Maternal and obstetric factors of hepatitis B immunisation failure in Hong Kong: a multicentre prospective study: abridged secondary publication

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KEY MESSAGES

Viral load of 8 $\log_{10}$ copies/mL at 28 to 30 weeks of gestation could be the optimal hepatitis B virus DNA cutoff to predict immunoprophylaxis failure. Starting antiviral treatment at 30 weeks could reduce the viral load and hence the immunoprophylaxis failure rate.

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Introduction

Hepatitis B virus (HBV) infection remains the most common form of chronic hepatitis worldwide. The risk of vertical transmission leading to chronic infection is dramatically reduced by administering hepatitis B immunoglobulin to newborns at birth together with a complete course of HBV vaccination.[1] A high maternal HBV DNA level during pregnancy is the strongest risk factor leading to immunoprophylaxis failure.[2] The optimal HBV DNA level to identify pregnancies associated with subsequent immunoprophylaxis failure remains unclear, owing to the retrospective nature[3] and heterogeneity of the studied population,[4] and different or unknown timing of HBV DNA quantification.[3-5] We aimed to evaluate the risk of immunoprophylaxis failure in relation to the maternal HBV DNA level at 28 to 30 weeks of gestation.

Methods

This prospective multicentre study was conducted from January 2014 to December 2016 at five hospitals in Hong Kong. Pregnant women were tested for hepatitis B surface antigen (HBsAg) during their first antenatal visit. Women with a positive HBsAg status were recruited. Women receiving antiviral treatment during pregnancy were excluded. All women provided written informed consent and were enrolled under protocols approved by the institutional review board of each hospital.

Maternal hepatitis B e antigen (HBeAg) was tested once upon recruitment, and the HBV DNA was quantified at 28 to 30 weeks using the COBAS TaqMan HBV Monitor Test coupled with the COBAS Ampliprep extraction system (both Roche Diagnostics, Branchburg, NJ), with a lower limit of detection of 100 copies/mL (~17.2 IU/mL) and upper limit of 990 000 000 copies/mL (~170 103 092 IU/mL) (1 IU=5.82 copies). All newborns received both 10 μg HBV vaccines (Engerix-B, GlaxoSmithKline, Belgium) and 110 IU hepatitis B immunoglobulin (HyperHEP B, Grifols [CA], USA) intramuscularly at a different site within 12 hours of birth, followed by hepatitis B vaccine at the same dosage at 1 and 6 months of life. HBsAg of infants was examined at age 9 to 12 months. Immunoprophylaxis failure of infants was defined as HBsAg positive status at age 9 to 12 months.

The sample size was calculated based on comparing the proportions of immunoprophylaxis failure in infants between high and low maternal pre-delivery HBV DNA levels. The proportions were assumed to be 2.5% and 0.01% for the groups of high and low maternal pre-delivery HBV DNA levels, respectively. A total of 624 subjects were required to have a power of 80% and a type I error of 5%. The Student's *t* test or Wilcoxon rank sum test was used to compare quantitative variables, and the Chi-square test or Fisher's exact test was used to compare qualitative variables. A P value of <0.05 was considered statistically significant. Data

were analysed with SAS software (version 9.2, SAS Institute. Cary [NC], USA).

Results and discussion

Data from 641 women and 654 infants (13 pairs of twins) were available for final analysis. All infants received hepatitis B immunoglobulin within 12 hours of birth and completed the whole course of hepatitis B vaccine on schedule. Of the women, 155 (24.2%) were HBeAg positive. There were seven (1.1%) cases of immunoprophylaxis failure; all born to women with positive HBeAg status and HBV DNA of >8 $\log_{10}$ copies/mL (>17 000 000 IU/mL). The risk of immunoprophylaxis failure with HBV DNA level of <8, 8-8.99, >9 $\log_{10}$ copies/mL were 0%, 8.6%, and 3.1%, respectively (Table). Significant predictors of immunoprophylaxis failure at 28 to 30 weeks were positive HBeAg (4.5% vs 0%, P<0.0001) and HBV DNA of ≥8 $\log_{10}$ copies/mL (≥17 000 000 IU/mL) [5.8% vs 0%, P<0.0001].

TABLE. Immunoprophylaxis failure rate in different hepatitis B virus (HBV) DNA levels and hepatitis B e antigen (HBeAg) statuses

HBV DNA at 28-30 weeks, $\log_{10}$ copies/mL	No. of patients	Immunoprophylaxis failure rate	
		No. (%)	95% confidence interval
<6 (~171 821 IU/mL)	474	0	0-0.78
6-6.99	24	0	0-14.25
7-7.99	22	0	0-15.44
≥8 (~17 000 000 IU/mL)	121	7 (5.79)	2.36-11.56
8-8.99	58	5 (8.62)	2.86-18.98
≥9 (~170 000 000 IU/mL)	63	2 (3.17)	0.39-11.00
HBeAg status			
Negative	486	0	0-0.76
Positive	155	7 (4.52)	1.83-9.08

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Disclosure

The results of this research have been previously published in:

1. Cheung KW, Seto MTY, Kan ASY, et al. Immunoprophylaxis failure of infants born to hepatitis B carrier mothers following routine vaccination. Clin Gastroenterol Hepatol 2018;16(1):144-145.

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