



Prediction of Mother-to-child Transmission of Hepatitis B Virus Infection by Using Perinatal Maternal Quantitative Surface Antigen

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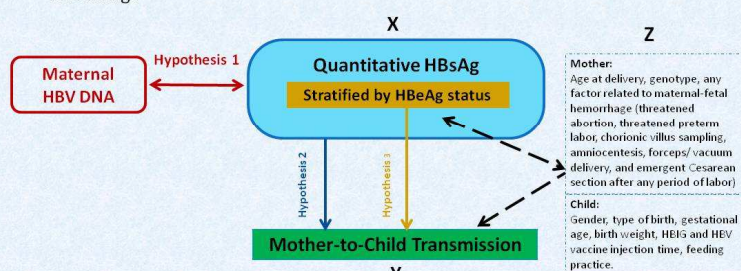
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Background

- To eliminate hepatitis B virus mother-to-child transmission, it is necessary to detect pregnant women with high HBV DNA and then give additional prevention strategy before delivery.
- Quantitative HBsAg is a newly developed method with a unit price much lower than that of HBV DNA.

Aims

- To evaluate the correlation between serum quantitative HBsAg and HBV DNA.
- To predict mother-to-child transmission by using quantitative HBsAg.
- To assess the feasibility of replacing HBV DNA by quantitative HBsAg in high risk screening.



Material and Methods

- This is a prospective cohort study conducted at the National Taiwan University Hospital, Cardinal Tien Hospital, and Tzu-Chi General Hospital Taipei Branch.
- All HBsAg positive mothers aged 18 to 45 years who had deliveries between April 2007 and June 2012 in these study hospitals were invited to participate in the study at postpartum wards.
- Serum HBsAg, HBeAg and HBV DNA level of these mothers were measured.
- Infants were followed up to 1-1.5 years old and had two separate serum HBsAg tests.
- Spearman's correlation coefficient was used to examine the correlation between quantitative HBsAg and HBV DNA. Logistic regression analyses were used to assess the predictive ability of HBV DNA, quantitative HBsAg, and other risk factors of mother-to-child transmission.

Results

- Among the 461 children, 16 children were found to be infected with HBV. All of them were born to HBeAg positive mothers with high HBV DNA ($7.9 \pm 0.74 \log_{10} \text{ IU/ml}$) and high quantitative HBsAg ($4.7 \pm 0.2 \log_{10} \text{ IU/ml}$).
- Quantitative HBsAg had a significant positive correlation with HBV DNA level ($r=0.64$, $p<0.0001$) in all subjects and in HBeAg positive subjects group ($r=0.62$, $p<0.0001$). The optimum cut-off point for HBV DNA concentration of $7 \log_{10} \text{ IU/ml}$ was $4.26 \log_{10} \text{ IU/ml}$, with a sensitivity of 93%, specificity of 97%.
- After adjusting possible confounders, quantitative HBsAg could significantly predict mother-to-child transmission.

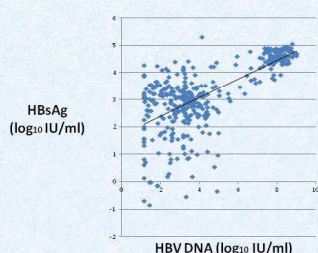


Figure 5-1 Correlation between HBsAg and HBV DNA
 $r=0.64$ $p<0.0001$

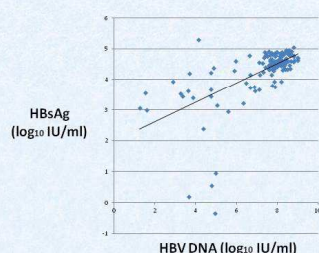


Figure 5-2 Correlation between HBsAg and HBV DNA in HBeAg positive mothers
 $r=0.62$ $p<0.0001$

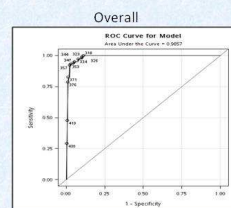


Figure 5-4 The predictive value of quantitative HBsAg for high HBV DNA ($\geq 7.0 \log_{10} \text{ IU/ml}$) in HBeAg positive pregnant women was assessed by an ROC curve

Cut-off point: HBsAg: $4.26 (\log_{10} \text{ IU/ml})$
Sensitivity: 93%; Specificity: 97%

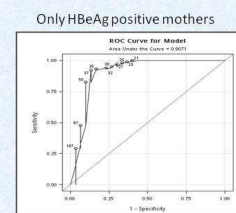


Figure 5-5 The predictive value of quantitative HBsAg for high HBV DNA ($\geq 7.0 \log_{10} \text{ IU/ml}$) in HBeAg positive pregnant women was assessed by an ROC curve

Cut-off point: HBsAg: $4.30 (\log_{10} \text{ IU/ml})$
Sensitivity: 92%; Specificity: 87%

Table 5-2 Characteristics between children infected and children uninfected

Characteristics	Children infected (N=16)	Children uninfected (N=445)	P
Maternal age at delivery (yr), mean \pm SD (range)	33.1 \pm 3.9 (23.3-41.6)	33.70 \pm 4.3 (19.5-45.1)	0.56
HBsAg status			
Positive	16 (100%)	0 (0%)	-
Negative	0 (0%)	445 (100%)	
HBV DNA ($\log_{10} \text{ IU/ml}$) mean \pm SD (range)	7.9 \pm 0.74 (6.0-9.0)	4.3 \pm 2.4 (1.2-9.0)	<0.0001
HBV DNA ($\log_{10} \text{ IU/ml}$)			
<7.0	1 (6.3%)	273 (75.6%)	<0.0001
≥ 7.0	15 (93.7%)	88 (24.4%)	
HBsAg ($\log_{10} \text{ IU/ml}$) mean \pm SD (range)	4.7 \pm 0.2 (4.2-4.9)	3.0 \pm 1.3 (-2.5-3)	<0.0001
HBsAg ($\log_{10} \text{ IU/ml}$)			
Low	0 (0%)	153 (34.4%)	<0.0001 *
Mid	0 (0%)	154 (34.6%)	
High	16 (100%)	138 (31.0%)	
Maternal ALT			
$\leq \text{ULN}$ (40 U/L)	14 (87.6%)	398 (91.3%)	0.66
1-2 \times ULN	1 (6.2%)	27 (6.2%)	
2-5 \times ULN	1 (6.2%)	11 (2.5%)	
HBV genotype			
B	12 (75%)	180 (73.5%)	0.88
C	4 (25%)	61 (24.9%)	
B+C	0 (0%)	4 (1.6%)	
Type of birth			
NSD	11 (68.8%)	180 (40.4%)	0.0361
C/S	5 (31.2%)	265 (59.6%)	
Any factor related to maternal-fetal hemorrhage†			
Yes	7 (43.8%)	238 (55.9%)	0.34
No	9 (56.2%)	188 (44.1%)	
Gestational age	37.9 \pm 2.2 (33.0-41.0)	38.7 \pm 1.3 (31.3-41.4)	0.16
Gender			
Male	9 (56.2%)	235 (52.8%)	0.79
Female	7 (43.8%)	210 (47.2%)	
Birth weight(kg)	3.0 \pm 0.5 (1.9-3.7)	3.1 \pm 0.4 (1.8-4.5)	0.32
Delayed injection of first dose of HBV vaccine			
No	15 (93.8%)	420 (95.2%)	0.55
Yes	1 (6.2%)	21 (4.8%)	
Vaccine (On schedule)			
Yes	13 (81.3%)	366 (85.5%)	0.72
No	3 (18.7%)	62 (14.5%)	
Feeding practice§			
Breast milk	8 (50%)	192 (44.0%)	0.29
Formula	4 (25%)	61 (14.0%)	
Both breast milk & formula	4 (25%)	183 (42.0%)	

Table 5-3 Potential risk factors of HBV mother-to-child transmission -- Multivariate logistic regression

Variables	Model 1		Model 2	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Maternal HBsAg (per $\log_{10} \text{ IU/ml}$ increase)	17.62 (3.63-85.41)	0.0004	-	-
Maternal HBV DNA (per $\log_{10} \text{ IU/ml}$ increase)	-	-	2.29 (1.44-3.63)	0.0004
Type of birth*	1.54 (0.46-5.21)	0.49	1.29 (0.40-4.18)	0.68
Gestational age (per 1 wk increase)	0.78 (0.54-1.12)	0.18	0.72 (0.50-1.04)	0.08
Delayed injection of first dose of HBV vaccine	0.33 (0.02-6.20)	0.46	0.37 (0.02-5.70)	0.48
Feeding practice†	1.11 (0.29-4.33)	0.88	0.83 (0.21-3.02)	0.78
Hosmer and Lemeshow test	-	0.9992	-	0.9606

*Feeding practice during the first 6 months; Reference group: formula milk
Abbreviation: CI, confidence interval

Conclusions

- Our study documents that quantitative HBsAg is highly correlated with, and as predictive as HBV DNA for mother-to-child transmission.
- With the concern of the screening cost, quantitative HBsAg may be used as a new screening tool during pregnancy.