Is maternal HBsAg carrier status associated with adverse pregnancy outcome?

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Abstract

Objective. *Although various studies have suggested that chronic hepatitis B virus infection is associated with several pregnancy and neonatal complications, the scientific information is still conflicting.* ***Methods.*** *In an attempt to clarify these suppositions we conducted a retrospective case-control study on 52 hepatitis B surface antigen (HBsAg) positive pregnant women (case group) and 111 HBsAg negative women (control group). The main outcome was to evaluate the effect of maternal HBsAg carrier status on pregnancy outcome in terms of preterm birth, preterm premature rupture of membranes (PPROM), prelabor rupture of membranes (PROM), hemorrhagic complications (abruptio placentae, postpartum hemorrhage), fetal weight and Apgar score.* ***Results.*** *No case of HBsAg vertical transmission was registered, irrespectively of the delivery way. No significantly association was found between HBsAg carrier status and preterm birth (13,21% vs. 20,72%, p=1,24), PPROM (7,69% vs. 9,91%, p=0,63), PROM (18,87% vs. 23,42%, p=0,36), large for gestational age (3,85% vs. 4,50%, p=0,59), small for gestational age (7,69% vs. 6,31%, p=0,38), antepartum hemorrhage (p=0,51), postpartum hemorrhage (p=0,62) and Apgar Score (p=0,72).* ***Conclusions.*** *According to our findings, there is no association between HBsAg carrier status and adverse pregnancy and maternal perinatal outcome.*

Keywords: *hepatitis B surface antigen, pregnancy outcome, perinatal outcome, vertical transmission*

Introduction

Approximately 350 million people are infected with hepatitis B virus (HBV) worldwide and 50% of them have acquired their infection in the perinatal or neonatal period, especially in countries where HBV has a high prevalence. The global prevalence of chronic HBV infection varies widely, from high (>8%) in Africa, Asia and Western Pacific to intermediate (2-7%) in Southern and Eastern Europe and low (<2%) in Western Europe, North America and Australia. In Romania prevalence of HBV infection varies between 4.9-6%[1].

HBV infection is still a major public health concern all over the world, and researches must rely upon the various aspects of this issue. Infection with hepatitis B virus in pregnant women is a threat for both mother and fetus. All pregnant women should be screened for hepatitis B surface antigen (HBsAg) at first antenatal visit. Despite its prevalence, there are little data on the effect of maternal chronic HBV infection regarding pregnancy outcome[2,3].

Worldwide, vertical transmission remains the most frequent route of infection, particularly in endemic areas where up to 20% of women of childbearing age may have HBV[4].

Studies have suggested that chronic HBV infection is associated with gestational diabetes mellitus, fetal macrosomia, antepartum hemorrhage, threatened premature labor and lower Apgar score[5,6,7,8].

Review of articles on this issue though demonstrated controversial findings. Some studies reported increased maternal and neonatal complication in HBsAg carrier women[2,9] and other showed that hepatitis B surface antigenic determinant in pregnant women does not put additional risk for pregnancy[10].

In HBsAg seropositive women the transmission rate is 10-20%, in the absence of immunoprophylaxis. In the cases were exists both HBsAg and hepatitis B 'e' antigen (HbeAg) seropositivity vertical transmission rate is up to 90%[16].

Some studies using multivariable analyses showed that association between HBV or hepatitis C virus (HCV) carrier status and perinatal mortality, congenital malformations and low birth weight remains significant[7]. Nevertheless, maternal HBV or HCV carrier status is an independent risk factor for adverse perinatal outcome and careful surveillance is warranted[7].

In order to evaluate the relationship between maternal HBsAg carrier status and perinatal outcome, we conducted a two-year retrospective study in our hospital.

Methods

A retrospective case-control study was carried out over a two years period from January 2011 to December 2012 on HBsAg positive women attending the labor ward at University Hospital of Obstetrics and Gynecology of Brasov from Romania.

The study included 52 HBsAg positive women (case group) and 111 HBsAg negative women (control group). Among the 52 HBsAg positive women, two were also HbeAg positive.

All newborns from HBsAg positive mothers had received immune prophylaxis within the first 12 hours after birth (most of them in the first hour after birth) using hepatitis B immunoglobulin (0,4ml/kg, HEPATECT-CP) and single-antigen hepatitis B vaccine (ENGERIX, 10µg/0.5 ml), within 12 hours of birth, according to guidelines.

Control group was identified and selected from Delivery Registry at random, matched for age, parity, antenatal surveillance and year of delivery with case group because we considered that these characteristics had important effects on pregnancy outcome. Data about antenatal assesment were extracted from the patient records available in our hospital.

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Inclusion criteria

- Documented serum HBsAg presence;
- Singleton pregnancies;
- Cephalic presentation;
- Women with the same antenatal screening and checkup;
- All newborns from HBsAg positive mothers received immunoprophylaxis according to guidelines.

Exclusion criteria

- Concurrent infection with HCV, hepatitis D virus, human immunodeficiency virus or *Treponema pallidum*;
- One or more known primary or secondary causes of liver disease other than hepatitis B (alcoholism, autoimmune hepatitis, malignancy with hepatic; involvement), other congenital or metabolic conditions affecting the liver;
- Women with chronic or active hepatitis from any cause at any time during;
- Pregnancy;
- Multiple pregnancy;
- Other pathological conditions that may affect the pregnancy outcome such as: placenta praevia, diabetes, severe hypertension etc.

Our main outcome was to evaluate the effect of maternal HBsAg carrier status on pregnancy outcome in terms of preterm labor, preterm birth, preterm premature rupture of membranes (PPROM), hemorrhagic complications (*abruptio placentae*, postpartum hemorrhage), fetal weight and Apgar score.

Statistical analysis was performed using SPSS for Windows version 9.1. Odds ratio and corresponding 95% confidence intervals were calculated using chi-square test or Fisher's exact test, for perinatal outcomes in the study groups.

Results

There was no significant difference in the mean age and parity between the case and control groups (Table 1).

Results indicated that preterm birth risk was not significantly different in the case group where compared with control group (p=1.24). Similarly, there was no significantly association with obstetrical hemorrhage (p>0.05), preterm premature rupture of membranes (p=0.63) and pre labor rupture of membranes (p=0.36) (Tables 2 and 3).

The effects of HBsAg carrier status on the neonatal outcome was also analyzed and there was no significantly association between HBsAg status and low Apgar score (p=0.72), small for gestational age (p=0.38) or large for gestational age (p=0.59).

Our findings determined that there were no case registers of vertical transmission of hepatitis B virus in the study group.

Discussion

Some studies reported an increased incidence of maternal and neonatal morbidity such as gestational diabetes, preterm labor, PPROM in the HBsAg positive mothers[2,11,12].

Table 1 Maternal demographic parameters with respect to HBsAg status

Parity	HBsAg positive (n=52)*	HBsAg negative (n=111)*
Primiparous	28 (52.83%)	62 (55.86%)
Multiparous	24 (45.28%)	49 (44.14%)
Age (years)	27.96 ± 4.80	28.48 ± 4.33

**Results are expressed in percentage (%) or mean ± standard deviation (SD).*

Table 2 Maternal outcome with respect to HBsAg status

	HBsAg positive	HBsAg negative	p-value	OR*** (95% CI****)
Preterm birth <37 weeks	7 (13.21%)	23 (20.72%)	1.24	0.59 (0.23-1.49)
PPROM*	4 (7.69%)	11 (9.91%)	0.63	0.38 (0.038-3.78)
PROM**	10 (18.87%)	26 (23.42%)	0.36	0.77 (0.34-1.76)
Antenatal maternal hemorrhage	2 (3.85%)	3 (2.70%)	0.51	0.69 (0.11-4.29)
Postpartum hemorrhage	1 (1.92%)	3 (2.70%)	0.62	1.42 (0,14-13,95)

**PPROM= preterm premature rupture of membranes, **PROM= prelabor rupture of membranes; ***OR= Odds ratio; ****CI= confidence interval*

Table 3 Neonatal outcome with respect to HBsAg status

	HBsAg positive	HBsAg negative	p-value	OR*** (95% CI****)
LGA*	2 (3.85%)	5 (4.50%)	0.59	0.72 (0.27-2.95)
SGA**	4 (7.69%)	7 (6.31%)	0.38	1.59 (0.58-4.35)
Apgar score <7	2 (3.85%)	4 (3.60%)	0,72	1.07 (0.19-6.03)
Apgar score (mean + SD)	9.04 ± 0.65	9.19 ± 0.66		

**LGA= large for gestational age; **SGA= small for gestational age; ***OR= Odds ratio; ****CI= confidence interval.*

A study of Tse and contributors showed that HBsAg carriers had higher incidences of threatened preterm labor at <37 weeks (11.9% versus 6.3%, p=0.030), preterm birth at <34 weeks (4.7% versus 1.2%, p=0.033), gestational diabetes mellitus (19.0% versus 11.1%, p=0.012) and antepartum hemorrhage (11.5% versus 5.5%, p=0.026) and their infants had lower Apgar scores at the 1st (p=0.001) and 5th minute (p=0.007)[8].

A recent study of Lu and contributors demonstrated that HBsAg carrier status can increase the risk of preterm delivery in pregnancy, but it does not seem to affect the fetal growth[13]. Also recently, another study suggested that the HBsAg positive women were associated with increased risk of fetal macrosomia[6,13]. The same study reported that the incidences of gestational hypertension, preeclampsia, gestational diabetes mellitus, abnormal glucose tolerance, premature rupture of membranes, cesarean delivery, and postpartum hemorrhage showed no significant differences between the two groups (p>0.05), nor did the fetal birth weight, height, head circumference or Apgar scores[13].

A significantly association was reported in a recent study between HBsAg carrier status in pregnant women and infant birth weight with increased risk of obesity, diabetes mellitus and various forms of malignancies from childhood to adulthood, but further studies are needed[6]. Other reports on the effects of chronic HBV infection indicated no association with adverse pregnancy outcomes in carriers[10].

Delivery method has been also examined as a potential risk factor for HBV transmission. Nowadays studies reported that there are no significant effects of delivery mode according to HBV transmission in newborns and caesarean section does not reduce the incidence of immune prophylaxis failure[14,15,16,17,18].

In one of our previously study we showed that Endometrial Toll like Receptors (TLR) are involved in pathogen recognition and linking them, stimulating thus secretion of endometrial cytokines and chemokines, important both for immunity and reproduction. The immune response in endometriosis is characterized by low number TRL 3 and 4 at ectopic endometrial cells, which could reduce the immune function, without having any negative effects on the further pregnancies[19].

In our study no case of maternal-fetal transmission of HBV was reported. According to this, due also to systematic anti-HBs immunoprophylaxis in the very first hour after delivery, we can say in correspondence with last years data that method of delivery does not influence the transmission of HBV to newborn.

Because there was no significant difference between the two groups in our study, we can assert that there is no association between HBsAg carrier status and adverse pregnancy and perinatal maternal outcome.

Conclusions

Pregnant women HBsAg carriers do not have additional risk for the pregnancy and perinatal outcome in terms of preterm labor, preterm birth, PPROM, hemorrhagic complications, fetal weight and Apgar score. ■

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