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RESEARCH ARTICLE

PERINATAL TRANSMISSION OF THE HEPATITIS B VIRUS: THE GHANAIAN SITUATION

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ABSTRACT

Vertical transmission of hepatitis B virus (HBV) from infected mothers to their fetuses or new born either in utero or peripartum remain a major source of perpetuating the reservoir of chronically infected individuals globally. The main aim of this study is to determine perinatal transmission of the HBV in the Ghanaian setting. One hundred and sixty one (161) pregnant women who were positive for HBV and their respective neonates were enrolled in the study. Viral loads of the mothers were determined using peripheral blood sample and analyzed by PCR. Cord blood of the neonates was assessed for HBV DNA using PCR. The mothers were categorized as having high or low viral load using 10^6 copies/ml as the reference point. Socio-demographic and obstetrical data were collected using a pre-tested checklist. The babies were assessed for birth weight, prematurity and any abnormalities. Sixty neonatal cord bloods were positive for HBV DNA, a perinatal transmission of 37.3%. The study revealed a positive association between maternal viral load ($p<0.001$) and neonatal HBV DNA status. The male sex ($P<0.001$) is at a higher risk for vertical transmission than the females. Preterm delivery and birth weight were comparable between the two groups. Screening of pregnant women for HBV is necessary for the required intervention to reduce MTCT.

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INTRODUCTION

Despite the successes with combination screening, infant post exposure prophylaxis, antiviral therapy and post vaccination testing, transmission from the pregnant woman with chronic hepatitis B infection to the neonate remain a substantial problem (Nelson *et al*, 2014). Vertical transmission of HBV from infected mothers to their fetuses or new born either in utero or peripartum remain a major source of perpetuating the reservoir of chronically infected individuals globally (Dionne-Odom *et al*, 2016). Chronic HBV infection will develop in up to 90% exposed neonates who did not receive appropriate immunoprophylaxis in contrast to 10-25% in children and only 5-10% in immunocompetent adults (Pan *et al*, 2012). Screening of pregnant women for chronic HBV infection and proper management of positive individuals has had a major impact in decreasing the risk for neonatal infection (Shui-lam & Kwok-Yin, 2013; Gentile and Borgia, 2014;Nelson *et al*, 2014). Test for HBsAg in the serum, the universally available screening process, will miss some potential infectious mothers. The use of highly sensitive nucleic acid amplification test have shown that up to 30% individuals with past history of HBV infection retain viral DNA. Such individuals have so called occult HBV infection and could transmit HBV vertically (Copolla *et al*, 2013). The need for a more effective routine screening process cannot be over emphasized (Sharma *et al*, 1996; Siakwa *et al*, 2014). A number of factors have been identified to influence utero placental transmission. These include male fetus, amniocentesis, pregnancy complication, prolonged labour, threatened preterm labour, maternal menstrual irregularity, severe nausea during the first trimester and antigenimia in siblings (Pan *et al*, 2012; Guo *et al*, 2013; Pan *et al*, 2013; Li *et al*, 2014; Yi *et al*, 2014). Despite the

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contributions of these factors to MTCT, serum HBV DNA level has been identified as the single most important predictor and independent of other risk factor for MTCT (Liu *et al.,* 2011). The risk of MTCT was found to increase with increasing maternal viral load irrespective of the administration of passive-active immunoprophylaxis to the neonate (Singh *et al.*, 2011;Zou *et al.*, 2011; Liu *et al.*, 2012; Pan *et al*., 2012; Nelson *et al.*, 2014). Though interventions for MTCT have been recommended by the WHO resources for their implementation are lacking in resource poor countries (Essan *et al.*, 2013; Olaleye *et al.*, 2013; Siakwa *et al.*, 2014) With HBV prevalence rate of 10.5%among pregnant women (Cho *et al.*, 2012), the only widely implemented policy for MTCT intervention in Ghana is active vaccination of the new born. The main of the present study is to determine perinatal transmission among pregnant women with chronic HBV infection in the Ghanaian setting.

MATERIALS AND METHODS

This cohort study was conducted in the Cape Coast Teaching Hospital, the major tertiary health institution in the Central Region of Ghana between December 2006 and September 2012. The Institutional Review Board of the University of Cape Coast approved the study.

Recruitment of Patients

One hundred and sixty one (161) pregnant women who were positive for hepatitis Bin a previous study (Siakwa *et al*., 2014) and their respective neonates were enrolled in the study to determine perinatal transmission of HBV from the infected mothers to their respective neonates. Viral loads of the mothers were determined using peripheral blood sample and analyzed by PCR as described earlier (Siakwa *et al.,* 2014). Cord blood of the neonates was assessed for HBV DNA using PCR to establish perinatal transmission. Samples of the cord blood were taken as described by Li *et al.* (2015) to avoid contamination. The mothers were categorized as having high or low viral load using 10^6 copies/ml as the reference point (Pan *et al*, 2012).Socio-demographic and obstetrical data were collected using a pre-tested checklist. The babies were assessed forbirth weight, prematurity and any abnormalities.

Data Analysis

Data was entered into the computer using SPSS for windows (version22.0) and double checked before analysis. Means and proportions of the socio-demographic, obstetrical and neonatal characteristics were calculated and compared between HBV DNA positive and HBV DNA negative babies using the student t-test and Chi-square test. Multivariate analysis was done with Neonatal HBV DNA status as dependent variable and maternal viral load, parity, gestational age, sex and birth weight of the babies as independent variables. Differences between means were considered statistically significant at $p < 0.05$.

RESULTS

A total of 161 mothers who were HBV infected and their respective neonates were studied. Sixty neonatal cord bloods were positive for HBV DNA bringing perinatal transmission to 60/161 (37.3%). Majority of the mothers were aged 20-29 years (73%), have high viral load (56.5%) and primigravidae (62%). The study revealed a positive association between high maternal viral load ($p<0.001$) and neonatal HBV DNA status. The higher the viral load the higher the chance of MTCT. The sex ratio of the study neonates was 1:1, however, the male sex ($P<0.001$) is at a higher risk for vertical transmission than the females. Preterm delivery and birth weight were comparable between the two groups.

DISCUSSION

The aim of the present study is to determine the rate of mother to child transmission of HBV among pregnant women in the study population. One hundred and sixty one infected mothers and their respective infants were assessed for trans placental transmission of the HBV. Several studies have reported MTCT before and after immunoprophylax is (Pan *et al*, 2012; Xu *et al*, 2014; Yi *et al*, 2014; Nelson *et al*, 2015; Donne-Odom *et al*, 2016). Globally, HBsAg positivity was reported in 16.2% (ranging from 0-72%) in cord blood of infants born to carrier mothers. The positive rate was 42, 1% (from 0- 100%) in infants born to carrier mothers without passive-active

Table. Characteristics of studied Mothers and Neonates

Parameters	Variable	Positive HBV DNA	Negative HBV DNA	p-value
		n=60	n=101	
Maternal Characteristics				
Age	< 20	5	6	0.1667
	20-29	38	80	
	30-39	12	10	
	≥40	5	5	
Parity	Primigravidae	42	58	0.1550
	Multigravidae	18	42	
Maternal Viral Load	<10 copies/ml	14	56	0.00139
	≥10 copies/ml	46	45	
Neonatal Characteristics				
Sex	Male	45	37	0.0000
	Female	15	64	
Birth Weight	< 2500g	26	51	0.4370
	≥ 2500g	34	50	
Gestational Age	<37 weeks	22	24	0.1110
	≥37 weeks	38	77	

immunoprophylaxis and 2.9% (from 0.0-21.0%) in infant born to carrier woman with passive-active immunoprophylaxis (Li *et al*., 2015). Li *et al.* (20015) also reported that postpartum infection contributes significantly to MTCT while passive-active immunoprophylaxis effectively reduces HBV infection to infants. The present study observed 37.3% MTCT rate in the absence of immunoprophylasis. This finding is consistent with what has been reported by Olaleye *et al.* (2013) from Nigeria. The regional variations observed in the transmission rates of HBV were attributed to the HBV types in circulation. Zou *et al.* (2012) asserted same as the probable explanation for the high incidence of the HBV in China. Some studies have also reported that different human race have different susceptibility to HBV infection (Guo *et al*., 2011; Hu *et al.,* 2012; Ji *et al*., 2014; Li *et al*., 2014). They explained that different human race might possess different pattern of single nucleotide polymorphorsms that are responsible for different genetic susceptibility to the chronic infections (Li *et al*., 2015; Ji *et al*., 2015). The high incidence of the HBV among Chinese was probably due to the race's genetic susceptibility to the HBV (Li *et al*, 2015). Several studies have reported increased MTCT with increased maternal viral load with or without immunoprophylaxis (Guo *et al*., 2013; Pan *et al*., 2013; Li *et al*., 2014; Yi *et al*., 2014; Ji *et al*., 20154). The findings in the present study are consistent with what has been reported elsewhere. HBV DNA greater than 10^6 copies/ml is a risk for MTCT.

This finding was the basis for the recommended antiviral therapy in the third trimester for HBV infected pregnant women with viral load $>10^6$ copies /ml. Telbivudine, tenofovir and lamivudine have been recommended for mothers with high viral load to prevent MTCT, however the use of lamivudine is being discourage due to the development of antiviral resistance (Pan *et al*., 2012; Nelson *et al*., 2014). Gentile and Borgia (2014) recommended antiviral prophylaxis starting 28 weeks gestation. Tenofovir is the recommended drug of choice due to non- resistance as well as negligible toxicity to both mother and fetus. Chronic HBV infection occurs more frequently in males than in females infected children (Li *et al*., 2014). The difference observed in chronic HBV carrier rate between males and females is apparently due to difference in susceptibility of the two sexes to development of the chronic carrier state (Li *et al*., 2014). Consistent with what has been reported earlier the present study found a significant different between the male and female sexes with the male being more susceptible.

Conclusion

Perinatal transmission rate of HBV is high among the study population. Higher maternal viral load increased the rate of vertical transmission. Males are more susceptible to HBV infection than females. Screening of HBV infected mother for viral load would help identify high-risk group for initiation of antiviral therapy. Passive-active immuneprophylaxis is recommended for neonates born to HBV infected mothers.

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