Original Article

Characteristics, Prevalence, and HBeAg Correlation of Hepatitis B in Pregnancy: A Siriraj Hospital Experience

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Objective: To describe the characteristics, prevalence, and HBeAg correlation of pregnant women with hepatitis B virus (HBV) at Siriraj Hospital, Mahidol University.

Materials and Methods: This retrospective medical chart review was conducted in pregnant women with HBV who came for antenatal care (ANC) at Siriraj Hospital between July 2015 and December 2018. All of them were asked to complete self-administered questionnaires at the first visit to the Siriraj Female Sexually Transmitted Infection (STI) Clinic. Blood testing for HBsAg was used to diagnose the infection. After that, HBeAg was routinely checked. HBV viral load (VL) was sent at the patients' own expense.

Results: Of the 28,214 pregnant women who came for ANC during the present study period, 395 were positive for HBsAg (1.4%). The mean age was 31.1±5.7 years. Of them, 110 knew the positive HBV serostatus before this pregnancy (27.9%) and 285 were newly diagnosed cases. The gestational age (GA) at diagnosis were less than 14 weeks in 157 (55.1%), 14 to 19 weeks in 72 (25.3%), 20 to 27 weeks in 26 (9.1%), and 28 weeks or more in 30 (10.5%). HBeAg was tested positive in 140 pregnant women (35.4%). Of the 57 women who were tested for HBV VL (15 known cases, 42 new cases), there was a significant association between HBeAg and VL of 200,000 IU per mL or more in that 85% of the positive HBeAg women had a HBV VL of 200,000 IU per mL or more. Of all participants, 303 male partners (76.7%) had never been tested for HBV infection.

Conclusion: Despite the success of the program to prevent the in-utero HBV infection, the standard of care, especially the routine evaluation of HBV VL is still not met. The present finding may raise awareness of the missing jigsaw in the health care of pregnant women with HBV at the national level.

Keywords: Pregnancy, Hepatitis B, Characteristics

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Hepatitis B virus (HBV) infection has been known as an important cause of chronic liver disease, cirrhosis, and liver cancer[(1)]. This has called for the prevention measure of transmission from mother to child across the globe. It is estimated that more than 240 million people worldwide are infected with this virus[(1)]. In Thailand, the prevalence of chronic HBV carriers is 5.1%[(2)]. The transmission of HBV from mother to child prenatally or perinatally is a mystical health care problem in many developing countries, especially in some Asian countries. The authors' previous report of data collection between 2004 and 2015 (n=107,183) showed that 3.3% of Thai pregnant women who came for antenatal care (ANC) at Siriraj Hospital were HBV-infected[(3)]. This group deserves the greatest attention, because as known, 90% of perinatally HBV-infected newborns will become chronic carriers.

Routine screening for HBV infection, human immunodeficiency virus (HIV) infection, and syphilis is done in pregnant women at their first ANC visit and during gestational age (GA) 28 to 32 weeks if the first test results are negative. Concurrent with the development of antiviral drugs, it results in a huge decline of the vertical transmission. In 2015, Thailand was announced by the World Health Organization's

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(WHO) as the first Asian country to achieve the targets, which is less than 2%[4]. Following the success of HIV, the management guideline for preventing the vertical transmission of HBV has been launched[2]. Basic laboratory investigations include hepatitis B e antigen (HBeAg), HBV viral load, and liver enzyme. HBeAg is a serum marker to indicate the high level of infection, so called "infectivity" in the person or pregnant women, and it can be detected very early after acquisition of the hepatitis B infection for a few months. Antiviral drug is initiated during pregnancy, and post-natal active and passive vaccination must be available within 12 hours. However, first and fundamental is that the current situation in Thailand should be acknowledged. Thus, the present study aimed to show the biggest series of Thai pregnant women living with HBV. Hopefully, the present study can inspire the health professionals across the globe to look at the hepatitis B infection in pregnancy, as well as to improve the ANC of this special group, aiming to reduce the vertical transmission from mother to child.

Materials and Methods

The present study was a retrospective chart-review that was ethically approved by the Siriraj Institutional Review Board, Mahidol University (COA no. Si 120/2018).

All pregnant women attending ANC clinic at Siriraj Hospital were blood-tested for HIV infection (anti-HIV), syphilis (venereal disease research laboratory; VDRL), and HBV infection (hepatitis B surface antigen; HBsAg). If any tests were positive, they would be sent to the Siriraj Female Sexually Transmitted Infection (STI) Clinic for ANC. All of them were asked to complete self-administer questionnaires regarding demographic data and sexual health risks. Those who attended the Clinic between July 2015 and December 2018 were included in the present study.

All HBV-infected women had their blood tested for HBeAg as the present study routine service. However, the decision to evaluate HBV viral load and liver enzyme depended on the patients' expense reimbursement and consent. Since late 2017, the counseling regarding complete blood testing has been done due to the many guidelines for preventing the vertical transmission of HBV. Additionally, partner evaluation or treatment as well as the interdepartmental corporation, mainly Internal Medicine, Obstetrics and Gynecology, and Pediatrics, have been enhanced.

Statistical analyses using Stata, version 12.1 (StataCorp LP, College Station, TX, USA) was done. In particular, descriptive statistics such as n (%), mean ± standard deviation (SD), and median with range were used. Chi-square was used to explore the association between categorical data. A p-value of less than 0.05 was considered as statistical significance.

Results

Of the 28,214 pregnant women who came for ANC during the present study period, 395 were positive for HBsAg (1.4%). The mean age was 31.1±5.7 years. Of them, 110 knew the positive HBV serostatus before this pregnancy (27.9%), and 285 were newly diagnosed cases. The GA at diagnosis were less than 14 weeks in 55.1%, 14 to 19 weeks in 25.3%, 20 to 27 weeks in 9.1%, and 28 weeks or more in 10.5%. Most of them finished secondary or vocational schools and currently had temporary jobs (Table 1).

Half reported one life-time sex partner, and all declared one current partner to be notified. Forty percent of them were alcohol drinkers, whereas 9.4% were cigarette smokers and 3.5% were illicit drug users. Eleven had history of STIs, including genital warts (4), trichomoniasis (3), herpes genitalis (2), gonorrhea (1), and chlamydial infection (1). Concurrent with the diagnosis of HBV infection, one had syphilis and one had HIV infection (Table 1).

Of the 57 women tested for HBV viral load (15 known cases, 42 new cases), there was significant association between HBeAg and viral load of 200,000 IU per mL or more, in that 81% of positive HBeAg women had HBV viral load of 200,000 IU per mL or more (Table 2). The level of HBV viral load was significantly higher in those with positive HBeAg as presented in Figure 1, at 1,840,000 (647,000 to 1,489,280) versus 143 (125 to 1,080), p=0.001. Table 3 shows that most of the sex partners did not come for the blood testing. Nine were living with HBV infection and one was HIV-infected.

Discussion

The prevalence of HBV infection declines over time in Thailand as being shown in the authors' previous report, that around 3.3% of pregnant women who attended the Siriraj ANC Clinic between 2004 and 2015 had HBV infection[3]. This is due to the effective national vaccination program against HBV infection starting in 1992. ANC is one of the best methods of HBV secondary prevention as it detected HBV infection in most of the present study population. At the moment, routine ANC blood

Table 1. Socio-demographic data of women (n=395)

Category	n (%)
Age (year); mean±SD (min-max)	31.2±5.7 (18 to 48)
≤19	7 (1.8)
20 to 29	148 (37.5)
30 to 39	213 (53.9)
≥40	27 (6.8)
Highest education level	
Primary and lower	83 (21.0)
Secondary/vocational school	181 (45.9)
University	131 (33.1)
Marital status: married	389 (98.5)
Occupation	
None/unemployment/housewife	82 (20.8)
House/office cleaner/laborer	170 (43.0)
Small business owner	49 (12.4)
Officer	94 (23.8)
Family income (Baht)	
≤15,000	113 (28.6)
15,001 to 35,000	199 (50.4)
≥35,001	83 (21.0)
Previous miscarriage	81 (20.5)
Gestational age at first antenatal care	
<14 weeks	148 (37.5)
14 to 19 weeks	109 (27.6)
20 to 27 weeks	54 (13.7)
≥28 weeks	84 (21.2)
Number of partner in the past	
1	204 (51.6)
2	109 (27.6)
≥3	82 (20.8)
Cigarette smoking	37 (9.4)
Alcoholic drink	161 (40.8)
Illicit drug use	14 (3.5)
Having tattoo	58 (14.7)
History of STDs	11 (2.8)
Been in prison	3 (0.8)

SD=standard deviation; STDs=sexually transmitted diseases

Table 2. Association with HBV viral load of HBeAg, diagnosis prior to pregnancy, diagnosis before GA 14 weeks, and alanine transferase ≥25 IU/mL (n=57)

	HBV viral load (IU/mL)		p-value
	<200,000	≥200,000	
Positive HBeAg (n=57)	4/37 (10.8)	17/20 (85.0)	<0.001
Diagnosis prior to pregnancy (n=57)	9/37 (24.3)	6/20 (30.0)	0.642
Diagnosis before GA 14 weeks (n=42)	12/28 (42.9)	4/14 (28.6)	0.367

HBV=hepatitis B virus; HBeAg=hepatitis B e antigen; GA=gestational age

Table 3. Blood testing for HIV infection, HBV infection and syphilis in the patients' sex partners (n=395)

	n (%)
Hepatitis B virus infection	
Yes	9 (2.3)
No	83 (21.0)
Not known	303 (76.7)
Human immunodeficiency virus infection	
Yes	1 (0.3)
No	112 (28.4)
Not known	282 (71.3)
Syphilis	
Yes	0 (0.0)
No	184 (46.6)
Not known	211 (53.4)

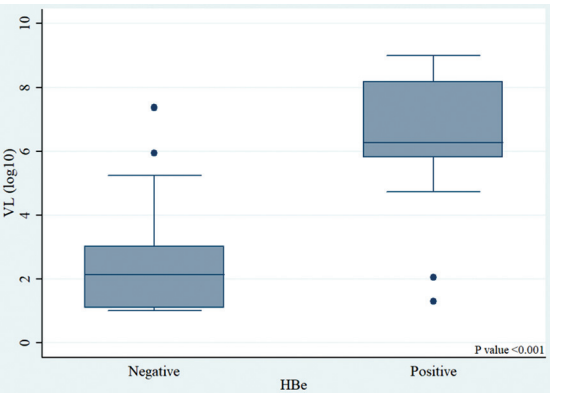

Figure 1. Level of hepatitis B viral load by status of hepatitis B e antigen.

VL=viral load

testing in Thailand involves many national common diseases, apart from STIs, such as thalassemia, diabetes mellitus, and anemia. The program is highly effective in minimizing new incidence of Thalassemia cases and congenital STIs. In addition, it prevents complications of those correctable diseases, like anemia and diabetes mellitus. Following the success of elimination of congenital HIV infection, the HBV infection has a great potential.

Many guidelines for stopping the mother-to-child transmission of HBV have been launched by many academic bodies[2,5-7]. Post-natal active and passive vaccination program, including HBV vaccination and hepatitis B immunoglobulin (HBIg) is well organized and complied with. However, the high expense of viral load testing, which is an important part of all guidelines, appears to be a big challenge. The present study demonstrates that only 14.4% (57/395) had the blood tested and almost all did because of full reimbursement. The alternatives of viral load that can be used to monitor the patients' status before and after treatment are clearly needed, especially in low-income settings.

HBeAg, as a routine test, is an extremely useful test. It is not only an independent factor of the vertical transmission but also reflects high level of viral load. HBeAg is one of the few HBV proteins that crosses placenta to impair fetuses' cell-mediated immunity, resulting in the greatest likelihood of becoming chronic carriers once being infected[8]. Moreover, the present study showed that 85% of the pregnant women with positive HBeAg had viral load of more than 200,000 IU per ml. Nonetheless, HBeAg cannot be the test used to make the decision to commence antiviral drugs.

Antiviral drug is a key factor for the prevention and a single agent of tenofovir disoproxil fumarate (TDF) is the most recommended drug for pregnant women. In 2016, a meta-analysis focusing on the effects of antiviral drugs in pregnant women and HBV fetal infection showed a 70% reduction rate[9]. This is compatible with the outcome of a randomized controlled trial (RCT) in 200 Chinese pregnant women with both positive HBeAg and viral load of more than 200,000 IU per mL. In that study, there was no HBV-infected infant in TDF group, whereas there was 18% in the placebo group[10]. In contrast, another RCT being conducted in 331 Thai pregnant women with positive HBeAg showed no significant difference of incidence when TDF or placebo was commenced at GA 28 weeks onwards[11]. The inhomogeneous findings may be the next challenge for the national policy makers.

Compared with general female population or women with other STIs, the characteristics of the participants are unremarkable[12] except that 40.8% used to be alcohol drinkers and 14.7% had tattoos. Both risks should be seriously taken into consideration. Alcohol consumption obviously degrades one's consciousness resulting in unsafe sex. Moreover, alcohol can further damages liver cells on top of HBV per se. The poor hygienic condition of some tattoo shops in Thailand can be another transmission source. Sanitation awareness should be raised in everyone's mind to protect oneself, and there should be some tools from the local health authority to control the quality.

The present study showed the sex partners' immense ignorance of self-health awareness for not only HBV infection but also HIV infection and syphilis. Partner notification is widely accepted as an important part of treating STI patients. The authors' previous report showed that enhanced partner notification using medical personnel or video can raised the notification rate to around 80%[12]. In addition, if the clinic was easily accessible and user-friendly, all partners would come for the blood test[12]. In fact, once a HBV-infected patient is detected, not only the sex partner(s) but also the whole family members should be blood-tested. As such, there remains room for improvement in terms of caring for HBV-infected patients.

The limited data in the Thai population is the strength of the study. National health policy makers may look at the data and re-consider the tailor-made management guideline for Thai people. Because of the low number of patients that had their blood tested for HBV viral load should alert all authorities involved in budget subsidization. Better STI treatment network should be strengthened as this group of diseases is more a social problem than an individual one. Finally, multidisciplinary care team is required for the holistic care of each indexed patient and all contacted people. The limitation of the present study is that it does not involve perinatal and post-natal outcomes, especially the uptake rate of HBV and HBIg.

Conclusion

Hepatitis B infection among Thai pregnant women is still a big problem that needs close medical care and attention because it implies more than one HBV-infected person. Many guidelines to prevent the vertical transmission of HBV have been launched but compliance may be obstructed by financial reason and inadequate knowledge. The unknown status of the HBeAg and hepatitis B viral load is the area to look at and to reduce the vertical transmission that may create the chronic infection of the hepatitis B and the family health problems beyond the neonates.

What is already known on this topic?

Routine screening in antenatal clinic for hepatitis B infection in pregnancy has been done for decades

to identify pregnant women at risk without the proper assessment of characteristics, prevalence, and HBeAg correlation. The unknown status of this valuable information can mislead the health professionals, particularly the perinatal period treatment to reduce the vertical transmission. Nowadays, the antiviral drug can be safely offered antenatally to the pregnant women with hepatitis B but the hepatitis B viral load and HBeAg need to be looked at carefully before starting the antiviral drug. We already known that the hepatitis B infection need to be well controlled from the start of the antenatal period to prevent the vertical transmission, but nothing much has been changed to improve our ANC in Thailand.

What this study adds?

The hepatitis B viral load blood test during pregnancy is the key of success to improve the ANC as well as to reduce the vertical transmission from mother to child. Unfortunately, the financial cost of this valuable test is expensive and not included in the universal healthcare coverage in Thailand. However, the proper and intensive counseling still have the role to raise the awareness among the pregnant women. Appreciation of the hepatitis B viral load blood test to be done is the crucial step to combat the hepatitis B infection in pregnancy. The hepatitis B infection among the pregnant women is still a problem that needs close medical care and attention from the health professional.

Conflicts of interest

The authors declare no conflict of interest and this article has no funding source.

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