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Hepatitis B seropositivity of pregnant women and the review of Turkish literature

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Abstract

Objective: The aim of the study was to show the progress of hepatitis B seropositivity rates of pregnant women in Turkey for the last two decades by regions and years and to evaluate the current condition in consideration of the studies published.

Methods: The studies investigating hepatitis B seropositivity of pregnant women in Turkey were analyzed by reviewing the databases and the literature. On this topic, 64 studies performed between 1975 and 2016 were found. The studies published within the last 2 decades (1996–2016) were arranged by their publication years. Additionally, the data of the women delivered in our clinic between 2012 and 2015 were reviewed retrospectively and the result of HBsAg seropositivity rate was determined.

Results: It was seen that the rate of HBsAg seropositivity in the studies published in Turkey was between 1.2 and 19.2%. Considering the studies performed within the last two decades, the highest rate was 9.3%, and no HBsAg seropositivity higher than 6% was found in the studies performed in the last 7 years with the contribution of vaccine program carried out throughout the country. In the study we performed in our clinic, we found the rate 2.16% in 4037 pregnant women.

Conclusion: In Turkey, it is fought against the perinatal contagion of hepatitis B virus by antenatal HBsAg screening, routine hepatitis B virus vaccine of newborns and passive and active immunization practices applied on newborns of the mothers who are positive for HBsAg. In addition, high risk groups are vaccinated against hepatitis B and with all these methods, it is expected to decrease the rate of hepatitis B in future years in Turkey.

Keywords: Hepatitis B, pregnancy, seropositivity, Turkey.

Özet: Gebelerde hepatit B seropozitifliği ve Türk literatürüne bir bakış

Amaç: Türkiye'de yaşayan gebelerde son 20 yıl içindeki hepatit B seropozitiflik oranlarının bölgeler ve yıllara göre seyrinin gösterilmesi, yapılan çalışmalar ışığında güncel durumun değerlendirilmesi amaçlanmıştır.

Yöntem: Türkiye'de yaşayan gebelerde hepatit B seropozitifliğinin araştırıldığı çalışmalar veri tabanları ve literatür taramaları yapılarak incelendi. Bu konuda 1975–2016 yılları arasında yapılmış 64 çalışma tespit edildi. Son 20 yıl içindeki (1996–2016) çalışmalar yayınlandığı yıla göre düzenlendi. Ek olarak kliniğimizde 2012–2015 yılları arasında doğum yapan kadınların verileri retrospektif olarak incelenerek ulaşılan HBsAg seropozitiflik oranı sonucu belirtildi.

Bulgular: Türkiye'de HBsAg seropozitiflik oranının yayınlanan çalışmalarda %1.2–19.2 arasında olduğu görüldü. Son 20 yılda yapılan çalışmalar incelendiğinde en yüksek oranın %9.3 olduğu, yurt genelinde uygulanan aşılama programının da etkisiyle son 7 yılda yapılan çalışmalarda %6'nın üzerinde bir HBsAg seropozitifliğine rastlanmadığı görüldü. Kliniğimizde yaptığımız çalışmada ise bu oran 4037 gebede %2.16 olarak bulundu.

Sonuç: Türkiye'de antenatal HBsAg taraması, yenidoğanlara rutin hepatit B virüsü aşısı ve HBsAg pozitif annelerden doğan bebeklere uygulanan pasif ve aktif immunizasyon uygulamalarıyla hepatit B virüsünün perinatal bulaşı ile mücadele edilmektedir. Bunlara ek olarak yüksek riskli gruplara da hepatit B aşısı yapılmakta ve tüm bu yöntemlerle gelecek yıllarda hepatit B oranlarının ülkemizde daha da düşmesi beklenmektedir.

Anahtar sözcükler: Hepatit B, seropozitivite, gebelik, Türkiye.

Introduction

The infection of hepatitis B virus is still considered as one of the leading public health problems in the world. According to the recent data of WHO, there are about 240 millions of individuals have been exposed to the chronic hepatitis B infection worldwide. The incidence of hepatitis B varies according to the geographical regions and they are classified as high, medium and low

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endemic regions. According to this classification, Turkey is among the medium endemic regions.

Hepatitis B virus seropositivity is evaluated with hepatitis B surface antigen (HBsAg) and HBsAg seropositivity rate is 5% in women in the world which varies between 0.6 and 20% according to the endemic regions.[1]

Hepatitis B virus (HBV) is transmitted by body fluids such as infectious blood, saliva and vaginal fluid/semen or percutaneous or mucosal contact. On the other hand, perinatal contagion is blamed particularly in the high endemic regions. Infection contagion from HBsAg positive mother to baby can occur during intrauterine, intrapartum or postpartum period. While contagion during intrauterine period is rare, it is more frequent during intrapartum or postpartum period when baby may contact with infected maternal fluids.

It was found that hepatitis B e antigen (HBeAg) and serum HBV DNA levels of mother are effective in the contagion of the infection from HBV carrier mother to the baby during perinatal period.[2] It was reported in a study that the risk of contagion from mothers negative for HBeAg was 10–40% and that the risk increases to 70–90% in positive women.[3] When it is transmitted from mothers positive for HBeAg, it is considered that the rate of the disease being chronic in the infected baby also increases.[4] Thanks to the active and passive immunization applied together with the birth, the risk of contagion to babies born from mothers positive for HBsAg/HBeAg is decreased. In Turkey, all newborns have been vaccinated routinely for hepatitis B since 1998.

As the perinatal contagion of hepatitis B is still important today, we aimed in this study to explain the seropositivity of hepatitis B virus of pregnant women in the light of the studies carried out in Turkey and to show the progress of HBsAg seropositivity rate by regions and years.

Methods

The studies on HBV seropositivity in pregnant women were screened in the databases of ULAKBIM Medical Database (Turkish Medical Index), TürkMedline and Turkish Citation Index. The studies were researched by using the keywords "hepatit B" *(hepatitis B)*, "HBsAg", "gebe enfeksiyon" *(infection in pregnant women)*, "gebe hepatit B" *(hepatitis B in pregnant women)*, and "gebe HBsAg" *(HBsAg in pregnant women)*. Other studies were found by analyzing the studies found in the databases. Except the theses published in Turkey, the theses found during the database investigation were reviewed in terms of the literature. On this topic, 64 studies performed between 1975 and 2016 were found. The studies performed within the last 2 decades (1996–2016) were arranged by their publication years (**Table 1**).

Table 1. The studies carried out on HBsAg seropositivity of pregnant women in Turkey within the last 20 years.

First author	Year	Region	Number	HBsAg positivity (%)
Çepni[9]	1996	Istanbul	4078	4.4
Kuru[10]	1996	Istanbul	5366	4.2
Kadanalı[11]	1997	Erzurum	282	6.3
Kaleli[12]	1997	Denizli	312	7.7
Akın[13]	1997	Bursa	310	5.5
Gül[14]	1998	Van	98	4.08
Biri[15]	2001	Ankara	451	7
Aslan[16]	2001	Şanlıurfa	450	4.6
Yücel[17]	2001	Ankara	644	3.2
Sağsöz[18]	2002	Kırıkkale	157	4.9
Karaca[19]	2003	Istanbul	460	4.7
Yegane Tosun[20]	2003	Izmir	760	4.2
Harma[21]	2003	Şanlıurfa	136	7.3
Yılmazer[22]	2004	Afyon	244	2.9
Tekay[23]	2006	Şanlıurfa	2335	5.1
Madendağ[24]	2007	Ankara	90351	2.1
Çakmak[25]	2008	Niğde	4831	1.2
Sırmatel[26]	2008	Gaziantep	397	9.3
Uyar[27]	2009	Samsun	2654	2.1
Atılgan[28]	2009	Rize	1130	2.56
Dündar[29]	2009	Istanbul	3503	2.2
Kölgelier[30]	2009	Adıyaman	660	4.7
Api[31]	2009	Istanbul	228	3.9
Altınbaş[32]	2010	Ankara	4700	2.8
Köksaldı Motor[33]	2010	Hatay	5410	1.5
Akdemir[34]	2010	Ankara	1422	1.2
Karlıdağ[35]	2011	Elazığ	5120	1.9
Coşkun[36]	2011	Istanbul	795	3.7
Araz[37]	2011	Gaziantep	11840	2.1
Gönen[38]	2011	Düzce	1028	3.3
Varol[39]	2011	Edirne	1526	3
Deveci[40]	2011	Mardin	1570	2.9
Çopur Çiçek[41]	2012	Şanlıurfa	56275	3.5
Kölgelier[3]	2012	Adıyaman	9420	4.7
Çakmak[42]	2012	Kocaeli	3756	2.2
Yıldız[43]	2012	Diyarbakır	2900	2.66
Özlü[44]	2013	Bolu	653	1.8
Balık[45]	2013	Rize	5894	5.7
Koruk[46]	2013	Şanlıurfa	261	3.2
Doğan[47]	2014	Istanbul	2011	1.2
Özcan Dağ[48]	2015	Kırıkkale	8442	3.47
Aynıoğlu[49]	2015	Zonguldak	1084	4

Additionally, the data of the women delivered in our clinic between 2012 and 2015 were reviewed retrospectively and the result of HBsAg seropositivity rate was determined in our study.

Results

There are more than 60 studies, investigating HBsAg seropositivity of pregnant women in Turkey, performed in different years and in the same and different cities. While these studies show that HBsAg seropositivity varies between 1.2 and 19.2% in Turkey, no higher positivity was found in other studies after the study reporting the rate as 19.2%. It is seen that the highest rate reported by the studies performed within the last two decades is 9.3% (**Table 1**). It is seen that the rate is less than 6% in the studies performed in the last 7 years with the contribution of vaccine program carried out throughout the country.

In our study that we investigated the rate of HBsAg seropositivity of pregnant women, we found this rate as 2.16% in 4037 pregnant women. In the study, we retrospectively analyzed the data of pregnant women who delivered at our clinic between 2012 and 2015 and found that 8.22% of the pregnant women were of foreign nationality, the mean age was 28.64 (±5.77), mean week of gestation was 38.57 (±2.72), gravida was 2.51 (±1.44) and parity was 1.20 (±1.16).

Discussion

Hepatitis B virus is an infectious agent which progress with mortality and may cause chronic liver diseases, cirrhosis and hepatocellular carcinoma. HBV is transmitted essentially by infected blood and body fluids as well as percutaneous or mucosal contact. On the other hand, perinatal contagion is blamed particularly for the incidence of hepatitis B in the high endemic regions. The presence of this infection is important in terms of obstetrics as it is considered that HBV infection has adverse effects on gestational outcomes. Infection contagion from carrier mother to baby can occur during intrauterine, intrapartum or postpartum period. It is thought that the reasons such as skin scars, mucosal penetration, swallowing maternal blood and fetomaternal bleeding due to placental injury have a role in the intrapartum contagion.[5]

There are many studies in the literature investigating the effects of HBV infection on gestational outcomes. In a study, it was reported that preterm labor rate is higher in pregnant women positive for HBsAg than the pregnant women in the control group and that the rates of gestational diabetes, preterm labor and low birth weight are higher in carrier women positive for HBsAg than the carrier women negative for HBsAg.[6] In another study, it is claimed that HBsAg seropositivity is associated with antepartum hemorrhage and low APGAR scores.[7]

There are more than 60 studies, investigating HBsAg seropositivity of pregnant women in Turkey, performed in different years and in the same and different cities. While these studies show that HBsAg seropositivity is between 1.2 and 19.2% in Turkey, the study of Turhanoğlu et al. in 1987 which was conducted on pregnant women in Diyarbakır found the rate 19.2%[8] and no such positivity has been seen in all other studies published afterwards.[8] When we evaluate the studies performed in the last two decades (**Table 1**),[9–49] we see that the highest rate is 9.3%.[26] It is seen that HBsAg seropositivity rate is lower in the studies performed with high number of pregnant women than those with less number of pregnant women. In the first three studies with the highest pregnant woman population, the rates of HBsAg seropositivity were 2.1% (90,351 pregnant women),[24] 3.5% (56,275 pregnant women)[41] and 2.1% (11,840 pregnant women).[37] It is remarkable in this regard that the numbers of pregnant women in studies with the rate above 7% are 397, 312 and 136.[26,12,21] The variety among the rates of HBsAg positivity in the studies shown in **Table 1** may have many reasons. While some of these studies were carried out in reference centers such as university and training and research hospitals, some of them were performed in rural areas and maternal-pediatric health centers.[38,13] In this regard, it should be remembered that the studies carried out in the clinics which are reference centers cannot reflect the entire society. The rates also vary by regions and years. In recent years, HBsAg seropositivity rates tend to decrease in pregnant women as in the general population. With the help of country-wide vaccination program which has been conducted since 1998, no HBsAg seropositivity over 6% has been found in the studies carried out in the last 7 years.

In the studies investigating perinatal contagion, cord blood of babies of HBsAg seropositive mothers was checked and while a study found 45% HBsAg seropositivity in cord blood,[50] another study found no

HBsAg seropositivity in the cord blood.[40] Kuru et al.[51] conducted screenings on the children as well as husbands of HBsAg seropositive cases and they found anti-Hbs rate over 20%. In the same study, there was no statistically significant difference between seropositive and seronegative cases in terms of age, number of pregnancy, socioeconomical status, intravenous injection, and applying blood and blood products.

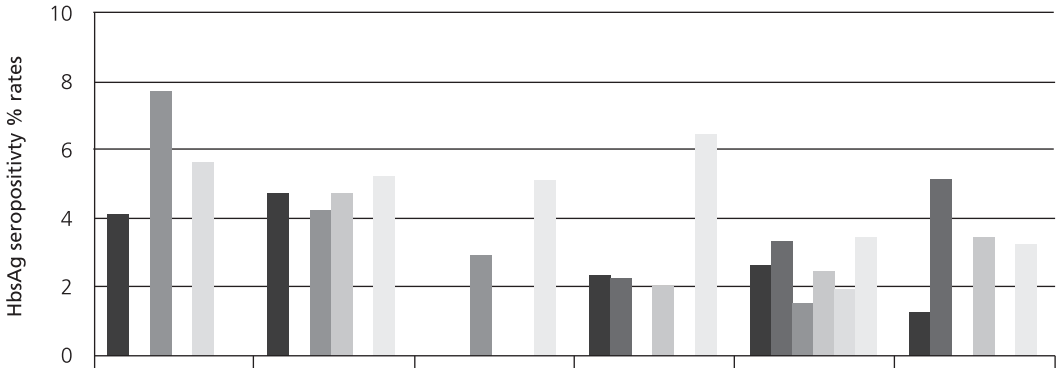
We found the rate of HBsAg seropositivity of pregnant women in our clinic 2.16% in 4037 pregnant women. In this study, we retrospectively analyzed the data of pregnant women who delivered at our clinic between 2012 and 2015, and investigated HBsAg results checked with ELISA method in the peripheral blood samples collected routinely from the pregnant women at antenatal period. Of the pregnant women, 8.22% were foreign. Of those included in the study, mean age was 28.64 (±5.77), mean week of gestation was 38.57 (±2.72), gravida was 2.51 (±1.44) and parity was 1.20 (±1.16). We found that the HBsAg seropositivity rate in our clinic was consistent with the rates found in similar studies conducted in Istanbul in recent years.

When we look at the **Table 1** which shows the progress of HBsAg seropositivity in different cities within last 20 years, we see that the rate is slightly above 4% in Istanbul for the first 10 years while it decreases to the level below 4% in the last 10 years. Although the rate reported in the study of Doğan et al. published in 2014 decreases to 1.2%,[47] the reasons for the slight increase in our study are considered to be the increased migration to Istanbul from other cities and the Middle East, and our clinic being one of the reference centers.

When we look at the distribution among the reasons, we see that there is a clear decrease in HBsAg seropositivity of pregnant women in Marmara, Mediterranean/Aegean and Eastern Anatolia regions while the rates fluctuate in Central and Southeastern Anatolia regions. On the other hand, the rate in Black Sea region increased from 2.2% to 5.1% in the last 10 years (**Fig. 1**). This result shows that further studies are required to investigate the reasons for the increase in Black Sea region.

Conclusion

As perinatal contagion maintains its importance in the endemic regions, it is necessary to investigate HBV of



	1996–1998	2001–2003	2004–2006	2007–2009	2010–2012	2013–2015
Marmara	4.1	4.7		2.3	2.6	1.2
Black Sea				2.2	3.3	5.1
Mediterranean/Aegean	7.7	4.2	2.9		1.5	
Central Anatolia		4.7		2	2.4	3.4
Eastern Anatolia	5.6				1.9	
Southeastern Anatolia		5.2	5.1	6.4	3.4	3.2

Fig. 1. Distribution of HBsAg seropositivity of pregnant women within the last 20 years by regions and years.

pregnant women in these regions and to take protective precautions against this infection. In Turkey, it is fought against the perinatal contagion of HBV by antenatal HBsAg screening, routine HBV vaccine of newborns and passive and active immunization practices applied on newborns of the mothers who are positive for HBsAg. In addition, high risk groups are vaccinated against HPV and with all these methods, it is expected to decrease the rate of hepatitis B in future years in Turkey.

Conflicts of Interest: No conflicts declared.

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