ORIGINAL ARTICLE

Perinatal Outcomes of Patients with Hepatitis B Viral Infection in Pregnancy

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Abstract

Purpose: Hepatitis B virus (HBV) virus has been established to infect about 350 million individuals on a worldwide scale. Nearly half of the infection is acquired either perinatally or in early childhood. The infection represents a significant cause of cirrhosis and hepatocellular carcinoma–related morbidity and mortality.

Materials and methods: This is a retrospective record study conducted at a tertiary care hospital (St John's Medical College Hospital, Bengaluru) by review of records over the past 5 years (January 2015–June 2021).

Results: We identified 85 pregnant women diagnosed as HBsAg-positive during our study period; of which 67 (78.8) patients were <30 years of age while the remaining 18 (21.2) were >30 years of age. The mean gestational age at the time of admission was 37.6 ± 2.5 weeks of gestation. Women who were >30 years of age who are married for >5 years 10 (55.6) and those who are <30 years of age and married for 1–5 years 33 (49.3) were HBsAg-positive, $p = 0.014^{b}$. It was noticed that gamma-glutamyl transferase was two times elevated in primigravida when compared to multigravida, which was statistically significant ($p = 0.037$). Meconium-stained liquor 3 (3.5) was the most common intraoperative finding seen in pregnant women who were HBsAg-positive.

Conclusion: The development of chronic hepatitis B infection is inversely proportional to the age at which infection occurs. Close monitoring of liver function tests, particularly gamma-glutamyl transferase and antepartum fetal surveillance is important to increase the chance of good outcomes in these pregnancies.

Keywords: Hepatitis B, Hepatitis B surface antigen, Lower-segment cesarean section, Pregnancy, Prematurity.

Key message: The better association of gamma-glutamyl transferase to obstetric score in HBsAg-positive pregnant women.

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Introduction

Hepatitis B virus (HBV) has been established to infect about 350 million individuals on a worldwide scale.[1–4] Nearly half of the infection is acquired either perinatally or in early childhood.[1,3,5] The infection represents a significant cause of cirrhosis and hepatocellular carcinoma–related morbidity and mortality.[3,4] The estimated burden of death with HBV infection is 5 lakhs to 1.2 million per year.[1]

The prevalence of HBV infection in pregnant women is at its highest in Asian women being 6% while the rates are 1, 0.6, and 0.41% in black, white, and Hispanic women, respectively.[2,4] It is transmitted through perinatal, percutaneous, and sexual routes.[6] China, Far East countries, and Africa have proportionately higher rates of infection which is attributed to higher endemicity of infection.[2,6,7] The risk of development of chronic HBV is a link to age exposure and varies approximately from 90% in infants to 5% in adults.[3,8]

Acute or chronic HBV infection that presents in pregnancy is similar to that of the general population.[1,5] HBV infection is not known to cause mortality or teratogenic effects in pregnancy.[1] Low birth weight, prematurity, gestational diabetes mellitus (GDM), antepartum hemorrhage, and preterm delivery are more frequent with HBV-infected mothers rather than the general population.[1,9,10] Fetal loss can also occur in 50% of HBsAg-positive mothers.[1]

Although HBV infection in pregnancy mandates a unique set of management, there must be amble consideration of maternal and fetal effects during the course of the antenatal period.[2] Chronic HBV infection is usually mild but can flare shortly after delivery.[2,5,10,11] Management of the disease in pregnancy possesses difficulty due to the similarity it presents with other acute liver diseases that also present during pregnancy (cholestasis of pregnancy).[1] Maternal complications, such as rupture of esophageal varices, hepatic decompensation, and rupture of a splenic aneurysm, increase during the second trimester and are maximum during labor.[1,7] Treatment with lamivudine, tenofovir, and telbivudine may be started early in pregnancy based on active liver disease as seen by elevated liver function tests or HBV DNA levels.[4,8,10,12] Management with beta-blockers, vasopressin, diuretics, lactulose, rifaximin, etc., might have to be given as a treatment modality in mothers with liver complications due to HBV despite having occasional fetal effects.[1] The literature review states that a vaginal delivery is well preferred than a cesarean section except in women with large varices.[1]

Although a vaccination protocol exists, reports of failed immunoprophylaxis have been reported to be 10–30% of infants born to HBsAg-positive mothers probably due to high maternal viremia, intrauterine infections, and mutated proteins of the HBV virus.[2,3,6,11] As minimal studies have looked into the obstetric and

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perinatal outcomes of hepatitis B infection in pregnancy in the South Indian population, we decided to look into the effects of HBV infection on pregnancy.[4]

Methods

This is a retrospective record study conducted at a tertiary care hospital (St John's Medical College Hospital, Bengaluru) by review of records over the past 5 years (January 2015–June 2021). Pregnant women with HBV infection during pregnancy who were diagnosed either clinically by signs and symptoms, altered biochemical markers, positive viral loads, HBsAg-positivity on routine antenatal investigations, etc., were included in the study. Those women with other established causes of cholestasis, such as cholestasis of pregnancy, gallstones, fatty liver in pregnancy, etc., were excluded. Ethics approval was procured from the institutional ethics committee before the start of the study (IEC Ref No.229/2021).

Maternal Variables

Maternal well-being, antenatal visits, fetal growth assessment, decreased fetal movements, pain abdomen, bleeding per vagina, leaking per vagina, jaundice, itching, ascites, features of encephalopathy, etc., were reviewed. Changes in liver function tests and association with other biochemical tests and viral markers were also noted. Obstetric complications, such as severe preeclampsia, GDM, oligohydramnios, polyhydramnios, antepartum hemorrhage, etc., were taken into consideration. Medical complications, such as hypothyroidism, anemia, hypertension, diabetes mellitus, bronchial asthma, etc., were also looked into. Pregnancy outcomes, such as the need for induction of labor, mode of delivery, and even need for instrumentation with forceps or vacuum were noted. Mode of therapy with antivirals, such as tenofovir, etc., dosing of medication and use of newer treatment modalities, and admission into intensive care unit were also documented. Intrapartum and postpartum complications like postpartum hemorrhage, puerperal sepsis, etc., were studied.

Fetal Variables

Complications at birth, preterm birth, Apgar (appearance, pulse rate, grimace, activity, respiration) scores, need for neonatal intensive care unit admission, birth weight, and placental weight for individual cases were obtained. Neonatal immunization in HBsAg-positive mothers was also evaluated.

In our hospital, management of HBV in pregnant women is similar to the study conducted by Ayoub et al.[13] At the first pregnancy visit, routine screening of all mothers for HBsAg is done. If HBsAg is negative, then vaccinate high-risk patients as well as infants at birth. If HBsAg is positive, check HBV DNA levels and at 28 weeks check alanine transaminase, hepatitis B e-antigen (HBeAg), and hepatitis B e-antibody (anti-HBe). If HBV DNA levels <2 lakhs IU/mL, no antiviral therapy is required but the infant receives hepatitis B vaccine and hepatitis B immunoglobulin (HBIg) at birth whereas for HBV DNA levels >2 lakhs IU/mL, consider treatment at 28–32 weeks with antivirals and can consider stopping therapy 0–3 months after delivery while monitoring for flare in the postpartum period with alanine transaminase and HBV DNA at 1, 3, and 6 months.

In our hospital, standard active and passive immunoprophylaxis with hepatitis B vaccine and HBIg administered immediately after birth in a matter of 12 hours to HBsAg-positive mothers is the planned protocol. This is followed by two additional doses of the vaccine at 6–12 weeks. This protocol prevents nearly 95% of transmission as stated by Tran.[3,14] Without immunoprophylaxis in mothers who are both HBsAg and HBeAg-positive, the risk of transmission is 70 and 90% by 6 months of age. If HBsAg is positive and HBeAg-negative, the risk of transmission is <10%. In our hospital, for infants born to HBsAg-positive mothers, we have active and passive immunoprophylaxis with a hepatitis B vaccination protocol—0.5 mL intramuscular injection—and HBIg administered within 24 hours of birth reduces the risk of transmission by 85–95% followed by a routine vaccination schedule at 6, 10, and 14 weeks. In special situations, such as unknown HBsAg status of the mother, the birth dose of hepatitis B vaccine and HBIg are given within 72 hours of delivery if the mother is tested positive. For preterm babies born to HBsAg-positive mothers, hepatitis B vaccine is given even if <2 kg of birth weight (under normal scenarios, for preterm and <2 kg of birth weight, hepatitis B vaccine is not given because of reduced immunogenicity). Breastfeeding is not contraindicated as it does not increase the risk of transmission provided the baby has received immunoprophylaxis. For follow-up, a test for HBsAg and hepatitis B surface antibody (anti-HBs) titers is done at 9–18 months of age, at least 1 month after the last dose in infants. Normally, anti-HBs titers should be >10 IU/mL; if <10 IU/mL, then revaccinate with a three-dose schedule, but if HBsAg is positive, then we have to closely follow up.

Analysis

Data were analyzed using SPSS version 16, after which they were entered manually in version 10. Interquartile ranges were used for variables like age, gestational age, birth weight, etc., for the analysis of pregnancy outcomes in women with HBV infection. The Pearson's Chi-square, Fisher's exact, was used as the test for significance, and a value of <0.05 was considered significant.

Results

Demographic Details

We identified 85 pregnant women diagnosed as HBsAg-positive during our study period; of which 67 (78.8) patients were <30 years of age, while the remaining 18 (21.2) were >30 years of age. Although the majority of patients were booked 77 (90.6), 8 (9.4) of them were unbooked. Forty (47.1) women were primigravidae while 45 (52.9) of them were multigravidae. The mean gestational age at the time of admission was 37.6 ± 2.5 weeks of gestation. One-sixth of the patients 12 (14.1) had a prior history of intrauterine death (IUD). There were more numbers of girl babies 45 (52.9) born when compared to boy babies 40 (47.1) seen in Table 1.

Antenatal Period

Various medical complications were encountered during pregnancy in these HBsAg-positive mothers, such as hypothyroidism 15 (17.6), chronic hypertension 1 (1.2), anemia 9 (10.6), overt diabetes 1 (1.2), human immunodeficiency virus positive 1 (1.2), thrombocytopenia 1 (1.2), immune thrombocytopenic purpura 1 (1.2), cholestasis 1 (1.2), bronchial asthma 2 (2.4), and treponema pallidum hemagglutination (TPHA) positive VDRL negative 2 (2.4). Obstetric complications like malpresentations [breech 2 (2.4), transverse lie 1 (1.2)], history of previous lower-segment cesarean section (LSCS) 9 (10.6), fetal growth restriction 1 (1.2), preeclampsia 15 (17.6), polyhydramnios 2 (2.4), oligohydramnios 4 (4.7), GDM 7 (8.2), antepartum hemorrhage 2 (2.4), premature rupture of membranes/preterm premature rupture of membranes (PROM/PPROM) 10 (11.8), bad obstetric history 2 (2.4), and Rh-negative 3 (3.5).

Table 1: Frequency of study population

Variables		*Frequency (Total N = 85)*	*Percentage*
	Booked	77	90.6
	Unbooked	8	9.4
Age (years)	<30	67	78.8
	>30	18	21.2
Obstetric score	Primigravida	40	47.1
	Multigravida	45	52.9
Married life (years)	<1	24	28.2
	2–5	38	44.7
	>5	23	27.1
Marriage	Consanguineous	3	3.5
	Nonconsanguineous	82	96.5
History of abortions in the past	1 abortion	8	9.4
	2 abortions	7	8.2
	3 abortions	2	2.4
History of intrauterine fetal death in the past		12	14.1
Intrauterine fetal death in this pregnancy		4	4.7
Gestational age (weeks)	$<36^{+6}$	14	16.5
	$37–40^{+6}$	70	82.4
	>41	1	1.2
Vaginal delivery	Full-term vaginal delivery	52	61.2
	Preterm vaginal delivery	6	7.1
	Forceps delivery	2	2.4
Lower-segment cesarean section	Emergency	21	24.7
	Elective	4	4.7
Gender	Boy	40	47.1
	Girl	45	52.9
Birth weight (kg)	<2.5	18	21.2
	2.5–3.5	48	56.5
	>3.5	15	17.6
Apgar at 1 minute	≤5	5	5.9
	6–7	21	24.7
	≥8	59	69.4
Apgar at 5 minutes	≤5	4	4.7
	6–7	1	1.2
	≥8	80	94.1
Placental weight (g)	<500	33	38.8
	≥500	52	61.2

The most common complication at the time of presentation was pain abdomen 34 (40) followed by decreased fetal movements 13 (15.3), leaking per vagina 11 (12.9), increased BP readings 5 (5.9), bleeding per vagina 1 (1.2), and oligohydramnios 1 (1.2). Twenty (23.5) women were admitted for safe confinement.

A high chance of coinfection in HBsAg-positive mothers was noticed in TPHA-positive women 2 (11.1), $p = 0.043^{b}$. It was also noticed that those women >30 years of age, who were HBsAg-positive, had antepartum hemorrhage 2 (11.1), $p = 0.043^{b}$. Women who were >30 years of age, who are married for >5 years 10 (55.6), and those who are <30 years of age and married for 1–5 years 33 (49.3) were HBsAg-positive, $p = 0.014^{b}$. HBsAg-positive primigravida 16 (40), as well as multigravida 22 (48.9) women who are married for 1–5 years had a higher chance of being HBsAg-positive, $p = 0.000^{b}$.

HBsAg-positive mothers who are multigravida had a higher chance of having a history of at least one IUD 12 (26.7). HBsAg-positive women who had a preterm pregnancy had a higher chance of having preeclampsia 8 (57.1), $p = 0.000^{b}$. Women who were HBsAg-positive at <37 weeks of gestation 2 (14.3) had a higher chance of polyhydramnios, $p = 0.049^{b}$. Women who are HBsAg-positive at <37 weeks of gestation had a higher chance of antepartum hemorrhage 2 (14.3), $p = 0.049^{b}$.

The history of one prior abortion was significantly associated in young primigravidae who were <30 years (p <0.05) as seen in Table 2.

Delivery Details

The majority of the patients were induced with PGE2 (dinoprostone) 24 (28.2) while others received PGE1 (misoprostol) 5 (5.9) and PGE1 + PGE2 4 (4.7) as seen in Table 3. The most common indication for induction was term gestation 20 (23.5), decreased fetal movements 5 (5.9), PROM/PPROM 4 (4.7), severe preeclampsia 2 (2.4), oligohydramnios 1 (1.2), and nonprogress of labor 1 (1.2). Thirty-one (36.5) underwent spontaneous vaginal delivery. Of the 40 primigravidae, 25 (62.5) had full-term vaginal delivery (FTVD), 3 (7.5) had preterm vaginal delivery (PTVD), and 2 (5) had forceps delivery when compared to the 45 multigravidae, where 27 (60) had FTVD, 3 (6.7) had PTVD, and none had a forceps delivery.

Primigravida had a higher chance of emergency LSCS 11 (73.3) and elective LSCS 4 (26.7). The most common indication for LSCS was a nonreactive nonstress test 8 (9.4) followed by a history of previous LSCS 5 (5.9), cephalopelvic disproportion 4 (4.7), failed induction 3 (3.5), malpresentation 2 (2.4), severe preeclampsia 2 (2.4), and abruption 1 (1.2). Meconium-stained liquor 3 (3.5) was the most common intraoperative finding seen in pregnant women who were HBsAg-positive.

Five children (5.8) had renal anomalies, such as pelviectasis, while one baby had a prominent stomach bowel meconium-filled colon rather than duodenum with grade I echogenicity of small bowel loops. Table 4 shows the significant association of birth weight (2.5–3.5 kg) and placental weight (>500 g) with gestational age at term (p <0.05^{b}). Similarly, good Apgar scores at 1 and 5 minutes of life are seen in the neonates born of HBsAg mothers (p <0.05^{b}).

When analyzing the parametric variables, such as hemoglobin, FBS, PPBS, creatinine, uric acid, AST, ALT, blood urea, direct bilirubin, and total protein using the independent t test, it was seen that there was no significant difference in these variables with respect to obstetric scores as seen in Table 5. Similarly, on performing Mann–Whitney test for TSH, platelet count, total count, total bilirubin, GGT, LDH, and ALP, it was seen that there was no significant difference in these variables with respect to obstetric scores as seen in Table 6. However, it was noticed that GGT was two times elevated in primigravida when compared to multigravida which was statistically significant ($p = 0.037$). On applying the Kruskal–Wallis test for nonparametric variables, a mean rank of 20.75 for gestational age <37 weeks and 32.36 for >37 weeks was shown to have a p value of 0.037.

Table 2: Relationship between age and obstetric score to abortions

	Abortion				
	No abortion	*One abortion*	*Two abortions*	*Three abortions*	*p value*
Age (years)					0.007[b*]
<30	57 (85.1)	6 (9)	2 (3)	2 (3)	
>30	11 (61.1)	2 (11.1)	5 (27.8)	0 (0)	
Obstetric score					0.000[b*]
Primigravida	39 (97.5)	1 (2.5)	0 (0)	0 (0)	
Multigravida	29 (64.4)	7 (15.6)	7 (15.6)	2 (4.4)	

[b]Fisher's exact; [*]Statistically significant at $\alpha = 5\%$ and $p < 0.05$

Table 3: Relationship between induction and type of delivery

	Induction					
Variables	*No induction*	*PGE1*	*PGE2*	*PGE1 + PGE2*	*Spontaneous*	*p value*
LSCS	18 (85.7)	1 (20)	3 (12.5)	2 (50)	1 (3.2)	0.000[b*]
FTVD	2 (9.5)	2 (40)	20 (83.3)	2 (50)	26 (83.9)	
PTVD	0 (0)	2 (40)	1 (4.2)	0 (0)	3 (9.7)	
Forceps	1 (4.8)	0 (0)	0 (0)	0 (0)	1 (3.2)	
Emergency LSCS	14 (66.7)	1 (4.8)	3 (14.3)	2 (9.5)	1 (4.8)	1.000[b]
Elective LSCS	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	

FTVD, full-term vaginal delivery; LSCS, lower-segment cesarean section; PTVD, preterm vaginal delivery; [b]Fisher's exact; [*]Statistically significant at $\alpha = 5\%$ and $p < 0.05$

Table 4: Relationship between gestational age and birth weight, Apgar at 1 and 5 minutes, placental weight

	Gestational age (weeks)			
	$<36^{+6}$	*$37–40^{+6}$*	*>41*	*p value*
Birth weight (kg)				0.001[b*]
<2.5	8 (66.7)	10 (14.7)	0 (0)	
2.5–3.5	1 (8.3)	46 (67.6)	1 (100)	
>3.5	3 (25)	12 (17.6)	0 (0)	
Apgar at 1 minute				0.006[b*]
≤5	4 (28.6)	1 (1.4)	0 (0)	
6–7	3 (21.4)	18 (25.7)	0 (0)	
≥8	7 (50)	51 (72.9)	1 (100)	
Apgar at 5 minutes				0.001[b*]
≤5	4 (28.6)	0 (0)	0 (0)	
6–7	0 (0)	1 (1.4)	0 (0)	
≥8	18 (71.4)	69 (98.6)	1 (100)	
Placental weight (g)				0.000[b*]
<500	13 (92.9)	20 (28.6)	0 (0)	
≥500	1 (7.1)	50 (71.4)	1 (100)	

[b]Fisher's exact; [*]Statistically significant at $\alpha = 5\%$ and $p < 0.05$

Postnatal Period

Most of the babies who were born to HBsAg-positive mothers have received HBIg soon after delivery and active immunization with hepatitis B vaccine, thereby reducing the risk of contracting hepatitis B infection in newborns.

Discussion

It is well known of the dilemma that exists due to the HBV infection in pregnancy.[15] Although there have been noted adverse pregnancy outcomes for both mother and the baby, this illness has been seldom looked into.[15,16]

An Asian study on chronic HBV-infected pregnant women stated that the mean age of their study participants was 30.7 ± 6 years.[17] Another study was with a mean age of 27.69 ± 5.67 years.[18] In our study, most of the participants were <30 years of age 67 (78.8). A retrospective cohort study on HBsAg-positive women showed that 12.8% were >35 years of age ($p = 0.016$[b]).[18]

The majority of the pregnant women were diagnosed as HBsAg-positive during routine antenatal investigations in the first trimester during their first pregnancy and those who were found with a high viral load were started on tenofovir 300 mg once a day. Some of the women were also found to be associated with TPHA-positive VDRL negativity and have received injection penicillin. It was also noticed that those women who were HBsAg-positive had a higher chance of presenting with other infections and some presented with yellowish discoloration of eyes.

A study done at Kaiqi et al. which looked into the association between HBsAg-positive status and pregnancy outcomes stated that the HBsAg-positive status was associated with the high risk of GDM (Odds ratio 1.24), intrahepatic cholestasis of pregnancy (Odds ratio 3.83), and preterm birth (Odds ratio 1.42).[19] Similar findings were seen by Qianving et al.[15] Our study showed contradiction wherein 8.2, 1.2, and 16.5% had GDM, intrahepatic cholestasis of pregnancy, and preterm, respectively. The study concluded that the HBsAg-positive status in pregnancy had an impact not only on the above complications but also inferred that neonatal asphyxia would occur.[19]

A review study conducted by Dalenda et al. stated that HBsAg viral transmission was by sexual contact.[20] Our study showed that in addition to sexual contact (as seen in those pregnancies wherein husbands were found to be HBsAg-positive), there must have existed other modes of transmission from close family members (father, mother, and siblings). Lamivudine and tenofovir were first-line therapies described by Stanialas et al., in our setup, tenofovir was the most preferred and commonly used medication which was highly efficacious and resulted in uneventful pregnancy

Table 5: Association of blood parameters in HBsAg-positive mothers in pregnancy

Variables	*N = 85*	*Mean*	*Standard deviation*	*p value**
Hemoglobin				
Primigravida	37	11.47	1.68	0.981
Multigravida	43	11.48	1.50	0.981
FBS				
Primigravida	24	79.08	10.00	0.106
Multigravida	37	84.59	14.32	0.082
PPBS				
Primigravida	17	105.65	20.64	0.168
Multigravida	15	125.6	53.97	0.195
Creatinine				
Primigravida	15	0.61	0.17	0.788
Multigravida	17	0.62	0.22	0.785
Uric acid				
Primigravida	12	5.35	1.48	0.557
Multigravida	11	5.00	1.23	0.554
AST				
Primigravida	36	25.86	16.72	0.256
Multigravida	38	22.21	10.09	0.263
ALT				
Primigravida	35	24.06	16.16	0.089
Multigravida	38	18.55	10.87	0.095
Blood urea				
Primigravida	15	15.52	4.00	0.232
Multigravida	16	13.35	5.69	0.228
Direct bilirubin				
Primigravida	31	0.16	0.12	0.935
Multigravida	36	0.16	0.11	0.936
Total protein				
Primigravida	33	6.44	0.51	0.504
Multigravida	36	6.36	0.47	0.505

ALT, alanine transaminase; AST, aspartate transaminase; FBS, fasting blood sugar; PPBS, postprandial blood sugar; **p* value calculated using the independent *t* test for parametric variables, and the significance of $p < 0.05$

Table 6: Association of liver function tests in HBsAg-positive mothers in pregnancy

Variables	*N = 85*	*Mean rank*	*p value**
TSH			0.22
Primigravida	33	39.77	
Multigravida	39	33.73	
Platelet count			0.169
Primigravida	23	33.85	
Multigravida	36	27.54	
Total count			0.289
Primigravida	17	21.18	
Multigravida	20	17.15	
Total bilirubin			0.556
Primigravida	33	33.52	
Multigravida	36	36.36	
GGT			0.037
Primigravida	32	38.56	
Multigravida	34	28.74	
LDH			0.411
Primigravida	11	14.36	
Multigravida	14	11.93	
ALP			0.177
Primigravida	32	37.36	
Multigravida	35	30.93	

ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; TSH, thyroid-stimulating hormone; **p* value calculated using the Mann–Whitney test for nonparametric variables, and significance of $p < 0.05$

outcomes.[21] Most of the pregnant women who were diagnosed as HBsAg-positive were HBeAg-negative, indicating the inactivity of the virus and low infectivity which is also confirmed by their low HBV DNA viral load and hence not requiring treatment.

A study in Thailand stated that there was no increased risk of complications, such as preeclampsia (6.3%, $p = 0.405$) and abortions (1.8%, $p = 0.166$) in HBsAg-positive pregnant women when compared to HBsAg-negative pregnant women.[18] Our study showed that among the 85 HBsAg-positive women, 15 (17.6) had preeclampsia and 17 (20) had a history of abortions in the previous pregnancy. The chances of IUD 4 (4.7) in the present pregnancy and history of IUD in the past pregnancy were significantly increased in HBsAg-positive women in our study 12 (14.1) whereas stillbirths 1.7% were reported in the Thailand study.[18] This difference in complications seen in HBsAg-positive women could be due to variations in the genetic inheritance.

In an Asian study, 57.1% of women had alanine transaminase elevation.[17] Our study showed elevation of alanine transaminase 24.06 ± 16.16 ($p = 0.089$), aspartate transaminase levels in primigravida 25.86 ± 16.72, and gamma-glutamyl transferase levels in primigravida 38.56 ($p = 0.037$). In multigravida, ALT, AST, and GGT levels were 18.55 ± 10.87 ($p = 0.095$), 22.21 ± 10.09 ($p = 0.263$), and 28.74 ($p = 0.037$), respectively. Although the study concluded the association of serum alanine transaminase elevation with hepatitis B and pregnancy, we bet to defer that gamma-glutamyl transferase was a better association between hepatitis B and pregnancy ($p = 0.037$).[17]

Literature review suggests the need for cesarean section in HBsAg-positive women.[22] In Thailand, it was seen that the rate of cesarean section (20.3%) was not increased in HBsAg-positive pregnancies when compared to the control group ($p = 0.176$).[18] The study also noted that with the causation of fetal distress (2.8%) to be the indication of a cesarean section, it was not a significant determining factor to estimate the preferred mode of delivery ($p = 0.988$).[18] In our study, we saw a predilection of LSCS 25 (29.4) in comparison to normal delivery [FTVD 51 (61.2), PTVD 6 (7.1)]. The major indications for LSCS in our patients were a nonreactive nonstress test 8 (9.4), followed by a history of previous LSCS 5 (5.9) and cephalopelvic disproportion 4 (4.7). This could be possibly due to the fact that women in the Indian population are less aware of the HBV infection and its effect on pregnancy and the importance of seeking medical care from the very start of pregnancy.

The birth weight of most babies born to HBsAg-positive mothers was between 2.5 and 3.5 kg 48 (56.5). Similarly, 15.8% of women delivered low birth weight babies as observed by Sirilert et al.[18] Apgar scores <7 at 1 minute (6.3) and <7 (3.0) at 5 minutes were not significantly increased in babies born of HBsAg-positive mothers.[18] Our study showed Apgar scores of <7, 26 (30.6) and 5 (5.9) at 1 and 5 minutes, respectively. This could be due to the timely neonatal resuscitation protocols followed at the institution noting the marked improvement in Apgar scores at 1 and 5 minutes of life.

Studies recommend breastfeeding in HBsAg-positive mothers.[23] Breastfeeding is not contraindicated as it does not increase the risk of transmission provided the baby has received immunoprophylaxis.

A Netherland study stated that the need for an antiviral drug, chiefly lamivudine, would be essential in the treatment of HBsAg-positive pregnancies in the third trimester.[24] We treated our patients with tenofovir and did not necessarily start it during the third trimester. The anomalies witnessed in these pregnancies were 5 (5.8) had renal anomalies, such as pelviectasis, while one baby had a prominent stomach bowel meconium-filled colon rather than the duodenum with grade I echogenicity of small bowel loops.

A need does exist for standard treatment protocols as varied guidelines have been stated based on the region of the prevalence of the viral infection.[25,26] At our institution, we follow a routine screening of all pregnant mothers for HBsAg. If HBsAg is negative, then vaccinate high-risk patients as well as infants at birth. If HBsAg is positive, check HBV DNA levels and at 28 weeks check alanine transaminase, HBeAg, and anti-HBe. If HBV DNA levels <2 lakhs IU/mL, no antiviral therapy is required but the infant receives hepatitis B vaccine and HBIg at birth whereas HBV DNA levels >2 lakhs IU/mL, consider treatment at 28–32 weeks with antivirals and can consider stopping therapy 0–3 months after delivery while monitoring for flare in the postpartum period with alanine transaminase and HBV DNA at 1, 3, and 6 months.

Conclusion

The development of chronic hepatitis B infection is inversely proportional to the age at which infection occurs. Chronic hepatitis B infection increases the risk of chronic liver disease, cirrhosis, and hepatocellular carcinoma. This tells us the importance of timely and efficient antepartum surveillance to identify pregnant women who are HBsAg-positive and to effectively start treatment in those women with a high viral load to reduce the risk of transmission to the newborns. Our study took into consideration both maternal and fetal effects of HBV infection during the antenatal period. Our study showed that HBsAg-positive women who had preterm pregnancies had a higher chance of having preeclampsia ($p = 0.000^{b}$), polyhydramnios ($p = 0.049^{b}$), and antepartum hemorrhage ($p = 0.049^{b}$). Also, we have identified the risk of the development of fetal anomalies, such as fetal pelviectasis (5.8), emphasising the importance of timely identification and the start of treatment to reduce the adverse fetal outcomes. Our study also showed the higher chances of abortions ($p = 0.000^{b}$) and IUD ($p = 0.000^{b}$) in HBsAg-positive women. All the above-mentioned complications showed the importance of conducting awareness programs for all the women to educate them about the HBV infection in pregnancy and its outcomes and the need to seek medical care during the antenatal period.

Close monitoring of liver function tests particularly gamma-glutamyl transferase and antepartum fetal surveillance increases the chance of good outcomes in these pregnancies.

Limitations

Mothers and infants could not be followed up postdelivery.

Importance

One among the first few papers which studied in detail the obstetric and perinatal outcomes of HBV infection in pregnancy in the South Indian population.

Scope for Future

Mother and Child Health Mission should take into consideration the importance of having separate awareness programs for HBV infection in pregnancy and have a standard set of management protocols.

Pros and Cons of the Study

Pros	*Cons*
This study viewed in detail the complications and management of HBsAg-positive mothers in pregnancy in the South Indian population	This study could have been a prospective study

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Declarations

Availability of data and material: The data can be published in an open-access forum without causing harm to the patients involved in the study.

Authors' Contributions

Dr Christy Vijay: (1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; (2) drafted the work or revised it critically for important intellectual content; (3) approved the version to be published; and (4) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Ashima K Thuruthayil: (1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; (2) drafted the work or revised it critically for important intellectual content; (3) approved the version to be published; and (4) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr Annamma Thomas: (1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; (2) drafted the work or revised it critically for important intellectual content; (3) approved the version to be published; and (4) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Dr Christy Vijay, Dr Ashima K Thuruthayil, and Dr Annamma Thomas. The first draft of the manuscript was written by Dr Christy Vijay and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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