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Obstetric Outcomes of Women With Elisa Positivity For HBV, HCV, or HIV

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ABSTRACT

ELISA positivity for Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Human Immunodeficiency Virus (HIV) may be associated with negative obstetric outcomes. The aim of this study is to compare the pregnancy complication rates of pregnant women based on ELISA positivity.

In this retrospective study, the obstetric outcomes of ELISA-positive and ELISA-negative pregnant women admitted to the delivery room unit of Kanuni Sultan Suleyman Training and Research Hospital between January 2014 and December 2014 were examined. Patients were grouped into two categories based on ELISA positivity or negativity for HBV, HCV, and HIV. In the study, 380 ELISA-positive and 294 ELISA-negative pregnant women were analyzed.

The demographic characteristics of both groups were similar. No statistically significant differences were observed between the two groups regarding average age, delivery method, premature birth, preterm membrane rupture (PROM), gestational diabetes mellitus (GDM), preeclampsia, intrahepatic cholestasis of pregnancy (ICP), poly/oligohydramnios, placenta previa, and congenital anomaly rates. The rates of fetal growth restriction (FGR), gestational hypertension (GHT), and increased pregnancy loss in the ELISA-positive group were found to be significantly higher than those in the ELISA-negative group.

In our study, we observed that the FGR and GHT rates in the ELISA-positive group were significantly higher than those in the ELISA-negative pregnant women, and their average birth weight was significantly lower. Therefore, we recommend that pregnancy follow-up for patients with positive serology be evaluated from these aspects.

Introduction

Viral infections are a common health concern worldwide. Among them, screening for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) is advised during pregnancy. HBV and HCV cause viral hepatitis that can eventually cause chronicity, liver failure, and perinatal complications (1).

Globally, the estimated prevalence of HBV is 3.5%; however, in endemic countries such as the Western Pacific and Africa, the prevalence rises to 6.1% and 6.2%, respectively (1). Turkey has an intermediate endemicity for hepatitis B, with an estimated frequency of 4.57% (2-8%) (2). In high- and intermediate-endemic locations, maternal-fetal transmission (MFT) accounts for almost 90% of the global incidence of the virus and is a common mode of transmission (1). In accordance with the mother's viral load and the problems caused by HBV, MFT in HBV might rise to 25% (3). Among pregnancy outcomes of HBV-infected pregnancies, an increase in preterm delivery (4) and gestational diabetes mellitus (GDM) were reported (5).

HCV is predicted to have a 2.5% prevalence, with women accounting for 30% of cases (6). According to US data, there are 29,000 births of HCV-positive mothers annually; however, global data are limited (7). Even though the prevalence of HCV is much lower, infection poses a risk for chronic liver disease and prenatal transmission during pregnancy. Chronic HCV infection has been linked to antepartum and postpartum hemorrhages, premature rupture of membranes (PROM), GDM, and intrahepatic cholestasis of pregnancy (ICP) in pregnant women (8, 9).

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Around 5000 HIV-positive women are thought to give birth in the USA each year, while 930,000 babies are thought to be born in low- and middle-income countries (10). Although the prevalence of HIV in Turey is low (0.1-0.3%), there is a propensity for an increase of 27% in the young population (11). Preterm birth and low birth weight risk have all been associated with maternal HIV infection (10).

This study was planned to assess the pregnancy outcomes of women with positive ELISA results for HIV, HBV, and HCV, compared to those of patients with negative results.

Materials and Methods

Our retrospective cohort investigation included patients who gave birth vaginally or by cesarean at Kanuni Sultan Süleyman Training and Research Hospital through January to December of 2014. The study we conducted was approved by the Ethics Board at Istanbul Medipol University (document number 10840098-604.01.01-E3210). In compliance with the Helsinki Declaration on Human Rights, the research was conducted.

Routine blood tests for total blood count, blood group assignment, and ELISA tests for HIV, HBV, and HCV were performed when pregnant patients were admitted to the maternity ward. All the patient files of patients who gave birth in 2014 were then screened in the archives department. After the identification of ELISA-positive patients, their demographic data were extracted. Those with positive ELISA testing for HIV, HCV, or HbsAg were referred to as the ELISA-positive group. Patients who were matched for age and parity with the ELISA-positive group among the ELISA-negative patients were designated as the control group. Multiple pregnancies and pregnancies shorter than 24 gestational weeks were not included in the study. Anti-HIV-positive patients with Ministry of Health confirmation were added to the ELISA-positive group, and those without were removed. Individuals with an uncertain last menstrual period were also excluded.

Indications for hospitalization, number and type of previous births, maternal age, week of gestation, and the presence of a known disease in the mother and baby were recorded in the files of all patients included in the study. Labor occurring prior to the 37th week of pregnancy was classified as preterm birth. Cesarean delivery was only considered for those with known HIV positivity.

Statistical Analysis: The NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package application was used to conduct the statistical analyses in this study.

Due to descriptive structure of the study power analysis was not conducted. All patients with positive ELISA tests were included for the analysis. Matching of the cases with control group was performed manually. Shapiro-wilk test was conducted for normal distribution of the patients. Results were given as mean and standard deviation as normal distribution was observed.

For data evaluation, continuous value comparison between paired groups was conducted using the independent t test, while the qualitative data comparison was conducted using the chi-square test.

An analysis of logistic regression was used to identify the variables influencing ELISA-positivity outcomes. The significance level for the results was set at $p<0.05$.

Results

The study included 674 postpartum women who gave birth by cesarean section or vaginally in tertiary hospital in Istanbul in 2014. Among the study attendees, 294 had negative ELISA results and 380 had positive results.

When clinical features such age, gravida, parity, birth weight, and mode of delivery were compared between the ELISA-positive and ELISA-negative groups of patients, no discernible variation in the distribution of these groups was found. Age and parity were similar in two groups confirming objective selection of control group (Table 1).

According to the study, gravida, or the number of pregnancies, was greater among ELISA-positive postpartum women than in ELISA-negative women ($p = 0.028$). In light of this, ELISA-positive pregnant women had an average of 2.78 ± 1.61 previous pregnancies, whereas ELISA-negative pregnant women had an average of 2.52 ± 1.38 previous pregnancies (Table 1).

As stated in Table 1 of the study, babies born to ELISA-positive postpartum women had an average birth weight of 3155.38 ± 643.73 g, while babies born to ELISA-negative postpartum women had an average birth weight of 3326.09 ± 347.31 g ($p = 0.0001$). The birth type distributions of the ELISA-positive and ELISA-negative groups did not differ statistically ($p = 0.053$).

Table 1: Demographic Data of the Patients

		ELISA (-) n= 294	ELISA (+) n=380	P Value
Age (Mean + SD)		25,94±4,69	26,33±5,2	0,321[a]
Parity (Mean + SD, Median, Min-Max)		2,22±1,15 2 (1-7)	2,32±1,26 2 (1-9)	0,299[a]
Gravida (Mean + SD, Median, Min-Max)		2,52±1,38 2 (1-7)	2,78±1,61 2 (1-10)	0,028[a]
Type of birth	Vaginal	208 (70.7%)	258 (67.8 %)	0,053[b]
	CS	86 (29.3%)	122 (32.2 %)	
Birth weight (g) (Mean + SD)		3326,09±347,31	3155,38±643,73	0,0001[a]
HbsAg positivity			321 (84,47%)	
HCV positivity			33 (8,68%)	
HIV positivity			26 (6.84%)	

CS: cesarean section
HbsAg: Surface antigen of Hepatitis B Virus
HCV: Hepatitis C Virus
HIV: Human Immunodeficiency Virus
SD: Standard deviation
Statistical analysis was used to compare two groups: a. an independent t-test and b. chi-square test.

Table 2: Pregnancy outcomes of the patients

	ELISA (-) n= 294	ELISA (+) n=380	P Value
Preterm Birth	9 (3.06%)	23 (6.05%)	0,07
FGR	8 (2.72%)	24 (6.32%)	0.03
PROM	2 (0.62%)	9 (2.37%)	0.086
GDM	8 (2.72%)	22 (5.79%)	0.055
Preeclampsia	21 (7.14%)	20 (5.26%)	0.311
Cholestasis	0	1 (0.26%)	0.379
GHT	1 (0.34%)	8 (2.11%)	0.048
Polyhydramnios	2 (0.62%)	6 (1.58%)	0.285
Oligohydramnios	6 (2.04%)	17 (4.47%)	0.084
Placenta Previa	3 (1.02%)	7 (1.84%)	0.382
Congenital anomaly	7 (2.38%)	11 (2.89%)	0.682

FGR: Fetal Growth Restriction
PROM: Preterm Rupture of Membranes
GDM: Gestational diabetes
GHT: Gestational hypertension
The chi-square test was used to compare the two groups.

Within the ELISA-positive group, 321 (84.4%) were HbsAg positive, 33 (8.6%) were Anti-HCV positive and 26 (6.8%) were Anti-HIV positive.

Preterm labor was found to be 3.06% in the ELISA-negative group and 6.05% in the ELISA-positive group when we looked at each potential pregnancy complication individually (Table 2). The ELISA-positive group had a higher risk of preterm birth, although the difference was statistically insignificant (p = 0.070). Likewise, PROM, which was 0.68% in the ELISA-negative group and climbed to 2.37% in the ELISA-positive group, Table 2 shows that these differences were statistically insignificant (p = 0.086, Table 2).

Compared to the ELISA-negative group, which had an incidence of 2.72%, the ELISA-positive

group had an incidence of 6.32% of fetal growth restriction (FGR) (p = 0.030, Table 2).

The ELISA-positive group had 5.79% GDM, while the ELISA-negative group had 2.72%. Despite the fact that the ELISA-positive group had a higher prevalence of GDM, this result was nearly at the threshold of statistical significance (p = 0.055, Table 2).

In patients with negative ELISA results, preeclampsia presented in 7.14% of cases, while in the ELISA-positive patients, it was observed in 5.26% of cases. GHT, on the other hand, was discovered to be 2.11% in the ELISA-positive group and 0.34% in the ELISA-negative group. The ELISA-positive group had a statistically significant higher prevalence of GHT than the ELISA-negative group (p = 0.048, Table 2).

ICP was 0% in the ELISA-negative group, 0.26% in the ELISA-positive group; polyhydramnios 0.68% in the ELISA-negative group, 1.58% in the ELISA-positive group; oligohydramnios was detected as 2.04% in the ELISA-negative group and 4.47% in the ELISA-positive group. Listed in Table 2, all of these findings were insignificant (p=0.379 and p=0.084 respectively).

The occurrence of placenta previa and congenital anomalies was similar in the two groups (p=0.382 and p=0.682, respectively, Table 2).

Discussion

We identified that lower birth weight, FGR, and GHT complicated the pregnancies of the ELISA-positive group, and that they also experienced greater rates of pregnancy loss in this retrospective case-control study. An increase in GDM incidence approached statistical significance. As the risk of these pregnancy complications increases with age and parity, in order to eliminate confounding effects linked to these factors, we tried to match the patients based on these two criteria during the study design.

Turkey is intermediate endemic for HBV, low endemic for HCV, and HIV (12). The significance of HBV and HCV infections lies in their increased potential to develop into chronic liver disease and exacerbate it, in comparison to other hepatitis viruses like Hepatitis A or Hepatitis E, which pose a larger risk to the mother and unborn child during pregnancy (1).

HBV positivity is thought to affect 3.3 million individuals in Turkey (2) and the percentage of pregnant women who test positive for HbsAg is 4.4% (range: 1.2–12.3%) (12). Given that Turkey has one million live births annually, between 10,000 and 100,000 pregnant women are predicted to be infected with HBV, which could result in a high burden of HBV complications (13).

Pregnancy loss in women infected with HBV and HCV has not been well researched compared to other pregnancy outcomes. Pregnancy loss was higher in the ELISA-positive group in our investigation, as the parities of the two groups were similar. Similar results were observed in a Polish cohort of individuals who tested positive for HBV or HCV; miscarriages rose considerably in HCV carriers (14). There have been contradictory findings from China, where groups of pregnant women with HBV-positive had comparable rates of miscarriages (15). Since our study cohort included all three infections, it may be speculated that HCV might have a greater impact on abortion rates. However, spontaneous abortion was less common in the HCV-positive group in a large cohort study conducted in the USA (16). The majority of HBV, HCV, and HIV studies on pregnant patients do not classify individuals based on the severity of their illness. Results from cohorts with more severe illnesses may differ from those of cohorts with stable carriers. As the severity of the infection increases, systemic inflammation arises (17). The systemic inflammation brought on by these infections may be the reason for the elevated tendency of pregnancy loss in the ELISA-positive group.

Numerous studies have demonstrated a decrease in the birth weight of newborns with HIV and HCV infections (10, 16, 18). Nonetheless, the results of HBV infections during pregnancy have contradictory findings, with lower birth weight (19-21). Among the 1446 HBV-positive pregnancies, Sirilert et al. revealed decreased birth weight, particularly in HBeAg-positive patients (21). On the other hand, different meta-analyses and retrospective cohorts revealed no connection between lower birth weight and HBV-positive individuals (19, 20). The risk of IUGR in HIV or HCV-positive pregnancies has been demonstrated in numerous studies (8, 10, 18). Contradictory data from HBV-positive pregnancies could be caused by different research designs or cohorts. Low birth weight or FGR in these populations may be caused by systemic inflammation, as was previously indicated. This conclusion coincides with the observation of low birth weight in HBe Ag-positive HBV patients (21).

Among the outcomes of our research was a higher risk of GHT. The Polish study, likewise reported an increase in GHT in HBV and HCV positive

patients, which is parallel to our findings (14). Preeclampsia risk did not differ in both groups while GHT risk increased in our ELISA-positive cohort. This result is consistent with the majority of research on HBV-positive patients, which show no increase in preeclampsia risk (1, 19, 21).

Both men and women are susceptible to developing type 2 diabetes mellitus due to HCV infection, and the risk of GDM increases during pregnancy (17). There are several studies and meta-analyses displaying an elevated risk of GDM in HBV-positive patients (5, 15, 19). However, as opposed to HCV, there isn't a strong correlation between GDM and HBV positivity. Wu et.al. reported increased risk for GDM but not for FGR, low birth weight, and GHT in a Chinese cohort, totally in contrast with our findings. (22). In their investigation, the HbsAg negative control group was younger and had lower parities, which could cause bias due to age and parity. Tse also showed increased risk for GDM, where patients were matched according to their age and parity (23). In response to the discrepancies in the research, particularly on the risk of GDM in HBV, Paramasivam hypothesized that most HBV studies have been published from regions with high epidemic rates, where GDM is also commonly observed. This could introduce bias and have an impact on the results of meta-analyses (17).

Few studies have been carried out to determine the underlying placental pathophysiology, despite the fact that there are many studies on the outcomes of ELISA-positive pregnancies. One explanation is that all three viruses promote systemic inflammation, which in turn causes placental inflammation, which can result in low birth weight, FGR, GDM, or premature birth (17). HBV infection was identified in villous trophoblast cells in the placenta, with the infection being more intense on the mother's side, presumably spreading by "cellular transfer" to the fetal side with a decreasing intensity (24). Vascular endothelial cells have been demonstrated to harbor HBV (24). Endothelial cells in the placenta support trophoblasts with nutrients and oxygen; however, infections and inflammation in these cells can interfere with these exchanges. The degree of inflammation in both trophoblast and endothelial cells may account for the differences in outcomes and their severity.

In conclusion, our study included a considerable number of pregnant women with HIV, HBV, and HCV infections, and every potential outcome was examined. Patients who receive a diagnosis early in their pregnancy should be made aware of the potential complications and managed appropriately. More prospectively designed studies should also be conducted to reveal possible underlying placental pathologies.

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Limitations: The retrospective design and small number of patients with HCV and HIV were the limitations of the study.

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