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Pattern and predictors of medical care received by hepatitis B carriers during pregnancy and after delivery

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ABSTRACT

Objective: The objective of the study is to evaluate the pattern and predictors of medical care received by hepatitis B virus (HBV) carriers during pregnancy and after delivery in Hong Kong.
Study design: The study is a retrospective analysis.
Methods: Pregnant HBV carriers and their infants were followed up for 9–12 months after delivery. Face-to-face interviews were conducted to investigate what medical care they received for HBV before, during and after pregnancy.
Results: Data were available for 412 HBV carriers. A total of 375 (91.0%) women were known HBV carriers before pregnancy. Routine antenatal screening picked out the remaining 37 (9.0%) HBV carriers; these women were younger, more likely to be smokers and had a lower level of education ($P < 0.05$) than known HBV carriers. In total, 356 of 412 (86.4%) HBV carriers did not receive any medical care for HBV during pregnancy. Known HBV carrier status, history of medical check-up and the use of antiviral treatment before pregnancy were significant predictors for HBV medical care during pregnancy ($P < 0.05$). The results show that 217 of 412 (52.6%) HBV carriers did not receive medical care for HBV after delivery. HBV medical care before pregnancy, use of antiviral treatment before pregnancy and a higher level of education were significant predictors for postpartum HBV medical care ($P < 0.05$). Multivariate analysis showed that HBV medical care before pregnancy (odds ratio [OR], 7.73; 95% confidence interval [CI], 3.21–18.65; $P < 0.001$) and the use of antiviral treatment (OR, 5.02; 95% CI, 1.41–17.81; $P = 0.013$) were associated with medical care during pregnancy. Medical care before pregnancy was also associated with postpartum HBV medical care (OR, 5.05; 95% CI, 3.29–7.51; $P < 0.001$).

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Conclusions: A significant proportion of HBV carriers did not receive HBV-related medical check-ups during and after pregnancy in Hong Kong despite the majority being aware of their carrier status. Medical care before pregnancy predicted antenatal and postpartum HBV medical care.

Introduction

Hepatitis B virus (HBV) infection is the most common form of chronic hepatitis in the world. It is a World Health Organization 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 immunisation 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 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 by initiating antiviral treatment in late pregnancy is essential to decrease the risk of immunoprophylaxis failure, which also facilitates monitoring of postpartum hepatic flare. However, little research has focused on the pattern and predictors of medical care to HBV carriers during and after pregnancy. In the US, a retrospective review of the healthcare system in Massachusetts found that 53% of newly diagnosed HBV carriers did not receive specialist care for HBV after delivery.[10] Another retrospective cohort study using an aggregate database from Massachusetts also revealed that half of the HBV carriers had not undergone postpartum laboratory testing.[11] In Hong Kong, free antenatal care is provided for all pregnant women, and hepatitis B surface antigen (HBsAg) is screened during the booking visit in early pregnancy. However, there are no local guidelines on maternal HBV DNA and hepatitis B e antigen testing, referral to hepatol- ogists/gastroenterologists for follow-up or the testing for HBV status in infants. Our aim is to evaluate the medical care of HBV carriers during and after pregnancy in Hong Kong and the factors impacting the care of these women.

Methods

The data of HBV medical care during and after pregnancy were collected from a previous prospective observational study,[9] which evaluated the factors leading to immunoprophylaxis failure. The study recruited women 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, between January 2014 and December 2016. All women provided 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 hospitals within the recruitment period, and 1592 women (5.4%) were HBsAg positive. Among the 750 participants in the original study, 412 women provided information regarding their attendance at HBV check-ups before, during and after pregnancy; these women were recruited into this retrospective study.

Basic demographics and clinical details, including age, race, gravida, parity, education level, smoking, drinking and HIV status, were recorded. Ex-smoker was defined as smoker quitted before pregnancy. Smoker was defined as smoking during pregnancy while drinker was defined as drinking alcohol during pregnancy. Drug abuser was defined as taking illicit drug during pregnancy. Maternal hepatitis B e antigen and HBV DNA were examined. At 9–12 months after delivery, the HBsAg status of infants was examined and a face-to-face interview was conducted by a research assistant to collect the information on the pattern of maternal HBV medical care during pregnancy and after delivery. Medical care was defined as any formal consultation for HBV disease with a primary practitioner, hepatologist or gastroenterologist, with or without laboratory testing. This study received ethical approval from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Data analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 22.0; IBM Corp, Armonk, NY). The results were presented as mean (standard deviation) or number (%). Student's *t*-test was used for continuous variables that were normally distributed, and the Mann–Whitney U test was used for skewed data. The chi-squared test or Fisher's exact test was used for dichotomous outcomes. Binary logistic multiple regression was performed on those factors showing statistical significance in univariate analysis to further investigate the predictors of attendance of medical follow-ups. The results were considered statistically significant when $P < 0.05$.

Results

The basic demographics of 412 HBV carriers are 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 receive any HBV medical care before pregnancy; these women had a higher gravida (2.4 vs 1.8) and parity (0.7 vs 0.4) and less antiviral use before pregnancy (0.6% vs 4.8%) than those who had HBV check-ups before pregnancy ($P < 0.05$) (Table 2).

Table 1 – Demographic data of the patients (n [%]).[a]

Characteristic	All (n = 412)	Positive HBeAg (n = 105)	Negative HBeAg (n = 307)	P-value
Age in years (mean [SD])	32.9 (4.6)	31.5 (4.2)	33.3 (4.6)	<0.001
BMI in kg/m^2 (mean [SD])	22.1 (3.0)	21.6 (3.0)	22.2 (3.1)	0.066
Gravida (mean [SD])	2.1 (1.2)	1.92 (1.0)	2.1 (1.3)	0.164
Parity (mean [SD])	0.5 (0.7)	0.4 (0.6)	0.5 (0.7)	0.250
Known HBV carrier status before pregnancy	375 (91.0)	97 (92.4)	278 (90.6)	0.572
Medical check-up for HBV 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
None	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)	
HIV 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

BMI, body mass index; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; SD, standard deviation.
[a] Unless stated otherwise.

Table 2 – The demographic data and obstetric characteristics of women with different awareness of HBV status and follow-up before pregnancy (n [%]).[a]

Characteristic	Known HBV carrier status before pregnancy			Medical check-up before pregnancy		
	No (n = 37)	Yes (n = 375)	P-value	No (n = 168)	Yes (n = 207)	P-value
Age in years (mean [SD])	31.1 (5.4)	33.0 (4.4)	0.015[b]	32.7 (4.3)	33.3 (4.6)	0.198[b]
BMI in kg/m^2 (mean [SD])	22.2 (3.3)	22.0 (3.0)	0.711[b]	22.0 (2.9)	22.1 (3.1)	0.956[b]
Gravida (mean [SD])	2.1 (1.3)	2.1 (1.2)	0.935[b]	2.4 (1.2)	1.8 (1.2)	<0.001[b]
Parity (mean [SD])	0.5 (0.9)	0.5 (0.7)	0.936[b]	0.7 (0.7)	0.35 (0.6)	<0.001[b]
Maternal HBeAg positive	8 (21.6)	97 (25.9)	0.572[c]	43 (25.6)	54 (26.1)	0.914[c]
Antiviral treatment before pregnancy	0 (0)	11 (2.9)	0.609[d]	1 (0.6)	10 (4.8)	0.026[d]
Smoker or ex-smoker	5 (13.5)	15 (4.0)	0.010	6 (3.6)	9 (4.3)	0.703[c]
Drinker	0 (0)	4 (1.1)	1.000[d]	2 (1.2%)	2 (1.0)	1.000[d]
Drug abuser	0 (0)	1 (0.3)	1.000[d]	1 (0.6%)	0 (0)	0.448[d]
Tertiary education or above	3 (8.12)	131 (34.9)	<0.001[d]	52 (31.0)	79 (38.2)	0.145[c]
Immunoprophylaxis failure	0 (0)	7 (1.9)	1.000[d]	5 (3.0)	2 (1.0)	0.250[d]

BMI, body mass index; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; SD, standard deviation.
[a] Unless stated otherwise.
[b] Student's t-test.
[c] Chi-squared test.
[d] Fisher's exact test.

There were 37 HBV carriers (9.0%) who discovered their status during routine antenatal check-ups; these women were younger (31.1 years vs 33.0 years), more likely to be smokers or ex-smokers (13.5% vs 4.0%) and likely to have a lower level of education (91.9% vs 65.1% with secondary or lower education) than the known HBV carriers ($P < 0.05$) (Table 2).

A total of 356 (86.4%) and 217 (52.6%) HBV carriers did not receive any medical care for HBV during pregnancy and after pregnancy, respectively. The predictors are shown in Table 3. Known HBV carrier status (98.2% vs 89.9%), medical check-up (87.5% vs 44.4%) and use of antiviral treatment (10.7% vs 1.4%) before pregnancy were significant predictors for receiving HBV medical care during pregnancy ($P < 0.05$). Medical check-up (71.3% vs 31.3%), use of antiviral treatment before pregnancy (5.6% vs 0%) and higher education level (tertiary or

Table 3 – Predictors of HBV medical care during and after pregnancy (n [%]).[a]

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

BMI, body mass index; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.
[a] Unless stated otherwise.
[b] Student's t-test.
[c] Chi-squared test.
[d] Fisher's exact test.

above) (38.0% vs 27.7%) were significant predictors for postpartum HBV medical care ($P < 0.05$) (Table 3).

Only higher education level (tertiary or above) was found to be positively associated with HBV awareness before pregnancy (odds ratio [OR], 5.31; 95% confidence interval [CI], 1.59–17.88; $P = 0.007$) when multivariate analysis was performed (Table 4). A higher chance of receiving HBV medical care during pregnancy was associated with medical care before pregnancy (OR, 7.73; 95% CI, 3.21–18.65; $P < 0.001$) and use of antiviral treatment (OR, 5.02; 95% CI, 1.41–17.81; $P = 0.013$). Receipt of HBV medical care after pregnancy was positively associated with medical care before pregnancy (OR, 5.05; 95% CI, 3.29–7.51; $P < 0.001$).

In the 37 carriers who were not aware of their HBV status before pregnancy, one carrier and 12 carriers received HBV care during pregnancy and after pregnancy, respectively. All seven immunoprophylaxis failure cases were women who knew that they were HBV carriers before pregnancy; however, only two received HBV medical care before pregnancy, and only one, during pregnancy.

Table 4 – Multivariate analysis of factors associated with awareness of HBV status before pregnancy and HBV medical care received.

Outcome	Factors	Coefficient or odds ratio (95% CI)	P-value	R^2
Known HBV 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 check-up before pregnancy				0.096
	Gravida	0.86 (0.68–1.08)	0.186	
	Parity	0.51 (0.34–0.77)	0.001	
HBV medical care during pregnancy				0.193
	Known HBV carrier status before pregnancy	1.31 (0.15–11.19)	0.808	
	Medical check-up for HBV before pregnancy	7.73 (3.21–18.65)	<0.001	
	Use of antiviral treatment before pregnancy	5.02 (1.41–17.81)	0.013	
HBV medical care after pregnancy				0.233
	Medical check-up for HBV 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	

HBV, hepatitis B virus; CI, confidence interval.

Discussion

The results of this study demonstrate that a high proportion of HBV carriers did not receive medical care for HBV and that the majority did not receive additional medical attention during pregnancy and after delivery. It is worth investigating this issue because antiviral treatment is recommended in highly viraemic carriers during pregnancy to reduce the risk of HBV vertical transmission. Knowing the possibility of hepatic flare after delivery should also prompt regular postnatal monitoring for these women to allow timely intervention to prevent cirrhosis, hepatocellular carcinoma and mortality.[12,13]

With regard to discussing the potential implications of HBV disease during pregnancy with HBV carriers, medical physicians and obstetricians can find it difficult because of a number of issues. First of all, despite being aware of the HBV carrier status, the asymptomatic nature of HBV disease in the early stages could lead to poor disease surveillance.[14] Second, maternal, obstetric 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, pre-eclampsia, gestational hypertension and antepartum haemorrhage, and 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] was shown by cohort studies and other meta-analyses. Furthermore, maternal HBV flare-up is possible during pregnancy, and maternal mortality has been reported.[20] Because the role of HBV DNA in predicting these complications remains unclear, the limited evidence from the literature may eliminate the need for monitoring maternal HBV DNA and hence the involvement of a hepatologist/gastroenterologist during pregnancy. Finally, insufficient knowledge of the obstetricians, the 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 recognised pregnancy and childbirth as a mode of HBV transmission, respectively.[21,22] Significant heterogeneity in the management of HBV carriers[23] and poor adherence to the guidelines[24] by medical physicians have been noted. Only 69% of hepatologists and 42% of non-hepatologist physicians were 'very comfortable' or 'comfortable' in managing pregnant HBV carriers.[23] Obstetricians were not familiar with the use of antiviral treatment during pregnancy,[25] and primary care physicians had even less knowledge on the subject, especially regarding foetal safety.

From a public health perspective, eradication of HBV disease should begin with early identification of HBV-infected individuals, followed by providing evidence-based disease surveillance strategies and treatment and preventing vertical and horizontal transmission. For early identification, the Centers for Disease Control and Prevention recommends universal screening of HBsAg during pregnancy.[26] This can identify HBV carriers who are unaware of their status and ensure that their newborns receive additional hepatitis B immunoglobulin at birth. Neonatal HBV immunisation programmes remain the most effective intervention to prevent vertical transmission.[3] The World Health Organization recommends all infants should receive a course of HBV vaccination, with the first dose preferably administered within 24 h.[27] HBV viral load assessment during pregnancy is crucial to assess the risk of immunoprophylaxis failure.[6] The use of antiviral treatment in highly viraemic HBV women in late pregnancy could reduce the risk of immunoprophylaxis failure, which is recommended by various authorities.[12,13] Multidisciplinary care involving hepatologists/gastroenterologists during pregnancy is necessary because they are more likely to provide timely and appropriate HBV disease assessment, monitoring and treatment than primary care physicians.[24,28] They can also jointly inform the safety and efficacy of antiviral treatment during pregnancy. Obstetricians have the initial contact with pregnant HBV carriers; therefore, they are responsible for initiating referral of the women to appropriate specialists for subsequent management of care. Provision of medical care to HBV carriers and HBV-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 policymakers should use this holistic approach during pregnancy, which 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 focussing on the management of HBV during pregnancy are necessary. However, practising this multidisciplinary approach may be difficult, and it can vary by location because of different public health systems, availability of specialists, financial support and resources. Local studies on the financial impact of different preventive strategies should be encouraged to obtain reliable data to guide regional policy.[4]

Our study is the first to evaluate the predictors of medical care among pregnant HBV carriers. We found that prepregnancy HBV medical care could be the key to improve the health care of HBV carriers during and after pregnancy. The government should promote regular prepregnancy HBV disease surveillance and enhance public awareness and knowledge by launching educational programmes. These may be achieved by using social media, short message services or 'apps' on mobile phones, which are widely available nowadays.[33] A referral and monitoring guideline at the primary care level can help disease surveillance and triage in complicated cases, for example, pregnant HBV carriers requiring specialist care.[12,13]

There are several limitations in our study. For the HBV carriers who received HBV-related care during and after pregnancy, we did not know the exact details of HBV care received by the carriers, whether they were under the care of hepatologists or primary care physicians or whether liver function tests and HBV DNA quantification had been performed. Without this information, it is difficult to guarantee a proper assessment, even with multidisciplinary care. The details of medical care could reflect the current management of pregnant HBV carriers and provide data to guide policy

planning or recommendation in their standard medical care. We also did not evaluate the obstetric and perinatal outcomes related to medical care. The risk of preterm delivery and gestational diabetes is increased in HBV carriers, particularly in women with active HBV disease (i.e., positive hepatitis B e antigen [HBeAg] or higher HBV DNA).[19,34] Whether provision of HBV medical care and early intervention in pregnancy could alter these adverse pregnancy outcomes requires further evaluation.

Conclusions

Our study highlights the deficiency in multidisciplinary HBV care during pregnancy and the lack of continuity of care after delivery. Eradication of HBV should begin with breaking the chain at birth, followed by long-term monitoring by practising evidence-based medicine with input from various stakeholders. However, a high proportion of HBV carriers in Hong Kong did not receive HBV medical care during and after pregnancy despite most of them being aware of their HBV carrier status. Strategies to improve HBV medical care during pregnancy and after delivery are needed.

Author statements

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Ethical approval

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

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Competing interests

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

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