Observational Study

Medicine®

OPEN

Hepatitis B virus serosurvey and awareness of mother-to-child transmission among pregnant women in Shenyang, China

An observational study

Qiu-Ju Sheng, MD, Sui-Jing Wang, MM, Yu-Yu Wu, MM, Xiao-Guang Dou, MD, Yang Ding, MD*

Abstract

Preventing hepatitis B virus (HBV) mother-to-child transmission (MTCT) is the key to controlling the prevalence of chronic HBV infection. Adequate awareness of hepatitis B in hepatitis B s antigen (HBsAg) positive pregnant women may be helpful to reduce HBV MTCT.

The aim of this study was to explore HBV seroprevalence among pregnant women and investigate the level of hepatitis B awareness among HBsAg positive pregnant women.

HBV serum biomarkers were tested among pregnant women visiting Shengjing Hospital of China Medical University. HBsAg-positive pregnant women received a HBV DNA test and completed a questionnaire. The different HBV DNA loads were interpreted as follows: 20 to $<2\times10^3$ IU/mL was low viral load, 2×10^3 to $<2\times10^6$ IU/mL was intermediate viral load and $\geq2\times10^6$ IU/mL was high viral load. The pregnant women with high viral load were treated with telbivudine (LdT). HBV DNA at different times was tested. The rate of HBV MTCT was confirmed at 28 weeks postpartum.

HBsAg prevalence among pregnant women was 3.1% (441/14314). There was significant difference in comparing HBsAg prevalence in different age groups ($\chi^2=13.86$, $P<.01$). Among 441 HBsAg-positive pregnant women, 151 (34.2%) were hepatitis B e antigen (HBeAg) positive and 112 (25.4%) had high viral load. After 4 weeks of treatment, the average HBV DNA load of 66 cases with high viral load was $(5.0\pm0.8)\log_{10}$ IU/mL. The average HBV DNA load at 4 weeks postpartum rebounded to $(7.9\pm1.0)\log_{10}$ IU/mL, which was not significantly different from that at baseline ($t=1.23$, $P=.22$). At 28 weeks postpartum, the rate of HBV MTCT in the treatment group was significantly lower than that in the observation group (0% vs 12.2%; $P=.02$). Only 23.4% of pregnant women knew their HBV status before gestation and 17.7% of pregnant women knew the HBV status before delivery. However, only 21.3% of pregnant women realized to need antiviral treatment to prevent MTCT.

The pregnant women in Shenyang had a low HBsAg prevalence. Antiviral treatment for pregnant women with high viral load can effectively reduce the rate of HBV MTCT. HBV screening and education among HBsAg-positive pregnant women should be strengthened.

Abbreviations: ALT = alanine aminotransferase, anti-HBc = hepatitis B c antibody, anti-HBe = hepatitis B e antibody, HBeAg = hepatitis B e antigen, HBIG = hepatitis B immunoglobulin, HBsAg = hepatitis B s antigen, HBV = hepatitis B virus, LdT = telbivudine, MTCT = mother-to-child transmission, TDF= tenofovir disoproxil fumarate.

Keywords: hepatitis B virus, mother-to-child transmission, pregnancy, questionnaire, telbivudine

1. Introduction

In China, mother-to-child transmission (MTCT) is the main transmission route of hepatitis B virus (HBV). Preventing HBV MTCT is the key to controlling prevalence of chronic HBV infection.[1] Despite immunoprophylaxis with hepatitis B vaccine and hepatitis B immunoglobulin (HBIG), the rate of HBV MTCT is still 10% to 15%, which involves in the women with high viral

Editor: Wenyu Lin.

Funding/support: This work was supported by National Science and Technology Major Project for Infectious Diseases Control [2017ZX10201201], Liaoning Province Natural Science Foundation [2014021007], and Liaoning Province Local Professional Technology Innovation Platform Construction Project [2016007013].

The Institutional Ethics Committee approved the study and the study conformed to the Helsinki declaration of 1977. Informed consent was obtained from all the study subjects before the study.

The authors report no conflicts of interest.

Department of Infectious Diseases, Shengjing Hospital of China Medical University, Shenyang, Liaoning, China.

** Correspondence: Yang Ding, Shengjing Hospital of China Medical University, 39 Huaxiang Road, Tiexi District, Shenyang 110022, Liaoning, China (e-mail: yding0903@sina.com).*

Medicine (2018) 97:22(e10931)

Received: 4 January 2018 / Accepted: 10 May 2018

http://dx.doi.org/10.1097/MD.0000000000010931

load and hepatitis B e antigen (HBeAg) positive.[2] Antiviral treatment during middle and late gestation in pregnant women with high viral load can effectively reduce HBV MTCT.[3,4] Aging women, hepatic flare, HBV mutation, and quasispecies may lead to a seroprevalence change in pregnant women with chronic HBV infection.[5–8] Measures such as improving hepatitis B awareness in hepatitis B s antigen (HBsAg) positive childbearing-age women, HBV screening and education before gestation, follow-up, and timely intervention during gestation can reduce HBV MTCT in HBsAg-positive women.[9,10]

2. Objectives

In this study, we investigated HBV seroprevalence among pregnant women in Shenyang, China. We also tested the dynamic change of HBV DNA load for pregnant women with high viral load during antiviral treatment. We further investigated the level of hepatitis B awareness among HBsAg-positive pregnant women by a questionnaire survey.

3. Study design

All pregnant women visiting Shengjing Hospital of China Medical University between January and December 2016 were enrolled. HBV serum biomarkers were tested for all pregnant women. HBsAg-positive pregnant women also received a HBV DNA test and completed a questionnaire.

HBV serum biomarkers were tested with chemiluminescence microparticle immunoassay (Architect I8200_C; Abbott, IL). Negative was defined as HBsAg < 0.05 IU/mL, HBeAg < 1.0 s/co, hepatitis B e antibody (anti-HBe) > 1.0 s/co, and hepatitis B c antibody (anti-HBc) < 1.0 s/co, respectively. HBV DNA was tested with real-time quantitative PCR (COBAS AmpliPrep/TaqMan 48 analyzer; Roche, CA). The different HBV DNA loads were interpreted as follows: < 20 IU/mL as negative, 20 to $< 2 \times 10^3$ IU/mL was low viral load, 2×10^3 to $< 2 \times 10^6$ IU/mL was intermediate viral load, and $\geq 2 \times 10^6$ IU/mL was high viral load. The pregnant women with high viral load signed informed documents and were divided into the treatment group and observation group according to their own preference. Telbivudine (LdT, 600 mg, once daily; Beijing Novartis Pharmaceutical Co., Ltd., Beijing, China) was orally administered from 24 to 28 weeks gestation and immediately discontinued after delivery in the treatment group. HBV DNA was tested at baseline, after 4 weeks of treatment, before delivery, and at 4 weeks postpartum in the treatment group. HBV DNA was tested at baseline and 4 weeks postpartum in the observation group. All these infants received 100 IU HBIG (Hualan Bioengineering Co., Ltd., Xinxiang, China) and 10 μg hepatitis B vaccine (Kangtai Biological Products Co., Ltd., Shenzhen, China) intramuscularly within 12 hours after birth. The other 2 doses of 10 μg hepatitis B vaccines were scheduled at 1 and 6 months of age. The rate of HBV MTCT was defined as the proportion of infants with HBV DNA and HBsAg-positive in the infants born to HBsAg-positive mothers at 28 weeks of age.

The HBsAg positive pregnant women were requested to complete a written questionnaire survey anonymously. They were taken into a separate room to allow privacy during the survey. The questionnaire was jointly developed by the study team. Content was intensely discussed among the study team. The questionnaire consisted of 10 items, divided into 3 parts: The time when HBsAg status was known (4 items: Q1, Q2, Q3, Q4), their knowledge of HBV MTCT (3 items: Q5, Q6, Q7), and strategies of preventing HBV MTCT (3 items: Q8, Q9, Q10). For each item there were 2 response options: "yes" or "no."

Data generated were analyzed with SPSS 22.0 software (IBM, Armonk, NY). Baseline characteristics and laboratory results were summarized by mean values including percentage and mean ± standard deviation. The *t* test or Mann–Whitney *U* test was employed in the comparison of continuous data and the Chi-square test was used for the comparison of count data. $P < .05$ (bilateral test) was statistically significant.

Table 1

HBsAg prevalence among pregnant women in different age groups.

Age, y	N	HBsAg positive (%)	HBsAg negative (%)	OR	95% CI
19~25	1035	12 (1.2%)	1023 (98.8%)	1.0	
26~35	8862	284 (3.2%)	8578 (96.8%)	2.8	1.58–5.05
36~45	4417	145 (3.3%)	4272 (96.7%)	2.9	1.60–5.23
χ^2	13.86				
P	.001				

The HBsAg prevalence in the group 19–25 years of age was lowest (1.2%). Whereas, the HBsAg prevalence in the group 26–35 and 36–45 years of age were 2.8 and 2.9 times than that in the youngest group. There was significant difference in comparing HBsAg prevalence in different age groups ($\chi^2 = 13.86$, $P < .01$).

4. Results

4.1. HB seroprevalence among pregnant women

4.1.1. HBsAg prevalence among pregnant women. There were 14,314 pregnant women visiting Shengjing Hospital of China Medical University from January to December 2016. The age range of these pregnant women was 19 to 45 years and the average age was (31.1 ± 4.5) years. The HBsAg prevalence among these pregnant women was 3.1% (441/14314). The HBsAg prevalence among pregnant women in different age groups is summarized in Table 1. The HBsAg prevalence in the group 19 to 25 years of age was lowest (1.2%). Whereas, the HBsAg prevalence in the group 26 to 35 and 36 to 45 years of age were 2.8 and 2.9 times than that in the youngest group. There was significant difference in comparing HBsAg prevalence in different age groups ($\chi^2 = 13.86$, $P < .01$).

4.1.2. HBeAg status and HBV DNA level among HBsAg-positive pregnant women. HBeAg status and HBV DNA load among 441 HBsAg-positive pregnant women are summarized in Table 2. Among 441 HBsAg-positive pregnant women, 151 (34.2%) were HBeAg positive, and 207 (46.9%) were HBV DNA

Table 2

HBeAg status and HBV DNA load among 441 HBsAg-positive pregnant women.

HBV DNA	Total n = 441	HBeAg positive n = 151	HBeAg negative n = 290
Negative	234 (53.1%)	9 (5.9%)	225 (77.6%)
Low viral load	44 (9.9%)	6 (4.0%)	38 (13.1%)
Intermediate viral load	51 (11.6%)	29 (19.2%)	22 (7.6%)
High viral load	112 (25.4%)	107 (70.9%)	5 (1.7%)

Among 441 HBsAg-positive pregnant women, 151 (34.2%) were HBeAg positive, and 207 (46.9%) were HBV DNA positive. There were 112 (25.4%) pregnant women with high viral load. Among 112 pregnant women with high viral load, 107 cases were HBeAg positive and the remaining 5 cases were HBeAg negative.

Table 3

Comparison of the baseline conditions between treatment group and observation group.

Items	Treatment group (n=66)	Observation group (n=46)	*t*	*P*
Age, y	31.3±4.4	30.4±4.2	1.01	.315
Alanine aminotransferase, U/L	27.4±11.0	25.1±12.3	1.05	.295
HBV DNA, $\log_{10}$IU/mL	8.1±0.4	7.9±0.5	1.89	.061

There was no significant difference in age, alanine aminotransferase, and HBV DNA load between the 2 groups.

positive. There were 112 (25.4%) pregnant women with high viral load. Among 112 pregnant women with high viral load, 107 were HBeAg positive and the remaining 5 cases were HBeAg negative.

4.1.3. Dynamic change of HBV DNA after antiviral treatment among the pregnant women with high viral load. One hundred twelve pregnant women with high viral load were divided into the treatment group (n=66) and observation group (n=46). All pregnant women in the treatment group were treated for more than 8 weeks and no subject was prematurely delivered before 28 weeks gestation. The baseline conditions in the 2 groups are described in Table 3. There was no significant difference in age, alanine aminotransferase (ALT), and HBV DNA load between the 2 groups. The change of HBV DNA load at different times in the treatment group is described in Fig. 1. After 4 weeks of treatment, the average HBV DNA load was (5.0±0.8) $\log_{10}$IU/mL, which decreased by 3.1 $\log_{10}$IU/mL compared with that at baseline ($t=29.78$, $P<.01$). The average HBV DNA load continued to decrease an extra 0.9 $\log_{10}$IU/mL to (4.1±0.8) $\log_{10}$IU/mL before delivery ($t=7.10$, $P<.01$). The average HBV DNA load at 4 weeks postpartum rebounded to (7.9±1.0) $\log_{10}$IU/mL, which was not significantly different from that at baseline ($t=1.23$, $P=.22$). The average HBV DNA load was (7.8±0.6) $\log_{10}$IU/mL at 4 weeks postpartum in the observation group, which was not significantly different from that at baseline ($t=1.54$, $P=.13$).

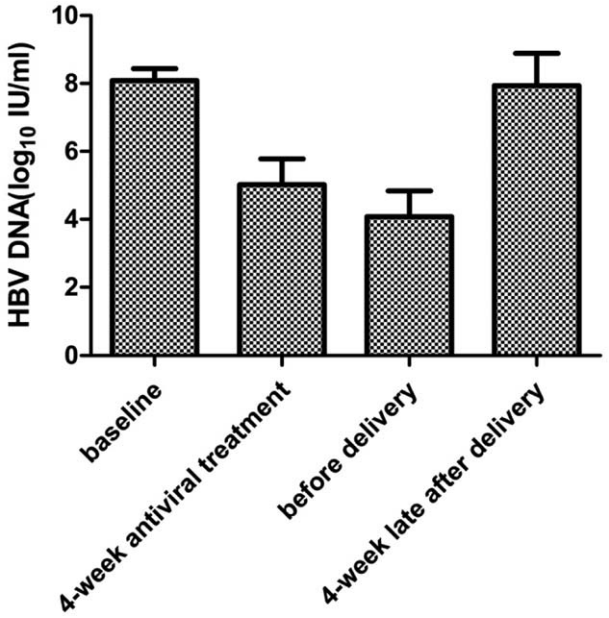

Figure 1. Change of HBV DNA level at different time points in the treatment group. After 4 weeks of treatment, the average HBV DNA load was (5.0±0.8) $\log_{10}$IU/mL, which decreased by 3.1 $\log_{10}$IU/mL compared with that at baseline ($t=29.78$, $P<.01$). The average HBV DNA load continued to decrease an extra 0.9 $\log_{10}$IU/mL to (4.1±0.8) $\log_{10}$IU/mL before delivery ($t=7.10$, $P<.01$). The average HBV DNA load at 4 weeks postpartum rebounded to (7.9±1.0) $\log_{10}$IU/mL, which was not significantly different from that at baseline ($t=1.23$, $P=.22$).

Table 4

Questionnaire survey among HBsAg-positive pregnant women.

Items N	(%)
1 Knowing HBsAg positive before gestation	103 (23.4%)
2 Knowing HBsAg positive at early gestation	136 (30.8%)
3 Knowing HBsAg positive at middle or late gestation	124 (28.1%)
4 Knowing HBsAg positive before delivery	78 (17.7%)
5 HBV MTCT can happen in HBsAg-positive pregnant women	292 (66.2%)
6 HBV MTCT can be blocked	265 (60.1%)
7 HBV MTCT is prone to happen in women with high viral load	216 (51.3%)
8 Pregnant women with high viral load need antiviral treatment to prevent MTCT	94 (21.3%)
9 Inoculation of hepatitis B vaccine and HBIG can prevent MTCT in neonates	305 (69.2%)
10 Hepatitis B vaccine and HBIG need to be inoculated within 12 h after delivery	273 (61.9%)

Only 23.4% (103/441) of HBsAg-positive pregnant women knew their HBV status before gestation and 17.7% (78/441) of HBsAg-positive pregnant women knew their HBV status before delivery. There were 66.2% (292/441) of HBsAg-positive pregnant women who knew that a HBsAg-positive mother could transmit HBV to her children; however, only 21.32% (94/441) of HBsAg-positive pregnant women knew that pregnant women with high viral load should need antiviral treatment to prevent MTCT. About 69.2% (305/441) of HBsAg-positive pregnant women were aware of the need for the inoculation of hepatitis B vaccine and HBIG in neonates.

4.2. Questionnaire survey among HBsAg-positive pregnant women

Four hundred forty-one questionnaires completed by HBsAg-positive pregnant women were collected with the results described in Table 4. Only 23.4% (103/441) of HBsAg-positive pregnant women knew their HBV status before gestation and 17.7% (78/441) of HBsAg-positive pregnant women knew their HBV status before delivery. There were 66.2% (292/441) of HBsAg-positive pregnant women who knew that a HBsAg-positive mother could transmit HBV to her children; however, only 21.32% (94/441) of HBsAg-positive pregnant women knew that pregnant women with high viral load should need antiviral treatment to prevent MTCT. About 69.2% (305/441) of HBsAg-positive pregnant women were aware of the need for the inoculation of hepatitis B vaccine and HBIG in neonates.

4.3. The rate of HBV MTCT

All these infants received immunoprophylaxis with hepatitis B vaccine and HBIG and visited follow-up. At 28 weeks postpartum, the rate of HBV MTCT among the infants born to mothers in the treatment group was significantly lower than that in the observation group (Fig. 2). The rate of HBV MTCT in the treatment group was 0% (0 of 66 infants) versus 12.2% (5 of 46 infants) in the observation group ($\chi^2=5.18$, $P=.02$).

5. Discussion

According to the data reported by the Chinese Disease Control and Prevention Center in 2007, HBsAg prevalence among

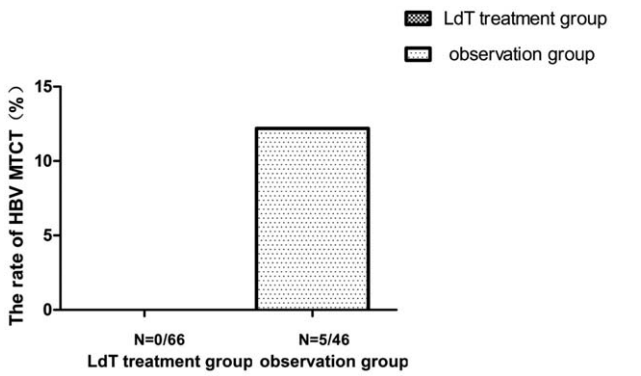

Figure 2. The rate of HBV MTCT. The rate of HBV MTCT was 0% (0 of 66 infants) in the treatment group versus 12.2% (5 of 46 infants) in the observation group. The rate of HBV MTCT among the infants born to mothers in the treatment group was significantly lower than that in the observation group. ($\chi^2 = 5.18$, $P = .02$). HBV = hepatitis B virus, LdT = telbivudine, MTCT = mother-to-child transmission.

childbearing-age women in China was 8.16%[11]. Various measures such as improving the clinical care, HBV screening, immunoprophylaxis, effective treatment, and close follow-up can significantly prevent HBV MTCT and mitigate the family, society, and individuals burden brought by chronic HBV infection.[12] Although immunoprophylaxis with hepatitis B vaccine and HBIG in neonates can remarkably reduce HBV infection, still cannot block HBV MTCT completely.[13,14] To further reduce HBV infection in neonates, it is recommended that HBeAg-positive pregnant women with high viral load should receive antiviral treatment during middle and late gestation.[15–18] Therefore, it is important to understand the HBV seroprevalence, HBeAg status, and viral load among pregnant women.

HBsAg prevalence among pregnant women in Shenyang previously reported was 5.49% with the average age of (26.1 ± 3.2) years. The immunization of hepatitis B vaccine effectively reduced HBsAg prevalence in this area.[19] Our study showed that HBsAg prevalence among pregnant women in the area in 2016 was 3.1% with the average age of (31.1 ± 4.5) years. Moreover, there was significant difference in comparing HBsAg prevalence in different age groups. Because of 2-child policy, the pregnant women are older. The older pregnant women may not have been vaccinated in their childhood. Hence, HBsAg prevalence in older age groups was significantly higher than that in the youngest age groups.

Previously, pregnant women with chronic HBV infection were generally younger and majority were in immune tolerance status. Currently, due to aging pregnant women, more women may have hepatic flare before or during gestation, which cause certain health risks to mothers and fetus.[20–22] The aim of antiviral treatment with LdT or tenofovir disoproxil fumarate (TDF) during gestation is to maintain stable liver function of pregnant women, ensure the continuation of gestation, and reduce HBV MTCT. Whether aging pregnant women would affect HBV seroprevalence and HBV DNA load, we found that the majority of pregnant women were HBeAg negative. However, in our previous investigation,[19] the majority of pregnant women were HBeAg positive (67.1%). It was inconclusive whether the change was caused by HBV genome variation, which was either introduced during viral replication due to the lack of proof-reading activity of the reverse transcriptase or induced by antiviral drugs pressure.[23,24]

A consensus is to treat pregnant women with high viral load in middle or late gestation. Therefore, it is of clinical significance to understand HBV DNA load among pregnant women.[25,26] In our study, the proportion of pregnant women with HBV DNA positive in 2016 was 46.9%, which was lower than that in 2010 (81.93%). The reason may be that some pregnant women received antiviral treatment before or during gestation because of hepatic flare. The proportion of pregnant women with high viral load was 25.4%. High viral load can occur in both HBeAg-positive and negative pregnant women (although in the minority).

In this study, 66 pregnant women with high viral load were treated orally with LdT. After 4 weeks of treatment, HBV DNA load significantly decreased. HBV DNA load at 4 weeks postpartum approximately rebounded to that at baseline. At 28 weeks postpartum, the rate of HBV MTCT in the treatment group (0%) was lower than that in the observation group (12.2%). After antiviral treatment, the dynamic change of HBV DNA in pregnant women and the rate of HBV MTCT were consistent with previous reports.[27] However, the latest study by Jourdain et al [28] in Thailand failed to obtain a positive result on their issue. Their result was generalized to pregnant women in the area with lower MTCT rate (MTCT rate in Thailand is 2%). It should not be generalized to pregnant women in the area with higher MTCT rate (MTCT rate in China is 10–15%).

It is necessary for HBsAg-positive pregnant women to have adequate awareness of hepatitis B, which has important influence on the screening and follow-up during gestation. Our survey was administered among HBsAg-positive pregnant women to determine the level of hepatitis B awareness. We found that relatively a few (23.4%) of HBsAg-positive pregnant women knew their HBV status before gestation. Only 21.3% of pregnant women knew that pregnant women with high viral load need antiviral treatment to prevent HBV MTCT. HBV screening and education among HBsAg-positive pregnant women still need to be strengthened. In China, the neonates born to HBsAg-positive mothers are provided free inoculation of hepatitis B vaccine and HBIG within 12 hours after delivery, which significantly decreases HBV MTCT. Over 60% of HBsAg-positive pregnant women knew about the HBV-free immunization policy.

The limitation of this study included potential long-term side effects of antiviral treatment on mothers and children. This aspect will require further investigation. These pregnant women treated with LdT were self-selected, and the questionnaire survey was not administered among HBsAg-negative pregnant women, which may be potential selective bias. It was still a limitation for the lack of the validation about our survey tool.

In 2015, China Foundation for Hepatitis Prevention and Control launched "Zero HBV MTCT Project" and standardized clinical management for preventing HBV MTCT. In 2016, the World Health Assembly endorsed World Health Organization global health sector strategies on hepatitis. These strategies call for the elimination of HBV MTCT by 2030.[29] Furthermore, HBV screening, education, as well as antiviral treatment in pregnant women are initiated. "Zero HBV MTCT " is expected to realize in China and all over the world.

Acknowledgment

We extend our thanks to all pregnant women involved in our study, who all agreed to be tested for HBV serum biomarkers, HBV DNA, and completed questionnaire survey. We disclosed they had no writing assistance.

Author contributions

Investigation: Qiuju Sheng, Suijing Wang, Yuyu Wu, YANG DING.
Writing – original draft: Qiuju Sheng, Xiaoguang Dou, YANG DING.
Data curation: Suijing Wang.
Funding acquisition: Xiaoguang Dou.
Supervision: YANG DING.

References

[1] Michielsen PP, Van Damme P. Viral hepatitis and pregnancy. Acta Gastroenterol Belg 1999;62:21–9.
[2] Liang X, Bi S, Yang W, et al. Epidemiological serosurvey of hepatitis B in China: declining HBV prevalence due to hepatitis B vaccination. Vaccine 2009;27:6550–7.
[3] Han GR, Jiang HX, Yue X, et al. Efficacy and safety of telbivudine treatment: an open-label, prospective study in pregnant women for the prevention of perinatal transmission of hepatitis B virus infection. J Viral Hepat 2015;22:754–62.
[4] Pan CQ, Duan ZP, Dai E, et al. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. N Engl J Med 2016;374:2324–34.
[5] Yang G, Liu Z, Yang J, et al. Quasispecies characteristics in mother-to-child transmission of hepatitis B virus by next-generation sequencing. J Infect 2017;75:48–58.
[6] Du Y, Chi X, Wang C, et al. Quantifying perinatal transmission of hepatitis B viral quasispecies by tag linkage deep sequencing. Sci Rep 2017;7:10168.
[7] Patton H, Tran TT. Management of hepatitis B during pregnancy. Nat Rev Gastroenterol Hepatol 2014;11:402–9.
[8] Cohen E, Tran TT. Hepatitis B in the female population. Gastroenterol Clin North Am 2016;45:359–70.
[9] Abara WE, Cha S, Malik T, et al. Hepatitis B Surface Antigen screening among pregnant women and care of infants of hepatitis B surface antigen-positive mothers - Guam, 2014. MMWR Morb Mortal Wkly Rep 2017;66:506–8.
[10] Dun-Dery F, Adokiya MN, Walana W, et al. Assessing the knowledge of expectant mothers on mother-to-child transmission of viral hepatitis B in Upper West region of Ghana. BMC Infect Dis 2017;17:416–25.
[11] Centers for Disease Control and Prevention. Progress in hepatitis B prevention through universal infant vaccination–China,1997-2006. MMWR Morb Mortal Wkly Rep 2007;56:441–5.
[12] Visvanathan K, Dusheiko G, Giles M, et al. Managing HBV in pregnancy. Prevention, prophylaxis, treatment and follow-up: position paper produced by Australian, UK and New Zealand key opinion leaders. Gut 2016;65:340–50.
[13] Guo Y, Liu JQ, Meng L, et al. Survey of HBsAg-positive pregnant women and their infants regarding measures to prevent maternal-infantile transmission. BMC Infect Dis 2010;10:26–30.
[14] Shao ZJ, Zhang L, Xu JQ, et al. Mother-to-infant transmission of hepatitis B virus: a Chinese experience. J Med Virol 2011;83:791–5.
[15] Chinese Society of Hepatology, Chinese Medical Association; Chinese Society of Infectious Diseases, Chinese Medical Association. The guideline of prevention and treatment for chronic hepatitis B: a 2015 update (in Chinese). Zhonghua Gan Zang Bing Za Zhi 2015; 23: 888–905.
[16] Ransom CE, Huo Y, Patel K, et al. Infant growth outcomes after maternal tenofovir disoproxil fumarate use during pregnancy. J Acquir Immune Defic Syndr 2013;64:374–81.
[17] Pan CQ, Han GR, Jiang HX, et al. Telbivudine prevents vertical transmission from HBeAg-positive women with chronic hepatitis B. Clin Gastroenterol Hepatol 2012;10:520–6.
[18] Zhang H, Pan CQ, Pang Q, et al. Telbivudine or lamivudine use in late pregnancy safely reduces perinatal transmission of hepatitis B virus in real-life practice. Hepatology 2014;60:468–76.
[19] Ding Y, Sheng QJ, Ma L, et al. Chronic HBV infection among pregnant women and their infants in Shenyang, China. Virol J 2013;10:17.
[20] Sinha S, Kumar M. Pregnancy and chronic hepatitis B virus infection. Hepatol Res 2010;40:31–48.
[21] Bzowej NH. Optimal management of the hepatitis B patient who desires pregnancy or is pregnant. Curr Hepat Rep 2012;11:82–9.
[22] Tse KY, Ho LF, Lao T. The impact of maternal HBsAg carrier status on pregnancy outcomes: a case-control study. J Hepatol 2005;43:771–5.
[23] Ma Y, Zhu NC, Dou XG, et al. Clinical and genetic mutation profile on therapy in chronic hepatitis B with lamivudine (in Chinese). China J Mod Med 2005;15:961–5.
[24] Sheldon J, Rodes B, Zoulim F, et al. Mutations affecting the replication capacity of the hepatitis B virus. J Viral Hepat 2006;13:427–34.
[25] Sellier P, Maylin S, Amarsy R, et al. Untreated highly viraemic pregnant women from Asia or sub-Saharan Africa often transmit hepatitis B virus despite serovaccination to newborns. Liver Int 2015;35:409–16.
[26] Jackson V, Ferguson W, Kelleher TB, et al. Lamivudine treatment and outcome in pregnant women with high hepatitis B viral loads. Eur J Clin Microbiol Infect Dis 2015;34:619–23.
[27] Sheng QJ, Ding Y, Li BJ, et al. Telbivudine for prevention of perinatal transmission in pregnant women infected with hepatitis B virus in immune-tolerant phase: a study of efficacy and safety of drug withdrawal (in Chinese). Zhonghua Gan Zang Bing Za Zhi 2016; 24:258–64.
[28] Jourdain G, Ngo-Giang-Huong N, Harrison L, et al. Tenofovir versus placebo to prevent perinatal transmission of hepatitis B. N Engl J Med 2018;378:911–23.
[29] World Health Organization. Combating Hepatitis B and C to Reach Elimination by 2030. Available at: http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/. Accessed May 2016.