Türk Kadın Sağlığı ve Neonatoloji Dergisi

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Original Article

Hepatitis B, Hepatitis C and HIV seroprevalence in pregnant women: Six years of experience

Gebelerde Hepatit B, Hepatit C ve HIV Seroprevalansı: Altı yıllık deneyim

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Abstract

Aim: To determine the seroprevalence of hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV) in pregnant women who presented to the pregnancy outpatient clinic at Umraniye Training and Research Hospital between January 1, 2014, and December 31, 2019, and to reveal the distribution of cases by year.

Material and method: Hepatitis B surface antigen (HBsAg), hepatitis B surface antigen-antibody (Anti-HBs), hepatitis C virus antibody (Anti-HCV), and HIV antibody (Anti-HIV) results from blood samples taken from pregnant women admitted to our hospital's pregnancy outpatient clinic were retrospectively scanned. The results of the line immunoassay validation test performed on patients with Anti-HIV reactivity were obtained from hospital records.

Results: Anti-HBs values were examined in 11,263 pregnant women, and positive results were found in 3,898 (34.61%). HBsAg values were examined in 55,639 pregnant women, with positive results in 822 (1.48%). Anti-HCV values were examined in 47,990 pregnant women, and the results were positive in 159 (0.33%). Anti-HIV values were examined in 44,107 pregnant women, and the result was found to be reactive in 40 (0.09%). HIV infection was confirmed in 5 pregnant women (0.01%). The seropositivity rates by year between 2014 and 2019 were 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% for Anti-HBs; 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.36% for HBsAg; 0.25%, 0.40%, 0.32%, 0.39%, 0.29%, and 0.32% for Anti-HCV; and 0%, 0.07%, 0.13%, 0.07%, 0.15%, and 0.17% for Anti-HIV.

Conclusion: During the antenatal period, pregnant women should be screened for HBV, HCV and HIV. Early diagnosis and treatment of HCV and HIV in pregnancy is vital to prevent long-term complications of infections and to reduce the transmission from the mother to the infant.

Key words: Antenatal screening; pregnancy; Hepatitis B virus; Hepatitis C virus; Human immunodeficiency virus

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Öz

Amaç: 01 Ocak 2014 ile 31 Aralık 2019 tarihleri arasında Ümraniye Eğitim ve Araştırma Hastanesi'nin gebe polikliniğine başvuran gebelerdeki Hepatit B (HBV), Hepatit C (HCV) ve İnsan İmmun yetmezlik Virüsü (HIV) seroprevalansını belirlemek ve yıllara göre vakaların dağılımını ortaya çıkarmaktır.

Gereç ve Yöntem: Hastanemizin gebe polikliniğine başvuran gebelerden alınan kan örneklerinden çalışılan Hepatit B yüzey antijen (HBsAg), Hepatit B yüzey antijen antikoru (Anti-HBs), Hepatit C virüs antikoru (Anti-HCV) ve HIV antikoru (Anti-HIV) sonuçları hastane kayıtlarından retrospektif olarak tarandı. Anti-HIV reaktivitesi olan hastalara yapılan Line Immunassay doğrulama testi sonuçlarına hastane kayıtlarından ulaşıldı.

Bulgular: 11,263 gebede Anti-HBs bakılmış, 3898 gebede sonuç pozitif olarak gelmiştir (%34,61), 55,639 gebede HBsAg bakılmış, 822 gebede sonuç pozitif olarak gelmiştir (%1,48), 47,990 gebede Anti-HCV bakılmış, 159 gebede (%0,33) sonuç pozitif olarak gelmiştir. 44,107 gebede Anti-HIV bakılmış, 40 gebede sonuç reaktif olarak gelmiştir (%0,09). Anti-HIV reaktif gelen 40 gebede doğrulama line immunassay yöntemi ile yapılmıştır ve 5 gebede HIV enfeksiyonu kesin olarak doğrulanmıştır (%0,01). 2014 ile 2019 yılları arasında yıllara sırası ile göre seropozitiflik oranları Anti-HBs için %26,16, %28,94, %32,20, %34,82, %39,66, %41,73; HBsAg için %1,54, %1,52, %1,46, %1,53, %1,45, %1,36; Anti-HCV için %0,25, %0,40, %0,32, %0,39, %0,29, %0,32 ve Anti-HIV için %0, %0,07, %0,13, %0,07, %0,15, %0,17 olarak tespit edilmiştir.

Sonuç: Antenatal dönemde gebeler HBV, HCV ve HIV açısından taranmalıdır. HCV ve HIV için gebelikte erken tanı ve tedavi enfeksiyonların uzun dönem komplikasyonlarının önlenmesi ve anneden bebeğe olan geçişin azaltılması için önemlidir.

Anahtar kelimeler: Antenatal tarama; gebelik; Hepatit B Virüsü; Hepatit C Virüsü; İnsan İmmun Yetmezlik Virüsü

1. Introduction

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are viral agents known to cause significant health problems around the world and in our country. HBV and HCV infections may progress from active hepatitis to chronic hepatitis, to liver cirrhosis and hepatocellular carcinoma. HIV may suppress an individual's immune system, giving way to various opportunistic infectious agents that may cause illness or death.

According to the World Health Organization (WHO) records, 257 million people were living with chronic HBV infection, and 71 million people were living with chronic HCV infection in 2015. In the same year, viral hepatitis, in general, resulted in 1.34 million deaths worldwide, with 720,000 caused by cirrhosis and 470,000 by hepatocellular carcinoma (1). Besides, in 2019, 38 million people were recorded as living with HIV or acquired immunodeficiency syndrome (AIDS), and 690,000 people died of HIV-related illnesses (2).

Countries are divided into three groups in terms of the prevalence of HBV infection: high (≥8%), moderate (2%–7%), and low (<2%) endemic countries. Our country is considered to be in the middle endemic group in terms of HBV carriers. According to current data, approximately 3.3 million individuals are reported to be infected with chronic HBV (3). In our country, a routine HBV vaccination program for newborn babies began in 1998. Previously, between 70% and 90% of babies born from an HBeAg-positive pregnant woman would have been infected with HBV, and 90% of the cases of babies with hepatitis would have resulted in chronic infection. Currently, infection in 85% to 95% of newborns can be prevented with HBV vaccines and immunoglobulins, which are administered to babies born of mothers who are HBV carriers (4).

HCV infection is a significant public health problem, but most people are unaware of the ongoing infection (5). According to 2016 data of the Ministry of Health, the HCV antibody (Anti-HCV) was found in 3.8% of hemodialysis patients, 1.7% of peritoneal dialysis patients, 1.96% of patients with kidney transplantation, and 7.6% of patients with liver transplantation. As of 2013, it was estimated that 514,000 individuals were infected with HCV (3).

In our country, HIV and AIDS are included in the list of reportable diseases, and surveillance has been carried out by the relevant departments of the Ministry of Health since the first case was reported in 1985. Between 1985 and June 30, 2019, there were 20,202 HIV-positive cases and 1,786 cases of AIDS, 89 of which were in the 0-age group, whose verification test was determined and reported. There were 676 HIV-positive cases in

our country in 2011, but this number increased more than five times in 2018, with 3,678 positive cases (6). HIV infection, which is increasingly seen among women in their reproductive years, is a siginificant risk factor for the proper course of pregnancy and newborn health.

The purpose of this study was to determine the seroprevalence of HBV, HCV, and HIV in pregnant women who presented to our hospital for their pregnancy follow-up between 2014 and 2019 and to reveal the distribution of cases by year during this period.

2. Material and Method

In this study, hepatitis B surface antigen (HBsAg), hepatitis B surface antigen-antibody (Anti-HBs), hepatitis C antibody (Anti-HCV), and HIV antibody (Anti-HIV) results, sampled from pregnant women who presented to the obstetric outpatient clinic at Umraniye Training and Research Hospital in their first or second trimester between January 1, 2014, and December 31, 2019, were obtained retrospectively from the hospital records. Blood samples taken from the patients were studied using the Abbott Architect i1000SR device using the chemiluminescence microparticle immunoassay method, according to the manufacturer's recommendations. The limit value for Anti-HBs was 9.99 mIU/mL, and values of 10.0 mIU/mL and greater were considered positive. The limit value for HBsAg, Anti-HCV, and Anti-HIV was 0.99 S/CO; values of 1.00 S/CO and greater were considered positive. For reaffirmation, results that showed reactive Anti-HIV were studied twice, as were blood samples obtained from patients whose results showed reactive Anti-HIV. The blood samples were rechecked with the line immunoassay method, and HIV positivity was confirmed.

This study was reviewed by the appropriate ethics committee and was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2000. Administrative approval for the usage of medical data was obtained from the Umraniye Training and Research Hospital Ethics Committee (No: B.10.1.TKH.4.34.H.GP.0.01/250).

Statistical Analysis

The data were analyzed using SPSS 25.0 (IBM Corp., Armonk, NY). While evaluating the study data, frequency values and percentage distributions of these values were calculated as the descriptive statistics.

3. Results

During these six years, Anti-HBs values were examined in a total of 11,263 pregnant women, and the results were positive in 3,898 patients (34.61%). Anti-HBs seropositivity rates by year from 2014 to 2019 were determined as 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% (**Table 1)**. HBsAg was examined in 55,639 pregnant women, and the results were positive in 822 (1.48%). HBsAg seropositivity rates by year from 2014 to 2019 were determined as 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.48% (**Table 2**). Anti-HCV was examined in 47,990 pregnant women, and the results were positive in 159 (0.33%). Anti-HCV seropositivity rates by year from 2014 to 2019 were determined as 0.25%, 0.40%, 0.32%, 0.39%, 0.29%, and 0.32% (**Table 3**). Anti-HIV was examined in 44,107 pregnant women, and the results were reactive in 40 (0.09%). Confirmation of Anti-HIV results which were found to be reactive in 40 pregnant women, was made using the line immunoassay method, and HIV infection was confirmed in 5 pregnant women (0.01%) (**Table 4**).

Table 1. Distribution of Anti-HBs results by years in pregnant women admitted to our hospital

	Anti-HBs Positive		Anti-HBs Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	231	26.16	652	73.84	883
2015	531	28.94	1,304	71.06	1,835
2016	757	32.20	1,594	67.80	2,351
2017	788	34.82	1,475	65.18	2,263
2018	945	39.66	1,438	60.34	2,383
2019	646	41.73	902	58.27	1,548
Total	3,898	34.61	7,365	65.39	11,263

Table 2. Distribution of HBsAg results by years in pregnant women admitted to our hospital

	HBsAg Positive		HBsAg Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	98	1.54	6,258	98.46	6,356
2015	131	1.52	8,498	98.48	8,629
2016	159	1.46	10,710	98.54	10,869
2017	173	1.53	11,117	98.47	11,290
2018	148	1.45	10,049	98.55	10,197
2019	113	1.36	8,185	98.64	8,298
Total	822	1.48	54,817	98.52	55,639

Table 3. Distribution of Anti-HCV results by years in pregnant women admitted to our hospital

	Anti-HCV Positive		Anti-HCV Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number
2014	14	0.25	5,542	99.75	5,556
2015	31	0.40	7,708	99.60	7,739
2016	33	0.32	10,442	99.68	10,475
2017	34	0.39	8,663	99.61	8,697
2018	24	0.29	8,264	99.71	8,288
2019	23	0.32	7,212	99.68	7,235
Total	159	0.33	47,831	99.67	47,990

Table 4. Distribution of Anti-HIV results by years in pregnant women admitted to our hospital

	Anti HIV Reactive		Line Immunoassay Positive		Anti HIV Negative		Total
Years	Number	Rate (%)	Number	Rate (%)	Number	Rate (%)	Number
2014	0	0	0	0	8,274	100.00	8,274
2015	6	0.07	2	0.02	8,772	99.93	8,778
2016	8	0.13	0	0	6,276	99.87	6,284
2017	5	0.07	1	0.01	7,625	99.93	7,630
2018	11	0.15	2	0.03	7,146	99.85	7,157
2019	10	0.17	0	0	5,974	99.83	5,984
Total	40	0.09	5	0.01	44,067	99.91	44,107

4. Discussion

Both acute and chronic HBV infections in pregnancy are similar to those in the general adult population. HBV infection during pregnancy does not increase the maternal mortality rate and does not cause a teratogenic effect in the fetus (7). It is known that HBV can infect all types of cells in the placenta (decidual, trophoblastic, villous mesenchymal, and villous capillary endothelial cells). Maternal HBeAg-positive serological status, along with a high viral load, is the leading risk factor regarding the occurrence of HBV intrauterine infection (8).

Particularly in regions with high endemicity in terms of HBV, those with chronic infections acquire the infection during the perinatal or early childhood period (7). Our country has been reported as a moderately endemic country in terms of HBV; HBsAg seropositivity has been reported between 1.2% and 5.7% in studies among pregnant women (9, 10). Owing to the region where our hospital is located, our facility serves a population with low socioeconomic status, particularly refugees from Syria. In our study, we found that the HBsAg seropositivity among pregnant women was 1.54%, 1.52%, 1.46%, 1.53%, 1.45%, and 1.36% for the years from 2014 to 2019. During these six years, a total of 55,639 pregnant women were tested for HBsAg in the pregnancy outpatient clinic of our hospital. HbsAg positivity was found in 822 pregnant women, and HBsAg seropositivity was determined to be 1.48% overall.

The detection of women who are not immune to HBV before pregnancy and the administration of HBV vaccines is essential for preventive healthcare. Meanwhile, antenatal screening is vital in terms of detecting HBsAg-positive pregnant women, determining viral load, and determining antiviral treatments. Antiviral therapy with nucleoside reverse transcriptase inhibitors starting between 28 and 32 weeks of gestational age is recommended to reduce the risk of HBV perinatal transmission among HBsAg-positive pregnant women with an HBV deoxyribonucleic acid level of greater than 106 copies/mL (11). Besides, as soon as HBsAg-positive mothers are identified, their babies should receive passive and active immunoprophylaxis at birth to reduce vertical HBV transmission. The combination of hepatitis B immune globulin and HBV immunization, given within 12 hours of birth, has effectively reduced the rate of perinatal transmission from greater than 90% to less than 10%. Despite appropriate neonatal postexposure prophylaxis, however, perinatal transmission still occurs in approximately 2% of infants. Most of these cases occur in HBeAg-positive women with very high viral loads (12).

When invasive prenatal diagnostic testing is required for HBsAg-positive pregnant women, it is crucial to avoid a transplacental approach. The rate of neonatal HBV infection induced by amniocentesis may range up to 1.4% in newborns born of mothers positive for HBsAg, and 16% for hepatitis B e-antigen (13). In two meta-analysis studies that compared elective cesarean delivery with vaginal delivery in terms of the prevention of mother-to-child transmission (MTCT) at birth, it was determined that elective cesarean section significantly reduced the rate of maternal transmission of HBV (14, 15). In contrast, according to another meta-analysis published in 2019, vaginal delivery did not increase the MTCT incidence after immunoprophylaxis at six months or more, and the existing evidence does not support the conclusion that cesarean section can prevent MTCT in HBsAg-positive mothers after immunoprophylaxis (16). Cesarean delivery should not be performed only to prevent perinatal transmission, as the benefits have not been established in well-conducted controlled trials (12). Even though HBV DNA can be detected in breast milk, breastfeeding does not pose an additional risk of HBV infection. Mothers with chronic HBV infection who wish to breastfeed should be encouraged to do so (17). In our hospital, unless there is an obstetric indication, we do not encourage pregnant women who are HBV carriers to deliver by cesarean to avoid MTCT.

In studies conducted in various regions of our country, Anti-HBs seroprevalence has been reported between 3.7% and 45.8% in pregnant women (18-20). In this study, Anti-HBs was evaluated in a total of 11,263 pregnant women who presented to the pregnancy outpatient clinic of our hospital in a-six year period. Anti-Hbs was detected as seropositive in 3,898 of these pregnant women (34.61%). Between 2014 and 2019, we determined the

Anti-HBs seroprevalence by year to be 26.16%, 28.94%, 32.20%, 34.82%, 39.66%, and 41.73% (**Table 1**). The increase in Anti-HBs seroprevalence and the tendency of HBsAg seroprevalence to decrease over the years may indicate that the HBV vaccine is effective in preventing disease (**Figure 1**).

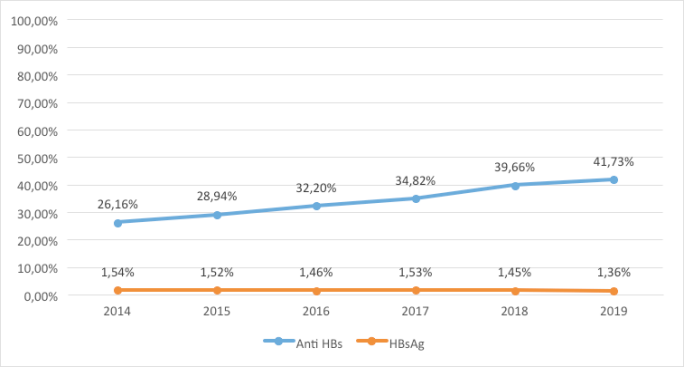

Figure 1. Distribution of Anti-Hbs and HBsAg seropositivity by years.

As many as 8% of pregnant women are known to be infected with HCV worldwide (21). Maternal well-being, MTCT, and the impact of maternal infection on pregnancy outcomes are the primary considerations regarding pregnancies with HCV infection. It has been reported that maternal HCV infection has been significantly associated with fetal growth restriction and low birthweight (22). The standard test used for HCV screening during pregnancy is Anti-HCV. Anti-HCV antibodies usually develop within 2 to 6 months after exposure. Therefore, even if the result in the first trimester is negative in pregnant women who are at risk for HCV, it is recommended that the test for Anti-HCV be conducted again in the later months of pregnancy (21). Anti-HCV was evaluated in 47,990 pregnant women in our outpatient clinic between 2014 and 2019, and the seropositivity was found in 159 patients (0.33%). The distribution of Anti-HCV seropositivity by years is shown in **Figure 2.** Other studies conducted in Turkey show Anti-HCV seropositivity rates ranging between 0.1% and 1.1% (10, 18-20, 23).

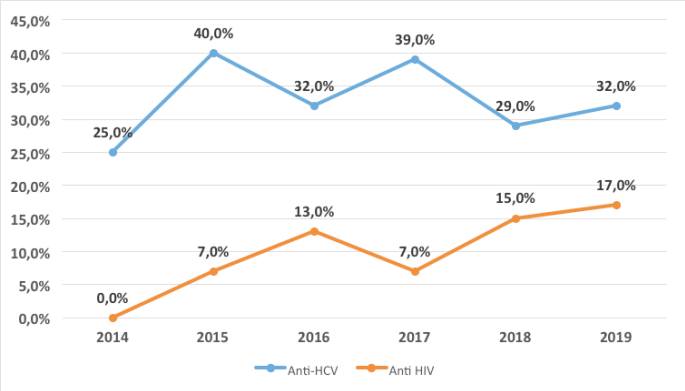

Figure 2. Distribution of Anti-HCV seropozitivity and Anti-HIV reactivity by years.

When an active HCV infection is confirmed in a pregnant woman, a quantitative HCV ribonucleic acid test should be performed to determine the baseline viral load. The risk of vertical transmission of HCV is 5.8% in women with chronic HCV infection who are HIV-negative, whereas the rate increases to 10.8% in HIV-positive women. The increased risk of vertical transmission in HIV-positive pregnant women may be the result of increased HCV viral load, issued by HIV-mediated immunosuppression (21). Should an invasive prenatal diagnostic testing be requested, amniocentesis is recommended rather than chorionic villus sampling. Amniocentesis does not appear to increase the risk of vertical transmission in Anti-HCV-positive pregnant women (13).

Studies have shown that there is no difference between vaginal birth and cesarean birth in terms of vertical transmission of HCV. It is recommended that obstetricians should avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labour in HCV-positive women. It has been stated that breastfeeding is safe in women with HCV infection. However, women should abstain from breastfeeding if there is preexisting nipple bleeding or cracked nipples (21). In our hospital, unless there is an obstetric indication, we do not encourage cesarean delivery for pregnant women who are HCV carriers only to avoid MTCT.

In our country, a total of 89 HIV-positive case reports were found in the 0-age group, whose validation test was determined between 1985 and 2019 (6). In most of these cases, HIV transmission occurred as MTCT. MTCT of HIV can occur during pregnancy, labour, delivery, or breastfeeding. A large prospective cohort study demonstrated that effective interventions such as performing antiretroviral therapies during pregnancy, planned pre-labor cesarean sections, and avoidance of breastfeeding would reduce the risk of MTCT of HIV from 20% to 1% (24). In light of such findings, it is feasible that antenatal screening for HIV is the proper course of action regarding the prevention of MTCT of HIV.

In a study conducted in Ankara, in 2007 by Madendağ et al. (4) to determine the Anti-HIV seropositivity in pregnant women, the authors detected Anti-HIV reactivity in 3 out of 60,562 pregnant women (0.004%). However, in 2017, a study conducted by Altuğlu et al (25), the authors detected Anti-HIV reactivity in 12 (0.1%) out of 8,803 pregnant women. In the current study, Anti-HIV was evaluated in 44,107 pregnant women between 2014 and 2019, with reactive Anti-HIV detected in 40 patients (0.09%). The distribution of Anti-HIV reactivity by year is shown in **Figure 2**. Forty patients with Anti-HIV reactivity were validated using the line immunoassay method, and only five patients had a positive result (0.01%). At our hospital, the Anti-HIV test is studied using the chemiluminescence microparticle immunoassay method. However, in Anti-HIV testing techniques,

some non-HIV-related proteins may be identified as HIV-specific antibodies, potentially leading to false-positive results. As a matter of fact, in our study, 35 of the 40 patients, whose Anti-HIV were found reactive, were also found to be false-positive. Particularly in societies where HIV prevalence is low, such as our country, false-positivities are one of the most common problems encountered concerning the identification of new HIV cases. It has been reported that pregnancy itself, or infections such as malaria, schistosomiasis, and human African trypanosomiasis, along with vaccines such as influenza, viral hepatitis, and rabies may be the cause of Anti-HIV false-positivity (26). Short confirmation of the newly detected Anti-HIV positivity in the near-term period may also prevent the newborn from receiving antiretroviral drug prophylaxis in vain.

If an invasive prenatal diagnostic testing is requested, amniocentesis in women infected with HIV under the antiretroviral therapy does not appear to significantly increase the risk of MTCT, mostly if the viral load is found to be undetectable. However, concerning women who are not taking antiretroviral therapy, the risk of MTCT has been found to increase with the performance of amniocentesis (13). In non-breastfeeding populations, the majority of MTCT of HIV occurs during late pregnancy and the intrapartum period. This issue indicates that appropriate intrapartum obstetric care is vital in HIV-positive pregnancies. In a randomized controlled trial, published in 1999, the MTCT rate for HIV was reported as 1.8% far planned cesarean section and 10.5% for vaginal delivery (27). Also, the level of maternal viral load at delivery was determined to be a primary factor in MTCT. Although cesarean section remains an essential strategy for those with untreated or poorly controlled HIV, vaginal delivery is now the recommended mode of delivery, as there is no obstetric indication for cesarean section concerning women with a viral load of fewer than 50 copies/mL (28). Concerning the breastfeeding of HIV-positive mothers, and considering the WHO guideline updated in 2016, it is recommended that mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer while being fully supported with anti-retroviral therapy adherence (29).

There were some limitations in the current single-center, the retrospectively designed study that should be noted. First, the inability of knowing the HBV vaccination status in pregnant women, the impossibility of distinguishing whether Anti-HBs positivity is the result of vaccination or a natural immune result obtained as a result of HBV infection, and the inability of knowing the immune status of babies born to pregnant women with positive HBsAg, Anti-HCV, and HIV verification results. Another limitation of our study is that the numbers of pregnant women examined for HBsAg, Anti-HBs, Anti-HCV, and Anti-HIV, respectively, was different. Although HBsAg is routinely requested from pregnant women who present to our hospital for pregnancy in the first or second trimester with the recommendation of the Ministry of Health, other examinations are requested by experts in the outpatient clinic.

In conclusion, pregnant women who present to the pregnancy outpatient clinic for antenatal care should be screened for HBV, HCV and HIV. For HCV and HIV, for which there is no vaccination, early diagnosis and taking necessary precautions during pregnancy is essential.

Declaration of Interest

The authors report no conflicts of interest.

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