Hepatitis Monthly 2009; 9(2): 146-149

BRIEF REPORT

Seroprevalence of Hepatitis B Virus among Pregnant Women in Northern Turkey

Yavuz Uyar [1, 2*], Cevat Cabar [1], Alaaddin Balci [3]

[1] Microbiology Laboratory, Samsun Maternity and Women's Disease and Pediatrics Hospital, Samsun, Turkey

[2] Refik Saydam National Public Health Agency (RSNPHA), Virology Reference and Research Laboratory, Sihhiye, Ankara, Turkey

[3] Department of Gynecology and Obstetrics, Samsun Maternity and Women's Disease and Pediatrics Hospital, Samsun, Turkey

Background and Aims: **Prevention of vertical transmission of hepatitis B virus (HBV) is extremely important because HBV infection in early life usually results in a chronic carrier state. The objective of this study was to assess the prevalence of HBV markers among pregnant women in the Middle Black Sea Region in Turkey.**

Methods: **Between March 2003 and May 2004, 2654 women in the first trimester of pregnancy who attended the Samsun Maternity and Women's Disease and Pediatrics Hospital pregnancy fallow-up clinics were enrolled into this study. Blood samples were taken and tested for hepatitis B surface antigen (HBsAg) by enzyme-linked immunosorbent assay (ELISA). Hepatitis B e antigen (HBeAg), antibody against hepatitis B e antigen (anti-HBe), hepatitis B surface antibody (anti-HBs), and total hepatitis B core antibody (anti-HBc) tests were studied for only HBsAg positive cases.**

Results: **HBsAg was found positive in 56 (2.1%; 95% confidence interval [CI]: 1.6%-2.7%) and negative in 2598 (97.9%) women. Serological markers of HBV could be investigated in 40 HBsAg-positive cases. HBeAg and anti-HBe were found positive in 5 (12.5%; 95% CI: 2.3%-22.8%) and 31 (77.5%; 95% CI: 64.6%-90.4%) cases, respectively. In all the 40 patients, anti-HBc was found positive and anti-HBs was negative.**

Conclusions: **Despite routine vaccination introduced in the Turkey national program, we suggest that pregnant women be routinely investigated for HBV infection. In this way, feto-maternal transmission of HBV may be reduced that might play an important role to break the cycle of HBV infection in Turkey.**

Keywords: **HBV, HBsAg, HBeAg, Prevalence, Pregnant Women**

Introduction

Hepatitis B virus (HBV) is a double-stranded DNA virus belonging to *Hepadnaviridae* family. The incubation period is six weeks to six months [(1)]. HBV infection affects over 350 million people worldwide and over one million die annually of HBV-related chronic hepatic disease. These chronically infected persons are at high risk of death from liver cirrhosis and cancer [(2)].

The prevalence of HBV infection, according to the geographical area, may be high (8%), intermediate (2%–7%) or low (<2%) [(3)]. In several studies from different regions of Turkey, the prevalence of hepatitis B surface antigen (HBsAg) among normal population was reported from a minimum of 2% to a maximum of 14.3%—average 6.8 % [(4)]. In Europe and America, chronic HBV carriers are found in <2% of the population [(5)]. In endemic areas, most individuals are infected by vertical transmission [(6)]. In Africa, more than half of

**** Correspondence:***
Yavuz Uyar, M.D.
Refik Saydam National Public Health Agency (RSNPHA), Virology Reference and Research Laboratory, Cemal Gürsel Cad. No 18 C Blok, Sihhiye - 06100 - Ankara, Turkey.

Tel: *+90 312 458 2452*
Fax: *+90 312 458 2388*

E-mail: *yavuz.uyar@rshm.gov.tr, yavuz_uyar@yahoo.com*

Received: *13 Jan 2009* ***Revised:*** *24 Apr 2009*
Accepted: *27 Apr 2009*

Hepat Mon 2009; 9 (2): 146-149

the population becomes HBV infected during their life time and about 8% of inhabitants become chronic carriers; most of the infections take place during delivery or infancy [5].

HBV is transmitted primarily through parenteral and sexual exposure to HBsAg positive blood or other body fluids, from those who are chronic HBV carriers or who have acute hepatitis B [3]. HBV is also transmitted perinatally. Prevention of vertical transmission is extremely important because HBV infection in early life usually results in a chronic carrier state. HBV infection does not appear to be teratogenic. Recent studies showed a higher incidence of low birth weight among infants born to mothers with acute infection during pregnancy [7]. The objective of this study was to assess the prevalence of HBV markers among pregnant women in the Middle Black Sea Region in Turkey (northern parts).

Patients and Methods

Subjects

Samsun is a city in the Middle Black Sea Region in northern Turkey, on the coast of the Black Sea, with a population of 1,324,000. Samsun Maternity and Women's Disease and Pediatrics Hospital is a 350-bed governmental hospital that serves patients in mid-Black Sea region of Turkey. The hospital offers an array of clinical services, ranging from primary to secondary care. The Hospital also provides services to other Middle Black Sea Region cities, such as Ordu, Tokat, Amasya, Çorum, and Sinop provinces with a total hinterland population of 2.5 million citizens. All the women in their first trimester of pregnancy who attended the pregnancy follow-up clinics between March 2003 and May 2004 were enrolled into this study. Blood samples collected from an antecubital vein were taken from the studied group, centrifuged on site within 1–2 hr and the serum was separated using a standard protocol.

Serology

HBsAg was tested in the study group using a commercial enzyme-linked immunosorbent assay (ELISA) kit (DiaSorin S.p.A., Italy) by an automated analyzer (Eti max, Italy). HBsAg-positive sera were stored at -20°C and were tested for hepatitis B e antigen (HBeAg), antibody against hepatitis B e antigen (anti-HBe), hepatitis B surface antibody (anti-HBs) and total hepatitis B core antibody (anti-HBc) markers (DiaSorin S.p.A., Italy). Samples were considered positive when the "sample optical density"/"assay cut off" (OD/OC) ratio was higher than 1.1 according to manufacturer's instructions.

Statistical analysis

SPSS, version 10.0, was used for descriptive statistics. A P value <0.05 was considered statistically significant.

Results

A total of 2654 pregnant women in their first trimester were enrolled into the study. The mean±SD age of the study group was 28.0±6.2 (range: 17–45) years. HBsAg was found positive in 56 (2.1%; 95% CI: 1.6%–2.7%). The mean±SD age in HBsAg-positive was 26.7±3.5 (range: 17–40) years; it was not statistically different from mean±SD age of HBsAg-negative subjects (28.4±4.2; range: 17–45 years).

For some limitations (e.g., insufficient sera, lost of samples, lose of contact with subjects, etc.) of 56 HBsAg-positive patients, only 40 (71%) could be evaluated for HBeAg and anti-HBe markers. HBeAg and Anti-HBe were positive in five (12.5%; 95% CI: 2.3%–22.8%) and 31 (77.5%; 95% CI: 64.6%–90.4%) of HBsAg-positive patients, respectively. All the 40 HBsAg-positive patients were positive for anti-HBc antibody and were negative for anti-HBs.

Discussion

Hepatitis B is a liver disease caused by HBV. It ranges in severity from a mild illness, lasting a few weeks (acute), to a serious long-term (chronic) illness that can lead to liver cirrhosis or cancer [1]. In patients with acute hepatitis B vertical transmission occurs in up to 10% of neonates when infection occurs in the first trimester and in 80%–90% of neonates when the infection occurs in the third trimester [8]. Ten percent to 20% of neonates born to HBsAg-positive mothers and 90% of those born to both HBsAg- and HBeAg-positive mothers will be infected with HBV [9, 10]. Immunization with hepatitis B immunoglobulin G (HBIG) and vaccine, starting at birth, reduces the risk of transmission to less than 10% among infants who have HBsAg/HBeAg positive mothers [11, 12]. HBIG has high levels of antibody to HBsAg; it is immediately effective, and seems to be protective for several months [13].

Several studies have been conducted on hepatitis

B and pregnancy. In the U.S., HBsAg positivity was reported in 5.8% of the Asians, 1.0% in non-Hispanic blacks, 0.6% of non-Hispanic whites and 0.1% of Hispanics [14]. HBsAg was found in 1.7% of pregnant women in Brazil [15]. In Africa, HBsAg was positive in 4.6% of pregnant women in Nigeria [16] and in 5.6% of pregnant women of Sudan [17]. In another study, the seroprevalence of HBsAg among the pregnant women in the countries of the Persian Gulf territory revealed a rate 7.1% in Oman, 1.0% in Qatar and 1.5% in UAE [18]. In France, HBsAg was positive in 0.29% of the pregnant women of French origin, 7.15% of Southeast Asian origin, and 6.52% for Sub Saharan African origin [19]. In a study conducted in six regions of Italy, HBsAg was positive in 1.1% of pregnant women born in Italy, but it was 5.9% among immigrants [20].

Turkey is geographically located between Europe and the Asia and Samsun province is at the Middle Black Sea Region, northern Turkey. However, the prevalence of HBsAg among pregnant women in our country was similar to other reports from Balkan and Black Sea countries. Other studies revealed an HBsAg seroprevalence rate of 3.87% for Greece [21], 1.1%–6.9% for Russia [22] and 8.4% for Romania [23]. In Turkey, according to a meta-analysis, HBsAg seropositivity was 4.4% (between 1.9% and 15.3% pooled from 22 reports) among pregnant women from different regions [4]. This meta-analysis showed that HBsAg seropositivity rate is widely different for region to region in Turkey. There are some other new reports about HBV among pregnant women from various regions of Turkey; HBsAg was positive in 3.2%–4.33% of pregnant women in Ankara [24, 25], in 3.75% in Kayseri [26] from Central Anatolia, in 3.5% in Mersin [27] from southern Turkey, in 12.3% in Diyarbakir [28] from southeastern Anatolia, and in 4.2% of the women in Istanbul [29] from Marmara region (northwestern Turkey). In our study, the HBsAg seropositivity was 2.1% in the Middle Black Sea region, northern Turkey. Compared to other reports form Turkey, it seems that the rate we observed is lower. This could be due to the higher social and economical status in northern and western Turkey compared to other regions and the level of hygiene and vaccination coverage in this region.

HBeAg is a seromarker related to infective HBV particles and its seropositivity might represent a high level of viral replication in hepatocytes [30]. In the absence of immunoprophylaxis, the risk of transmission from HBsAg/HBeAg-positive mothers is almost 90%. The risk of perinatal transmission is related to the maternal HBeAg status and HBV DNA load [31]. In a study from Turkey, Kuru *et al.,* [29] reported HBeAg positivity rate of 6.2% among HBsAg-positive pregnant women. We found a positive rate for HBeAg of 12.5% among HBsAg-positive pregnant women. In a study, the seroprevalence of HBsAg was found to be 91.6% in infants born from pregnant women who were positive for both HBsAg and HBeAg [28]. Therefore, HBeAg should be tested in HBsAg-positive pregnant women and measures must be employed to prevent vertical transmission of the HBV.

Pregnancy is not a contraindication for vaccination for HBV [31, 32]. No apparent risk for adverse events to developing fetuses has been demonstrated when HBV vaccine was administered to pregnant women—even in early pregnancy [32]. Therefore, those pregnant women who are identified at risk for HBV infection during pregnancy should be vaccinated [31]. World Health Organization (WHO) and Center for Disease Control and Prevention (CDC) advise that HBsAg should be examined in all pregnant women and that infants born to HBsAg-positive mothers should receive hepatitis B vaccine and 0.5 mL HBIG within 12 hours of birth [1, 2]. This offer has begun to be applied widely all around the world. In addition, viral hepatitis preventive board (VHPB) suggests routine screening of pregnant women for HBsAg; if one found positive, active and passive prophylaxis, and vaccination of the newborn to prevent the perinatally transmission of HBV [33] are recommended. Hepatitis B vaccination was first included in the National vaccination program in Turkey in 1998 by Turkish Ministry of Health. According to this campaign, infants were vaccinated with three doses of vaccine at 0, 3, and 9 months.

Conclusions

Turkey is in a region with intermediate prevalence of HBV. Routine vaccination was started in 1998, so there are already some unvaccinated women in childbearing age who are at risk for HBV infection. Despite routine vaccination introduced in the Turkey National program, we suggest that pregnant women be routinely investigated for HBV infection. If HBV carriers are detected, newborns must be immunized and HBIG must be given. In this way, fetomaternal transmission of HBV may be reduced that might play an important role to break the cycle of HBV infection in Turkey.

Acknowledgements

We thank everyone who collaborated in this study, particularly Samsun Maternity and Women's Disease and Pediatrics Hospital management, staff, the occupational physicians and nurses, and laboratory personnel. We thank to Dr. Alper Akcali for editing of the manuscript.

References

1. Sexually transmitted diseases treatment guidelines 2002. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2002;**51**(RR-6):1-78.
2. World Health Organization (WHO). Advanced Immunization Management (AIM). Hepatitis B. [cited 2005 August]; Available from: www.who.int/mediacentre/factsheets/fs204/en/.
3. Maddrey WC. Hepatitis B: an important public health issue. *J Med Virol*. 2000;**61**(3):362-6.
4. Mistik R, Balik I. [The Epidemiologic Analyzes Viral Hepatitis in Turkey]. In: Kılıçturgay K, Badur S, editors. *Viral Hepatitis*. İstanbul; 2001. p. 10-55.
5. Kane M. Global programme for control of hepatitis B infection. *Vaccine*. 1995;**13 Suppl 1**:S47-9.
6. Wright TL. Introduction to chronic hepatitis B infection. *Am J Gastroenterol*. 2006;**101 Suppl 1**:S1-6.
7. Shepard TH. *Catalog of Teratogenic Agents*. 9th ed. Baltimore, MD: Johns Hopkins University Press; 1998.
8. ACOG educational bulletin. Viral hepatitis in pregnancy. Number 248, July 1998 (replaces No. 174, November 1992). American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet*. 1998;**63**(2):195-202.
9. Chang MH. Chronic hepatitis virus infection in children. *J Gastroenterol Hepatol*. 1998;**13**(5):541-8.
10. Stevens CE, Beasley RP, Tsui J, Lee WC. Vertical transmission of hepatitis B antigen in Taiwan. *N Engl J Med*. 1975;**292**(15):771-4.
11. Andre FE, Zuckerman AJ. Review: protective efficacy of hepatitis B vaccines in neonates. *J Med Virol*. 1994;**44**(2):144-51.
12. Tosun SY, Yücetürk M, Benzergil S. [HBsAg Pozitif Gebelerden Dogan Bebeklerin ImmuNizasyonu]. *Ege J Med* 2002;**41**(1):21-3.
13. Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis. *BMJ*. 2006;**332**(7537):328-36.
14. Euler GL, Wooten KG, Baughman AL, Williams WW. Hepatitis B surface antigen prevalence among pregnant women in urban areas: implications for testing, reporting, and preventing perinatal transmission. *Pediatrics*. 2003;**111**(5 Part 2):1192-7.
15. Bertolini DA, Pinho JR, Saraceni CP, Moreira RC, Granato CF, Carrilho FJ. Prevalence of serological markers of hepatitis B virus in pregnant women from Parana State, Brazil. *Braz J Med Biol Res*. 2006;**39**(8):1083-90.
16. Obi SN, Onah HE, Ezugwu FO. Risk factors for hepatitis B infection during pregnancy in a Nigerian obstetric population. *J Obstet Gynaecol*. 2006;**26**(8):770-2.
17. Elsheikh RM, Daak AA, Elsheikh MA, Karsany MS, Adam I. Hepatitis B virus and hepatitis C virus in pregnant Sudanese women. *Virol J*. 2007;**4**:104.
18. Al Awaidy S, Abu-Elyazeed R, Al Hosani H, *et al*. Sero-epidemiology of hepatitis B infection in pregnant women in Oman, Qatar and the United Arab Emirates. *J Infect*. 2006;**52**(3):202-6.
19. Denis F, Ranger-Rogez S, Alain S, *et al*. Screening of pregnant women for hepatitis B markers in a French Provincial University Hospital (Limoges) during 15 years. *Eur J Epidemiol*. 2004;**19**(10):973-8.
20. Stroffolini T, Bianco E, Szklo A, *et al*. Factors affecting the compliance of the antenatal hepatitis B screening programme in Italy. *Vaccine*. 2003;**21**(11-12):1246-9.
21. Panagopoulos P, Economou A, Kasimi A, *et al*. Prevalence of hepatitis B and C in the maternity department of a Greek district hospital. *J Matern Fetal Neonatal Med*. 2004;**16**(2):106-10.
22. Kuzin SN, Ikoev VN, Shakhgil'dian IV, *et al*. [Patterns in perinatal infection with the hepatitis B virus in areas contrasted by the level of HBsAg and HBeAg carriage]. *Vopr Virusol*. 1990;**35**(4):304-6.
23. Woodruff BA, Popovici F, Beldescu N, Shapiro CN, Hersh BS. Hepatitis B virus infection among pregnant women in northeastern Romania. *Int J Epidemiol*. 1993;**22**(5):923-6.
24. Yucel A, Bozdayi G, Turgut I. Serological profile of hepatitis b, hepatitis c and human immunodeficiency viruses among pregnant women. *Gazi Med J*. 2001;**12**:103-5.
25. Erdem M, Sahin I, Erdem A, Gursoy R, Yildiz A, Guner H. Prevalence of hepatitis B surface antigen among pregnant women in a low-risk population. *Int J Gynaecol Obstet*. 1994;**44**(2):125-8.
26. Abaci IM, Düsünsel R, Patiroglu T, Çetin N, Kiliç H. [Gebelerde ve bebeklerinde hepatit virüs belirleyicileri ve doku antijenleriyle iliskisi]. *Mikrobiyol bült*. 1995;**29**:170-8.
27. Borekci G, Otag F. The investigation of the seroprevalence of hepatitis B virus, hepatitis C virus and human immunodeficiency virus and related risk factors in healthy pregnants. *Turk J Infect*. 2004;**18**(2):219-23.
28. Turhanoglu M, Arikan E. [Gebe Kadinlar Ve Yeni Doğan Bebeklerinde Hbv Serolojik Göstergelerinin Araştirilmasi Ve Perinatal Profilaksi İle İlgili Öneriler]. *Pamukkale niv Tip Fak Dergisi*. 2001;**7**(1):1-4.
29. Kuru U, Turan O, Kuru N, *et al*. Prevalence of hepatitis B virus infection in pregnant Turkish women and their families. *Eur J Clin Microbiol Infect Dis*. 1996;**15**(3):248-51.
30. Hsu YS, Chien RN, Yeh CT, *et al*. Long-term outcome after spontaneous HBeAg seroconversion in patients with chronic hepatitis B. *Hepatology*. 2002;**35**(6):1522-7.
31. Gambarin-Gelwan M. Hepatitis B in pregnancy. *Clin Liver Dis*. 2007;**11**(4):945-63, x.
32. Levy M, Koren G. Hepatitis B vaccine in pregnancy: maternal and fetal safety. *Am J Perinatol*. 1991;**8**(3):227-32.
33. Van Damme P. Viral Hepatitis. Report on the VHPB