Abstract

Objective: To evaluate the pattern of medical care of hepatitis B virus (HBV) carriers during pregnancy and after delivery in Hong Kong, and the factors affecting the medical care of these women.

Study design: Retrospective analysis

Methods: ~~Pregnancy~~ Pregnant HBV carrier~~s~~ ~~women~~ and their infants were followed up at 9-12 months after delivery. A face-to-face interview was conducted to enquire their medical care~~attendance~~ for ~~of~~ HBV ~~check-up~~ prior to, during and after pregnancy.

Results: Data were available in 412 HBV carriers. 375 (91.0%) women were known HBV carriers prior to pregnancy. Routine screening during the antenatal period picked up the remaining 37 (9.0%) carriers and they were younger, more likely to be smokers and had a lower education level ($p<0.05$). 356/412 (86.4%)

HBV carriers ~~infected women~~ did not have ~~attend~~ the medical care for HBV during pregnancy. Known HBV carrier status, history of medical checkup and use of antiviral treatment prior to pregnancy were significant predictors for medical care during pregnancy ($p<0.05$). 217/412 (52.6%) HBV carriers ~~infected women~~ did not have ~~receive HBV~~ medical care after delivery. Medical care~~checkup~~ before pregnancy, use of antiviral treatment prior to pregnancy and higher education level were significant predictors for postpartum medical care ($p<0.05$). Multivariate analysis showed medical care prior to the pregnancy (OR 7.73, 95%CIs 3.21–18.65,$p<0.001$) and use of antiviral treatment (OR 5.02, 95%CIs 1.41–17.81,$p=0.013$) were associated with medical care during pregnancy. Medical care prior to the pregnancy was also associated with postpartum medical care (OR 5.05, 95%CIs 3.29–7.51,$p<0.001$).

Conclusion: A significant proportion of HBV carriers did not ~~have~~ receive medical checkup ~~care~~ during and after pregnancy in Hong Kong~~,~~ despite the

majority ~~of them~~ were aware of their ~~HBV~~ carrier status. Medical care prior to ~~the~~ pregnancy predicted ~~the~~ antenatal and postpartum medical care.

Keywords: Hepatitis B virus; Infection; Infectious Disease Transmission, Vertical; Pregnancy

Introduction

Hepatitis B virus (HBV) infection is the most common form of chronic hepatitis in the world. It is a World Health Organization's goal to eradicate HBV infection by 2030 by promoting adequate prevention and effective treatment.[1] The risk of acquiring chronic infection is highest during the perinatal period[2] and active and passive immunization to the newborns of HBV carriers can effectively decrease the risk of vertical transmission.[3] However, HBV infection is still endemic in Asia.[4] The prevalence of HBV infection has been decreasing in Hong Kong ~~after~~ since the implementation of universal HBV vaccination in 1988.[5] The persistence of HBV infection could be due to immunoprophylaxis failure,[6] which occurs in 1-4% of infants of HBV carriers.[7-9] Appropriate medical evaluation of pregnant HBV carriers is essential to decrease the risk of immunoprophylaxis failure by initiating antiviral treatment in late pregnancy~~, and~~, which also facilitates monitoring ~~for~~ of postpartum hepatic flare ~~after delivery~~. However, little research has focused on the pattern and the predictors to medical care of HBV carriers during and after pregnancy ~~of HBV carriers~~. In the United States, a retrospective

review ~~of the data~~ of the~~a~~ ~~from a~~ health care system in Massachusetts found 53% of newly diagnosed HBV carriers ~~did~~ had not receive~~d~~ specialist care for HBV after delivery.[10] Another retrospective cohort study using aggregate database of~~in~~ Massachusetts also revealed half of the HBV carriers ~~did~~ had not receive~~d~~ postpartum laboratory testing.[11] In Hong Kong, ~~the government provides~~ free antenatal ~~and medical~~ care is provided ~~to~~ for all pregnant women and ~~.~~ Hepatitis B surface antigen (HBsAg) is ~~tested for every pregnant woma~~screene~~d~~~~n~~ during the booking visit in early ~~in the~~ pregnancy. However, there is no ~~existing~~ local guideline~~s~~ ~~for~~ on maternal HBV DNA testing, referral to hepatologist / gastroenterologist for follow up and infants' testing for HBV status. Our aim is to evaluate the medical care of HBV carriers during and after pregnancy in Hong Kong, and the factors affecting the care of these women.

Methods:

The data of medical care during and after pregnancy ~~was~~ were collected from a previously conducted prospective ~~multicenter~~ observational study ~~previously~~

~~conducted,~~[9] ~~to~~ which evaluated the factors leading to immunoprophylaxis failure~~,~~. It ~~studied~~ recruited women~~–~~ between January 2014 to December 2016 at five public regional hospitals in Hong Kong, including Kwong Wah Hospital, Queen Elizabeth Hospital, Queen Mary Hospital, Pamela Youde Nethersole Eastern Hospital and Tuen Mun Hospital. All women gave a written informed consent and were enrolled under protocols approved by the Institutional Review Board of each hospital. A total of 29,431 women were booked for delivery in the five ~~study~~ hospitals within the recruitment period and 1,592 women (5.4%) were HBsAg positive. Among the 750 subjects in the original study, 412 women provided their attendance of HBV check-up prior to, during and after pregnancy. They ~~,~~were recruited into this retrospective study.

Basic demographics and clinical details were recorded ~~with their written informed consent~~, which included the age, race, gravida, parity, education level, smoking, drinking, and human immunodeficiency virus status. Referral to hepatologist/gastroenterologist was offered at the discretion of the attending obstetricians. At 9-12 months after delivery, HBsAg of infants was examined and

a face-to-face interview by a research assistant was conducted to collect the information on the pattern of maternal follow up for HBV during pregnancy and after delivery ~~was enquired by a face-to-face interview by a research assistant~~. Medical care was defined by any formal consultation for HBV disease with primary practitioner, hepatologist or gastroenterologist with or without laboratory testing. This study received ethical approval from Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Data analysis was performed using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Results were presented as mean (standard deviation (SD)) or number (n) (%). Student's t test was used for continuous variables that were normally distributed and the Mann-Whitney U test for skewed data. Chi-square test or Fisher Exact test was used for dichotomous outcomes. Binary logistic multiple regression was performed on those factors showinged statistical significance in univariate

analysis to further investigate the predictors of attendance of medical follow-ups. Results were considered statistically significant when $p<0.05$.

Result

The basic demographics of 412 HBV carriers were shown in Table 1. A total of 375 women (91.0%) were known HBV carriers before pregnancy. Of these, 168 women (44.8%) did not have medical care prior to pregnancy. They had a higher gravida (2.4 vs. 1.8) and parity (0.7 vs. 0.4), and ~~less~~ fewer antiviral treatment use before pregnancy (0.6% vs. 4.8%) ~~when~~ compared with ~~to~~ those who had ~~having~~ follow up before ~~the~~ pregnancy ($p<0.05$) (Table 2). 37 carriers (9.0%) discovered their HBV status during routine antenatal checkup. They were younger (31.1 years vs. 33.0 years), more likely to be a smoker or ex-smoker (13.5% vs. 4.0%) and had a lower education level (91.9% vs. 65.1% with secondary or lower education) when compared with the known HBV carriers ($p<0.05$) (Table 2).

356 (86.4%) and 217 (52.6%) HBV carriers did not have medical care for HBV during and after pregnancy respectively. The predictors were shown in Table 3. Known HBV carrier status (98.2% vs. 89.9%), medical checkup (87.5% vs. 44.4%) and use of antiviral treatment (10.7% vs. 1.4%) prior to pregnancy were significant predictors for having medical care during pregnancy ($p < 0.05$). Medical checkup (71.3% vs. 31.3%), use of antiviral treatment prior to pregnancy (5.6% vs. 0%) and higher education level (tertiary or above) (38.0% vs. 27.7%) were significant predictors for postpartum medical care ($p<0.05$) (Table 3).

On multivariate analysis (Table 4), only higher education level (tertiary or above) was positively associated with HBV awareness before pregnancy (OR 5.31, 95% CIs 1.59 –17.88, p=0.007). A higher chance of attendance to ~~attending~~ medical care during pregnancy was associated with medical care prior to pregnancy (OR 7.73, 95% CIs 3.21 – 18.65, $p<0.001$) and use of antiviral treatment (OR 5.02, 95% CIs 1.41 – 17.81, p=0.013). The attendance of medical care after pregnancy

was positively associated with medical care prior to pregnancy (OR 5.05, 95% CIs 3.29 – 7.51, p <0.001).

In the 37 carriers who ~~did not know~~were not aware of their HBV status prior to pregnancy, one and twelve carriers received HBV care during and after pregnancy respectively. All seven immunoprophylaxis failure cases were born ~~of~~ to known HBV carriers prior to pregnancy, of which only two received medical care before pregnancy and one ~~of them received medical care before and~~ during pregnancy ~~respectively~~.

Discussion:

The results of this study demonstrated ~~that~~ a high proportion of HBV carriers ~~did not have~~had not had medical care for HBV and the majority of them ~~did~~ had not received extra medical attention during pregnancy and after delivery. It is worth looking into the issue because antiviral treatment is recommended in highly viremic carriers during pregnancy to reduce the risk of HBV vertical

transmission. ~~T~~Knowing the~~re is also~~ possibility of hepatic flare after delivery should also prompt one to offer ~~and subsequent long term~~ regular postnatal monitoring ~~of HBV status~~ ~~can to~~for these women in order to allow timely intervention to prevent cirrhosis, hepatocellular carcinoma and mortality.[12, 13]

First of all, despite being aware of the HBV carrier status, ~~A~~asymptomatic nature of HBV disease at an earlier stage could lead to poor~~prohibit regular~~ disease surveillance~~, despite being aware of the HBV status~~.[14] Secondly, maternal, obstetric~~s~~ and perinatal risks may be underestimated by the medical profession and general public. A meta-analysis did not show an increase in adverse pregnancy outcomes including preterm rupture of membranes, stillbirth, preeclampsia, gestational hypertension and antepartum haemorrhage.[15] It was suggested that HBV carriers without other risk factors could be managed as low risk pregnancy.[15] However, an increased risk of miscarriage[16], gestational diabetes[17] ~~,~~ and preterm delivery[18, 19] were shown by ~~two~~ cohort studies and other meta-analysis. Furthermore, maternal HBV flare up is possible during

pregnancy and maternal mortality has been reported.[20] Since the role of HBV DNA in predicting these complications remains unclear, the limited evidence from the literature may obviate the need of monitoring maternal HBV DNA and hence the involvement of hepatologist/ gastroenterologist during pregnancy. Finally, the knowledge of the obstetricians, hepatologists/ gastroenterologists and the HBV carriers may also contribute to the poor disease surveillance rate. In Hong Kong, only 67% and 58% of local women correctly recognized pregnancy and childbirth ~~w~~as a mode of HBV transmission.[21, 22] Significant heterogeneity in the management of HBV carriers[23] and poor adherence to the guidelines[24] by medical physicians were noted. Only 69% of hepatologists and 42~~.2~~% non-hepatologist were "very comfortable" or "comfortable" in managing pregnant HBV carriers.[23] Obstetricians were also not familiar with the use of antiviral treatment during pregnancy[25] and more so for primary care physicians~~primary practitioners~~ especially regarding fetal safety. All these may hinder the initiation to discuss~~and discussion of~~ potential implications of HBV disease to the pregnancy among HBV carriers, medical physicians and the

obstetricians.

Form the public health perspective, eradication of HBV disease should begin with early identification of HBV infected individuals, followed by offering evidence-based disease surveillance strategy and treatment, and preventing vertical and horizontal transmission. For early identification, the Center for Disease Control and Prevention recommends universal screening of HBsAg~~in pregnant women for HBsAg~~ during pregnancy.[26] This can ~~recognize~~ identify HBV carriers who are unaware of the~~ir HBV~~ statuses and their ~~identify~~ newborns who require additional hepatitis B immunoglobulin at birth. Neonatal HBV immunization program remains the most effective intervention to prevent vertical transmission[3]. World Health Organization recommends all infants should receive a course of HBV vaccination, with the first dose preferably within 24 hours[27]. HBV viral load qualification during pregnancy is crucial to assess the risk of immunoprophylaxis failure[6] ~~and~~ . T~~t~~he use of antiviral treatment in highly viremic HBV women in late pregnancy could reduce the risk of

immunoprophylaxis failure which is recommended by. Vvarious authorities published their recommendations on antiviral treatment to highly viremic women.[12, 13] Multidisciplinary care during pregnancy involving hepatologists/ gastroenterologists during pregnancy is necessary because they are more likely to provide timely and appropriate HBV disease assessment, monitoring and treatment when compared with primary care physicians.[24, 28] They can also jointly inform the safety and efficacy of antiviral treatment during pregnancy.

Since it is the obstetricians to look after pregnant HBV carriers at the initial encounter, it is important for them tothey may take up the responsibility to initiate referral of the women to appropriate subspecialists for subsequent management. Provision of medical care to HBV carriers and HBV affected infected infants should be continued after delivery by hepatologists/ gastroenterologists to look for maternal postpartum flare up[29] and provide long term HBV disease surveillance. Health policies, such as checking HBV viral load during pregnancy and referral to medical physicians for monitoring and treatment, are proven to be cost-effective.[30-32] Therefore, public health

practitioners and policy makers should employ this holistic~~comprehensive~~ approach during pregnancy, which ~~pregnancy~~ provides an excellent opportunity to eliminate HBV by breaking the chain at birth. Development of a national plan is often considered as the first indicator of political commitment towards HBV eradication.[4] Financial support and resource allocation focusing on the management of HBV during pregnancy are necessary. However, ~~practicality for~~ practicing this multidisciplinary approach may be difficult~~in managing the HBV carriers during pregnancy remains an issue~~. It varies in different places because of different public health systems, expertise availability, financial support and resources. Local studies on financial impact of different preventive strategies should be encouraged to obtain reliable data to guide ~~tailor-made~~individualized policy.[4]~~Unfortunately, this ideal modal was not shown in our study.~~

Our study is the first study to evaluate the predictors of medical care among pregnant HBV carriers. We found pre-pregnancy medical care could be the key to improve the health care of HBV carriers during and after pregnancy. ~~As the~~

~~pre-pregnancy medical care may improve the chance of medical care during and after pregnancy, government~~ Government should promote regular pre-pregnancy HBV disease surveillance and enhance public awareness and knowledge by launching educational programs. These may be achieved by using social media, short message service or 'apps' in mobile phone, which is widely available nowadays.[33] A referral and monitoring guideline ~~can help disease surveillance~~ at the primary care level can help disease surveillance and ~~allow~~ triage complicated cases, for example pregnant HBV carriers, ~~under~~ to receive subspecialist's care. ~~Guidelines have been setup for easy reference to policy markers.~~[12, 13]

~~However, practicality for multidisciplinary approach in managing the HBV carriers during pregnancy remains an issue. It varies in different places because of different public health systems, expertise availability, financial support and resources. Development of a national plan is often considered as the first indicator of political commitment towards HBV eradication.[4] Financial support~~

~~and resource allocation focusing on the management of HBV during pregnancy are necessary.~~There are several limitations of our study. For the HBV carriers who received HBV related care during and after pregnancy, we did not know the exact details of the HBV care, whether they were under the care of hepatologists or primary care physicians~~general practitioners~~ and ~~which laboratory investigations~~whether liver function test and HBV DNA quantification had been performed. Without these information, it would be difficult to guarantee a proper assessment even with multidisciplinary care.~~Therefore, proper medical evaluation cannot be guaranteed even with multidisciplinary care.~~[11] ~~Maternal assessment with liver function test and HBV DNA could identify women at risk of hepatic flare up and immunoprophylaxis failure. This information~~ The details of medical care could reflect the current ~~medical care~~ management of pregnant HBV carriers and provide data to guide policy planning or recommendation on their standard medical care ~~of pregnant HBV carriers~~. We also did not evaluate the obstetric and perinatal outcomes related to medical care. The risk of preterm delivery and gestational diabetes are increased in HBV carriers, particularly in

women with active HBV disease (i.e. positive HBeAg or higher HBV DNA)[19, 34]. Whether the provision of medical care and early intervention in ~~the~~ pregnancy could alter these adverse pregnancy outcomes would require further evaluation. ~~Further research could focus on the evaluation of details of HBV medical care during pregnancy and the effect on pregnancy outcomes.~~

Conclusion

Our study is important to draw the attention to the deficiency in multidisciplinary care during pregnancy and lack of continuity of care after delivery. Eradication of HBV should begin with breaking the chain at birth and subsequent long term monitoring by practicing evidence~~d--~~based medicine and input from various stakeholders. However, a high proportion of HBV carriers in Hong Kong did not have medical care during and after pregnancy, despite ~~the~~ majority of them were aware of their HBV carrier status. Strategies to improve medical care during pregnancy and after delivery are needed.

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Statements of ethical approval

This study received ethical approval from Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

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Disclosure

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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Table 1. Demographic data of subjects				
	All (n=412)	Positive HbeAg (n=105)	Negative HbeAg (n=307)	P value
Age (years)	32.9 (4.6)	31.5 (4.2)	33.3 (4.6)	<0.001
Body mass index (kg/m^2)	22.1 (3.0)	21.6 (3.0)	22.2 (3.1)	0.066
Gravida	2.1 (1.2)	1.92 (1.0)	2.1 (1.3)	0.164
Parity	0.5 (0.7)	0.4 (0.6)	0.5 (0.7)	0.250
Known hepatitis B carrier status before pregnancy	375 (91.0%)	97 (92.4%)	278 (90.6%)	0.572
Medical checkup for hepatitis B before pregnancy	207 (50.2%)	54 (51.4%)	153 (49.8%)	0.778
Chinese	409 (99.3%)	104 (99%)	305 (99.3%)	0.088
Smoker or ex-smoker	20 (4.8%)	7 (6.7%)	13 (4.2%)	0.317
Drinker	4 (1.0%)	0 (0%)	4 (1.3%)	0.240
Drug abuser	1 (0.2%)	0 (0%)	1 (0.3%)	0.558
Education				0.311
No	20 (4.9%)	8 (7.6%)	12 (3.9%)	
Primary	11 (2.7%)	4 (3.8%)	7 (2.3%)	
Secondary	247 (60.0%)	62 (59%)	185 (60.3%)	

Tertiary	129 (31.3%)	31 (29.5%)	98 (31.9%)	
Post tertiary	5 (1.2%)	0 (0%)	5 (1.6%)	
Human immunodeficiency virus infection	0 (0)	0 (0%)	0 (0%)	1.000
Use of antiviral treatment	11 (2.7%)	4 (3.8%)	7 (2.3%)	0.401
Mode of delivery				0.310
Normal spontaneous delivery	254 (61.7%)	70 (66.7%)	184 (59.9%)	
Vacuum extraction	27 (6.6%)	6 (5.7%)	21 (6.8%)	
Low forceps	9 (2.2%)	4 (3.8%)	5 (1.6%)	
Elective Caesarean section	59 (14.3%)	10 (9.5%)	49 (16%)	
Emergency Caesarean section	63 (15.3%)	15 (14.3%)	48 (15.6%)	
Immunoprophylaxis failure	7 (1.7%)	7 (6.7%)	0 (0%)	<0.001

Table 2. The demographic data and obstetric characteristics of women with different awareness of HBV status and follow up before pregnancy						
	Known HBV carrier status before pregnancy			Medical checkup before pregnancy		
	No (n=37)	Yes (n=375)	p value	No (n=168)	Yes (n=207)	P value
	Mean (SD) or n (%)	Mean (SD) or n (%)		Mean (SD) or n (%)	Mean (SD) or n (%)	
Age (year)	31.1 (5.4)	33.0 (4.4)	0.015 †	32.7 (4.3)	33.3 (4.6)	0.198 †
BMI (kg/m^2)	22.2 (3.3)	22.0 (3.0)	0.711 †	22.0 (2.9)	22.1 (3.1)	0.956 †
Gravida	2.1 (1.3)	2.1 (1.2)	0.935 †	2.4 (1.2)	1.8 (1.2)	<0.001 †
Parity	0.5 (0.9)	0.5 (0.7)	0.936 †	0.7 (0.7)	0.35 (0.6)	<0.001 †
Maternal hepatitis B e antigen positive	8 (21.6)	97 (25.9)	0.572 ‡	43 (25.6)	54 (26.1)	0.914 ‡
Antiviral treatment before pregnancy	0 (0)	11 (2.9)	0.609 §	1 (0.6)	10 (4.8)	0.026 §
Smoker or ex-smoker	5 (13.5)	15 (4.0)	0.010	6 (3.6)	9 (4.3)	0.703 ‡
Drinker	0 (0)	4 (1.1)	1.000 §	2 (1.2%)	2 (1.0)	1.000 §
Drug abuser	0 (0)	1 (0.3)	1.000 §	1 (0.6%)	0 (0)	0.448 §
Tertiary education or above	3 (8.12)	131 (34.9)	<0.001 §	52 (31.0)	79 (38.2)	0.145 ‡
Immunoprophylaxis failure	0 (0)	7 (1.9)	1.000 §	5 (3.0)	2 (1.0)	0.250 §

† student t test

‡ chi square test

§ Fisher's exact test

Table 3. Predictors of medical care during and after pregnancy						
	Medical care of HBV during pregnancy			Medical care of HBV after pregnancy		
	No (n=356)	Yes (n=56)	p value	No (n=217)	Yes (n=195)	p value
	Mean (SD) or n (%)	Mean (SD) or n (%)		Mean (SD) or n (%)	Mean (SD) or n (%)	
Age (year)	32.8 (4.6)	33.0 (4.6)	0.755 †	32.5 (4.5)	33.2 (4.5)	0.106 †
BMI (kg/m^2)	22.0 (3.0)	22.2 (3.3)	0.723 †	22.1 (3.0)	22.0 (3.1)	0.598 †
Gravida	2.1 (1.2)	1.9 (0.9)	0.165 †	2.1 (1.3)	2.0 (1.0)	0.198 †
Parity	0.5 (0.7)	0.4 (0.5)	0.191 †	0.5 (0.7)	0.5 (0.7)	0.525 †
Maternal hepatitis B e antigen positive	89 (25.0)	16 (28.6)	0.569 ‡	53 (24.4)	52 (26.7)	0.602 ‡
Known HBV status before pregnancy	320 (89.9)	55 (98.2)	0.043 ‡	192 (88.5)	183 (93.9)	0.057 ‡
Medical checkup for HBV before pregnancy	158 (44.4)	49 (87.5)	<0.001 ‡	68 (31.3)	139 (71.3)	<0.001 ‡
Antiviral treatment before pregnancy	5 (1.4)	6 (10.7)	<0.001 ‡	0 (0)	11 (5.6)	<0.001 §
Smoker or ex-smoker	18 (5.1)	2 (3.6)	1.000§	12 (5.5)	8 (4.1)	0.501 ‡
Drinker	3 (0.8)	1 (1.8)	0.444 §	4 (1.8)	0 (0)	0.125 §
Drug abuser	1 (0.3)	0 (0)	1.000 §	1 (0.5)	0 (0)	1.000 §
Tertiary education or above	111 (31.2)	23 (41.1)	0.142 ‡	60 (27.7)	74 (38.0)	0.026 ‡
Immunoprophylaxis failure	6 (1.7)	1 (1.8)	1.000 §	6 (2.8)	1 (0.5)	0.125 §

† student t test

‡ chi square test

§ Fisher's exact test

Table 4. Multivariate analysis of factors associated with awareness of hepatitis B before pregnancy and medical care attendance				
Outcome	Factors	Coefficient or Odds ratio (95% CI)	p value	R^2
Known hepatitis B carrier status before pregnancy				0.105
	Age	1.08 (1.00, 1.16)	0.068	
	Smoker or ex-smoker	0.441 (0.15, 1.34)	0.149	
	Tertiary education or above	5.31 (1.59, 17.88)	0.007	
Medical checkup before pregnancy				0.096
	Gravida	0.86 (0.68, 1.08)	0.186	
	parity	0.51 (0.34, 0.77)	0.001	
Medical care of hepatitis B during pregnancy				0.193
	Known hepatitis B carrier status before pregnancy	1.31 (0.15, 11.19)	0.808	
	Medical checkup for hepatitis B before pregnancy	7.73 (3.21, 18.65)	<0.001	
	Use of antiviral treatment before pregnancy	5.02 (1.41, 17.81)	0.013	
Medical care of hepatitis B after				0.233

pregnancy				
	Medical checkup for hepatitis B before pregnancy	5.05 (3.29, 7.51)	<0.001	
	Use of antiviral treatment before pregnancy	NA	0.999	
	Tertiary education or above	1.24 (0.79, 1.97)	0.353	