

ORIGINAL ARTICLE

## Investigation of intrauterine transmission of Hepatitis B Virus to children from HBsAg-positive pregnant women

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### ABSTRACT

**Objectives:** Hepatitis B virus is reported to cause fetal and neonatal hepatitis, with a high rate of vertical transmission. The aim of this study was to determine the rate of vertical transmission during the intrauterine period by determining HBsAg positivity in the cord blood of newborns whose mothers were hepatitis B carriers.

**Materials and methods:** Pregnant women, who were admitted at the Obstetrics and Gynecology Unit for delivery, were included. HBsAg, hepatitis B virus antigen (HBeAg), and antibody against hepatitis B virus antigen (anti-HBe) tests were performed from the pregnant women before delivery. Cord bloods of newborns whose mothers were HBsAg-positive were tested for HBsAg immediately after delivery. HBsAg, HBeAg and anti-HBe tests were conducted.

**Results:** Of the 1,570 pregnant women included in the study, 45 (2.9%) were positive for HBsAg. HBeAg was also found to be positive in 7 (15.6%) of the pregnant women, who were positive for HBsAg, while 38 (84.4%) of HBsAg-positive women were positive for anti-HBe. None of the newborns whose mother was HBsAg-positive was found to be HBsAg-positive.

**Conclusion:** Vertical intrauterine transmission of hepatitis B virus is rare. Screening of all pregnant women for hepatitis B should be recommended in Turkey since the country is of moderate endemicity for HBV seroprevalence. Newborns of HBV positive pregnant women should be vaccinated and hepatitis B immunoglobulin should be given after birth to prevent transmission of hepatitis B. *J Microbiol Infect Dis* 2011;1(1):14-16.

**Key words:** Hepatitis B virus, HBsAg, vertical transmission, intrauterine, cord blood, pregnant women.

### HBsAg pozitif gebe kadınlardan çocuklara Hepatit B Virüsü'nün intrauterin geçişinin araştırılması

#### ÖZET

**Amaç:** Hepatit B'nin, fetal ve yenidoğan hepatitine neden olduğu ve yüksek oranda vertikal geçişe sahip olduğu bildirilmektedir. Bu çalışmanın amacı Hepatit B taşıyıcısı gebelerden doğan bebeklerin kordon kanlarında Hepatit B yüzey antijeni (HBsAg) pozitifliğini araştırarak intrauterin dönemde oluşabilecek vertikal geçiş oranının belirlenmesi amaçlanmıştır.

**Gereç ve yöntem:** Bu çalışmaya Kadın Hastalıkları ve Doğum servisine doğum yapmak üzere yatırılan gebeler dahil edildi. Doğumdan önce gebelerden HBsAg, HBeAg ve anti-HBe tetkikleri istendi. HBsAg pozitif çıkan gebelerin bebeklerinde doğumdan hemen sonra kordon kanında HBsAg araştırıldı. HBsAg, HBeAg ve anti-HBe testleri hastanemiz mikrobiyoloji laboratuvarında makro-ELISA cihazında (AxSYM Plus System, Abbott, USA) üretici firmanın önerileri doğrultusunda çalışıldı.

**Bulgular:** Çalışmaya alınan 1570 gebenin 45'inde (% 2.9) HBsAg pozitif tespit edildi. HBsAg'si pozitif bulunan gebelerin 7'sinde (% 15.6) HBeAg de pozitif bulunurken 38 (% 84.4) gebede ise anti-HBe pozitif bulundu. HBsAg pozitif bulunan gebelerden doğan bebeklerden hiç birinin kordon kanında HBsAg pozitifliği tespit edilmedi.

**Sonuç:** Hepatit B virüsünün vertikal-intrauterin geçişi nadir görülmektedir. Ülkemiz hepatit B virüsü seroprevalansı açısından orta endemik bölgede bulunduğu için tüm gebeler hepatit B yönünden taranmalı, hepatit B virüsü pozitifliği belirlenen annelerden doğan bebeklere doğumdan sonra hepatit B virüsü aşısı ve hepatit B immünglobulini yapılarak bebeğe hepatit B virüsü bulaşı engellenmelidir.

**Anahtar kelimeler:** Hepatit B virüsü, HBsAg, vertikal geçiş, intrauterin, kordon kanı, hamile kadın.

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## INTRODUCTION

Acute and chronic hepatitis B virus (HBV) infection is an important public health problem worldwide. Transmission of hepatitis B virus occurs by the parenteral and percutaneous routes, through sexual intercourse, during labor and by perinatal vertical route from an infected mother.<sup>1</sup> Perinatal transmission is generally due to contact of the newborn with fluids of the hepatitis B virus-infected mother during or after delivery. Transmission during delivery is said to be through skin abrasions, mucosal penetration, and during cesarean section through contact with mother's blood and by mixing of fetal and maternal circulations following placental injury.<sup>2</sup>

Infections from an HBsAg-carrier mother to the newborn (vertical transmission) during the perinatal period are at the rate of 10-20%.<sup>1</sup> The rate is higher in HBeAg carriers.<sup>3</sup> Despite the absence of congenital anomaly and teratogenic effects of HBV, passage through the placenta has not been identified and transmission during the intrauterine period is rare. The rate of transmission during the third trimester of pregnancy varies between 5-10% due to transplacental bleeding.<sup>4</sup> This study was aimed at determining the transmission rate of hepatitis B virus during the intrauterine period, by investigation HBsAg positivity in cord blood of newborns who were born to hepatitis B carriers-mothers.

## MATERIALS AND METHODS

Pregnant women, who were admitted at the Obstetrics and Gynecology Unit of the Kiziltepe State Hospital for delivery between March 2010 and August 2010, were prospectively included in the study. A section of these women consisted of pregnant women who were previously being followed up, whereas the other section consisted of those without previous follow-up records. Routine HBsAg analyses were performed after patients were admitted to their various wards. HBeAg and anti-HBe markers were tested in pregnant women who were detected to be HBsAg positive. HBsAg positivity was investigated after delivery, in the cord blood of newborns whose mothers were detected with positive HBsAg. Newborns of HBsAg-positive pregnant women were vaccinated and prophylactic hepatitis B immunoglobulin was administered irrespective of the HBsAg results.

The HBsAg, HBeAg, and anti-HBe markers were detected in accordance with recommendations of the manufacturer (AxSYM Plus System, Abbott, USA) of the macro-ELISA kits in our microbiology laboratory. Evaluation of HBV DNA was not performed in our hospital laboratory due to the current conditions of the laboratory.

## RESULTS

A total of 1,570 pregnant women who were admitted for delivery at the Obstetrics and Gynecology Unit of the Kiziltepe State Hospital were included in the study. Their mean age was  $27 \pm 5.4$  years. Of these pregnant women 45 (2.9%) were detected to be HBsAg positive. The liver function tests (e.g. aspartate transaminase-AST, alanin transaminase-ALT) of HBsAg-positive patients were found to be within normal limits. HBeAg was also found to be positive in 7 (15.6%) of the pregnant women whose were positive for HBsAg, while 38 (84.4%) of HBsAg-positive women were positive for anti-HBe. No HBsAg positivity was detected in the cord blood of newborns which was investigated.

## DISCUSSION

HBV is transmitted by percutaneous and mucosal contact through infected blood and body secretions. Perinatal transmission is important for the chronicity of HBV infection in regions of high endemicity, through vertical transmission from the HBV-carrier mother. The risk of chronic HBV infection is high in newborns of mothers who are chronic HBV infection carriers and those with active HBV replication (HBeAg positive). This risk increases to 70-90% by the sixth month when hepatitis B vaccination is not performed and hepatitis B immunoglobulin is not administered immediately after delivery. On the other hand, the risk is lower (10-40%) in babies born to HBeAg negative mothers. However, chronicity of the infection is observed in almost all infected children.<sup>5</sup> HBsAg positivity is observed in 5-10% of children born to HBeAg-positive mothers despite hepatitis B immunoglobulin, standard active immunoprophylaxis and hepatitis B vaccine. This rate is reported to be related to a high viral load of the mother<sup>6</sup>, presence of intrauterine infection<sup>7</sup> or the presence of HBV surface protein mutations.<sup>8</sup>

In a case-control study including 402 newborns of HBsAg-positive pregnant mothers, HBsAg was evaluated within 24 hours of delivery and HBsAg was found to be positive in 15 (3.7%) of newborns. This condition indicates the presence of intrauterine infection. Kaleli et al, investigated HBsAg positivity in the cord blood of newborns of mothers with hepatitis B infection and reported HBsAg positivity in only one of the 13 pregnant women. The study demonstrated HBsAg-positivity of 7.7%, whereas the anti-HBe rate was reported as 70%.<sup>10</sup> In the study conducted by Abacı et al. on 400 pregnant women, HBsAg positivity was demonstrated in 3.75% of the pregnant women; meanwhile 4 HBsAg positivity was reported in the cord blood of newborns of 15 HBsAg-positive pregnant women who gave birth.<sup>11</sup> In another study<sup>12</sup> conducted in France, prevalence rate of HBsAg in pregnant women was found to be 1.24%, whereas this rate was reported as 11.6% in Nigeria, and 11-14% in Taiwan.<sup>13</sup>

In this study, the prevalence rate of HBsAg in pregnant women was reported as 2.9%, whereas that of anti-HBe positivity was found to be 84.4%. On the other hand, HBsAg positivity was not reported in any of the cord blood of newborns born to HBsAg-carrier mothers. Similarly, in another study where maternal and cord blood were compared, vertical transmission of HBsAg was not reported, however vertical transmission of anti-HBs antibodies was detected.<sup>14</sup> This study demonstrates that antibodies cross the placenta easier than antigens, whereas neonatal infection is less observed in asymptomatic HBsAg-carrier pregnant women.<sup>14</sup> The study by Harma et al. also demonstrated the absence of vertical transmission from 10 hepatitis B-carrier mothers.<sup>1</sup> A recent study reported HBsAg positivity in the cord blood of 16 (32%) of the newborns born to 50 HBsAg-positive pregnant women.<sup>15</sup>

In conclusion, intrauterine vertical transmission of hepatitis B virus was not identified in our region. This study was consistent with some literature studies,<sup>1,14</sup> whereas it was different from the study by Abacı<sup>11</sup> et al. Despite the rarity of intrauterine vertical transmission of hepatitis B virus, screening of all pregnant women for hepatitis B is highly recommended in Turkey since the

country is of moderate endemicity for HBV seroprevalence; newborns of HBsAg-positive pregnant women should also be vaccinated and prophylactic hepatitis B immunoglobulin should be administered immediately after birth, to prevent any possible risk of hepatitis B infection.

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