

Maternal Hbsag Carrier and Pregnancy Outcome

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Abstract: Background : Hepatitis B virus infection is still a major public health concern all over the world, and much research must be carried out on the various aspects of this issue. Since infection with hepatitis B virus in pregnant mothers is a threat for both mother and her fetus, this study was performed to To assess the impact of maternal HBsAg carrier status on pregnancy outcomes Materials and Methods: one hundred fifty carriers of hepatitis B surface antigen (HBsAg) with singleton pregnancy, were compared with two hundred controls matched for age and parity. Results: Women with HBsAg carriers had higher incidences of preterm labour (21.2% vs. 13.9%, $P=0.037$), gestational diabetes (23.2% vs. 11.6%, $P=0.003$), cesarean section (32.4% vs. 28.2, $P<0.000$), prelabor rupture of membranes (7.1% vs. 4.0%, $P=0.011$) and Apgar scores lower 7 in their infants at the 5th minute (16.8% vs. 9.0%, $P=0.006$). Conclusion: HBsAg carriers have increased risk of adverse pregnancy outcomes. The role of chronic HBV infection in pregnancy complications is not clear and needs more investigation.

Key words: CARRIER, PREGNANCY, antigen, rupture

INTRODUCTION

Hepatitis B virus (HBV) is a common cause of liver disease in the world. Over 2 billion people today have been infected with HBV and 400 million of them are chronically infected carriers without significant liver disease (Schenke *et al.*, 2008; Belongia *et al.*, 2008). Over 70% of the chronic hepatitis B patients in the world are Asians (Lai *et al.*, 2001; Lin 1990). Fortunately, as Alavian *et al.* have reported, since Iran's national vaccination program implementation in 1993, the number of HBV patients in the age group 2-14 has declined from 1.3% to 0.8% (Alavian *et al.*, 2007).

Consequently, all pregnant women are screened for hepatitis B surface antigen (HBsAg) at the first antenatal visit. Despite its prevalence, there are little data on the effect of maternal chronic HBV infection on pregnancy outcomes. (Ka *et al.*, 2005)

On the other hand, a recent study suggested that maternal HBsAg carrier status was the explanation for the increased maternal serum ferritin found in association with gestation diabetes mellitus. (Su *et al.*, 2002) As serum ferritin acts as an acute phase reactant, the findings of this study suggest, an increased chronic inflammatory state in the HBV infected women.

Review of few published articles on this issue demonstrated controversial findings. Gambarin-Gelwan *et al.* and Tse *et al.* have reported increased maternal and neonatal complication in HBsAg carrier mothers (Ka *et al.*, 2005; Gambarin-Gelwan, 2007). While according to the study made by Wong *et al.*, hepatitis B surface antigenemia in pregnant women does not pose additional risk for the pregnancy (Wong *et al.*, 1999). Therefore, in order to evaluate the situation in our country, we have conducted a retrospective case-control study to assess the impact of maternal hepatitis B antigenemia on maternal and neonatal outcomes.

MATERIALS AND METHODS

A retrospective case control study was carried out over a 3 year period from January 2005 to December 2008 on HBsAg positive women attending the labor ward in Imam Khomeyni, Sari, Iran. Since the impact of maternal HbsAg carriage on adverse pregnancy outcome remain unclear, we could not estimate the required sample size with confidence. Hence, We studied the patient delivered over a three-year period. The study included 150 HBsAg positive women (case group) and 200 HBsAg negative women (control group). Control group matched for age and parity with case group, was identified and selected from the Delivery Suite Registry

at random.

The result of the routine antenatal HBsAg screening was retrieved from patient records. Unfortunately, neither of the patients had HBeAg status record in their medical history. Only singleton pregnancies were selected and those patients who were diagnosed to have had active hepatitis from any cause at any time during their pregnancy were excluded from the subsequent analysis.

The demographic characteristics including age, parity, past medical history, body mass index (BMI), and antenatal complication such as caesarean section(Cs), gestational diabetes (GDM), preterm labor (PTL), prelabour rupture of membranes(PROM) and low Apgar score were retrieved from the records.

Statistical analyses were performed using SPSS -13. In the primary stage, continuous variables were analyzed and reported as means and tested by t-test for comparison between the HBsAg negative and positive groups. Categorical variables were analyzed using Chi-square test or Fisher's exact test and odds ratios with 95% confidence interval were calculated. In the second stage, Multinomial logistic regression was performed to determine the role of HBsAg status in the subsequent perinatal outcome complications, by considering confounding factor effects.

RESULT AND DISCUSSION

Among the 2953 singleton pregnancies delivered in this period, 150 HBsAg carriers (5.07%) and 200 HBsAg negative control mothers were identified. There was no significant difference in the demographic characteristics like age, parity and haemoglobin level at booking.(table1), or past medical history(table 2), between the cases and controls.

Table 1: Maternal demographic parameters with respect to HBsAg status.

	HBsAg +ve(n=150)	HBsAg -ve(n=200)
primiparous	73(48.6%)	91(45.5%)
multiparous	77(51.3%)	109(54.5%)
Age(years)	28.54±4.5	29.1±5.1
Hb at admission(g/dl)	11.8±1.6	11.74±1.8

Hb: hemoglobin. Results are expressed in number (%) or mean± standard deviation (SD) as indicated

Table 2: Maternal Past health with respect to HBsAg status.

	HBsAg +ve(n=150)	HBsAg -ve(n=200)
Hypertension	1(0.6%)	1(0.5%)
Diabetes mellitus	1(0.6%)	1(0.5%)
History of stillbirth	0(0.0%)	1(0.5%)
Liver disease	2(1.3%)	1(0.5%)

Results are expressed in number (%) or mean± standard deviation (SD) as indicated.

In the case group, there was a significantly higher incidence of gestational diabetes, preterm labor at less than 37 weeks, premature rupture of membranes, cesarean section and low Apgar score in 5th minute compared to control group.

Table 3: Maternal complications with respect to HBsAg status.

	HBsAg +ve n=150	HBsAg -ve n=200	P-value	OR (95% CI)
GDM	35 (23.2%)	23 (11.6%)	0.003	1.532 (1.190-1.972)
PTL	32 (21.2%)	27 (13.9%)	0.037	1.338(1.018 – 1.757)
PROM	14 (7.1%)	6(4.0%)	0.011	1.699 (1.2140-2.326)
Cs	64 (32.4%)	42(28.2%)	0.000	1.713 (1.362-2.155)
5 min Apgar score<7	25 (16.8%)	18 (9.0%)	0.006	1.899(1.405-2.568)

GDM: gestational diabetes mellitus; PTL: preterm labor; PROM: prelabour rupture of membranes; Cs: caesarean section

Discussion:

We have demonstrated a positive association between preterm labour (21.2% vs. 13.9%, $P=0.037$), gestational diabetes (23.2% vs. 11.6%, $P=0.003$), cesarean section (32.4% vs. 28.2, $P<0.000$), prelabour rupture of membranes(7.1% vs. 4.0%, $P=0.011$) and Apgar scores lower 7 in their infants at the 5th minute (16.8% vs. 9.0%, $P=0.006$) HBsAg carrier status.

An increased incidence of maternal and neonatal morbidity such as gestational diabetes, preterm labor, premature rupture of membranes in the HBsAg positive mothers was reported (Ka *et al.*, 2005;Gambarin-Gelwan, 2007; Saleh-Gargari *et al.*, 2009). Although other reports on the effects of chronic HBV infection indicated no association with adverse pregnancy outcomes in the carriers (Wong *et al.*, 1999),

there have been case reports and studies indicating an increased incidence of maternal and neonatal morbidity in HBV infection. (Yang *et al.*, 2009).

The reports of hepatitis B-related adult-onset Still's disease, polyarteritis nodosa, glomerulonephritis and vasculitis (Gambichler *et al.*, 2003), indicate that chronic HBV infection may be associated with a systemic inflammatory state that plays a causative role in these autoimmune diseases. Chronic HBV infection is associated with increased levels of pro-inflammatory cytokines such as IL-2, IL-6, IL-10, macrophage migration inhibitory factor, and tumour necrosis factor- α (TNF- α), which are more pronounced during active hepatitis. (Bozkaya *et al.*, 2000) Our findings of the association between the HBsAg carrier status with gestational diabetes mellitus, preterm birth could have, therefore, represented the effect of an accentuation of the normal systemic inflammatory response seen in pregnancy. (Luppi *et al.*, 2002) There is evidence that an exaggerated systematic inflammatory response could lead to certain obstetric complications. The pathogenesis of gestational diabetes mellitus is related to insulin resistance (Shao *et al.*, 2002) which in turn is influenced by chronic subclinical inflammation in which immune markers are raised (Festa *et al.*, 2000) TNF- α and its soluble receptors (sTNFR-1 and -2) were found to be elevated in patients with GDM. (Winkler *et al.*, 2002) It has been demonstrated that the levels of TNF and its receptors were raised in patients with chronic HBV infection. (Sheron *et al.*, 1991) Similarly, many studies have shown that increased serum concentrations of pro-inflammatory cytokines that include IL-2 receptors, IL-6, IL-8, TNF- α and thrombin play an important role in premature labour. (Gucer *et al.*, 2001) Therefore, the additional systemic inflammatory response induced by chronic HBV infection could be the central explanation of the findings in our study.

In our study, the Apgar scores at 1st and 5th minutes were lower in the HBsAg carrier status newborns and it was probably related to the higher incidence of preterm delivery.

In addition, our study showed HBsAg carriers have increased risk of adverse pregnancy outcome.

But in order to come to a definite conclusion for explaining the potential role of chronic HBV infection in pregnancy complications, more investigation with more data must be carried out in a prospective manner.

ACKNOWLEDGMENTS

We are thankful to the medical staff of Imam Khomeyni hospitals for their sincere cooperation in collecting patient's data.

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