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Impact of maternal HBsAg carrier status on pregnancy outcomes in Duhok city, Iraq



Amira S. Khalil¹, Nawfal R. Hussein^{2*}, Maida Y. Shamdeen¹

¹Department of Gynecology and Obstetrics, College of Medicine, University of Duhok, Duhok, Kurdistan Region, Iraq

²Department of Internal Medicine, Azadi Teaching Hospital, College of Medicine, University of Duhok, Duhok, Kurdistan Region, Iraq

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ABSTRACT

Objective: To investigate the relationship between hepatitis B virus (HBV) positivity and pregnancy outcomes. Also, the association between HBV-related risk factors and HBV status was studied.

Methods: A total of 100 HBV positive pregnant women were recruited and the pregnancy outcomes were compared with 301 HBV negative women. Blood samples were collected and tested for HBV by HBsAg ELISA. Data were collected for recruited subjects using interview questionnaire.

Results: Data analysis showed that 51/100 (51%) of the HBV-positive subjects gave a history of HBV in the family which was significantly higher than that of HBV-negative patients [41/301 (13.6%) $P = 0.001$]. A significant association was found between positive history of surgery and HBsAg positivity ($P = 0.009$). Then, pregnancy outcomes were stratified according to the HBV positivity. No significant association was found between HBV status and pregnancy outcomes ($P > 0.05$ for all).

Conclusions: Positive family history of HBV and previous surgical procedures are associated with higher rate of HBV positivity. No association is found between HBV positivity and pregnancy outcomes.

1. Introduction

Infection with hepatitis B virus (HBV) is a public health problem. Around 500 million subjects are chronically infected with the virus worldwide [1,2]. HBV can be transmitted through blood and blood products, hemodialysis, shared needles among drug abusers, surgeries and dental procedures [1,2]. Additionally, the virus can be transmitted sexually and certain sexual behaviors such as homosexuality increased the risk of infection [1–4]. HBV can also be transmitted vertically from mother to new born babies during delivery. The rate of infection in infants depends upon viral load and HBe antigen positivity. In mothers with HBe antigen positive HBV infection, the transmission rate may reach up to 90%, while the infectivity may decrease to as low as 10% in HBe antigen negative mothers [5]. Recent studies

have shown that mothers with HBV DNA levels $\geq 10^6$ copies/mL (≥ 200000 IU/mL) carried a higher risk of HBV transmission of the HBV to their infants [6–8].

The prevalence of HBV varies from region to region ranging from 8% in some areas in China to less than 1% in some European countries. In a study conducted in Iraq in which 7900 subjects were recruited, the prevalence of HBV was found to be less than 1% [9]. Different studies have shown conflicting results about the association of maternal chronic HBV infection and pregnancy outcomes. Some studies have shown no significant relationship between HBV infection and low birth weight, preterm labor, pregnancy induced hypertension and gestational diabetes [10,11]. Other reports have shown a relationship between chronic HBV and gestational diabetes mellitus and gestational hypertension [12]. This is important because gestational diabetes, hypertension and preeclampsia are major causes of maternal, fetal, and neonatal morbidity and mortality [13,14]. The re-activation and exacerbation of the infection during or after gestation is uncommon [15]. Few case reports described cases of fulminant hepatitis and liver failure in peripartum period [15,16]. In addition to health-related issues, HBV is associated with social stigma in our locality and a

*Corresponding author: Nawfal R Hussein, Department of Internal Medicine, Azadi Teaching Hospital, College of Medicine, University of Duhok, Duhok, Kurdistan Region, Iraq.

E-mail: Nawfal.hussein@yahoo.com (N.R. Hussein).

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misbelief that it is associated with negative pregnancy outcomes including abortion. To our knowledge, no study has been conducted in Kurdistan investigating the risk factors associated with HBV in pregnant women and the association between HBV positivity and pregnancy outcomes. Therefore, in this project, it was aimed at studying HBV-associated risk factors in pregnant women attending Duhok Maternity Hospital and investigating the pregnancy outcomes in HBV-infected pregnant women.

2. Materials and methods

2.1. Patients

The study was conducted from June 2015 to June 2016. During the period of the study, all HBV-positive women who visited Duhok Maternity Hospital were recruited. A total of 100 HBV-positive pregnant women were recruited; the average age of the recruited samples was (27.5 ± 6.1) years old. On the other hand, 301 HBV-subjects were recruited as a control group. There was no significant difference in age, BMI, education, address or parity between two groups ($P > 0.05$) (Table 1).

Blood samples were collected using a 5 cc syringe to collect approximately 5 mL blood from each subject. Then, the blood samples were centrifuged at 1500 rpm for 3 min to obtain serum that was frozen in -20°C until the test was performed. A questionnaire was filled in a face to face interview. The questionnaire covered history of blood transfusion, history of dental surgeries, history of surgical procedures, family history of HBV, previous history of abortion, and history of tattooing.

Primary pregnancy outcomes were: miscarriage (spontaneous abortion), prepartum hemorrhage, preterm (<37 weeks), or ectopic pregnancy. Other maternal outcomes included preeclampsia and eclampsia, gestational hypertension and gestational diabetes mellitus. The rate of cesarean section was not assessed because caesarean delivery rate was high in Kurdistan due to “social influence” rather than medical or obstetric indication.

2.2. HBsAg ELISA

HBsAg was studied by commercial Liaison-XL diagnostic system (USA) following manufacturer's instruction. First, specific monoclonal antibodies (anti HBsAg) were fixed to the surface of micro-wells. Subjects' serum was then added to the micro-well and secondary conjugated monoclonal antibody, conjugated with horseradish peroxidase, was added. Unbound serum proteins and horseradish peroxidase conjugate were then washed off. The substrate was added after blocking the enzymatic reaction and optical density was measured by an ELISA reader.

2.3. Ethics

The study was approved by the Scientific and Ethics Committee, board of Kurdistan for medical specialties. Oral consent was obtained from all subjects before data collection.

2.4. Statistics

Chi-squared test was applied to assess associations between HBV positivity and different variables. Mann–Whitney test was used to compare continuous data. P value of 0.05 or less was

regarded significant. All computations were carried out by SPSS version 21.

3. Results

3.1. HBV-associated risk factors

Data analysis showed that 51/100 (51%) of the HBV-positive subjects gave a history of HBV in the family which was significantly higher than that of HBV-negative patients [41/301 (13.6%)] ($P = 0.001$). Also, a significant association was found between a previous history of surgery and HBsAg positivity ($P = 0.009$). No association was found between history of tattoo, blood transfusion, abortion, or dental procedures and HBV-positivity (Table 2).

3.2. Pregnancy outcomes

According to the pregnancy outcomes, the recruited samples were classified into normal vaginal delivery, preterm labor, abortion and ectopic pregnancy. A total of 57/100 (57%) of the HBV-positive group was normal vaginal delivery versus 187/301 (62.1%) for the HBV-negative group. Pregnancy outcomes were compared according to the HBV-positivity and it was found that there was no significant association between HBV status and pregnancy outcomes (Table 3).

3.3. Pregnancy related complications

Also, the data were stratified according to pregnancy-related complications. No gestational diabetes mellitus was found in

Table 1

Characteristics of HBV-positive patients and HBV-negative patients.

Characteristics	HBV-positive	HBV-negative	P value
Age	27.50 ± 6.10	27.40 ± 6.08	0.570
BMI	28.7 ± 4.9	28.5 ± 4.5	0.540
Education	Primary/under	174 (76.3)	0.224
	Middle/high school	111 (71.6)	
Address	College or above	16 (88.9)	0.730
	City	40 (29.6)	
Parity	Rural	60 (22.6)	0.169
	Primy	35 (28.5)	
	Multi	213 (76.6)	

Table 2

Risk factors associated with HBV positivity.

History of actions	HBV-positive (n)	HBV-negative (n)	P value
Tattoo	Yes	72	0.400
	No	229	
Blood transfusion	Yes	37	0.440
	No	264	
Family history of HBV	Yes	41	0.001
	No	260	
Abortion	Yes	99	0.122
	No	202	
Dental procedures	Yes	140	0.200
	No	161	
Surgery	Yes	210	0.009
	No	91	

Table 3

Pregnancy outcomes according to the HBV-positivity.

Pregnancy outcome	HBV-positive (n)	HBV-negative (n)	P value
Normal vaginal delivery	82	223	
Preterm labor	4	16	0.60
Prepartum hemorrhage	1	14	0.12
Abortion	11	36	0.70
Ectopic	2	12	0.37
Total	100	301	

HBV-positive patients. A total of 2/100 (2%) of the HBV-positive subjects had preeclampsia versus 16/301 (5.3%) for HBV-negative patients ($P = 0.2$). No significant association was found between gestational hypertension and HBV positivity: 8/100 (8%) for HBV-positive patients versus 37/301 (12.3%) for HBV-negative patients ($P = 0.3$).

4. Discussion

Chronic HBV infection is associated with deleterious consequences such as cirrhosis and hepatocellular carcinoma. In addition, in our locality, such an infection is associated with social stigma and misbelief that it can cause negative pregnancy outcome such as abortion. Healthcare planners setup a plan to prevent the transmission of infection and eliminate the virus by 2030. To achieve such a plan, studying risk factors associated with HBV infection is important. Conducting population based study in our region is insuperable due to logistic and financial issues. Hence, we investigated HBV-associated risk factors in different groups such as in pregnant women in the region. In a study conducted in China, it was found that history of surgical operations was associated with HBV positivity [17]. In Turkey, dialysis, family history of HBV and sexual contact with HBV positive subjects were found as risk factors for acquiring HBV infection [18]. In our country, a significant association was found between previous history of surgical procedures and HBV positivity. These results should be confirmed and planning of preventive public health program should concentrate on such factors. Blood transfusion and dental surgeries were not predictive factors for HBV infection. This might trace back to the strict policy of testing blood and blood products in Duhok city.

Several studies have investigated the effect of chronic HBV on pregnancy outcomes. While some reports did not show any effects of chronic HBV infection on pregnancy and concluded no association with adverse pregnancy outcomes [11,19]. There have been reports showing a high incidence of maternal and neonatal morbidity associated with such an infection including fetal distress, premature delivery and meconium peritonitis [12,19–22]. In a recent study conducted in China, it was shown that the rates of stillbirth, preterm birth, gestational diabetes, premature rupture of the membrane, low birth weight or small for gestational age were not associated with HBV positivity [19]. However, the proportion of miscarriage was significantly higher among the HBV carriers than the controls [19]. In our study, no associations were found between HBV carrier status and abortion or ectopic pregnancy. Previously, a significant association between gestational diabetes and HBsAg carrier

status was shown [19]. In our study, no association was found between gestational diabetes and HBV positivity. This might be explained partially by the small sample size used in our study. Additionally, no association was found between HBV carrier status and gestational hypertension or pregnancy induced hypertension. Reddick *et al.* [11], showed no association between maternal HBV infection and preeclampsia. In another study conducted in Florida [23], no relationship was found between HBV and gestational hypertension or preeclampsia. In agreement with this, studies from Thailand [24], Germany [10], Israel [25] and Hong Kong [26] have shown no association between HBV and gestational hypertension or preeclampsia. However, a study in Iran [22], recruiting 450 HBV carriers and 450 controls showed increased risk of pregnancy induced hypertension with maternal HBV infection. On the other hand, two studies from Hong Kong, observed that maternal HBV infection could reduce the risk of hypertension [27]. It is speculated that this discrepancy might be explained by the difference in ethnicity, activity in the HBV status and other factors.

To conclude, positive family history of HBV and previous surgical procedures were associated with higher rate of HBV positivity. No association was found between HBV positivity and pregnancy outcomes. Our study is of exceptional importance as it gives a hint for healthcare planners about the risk factors associated with HBV in pregnant women in our locality. In addition, it negates the myths of association between HBV positivity and negative pregnancy outcomes. Further study is needed to investigate the effect on child health.

Conflict of interest statement

The author declares no conflict of interest.

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