jjogastroenterology.org

Japanese Journal of Gastroenterology

ISSN 2832-4870

DIRECTIVE PUBLICATIONS

Research Article

Miscarriages In HBV Patients - Time To Ponder.

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Abstract

Introduction: Hepatitis B virus (HBV) infection poses a significant global public health challenge. It is associated with increased miscarriage rate and studies also has confirmed that the miscarriage rate is higher in women with HBV, with one study finding a 71% increase in miscarriage risk in HBV carriers compared to a control group. Another study found a significantly higher rate of miscarriage in pregnant HBV carriers (9.66%) compared to the control group (5.81%). The potential contributing factors are HBV infection of embryos. Studies have detected HBV mRNA fragments in embryos from mothers with HBV, suggesting that direct infection of the embryo could be a cause of miscarriage and congenital malformations. HBV infection is associated with an increased risk of other complications that can contribute to miscarriage, such as gestational diabetes mellitus (GDM) and preeclampsia.

Aims and objectives: To determine miscarriage rate m pregnant patients with confirmed HBV infection.

Materials & Methods: It was a prospective study conducted at Medical Gastroenterology in collaboration with Obstetrics & Gynecology, PGIMS, Rohtak over a period of eight years and eleven months from 1.1.2017 to 30.11.2025. Three hundred (300) pregnant patients who were confirmed to be positive for Hepatitis B antigen (HbsAg) test on Enzyme linked Immunoassay test (ELISA) and HBV DNA quantitative on PCR testing and anti HCV antibody & anti-HIV antibody negative were enrolled in the study and followed. These three hundred patients were followed throughout pregnancy, delivery, post-partum period. The data of these 300 HBV confirmed pregnant patients was analysed in final analysis.

Results: Out of these 300 HBV patients, 104 patients (34.66%) had miscarriage. In these 104 patients with miscarriage, majority belonged to 21-30 yrs age group (74%). Majority of miscarriages were seen in first trimester of pregnancy (63.46%) and out of it also, maximum was seen in second month of pregnancy. Majority (58%) had single miscarriage followed by twice miscarriage and multiple ones were least common. Majority patients (80%) were non-cirrhotic with normal fibroscan score i.e. below 7 Kpa, followed by patients in F1 - F3 group but none was cirrhotic. One characteristic finding in our pool was that majority of patients (80.76%) were inactive carrier with low HBV viral load i.e. > 10^{2-3} I.U./ml,

Conclusion: Our study is an eye opener as it not only re-confirms the findings already available in literature regarding more prevalence of miscarriages in HBV females in comparison to normal population but also hints at more gravity of problem, then what is being thought and understood. Moreover, in comparison to HCV, HBV related miscarriages occur even at low viral load also.

Keywords: HbsAg, HBV DNA Quantitative, Miscarriage. Pre-term delivery, Breast feeding, anti-viral treatment

INTRODUCTION

Hepatitis B and C are the most common causes of chronic viral hepatitis in children and adults worldwide. Previous studies have found no link between maternal HBV infection and live birth, preterm birth, or pregnancy rates in women undergoing assisted reproductive technology [1,2]. Later on, infection with HBV has been linked to a higher risk of miscarriage and preterm birth in natural pregnancies [3]. Pregnant women with a high HBV viral load are at risk of transmitting the virus to the developing embryo, causing adverse pregnancy outcomes [4]. Studies have shown an increased risk of both newborn and maternal morbidity associated with HBV infection, including fetal distress, gestational diabetes mellitus, preterm delivery, and meconium peritonitis [5-9]. Also, antepartum hemorrhage causing placental abruption and placenta previa can increase. A lower Apgar score is the only perinatal complication [5,9]. However, there isn't much research on the mechanisms underlying these results [10]. Multiple cohort studies have found a significantly higher proportion of miscarriages among HBV carriers compared to non-HBV controls. One large study of over 21,000 pregnant women found that the miscarriage rate was 9.36% in HBV carriers versus 5.70% in controls, and after adjusting for other variables, women with HBV were 1.71 times more likely to miscarry.

AIMS AND OBJECTIVES

To determine miscarriage rate in pregnant patients with confirmed HBV infection.

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Email: drparveenmalhotra@yahoo.com.
Received: 22-Dec-2025, Manuscript No. JJOGASTRO - 5351 **; Editor Assigned:** 25-Dec-2025 **; Reviewed:** 08-Jan-2026, QC No. JJOGASTRO - 5351 **;**
Published: 13-Jan-2026.
Citation: **Parveen Malhotra**. Miscarriages In HBV Patients - Time To Ponder . Japanese Journal of Gastroenterology. 2026 January; 15 (1).

MATERIAL AND METHODS

It was a prospective study conducted at Medical Gastroenterology in collaboration with Obstetrics & Gynecology, PGIMS, Rohtak over a period of eight years and eleven months from 1.1.2017 to 30.11.2025. Three hundred (300) pregnant patients who were confirmed to be positive for Hepatitis B antigen (HbsAg) test on Enzyme linked Immunoassay test (ELISA) and HBV DNA quantitative on PCR testing and anti HCV antibody & anti-HIV antibody negative were enrolled in the study and followed. These three hundred patients were followed throughout pregnancy, delivery, post-partum period. The data of these 300 HBV confirmed pregnant patients was analysed in final analysis.

Stastical Analysis

All the data was entered in Microsoft Excel Data and analysed using SPSS 15.0 version.

OBSERVATION AND RESULTS

Three hundred (300) patients who were confirmed to be positive for HbsAg test on Enzyme linked Immunoassay test (ELISA) and HBV DNA quantitative on PCR testing were enrolled in the study and followed. Out of these 300 HBV patients, 104 patients (34.66%) had miscarriage. In these 104 patients with miscarriage, majority 77 patients (74,03%), belonged to 21-30 yrs age group. Majority of miscarriages were seen in first trimester of pregnancy i.e. 66 patients (63.46%) and out of it also, maximum was seen in second month of pregnancy. Majority,61 patients (58.65%) had single miscarriage followed by twice miscarriage and multiple ones were least common. Majority, 83 patients (79.80%) were non-cirrhotic with normal fibroscan score i.e. below 7 Kpa, followed by 21patients (20.20%) in F1 - F3 group but none was cirrhotic. One characteristic finding in our pool was that majority of patients (84 i.e. 80.76%) were inactive carrier with low HBV viral load i.e. > 10^{2-3} i.u./ml with normal liver function tests,

Table 1. Showing Percentage of HBV Patients with Miscarriages in study group

Total Number of HBV Patients	HBV Patients with Miscarriages	HBV Patients without any Miscarriages
300 (100%)	104 (34.66%)	196 (65.34%)

Table 2. Showing Age Group Distribution of HBV Patients with Miscarriages

HBV Patients with Miscarriages	10-20 yrs age	21-30 yrs age	31-40 yrs age	41-50 yrs age
104 Patients	4 (3.84 %)	77 (74.03 %)	25 (24.03%)	0 (0%)

Table 3. Showing Number of Miscarriages in HBV Patients in study group

Total Miscarriage	Single Miscarriage	Twice Miscarriage	Multiple Miscarriages
104 (100%)	61 (58.65%)	31 (29.80%)	12 (11.55%)

Table 4. Showing Distribution of Miscarriages according to Gestational Age in HBV Patients

HBV Patients with Miscarriages	First Month	Second Month	Third Month	Fourth Month	Fifth Month	Sixth Month	Seventh Month	Eight Month	Ninth Month
104 (100%)	10 9.61%	44 42.30%	12 11.53%	7 6.73%	7 6.73%	12 11.5%	9 8.65%	1 0.96%	2 1.92%

Table 5. Showing Fibrosis/Cirrhosis in HBV Patients with Miscarriages on Basis of Fibroscan

Patients with Miscarriages	Normal Liver	F1 Fibrosis	F2 Fibrosis	F3 Fibrosis	F4 Cirrhosis
104 (100%)	83 (79.80%)	9 (8.65%)	7 (6.73%)	5 (4.8%)	0 (0%)

Table 6. Showing HBV Viral Load in Patients with Miscarriages

HBV Viral Load in Miscarriage Patients	HBV Viral Load 10^2	HBV Viral Load 10^3	HBV Viral Load 10^4	HBV Viral Load 10^5	HBV Viral Load 10^6	HBV Viral Load 10^7
78 (100%)	52 (50%)	32 (30.76%)	10 (9.61%)	6 (5.76%)	4 (3.87%)	0 (0%)

DISCUSSION

According to available research, studies suggest that women with Hepatitis B infection in India have a higher prevalence of miscarriages compared to those without the virus, with some studies indicating a significant increase in miscarriage rates among pregnant women carrying hepatitis B; however, the exact prevalence of miscarriages specifically related to Hepatitis B in India is difficult to pinpoint due to limited data and variations in study methodologies. Studies have shown an increased risk of both newborn and maternal morbidity associated with HBV infection, including fetal distress, gestational diabetes mellitus, preterm delivery, and meconium peritonitis [11-15]. Zhang et al retrospectively analyzed the pregnancy outcomes of 9,699 HBsAg-positive and 73,076 HBsAg-negative pregnant women, and the result found that pregnant women who were HBsAg-positive were more likely to undergo PPH and intrahepatic cholestasis of pregnancy; in addition, HBsAg-positive pregnant women had a higher risk of placental abruption and premature birth in the vaginal delivery group [16]. According to the findings of another meta-analysis, the risk of preterm birth in pregnant women who had a chronic HBV infection was significantly higher than the risk of preterm birth in pregnant women who did not have an HBV infection; furthermore, the risk of preterm delivery rose by 16% [17]. Moreover, the presence of HBV was an independent risk factor for early preterm delivery, but the level of HBV DNA did not affect the increase in risk associated with early preterm delivery [18]. Peng et al demonstrated that baseline HBeAg status and HBV DNA level were not associated with GDM, despite the fact that maternal carrying of HBsAg was an independent risk factor for GDM [19]. The occurrence of GDM may be related to age (>35 years old) and abnormal liver function [20]. However, advanced age is a risk factor for GDM [21]. According to the findings of another study, chronic HBV infection was linked to a marginally increased risk of low birth weight and preterm birth, but HBeAg positivity led to an increased risk of low birth weight, preterm birth, and GDM [22]. In our study group, miscarriage rate of 34.66% was seen with maximum number of patients belonging to 21-30 yrs of age group. Majority of miscarriages were seen in first trimester of pregnancy and out of it also, maximum was seen in second month of pregnancy. Maximum number of patients had single miscarriage followed by twice miscarriage and multiple ones were least common. Majority patients were non-cirrhotic with normal fibroscan score i.e. below 7 Kpa. One characteristic finding in our pool was that miscarriages were occurring in majority of HBV pregnant patients, even at low viral load which is in contrast to HCV, as shown already by Malhotra etal [23]. Our study clearly highlights the significant higher miscarriage rate in HBV in comparison to HCV and general population [23]. Moreover, as majority of patients were with normal liver and none was having cirrhosis, it excluded cirrhosis reason for causing miscarriage. It stresses the need of timely recognition and treatment, if indicated of HBV before conception. Moreover, it warrants screening for HBV in pregnancy, cases of recurrent pregnancy loss & even in marriageable females in hot spot areas and they should be fully vaccinated against HBV, if not done in childhood.

CONCLUSION

Our study is an eye opener as it highlights a significantly higher miscarriage rate in HBV patients, then reported in literature. Moreover, the prominent risk factors associated with miscarriage are young age and first trimester of pregnancy. It will be wise decision to get tested for HBV before conceiving, at least in those areas which have high prevalence of HBV and get treated for the same. Moreover, it warrants screening for HBV in cases of recurrent pregnancy loss.

Conflict Of Interest

The authors declare that there was no conflict of interest and no financial aid was taken for the same.

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