conducted in Gian Sagar Medical College & Hospital, Patiala, Punjab, India. Hepatitis B antigen and Hepatitis C virus antibody testing of sera from specimens sent to the hospital laboratory for routine serological testing. The results were then linked to risk information, obstetric complications and pregnancy outcome.

Results: Overall HBsAg and anti-hepatitis C antibody prevalence was 1.2% (33/2031). Increased risk of transmission was associated with sexually transmitted diseases and previous surgical procedures. High rates of preterm labor pains, CD (27.27%), and non-reassuring fetal heart rate patterns and meconium stained liquor were found in the seropositive patients.

Conclusions: Maternal hepatitis B and C carrier status is an eminent risk factor for adverse pregnancy outcome.

Keywords: Hepatitis, Hepatitis B antigen, Anti-hepatitis C antibody, Pregnancy outcomes, Sero-prevalance, Risk factors

INTRODUCTION

Approximately one-third of world's population has serological evidence of past or present infection with HBV. About 350 million people worldwide are chronic carriers with nearly 6,00,000 dying of CHB complications (acute liver failure, cirrhosis and HCC annually).¹⁻³ The prevalence of HBsAg in gravid women alters with geographical location and ethnicity, being 6% in Asian women, 1% in African-Americans, 0.6% in non-Hispanic whites and 0.1% in Hispanics. In endemic areas such as China and South East Asia, it may be as high as 10-20%.⁴ The same in India is intermediate, with a

population prevalence of 4% and an estimated 1,40,000 carriers.

Likewise, prevalence of HCV infection is approximately 2.2-3.0% globally, with highest in African and Eastern Mediterranean region.^{5,6} The incidence of HCV during pregnancy is 1% -2.4%.⁷ Of infants born to seropositive women, 6 in 100 will acquire HCV perinatally, translating into almost 2500 perinatally acquired infections annually.⁷ Most persons acutely infected with HCV develop a persistent infection and nearly 70% experience chronic necro-inflammation of liver.

HBV is transmitted from infected mothers to infants via trans placental transmission, during parturition or postnatally through breast milk. Perinatal transmission appears to be the most important factor in determining the primacy in India. Before HBV vaccine was integrated into routine immunization program, proportion of babies becoming HBV carriers was roughly 10-30% for mothers who were HBsAg positive but HBeAg negative, increasing to 70-90% when mother was also HBeAg positive.⁸⁻¹⁰ The majority of perinatally acquired infection (>95%) results in CHB infection, due to induction of an immune tolerant state of variable duration. Therefore, prevention of perinatal transmission remains an imperative target in the struggle for global eradication of HBV infection.

HCV is transmitted through parenteral exposure, especially blood transfusions and the use of injectable drugs. The vertical, sexual and intra familial transmission of HCV have also been established.

Most antenatal women are recognized to be HBV/HCV carriers by their physicians from the commencement of their pregnancies. Viral hepatitis during pregnancy is associated with a high risk of maternal complications, high rate of vertical transmission (causing fetal and neonatal hepatitis) and is a leading cause of maternal mortality.¹¹ Epidemiological data on HBV/HCV infection is hence vital for obstetricians for optimal management of parturients and also program managers and health planners, to determine its morbidity and mortality, effect on parturition and transmission of infection to the newborn, to formulate preventive strategies. Though several studies on epidemiology of viral hepatitis in pregnancy are available from Africa, there is paucity of such up to date data among obstetric literature in India, especially regarding the potential adverse pregnancy outcomes related to maternal HBV/HCV carrier status.

The aim of this extant population-based study was thus to examine the sero-prevalence of HBsAg and HCV among pregnant women, possible risk factors for perinatal transmission of HBV/HCV infection and the impact of maternal HBV/HCV carrier status on pregnancy outcomes in a tertiary care hospital.

METHODS

The study was carried out at Gian Sagar Medical College & Hospital over a span of three years from April 2011 to June 2014. Women in any trimester of pregnancy, with or without jaundice, attending the daily antenatal clinic or emergency of the hospital were included. After informed consent, detailed history was taken and complete clinical examination was performed. Also 4 ml blood was collected and the sera obtained were tested for HBsAg and anti-HCV in laboratory using ELISA (Span Diagnostic Ltd, Surat, India). For the purpose of this study, we defined positive HBV status as having a

reactive HBsAg; and a positive HCV status as having a reactive anti-HCV result.

Women who tested positive for either of two underwent appropriate counseling and treatment, if warranted, and were then further evaluated for the virological characteristics of the hepatitis virus (HBsAg positive or negative, HBe antigen positive or negative and anti-HCV), co-infection with HIV. Socio-demographic profile, reproductive, medical and surgical history, as well as history pertaining to HBV/HCV infection and high-risk behaviors was extracted in detail from them. At the time of admission for delivery, history was reviewed along-with a thorough examination to note significant obstetric complications if occurred.

Additionally, woman's labor and delivery details, postpartum complications and neonatal outcomes were documented. Cord blood was collected at time of delivery and tested for HBsAg, HBeAg and HBV DNA; presence of HBV DNA in cord blood was taken as evidence of vertical transmission of HBV. The entire information was tabulated on a predesigned record proforma. An entire analysis was done using available Statistical Program for Social Sciences (SPSS 18 for Windows) after applying appropriate tests. P values <0.05 were considered as statistically significant.

RESULTS

HBsAg/HCV seroprevalence rate

Thirty three hepatitis seropositive pregnant women were identified out of 2031 deliveries (1.2%) during the study period, amongst which 27 were HBV carriers (81.88%) and 6 were HCV carriers. None of the women were co-infected with HBV and HCV. Since fetomaternal outcomes were comparable between HBV and HCV carriers with no significant differences observed, the two groups were combined for further analyses. One of the HBV carriers had a co-infection with HIV.

Socio-demographic profile

The mean age of seropositive patients was 23.8 years. The highest prevalence was perceived in the age group of 21-25 years (84.84%). An increasing trend in the prevalence of seropositivity was observed with higher parity, being 6 (18.18%) in primigravida, 10/ (30.30%) in 2nd gravida and 13 (39.39%) in 3rd gravida women. The prevalence rates in the first three parity groups were significantly different ($p < 0.05$) (Table 1).

The mean BMI of all these women, mostly Sikh and Hindu by religion, was $21.93 \pm 2.025 \text{ kg/m}^2$. Majority of subjects hailed from rural background (87.88%) and belonged to low (69.70 %) and middle (30.30%) socioeconomic status. A further breakup of socio demographic data revealed highest HBsAg/anti-HCV antibody positivity in illiterates. Nearly all were

housewives (96.96%) without any prior regular antenatal care. All these observations substantiated the section of society which attends the institute for its medical problems.

Table 1: Socio demographic Characteristics of 33 seropositive women for HBsAg/ anti-HCV antibody.

Characteristic	No. of seropositive women (n)	%
Age,(years)		
<20	0	0
21-25	28	84.84
26-30	4	12.12
31-35	1	3.03
Gravidity, no.		
1	6	18.18
2	10	30.30
3	13	39.39
≥4	4	12.12
Education		
Illiterate	25	75.75
Primary	4	12.12
Middle	1	3.03
High school	2	6.06
Secondary	1	3.03
Graduation/ Post graduation	0	0
Religion		
Hindu	15	45.45
Sikh	16	48.48
Muslim	2	6.06
Christian	0	0
Others	0	0
Address		
Urban	4	12.12
Rural	29	87.88
Socioeconomic status		
i	0	0
ii	0	0
iii	10	30.30
iv	20	60.60
v	3	9.09
Occupation		
Housewife	32	96.96
Working	1	3.03
Antenatal care		
Booked	2	6.06
Unbooked	31	93.93
BMI		
<18.9	5	15.15
19-24.9	22	66.67
25-29.9	4	12.12
30-34.9	2	6.06
35-39.9	0	0
>40	0	0

Medical and obstetric complications

Of the 33 seropositive gravid women, only three had acute hepatitis B while remaining were asymptomatic. Fortunately, the former did not seem to transmit infection to her baby. Common complications observed were preterm labour (18.18%), oligohydramnios (15%), and hypertensive disorders in pregnancy (12.12%) (Table 2).

Table 2: Medical and obstetric complications.

Complications	No. of seropositive women(n)	%
Deranged LFTs	3	9.09
Preterm delivery	3	9.09
HDP	4	12.12
IUGR	2	6.06
Oligohydramnios	5	15.15
PROM	6	18.18
Pulmonary embolism	0	0
Cholestasis	3	9.09
Coagulopathy	1	3.03
Placenta previa	1	3.03
Placental abruption	0	0
GDM	2	6.06
PGDM	1	3.03
polyhydramnios	0	0
Excessive wt gain (>11 Kg)	3	9.09

Risk factors for HBV/HCV infection in HBsAg positive/ anti HCV women

In all at least one of these significant risk factors was present in 24 (72.72 %) seropositive women.

Early age at marriage was present in 84.84% of seropositive parturients. One sero-positive women had history of tattooing, whilst 30% gave history of previous surgical procedures (dilatation and curettage in 11 and CD in 7). Information on status of husband was available only for 20 women as husbands of remaining 13 seropositive women declined HBsAg/anti HCV testing. Three husbands were HBsAg positive, while none was anti HCV positive. Past history of sexually transmitted infections like Molluscum Contagiosum was found in one of the HCV positive pregnant woman. None of the females reported known sero positivity in their sibling(s). History of blood transfusion within last 3-5 years was present in 6% women. One woman was a health care worker and a smoker also (Table 3).

Table 3: Prevalence of risk factors among 33 pregnant women seropositive for HBsAg /anti-HCV antibody.

Risk factors	No.of seropositive women(n)	%
Early age at marriage		
No	5	15.15
Yes	28	84.84
Multiparity		
No	6	18.18
Yes	27	81.81
Smoking		
No	32	96.96
Yes	1	3.03
Substance abuse		
No	32	96.96
Yes	1	3.03
Multiple sexual partners		
No	33	100
Yes	0	0
Fertility treatment		
No	28	84.84
Yes	5	15.15
Previous Surgical procedures		
No	15	45.45
Yes	18	54.54
Dilatation & curettage	11	33.33
Caesarean delivery	7	21.21
Acupuncture and/or tattooing		
No	32	96.96
Yes	1	3.03
Circumcision		
No	32	96.96
Yes	1	3.03
Positive status of partner		
No	30	90.90
Yes	3	9.09
History of jaundice		
No	31	93.93
Yes	2	6.06
Previous blood transfusion		
No	31	93.93
Yes	2	6.06
HIV positive status		
No	32	96.96
Yes	1	3.03
History of RTI/STD		
No	31	93.93
Yes	2	6.06
History of having received parenteral drugs from untrained personnel		
No	27	81.81
Yes	6	18.18
Family history of seropositivity		
No	32	96.96
Yes	1	3.03
Use of OCPs		
No	30	90.90
Yes	3	9.09

Table 4: Pregnancy outcomes in seropositive women for HBsAg /anti-HCV antibodies.

Outcome in seropositive group	No. of women	%
Pregnancy duration, wk		
<37	3	9.09
37–41	29	87.87
>41 01	1	3.03
Onset of labor		
Spontaneous	24	72.72
Induced	7	21.21
Fetal bradycardia		
Yes	5	15.15
No	28	84.84
Meconium-stained liquor		
Yes	9	27.27
No	24	72.72
Mode of delivery		
Vaginal	24	72.72
LSCS	9	27.27
Outcome		
Live born	31	93.93
Still born	2	6.06
Birth weight, g		
<2500	8	24.24
>2500	25	75.75
Apgar score at 1 min		
Low(< 7)	8	24.24
High(>7)	25	75.75
Sex of newborn		
Male	16	48.48
Female	17	51.51
Size of newborn		
SFD	3	9.09
AFD	30	90.90
Neonatal resuscitation required		
No	29	87.87
Yes	2	6.06
Admission to NICU		
No	0	0
Yes	31	93.93
Any gross CMF		
No	32	96.96
Yes	1	3.03
Neonatal jaundice (Pathological)		
No	31	93.93
Yes	0	0
Perinatal mortality		
No	31	93.93
Yes	0	0

Pregnancy outcomes (Table 4)

High rates of CD (27.27%), and non-reassuring fetal heart rate patterns and meconium stained liquor were found in the seropositive patients. Among the 9 women who had CD, 7 were performed in emergency while elective CD were done for malpresentation and placenta previa. 31 babies were delivered alive among which 14 (45.2%) showed evidence of vertical transmission. 24.4% babies were low birth weight and 24.4 % had low Apgar scores, with 2 of them requiring NICU care. One of the still born babies had anencephaly. None of the babies developed jaundice postnatally.

DISCUSSION

This is one of the largest studies demonstrating the prevalence of HBsAg /anti-HCV antibodies in symptomatic pregnant women from India. The HBsAg/anti HCV antibody sero-prevalence rate of 1.2% in this study indicates intermediate endemicity of HBV/HCV infection in the region. Sero-epidemiological studies of different populations show variations and differences (Table 5). This difference may be because of the type of population studied, different geographical regions, genetic and socioeconomic factors.

Table 5: Comparison of seroprevalence rates of HBsAg/ anti HCV among pregnant women in different populations.

Author, year and references	Population studied	Number of persons screened	HBsAg and /or anti HCV +ve (%)
Murad et al.2013 ¹¹	Yemen	400	10.8%
Makuwa et al. 2008 ¹⁸	Gabon	1,186	9.20
Kabiru et al. 2010 ¹	Nigeria	1,052	6.08%
Zahran et al. 2010 ¹⁹	Egypt	500	6.4 and 4%
Rasha M Elsheikh et al. 2007 ¹²	Sudan	728	5.6%
Mohammed et al. 2008 ²⁰	Saudi Arabia		1.60
Bertolini et al. 2006 ²¹	Brazil	3,188	1.5%
Present Study 2014	Punjab, India	2031	1.2%
Dwivedi et al 2008 ¹³	Allahabad, India	4,000	0.9%
A kumar et al 2004 ¹¹	New Delhi, India	1900	0.73%
Ari Safir 2009 ¹⁷	Sudan	186 619	0.4%

A finding similar to that by Elsheikh et al and Murad et al in this study is that none of the patients were infected by both HBV and HCV.^{11,12}

We noted high seropositivity in women between 21-25 age group in multiparous women. This was akin to the observations made by previous researchers.¹³ The majority of the mothers were from low socioeconomic backgrounds suggesting that the infection was more prevalent in those with a lower educational level.¹¹⁻¹³

The absolute number of only 33 positive cases precludes the detection of small differences in the prevalence of risk factors; however, the prevalence of HBsAg/anti-HCV antibodies have been reported to increase with age and to be the highest among women older than 40 years. The findings that 84.4% of the positive women had at least one significant risk factor clearly demonstrates that high risk screening of pregnant women is not a sensitive method, and that as many as a quarter of seropositive women may be lost by such practice. This justifies routine screening of all antenatal women in India for HBsAg and anti HCV antibody.

A much higher sexual transmission has been long recognized as a major source of HBV transmission in all areas of the world.^{14,15} It is therefore not astounding that early age at sexual debut and previous history of STIs were the significant risk factors for seropositivity in this study. However multiple sexual partners were not identified as a risk factor in our subjects owing to social inhibitions. Also, the current program of hepatitis B vaccination in infancy and children in India offers a long-term solution to HBV infection, but its impact on seroprevalence rates would take some time to establish. However, none of the known risk factors such as history of contact with jaundiced patient, tattooing, history of dental manipulation, circumcision in the extant study were found to be significantly associated with the HCV infection among gravid women.^{11,15,16} Also there is a slightly increased risk of seropositivity in individuals with a history of dilation and curettage or previous LSCS, insinuating a blood-borne mode of transmission. Unsterilized medical equipment is likely to be an important risk factor in these patients.

Drug abuse is known to be strongly associated with poor neonatal outcomes. Our population differ significantly from other studies investigating the outcome of patients with hepatitis, as smoking and substance abuse is extremely rare (3.03%). High rates of low birth weight, preterm deliveries and low Apgar scores (<7) at 1 min were noted. These were in concordance with studies published among other populations till date.¹⁵⁻¹⁷ An exception is the prevalence of gestational diabetes mellitus among hepatitis carriers, which was found to be higher only in women who had an excessive weight gain during their pregnancy. The differences in BMI values may explain the diversity of the results. Literature has related the adverse pregnancy outcomes to a chronic

inflammatory state in which increased serum concentrations of pro-inflammatory cytokines play an important role in premature labor and PROM.

Our study has few limitations. The population investigated consisted only of women able to access antenatal care, and the prevalence reported here may have underestimated the true prevalence among pregnant women in the community. Secondly, because of the test being expensive, only 6 seropositive parturients agreed to be further investigated for virological characteristics. Therefore, we were unable to show any significant correlation between higher viral loads at the time of pregnancy and adverse outcomes. Also, many patients did not have a follow-up regarding their liver disease during their pregnancies. Further prospective studies should focus on these critical factors, including careful observation and preconception consultation. Nevertheless, we agree with the management suggested by Jonas for hepatitis carriers during pregnancy, including recognition of maternal virological status and assessment of liver disease. We recommend the referral of those patients to high-risk pregnancy clinics with careful observation during pregnancy and delivery.

CONCLUSIONS

Maternal HBV or HCV carrier status is an independent risk factor for adverse perinatal outcome, and careful surveillance as high-risk pregnancy is warranted.

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