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RESEARCH ARTICLE

MATERNAL VIRAL LOAD AS A RISK FOR ADVERSE OBSTETRIC AND PERINATAL OUTCOME IN CHRONIC HEPATITIS B INFECTION

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ABSTRACT

Hepatitis B viral load is directly related to the risk of disease progression. Studies reporting outcomes and indication for treatment are interpreted in relation to viral load. The main objective of this study is to determine the relationship between viral load and obstetric and neonatal outcomes in hepatitis B virus (HBV) infected mothers. Two hundred and sixty two pregnant women whose HBV status was determined by PCR and HBsAg were recruited for the study. They were categorized based on their viral load; viral load $\geq 10^6$ copies/ml as case and $< 10^6$ copies/mlas control. Maternal and neonatal outcomes were assessed and compared between the two groups. The results revealed age, income and place of residence (whether rural or urban) were comparable between the two groups. However, there was an association between an infected mothers' educational level and serum HBV DNA level. Parity, PIH foul smelling liquor, and previous abortion were comparable between the two groups. PROM ($p<0.05$) and a history of STI/UTI ($p<0.05$) were associated with high maternal viral load. Mothers with viral load $>10^6$ copies/ml are at higher risk for PROM. The higher the viral load the greater the risk for having neonates with birth weight <2500g ($p<0.05$). Being preterm, asphyxiated and low APGAR scored neonate is not directly associated with maternal viral load. Routine screening of HBV infected pregnant women for viral load will determine the need for antiviral therapy to reduce adverse perinatal outcome and MTCT.

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INTRODUCTION

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 (Dionic-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). Identification of pregnant women with chronic HBV infection through universal screening has had a major impact in decreasing the risk for neonatal infection (Gentile and Borgia, 2014; Nelson *et al*., 2014). The present universal screening process test for HBsAg in the serum however, 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). Serum HBV DNA level has been identified as the single most important predictor and independent risk factor for MTCT. Many studies done before and after adoption of passive-active immunoprophylaxis have shown an increased risk of MTCT

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with higher HBV DNA. The prophylaxis effective rate (PER) of passive –active prophylaxis was 100% if maternal prelabour HBV DNA levels were less than 10^5 copies/ml as compared with 65%-68% observed risk if maternal HBV DNA were more than 10^5 copies (Singh *et al*., 2011; Pan *et al*., 2012; Nelson *et al*., 2014). Liu *et al*., (2012) observed that the risk of MTCT increased as maternal prelabour HBV DNA level rose above 10^7-10^8 copies/ml. Zou *et al*., (2011) demonstrated that immune prophylaxis failure only occurred in infants born to HBeAg positive mothers. When maternal predelivery HBV DNA was stratified immunoprophylaxis failure was found to increase with increasing viral load. Thus maternal HBV DNA level $>10^6$ copies/ml is the most important predictor (Pan *et al*., 2012). Host factors related to HBV transmission are mainly placenta and genetic. Prolonged uterine contraction during normal labour and/or threatened preterm labour might disrupt placenta function increasing MTCT (Xu *et al*., 2002; Wiseman *et al*.,, 2009; Singh *et al*., 2011). Though some studies reported viral load is independent of HBV infection progression to cirrhosis and hepatocellular carcinoma (Shaheen *et al*., 2010), HBV DNA levels have been shown to be directly related to disease progression in an infected individual (del Canho *et al*., 1997). Studies reporting outcomes and indication for treatment are usually interpreted in relation to viral load (Borgia *et al*., 2012). The implementation of the passive-active immunoprophylaxis has reduced MTCT of HBV (Singh *et al*., 2011; Dunkelberg *et al*., 2014). However, it has been reported that HBV DNA $>10^6$ copies/ml increased the risk for MTCT despite passive-active immunoprophylaxis (Pan *et al*., 2012).
Our previous study reported, a progression of HBV infection from asymptomatic to symptomatic increased the risk for adverse maternal and perinatal outcomes (Siakwa *et al*., 2016). There is paucity of literature on the relationship between maternal HBV DNA levels and maternal and perinatal outcomes. The main objective of this study is to determine the relationship between Maternal HBV DNA levels and obstetric and neonatal outcomes.

MATERIALS AND METHODS

This descriptive comparative study was conducted in the Cape Coast Teaching Hospital, the major tertiary health institution in the Central Region of Ghana. The Institutional Review Board of the University of Cape Coast approved the study.

Recruitment of Patients

Two hundred and sixty two (262) pregnant women who were positive for hepatitis Bin a previous study (Siakwa *et al*., 2014) were enrolled in the study to determine differences in birth outcomes between pregnant HBV infected women with high viral load $>10^6$ copies/ml (as case) and those with low viral load $<10^6$ copies/ml (as control). Participants gave their consent in writing and were screened for any underlying obstetric and medical complications for exclusion and further categorized into high viral load and low viral load on the basis of PCR analysis of HBV DNA as described earlier (Siakwa *et al*., 2014). Socio-demographic, medical and obstetrical data were collected using a pre-tested checklist. Participants were monitored on each antenatal visit through their pregnancy until delivery and their babies were assessed for Apgar score at minute one and five, birth 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, medical, obstetrical and neonatal characteristics were calculated and compared between the high viral load and low viral load groups using the student t-test and Chi-square test. Multivariate analysis was done with high viral load/low viral load as dependent variables and socio-demographic, medical, obstetrics and neonatal variables as independent variables. Differences between means were considered statistically significant at $p < 0.05$.

RESULTS

Table 1 show the socio demographic characteristics of the participants. Age, income and place of residence (whether rural or urban) are comparable between the two groups. However, there is an association between an infected mothers' educational level and serum HBV DNA level.

Table 2 shows maternal obstetric characteristics of the participants. Parity, PIH, foul smelling liquor, and previous abortion are comparable between mothers with high maternal viral load and those with low viral load. PROM ($p<0.05$) and a history of STI/UTI ($p<0.05$) are associated with high maternal viral load. Mothers with viral load $>10^6$ copies/ml are at higher risk for PROM.

Table 1. Socio-demographic Characteristics of Respondents

Parameters	Variables	Case (n=160)	Control (n=102)	X^2	p-value
Age	<20	5	6		
	20 – 29	101	48		
	30 – 39	37	34	6.8567	0.07661
	≥ 40	17	14		
Income	Low	92	52		
	Medium	38	30	1.2751	0.5286
	High	30	20		
Educational Level	Illiterate	28	9		
	Primary	80	31		
	Secondary	42	40	24.2867	0.00002
	Tertiary	10	22		
Residence	Rural	92	62		
	Urban	70	40	0.2629	0.6081

Table 2. Maternal Obstetric Characteristics of Respondents

Parameters	Variables	Case (n=160)	Control (n=102)	X^2	P-Values
Parity	1	82	63		
	2	60	33	3.6684	0.1597
	≥ 3	18	6		
PROM	Present	62	22		
	Absent	98	80	7.6715	0.0056
PIH	Present	37	34		
	Absent	123	68	2.7894	0.0949
Foul Smelling Liquor	Present	22	10		
	Absent	138	92	0.574	0.4487
Previous Abortion	Present	23	20		
	Absent	137	92	0.3671	0.5446
HO/UTI/STI	Present	50	17		
	Absent	110	85	6.2151	0.0127

Table 3. Neonatal Characteristics of Infants Born to Respondents

Parameters	Variables	Case (n=160)	Control (n=102)	Chi Square	P-Values
Gestational Age	Preterm	42	20		
	Term	118	80	1.0019	0.3168
Birth Weight	<2500g	50	16		
	≥2500g	110	86	7.202	0.0073
Apgar Score at 1 min	< 7	62	35		
	≥ 7	98	67	0.3527	0.5526
Apgar Score at 5 min	< 7	40	28		
	≥ 7	120	74	0.0881	0.7667
Birth Outcome	Live	152	99		
	Still Birth	8	3	0.2444	0.6211
Asphyxia	Present	18	11		
	Absent	142	91	0.0072	0.9324

Table 3 shows neonatal outcomes among neonates born to participants. There was an association between viral load and birth weight of neonates born to the participants. The higher the viral load the greater the risk for having neonates with birth weight <2500g ($p<0.05$). Having preterm or asphyxiated neonates is not associated with maternal viral load. Also having a child with low APGAR score or stillbirth is comparable between the two groups.

DISCUSSION

The study considered the relationship between viral load and maternal and neonatal outcome in HBV infected pregnant women. A total of 262 pregnant women were monitored. The majority of the respondents were aged 20-29 years, were rural dwellers, belonged to the low to middle income group with low educational levels. Similar findings were reported earlier (Ott *et al*., 2012; El-shabrawi *et al*., 2013; Fomulu *et al*., 2013; Esan *et al*., 2014). Women who live in rural settings and are of lower income status are more likely to engage in risky behaviors that will expose them to the infection. Sharma *et al*., (1996) and Chandan *et al*., (2012) also asserted women in rural settings with low educational background had insufficient knowledge regarding HBV infection and its mode of transmission. Majority of the participants 160/262 had HBV DNA $>10^6$ copies/ml. The study found a positive association between low education and high maternal HBV DNA. HBV viral load is directly related to the risk of disease progression in infected adults (Pan *et al*., 2012; Xu *et al*., 2014; Dionnic-Odom *et al*., 2016). It was also reported that most HBV infections are asymptomatic (WHO, 2015) and would be come symptomatic with increased HBV DNA levels. Earlier report found positive association between symptomatic HBV infection and foul smelling liquor, PROM, previous abortion and a history of STI/UTI (Siakwa *et al*., 2014). Such association was expected with increased HBV DNA levels. The present study found high HBV DNA levels to be associated with PROM and a history of STI/UTI. The pathogenesis of PROM is explained by the role of pro inflammatory cytokines in HBV infected individuals (Lupii *et al*., 2002). Similar assertion was made for the high prevalence of PROM in STI/UTI. Increased viral load will increase the production of pro inflammatory cytokines which would affect inflammation of the membranes. HBV infection in pregnant mothers was reported to be associated with preterm delivery, low Apgar score and low birth weight (Leobstein *et al*., 2011; Lao *et al*., 2012; Siakwa *et al*., 2014). The current study found a significantly increased risk of low birth weight with high HBV DNA levels. It was reported that inflammatory cytokines affect placenta function (Xu *et al*., 2002, 2009& 2014). Fetal oxygen and nutrient supply would be affected leading to intra uterine growth retardation hence low birth weight.

Conclusion

High maternal HBV DNA level increased an infected mother's risk for PROM and delivery of low birth weight babies.

Screening of HBV infected mother for viral load would help identify high-risk group for initiation of antiviral therapy not only to reduce the incidence of PROM and low birth weight but also prevent MTCT.

REFERENCES

Borgia G, Carleo MA, Gaeta GB, Gentile I 2012. Hepatitis B in pregnancy. *World J. Gastroenterol.,*18(34): 4677 - 4683.

Chandan KS, Sanjoy KD, KamrulHS *et al*. 2012. Neonatal Sepsis: A Review. *Bangladesh J. Child Health,* 36(2): 82 - 89.

Cho, Y., Bonsu, G., Akoto, A. A, *et al*. 2012. The prevalence and risk factors for hepatitis B surface Ag positivity in pregnant women in Eastern Region of Ghana. *Gut Liver. 6*(2):235 - 240. 14.

Copolla N, Loquercio G Tonziello G *et al*. 2013. Hepetitis B virus transmission from an occult carrier with five mutation in the major hydrophilic region to immunosuppressed plasma recipient. *J clin. Virol.*, 58(1): 315-317

delCanho R, Groshede PM, Mazel JA *et al*. 1997. Vaccination program The Netherland 1982-1992protective efficacy and long-term immunogenicity. *Vaccine,* 15:16244-50

Dionnic –Odom J, Tita ATN, Silverman NS 2016. Hepatits B in pregnancy screening, treatment and prevention of vertical transmission. *Am. J Obst and Gynaecol.,* 38:6-14.

Dunkelberg, J. C., Berkley, E. M. F., Thiel, K. W., & Leslie. K. K. 2014. Hepatitis B and C in pregnancy: a review and recommendations for care. *J Perinatol* 34: 882–891; doi:10.1038/jp.2014.167. Retrieved at http://www.nature.com/jp/journal/v34/n12/full/jp2014167a.html

El-Shabrawi M, Mohamed FM *et al*. 2013. Prevalence of hepatitis B virus infection among Egyptian pregnant women - A single center study. *Int. J. of Trop. Dis. and Health*, 3(2): 157 – 168.

Esan AJ, Omisakin CT, Ojo-Bola T *et al*. 2014. Sero-prevalence of hepatitis B and hepatitis C virus co-infection among pregnant women in Nigeria. *Am. J. Biomed. Res*., 2(1): 11 - 15.

Fomulu, N.J., Morfaw, F.L., Torimiro, J *et al*. 2013. Prevalence, correlates and pattern of Hepatitis B among antenatal clinic attenders in Yaounde-Cameroon: is perinatal transmission of HBV neglected in Cameroon? *BMC Pregnancy and Childbirth*, 13: 158.

Gentile I & Borgia 2014. Vertical transmission of hepatitis B virus Challenges and solutions. *Int. J Women Health*, 6:605-611

Giogiana, F.B., Ioan, S., Ioan, M. *et al*. 2010. Sepsis in newborns. TMI. 60 (4).

Kowdley, K.V., Wang, C.C, Welch, S. 2012. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatol* 56:422. Retrieved on 15/10/2015 at www.uptodate.com/contents/epidemiology-transmission-and-prevention-of-hepatitis-b-virus-infection/abstract/4

Lao, T.T., Sahota, D.S., Suen, S.S.H. *et al*. 2012. Maternal HBsAg status and infant size – a Faustian bargain? *J. Viral Hep.* 19:519- 524.

Lobstein S, Faber R, Tillmann HL 2011. Prevalence of hepatitis B and its impact on Germany. *Digestion.* 83: 76 – 82

Nelson PN, Jamieson DJ, Murphy TV. 2014. Prevention of perinatal hepatitis B virus transmission. *J Paed. Infect Dis.*, 3(1): S7-S12

Ott, J.J., Stevens, G.A., Groeger, J., Wiersma, S.T. 2012. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBs Agseroprevalence and endemicity. *Vaccine* 2012; 30:2212.

Pan CQ, Duan ZP, Bhamidimani RR *et al*. 2012. An Algorithm for risk assessment and intervention of mother to child transmission of hepatitis B virus; *Clin. Gastroenterolhepat,* 10:452-9

Pan CQ, Mi LJ, Bhamidimani RR *et al*., 2012. Tonofovir Dispproxil Fumurate for prevention of vertical transmission of hepatitis B virus infection by highly viremicwomen ; A case series. *Dig Dis Sci.,* 57(9) 2423-2429

Safir, A., Levy, A., Sikuler, E., Sheiner, E. 2010. Maternal Hepatitis B virus or Hepatitis C virus carrier status as an independent Risk Factor for adverse perinatal outcome. *Liver Int.*, 30:765 - 770.

Shaheen, A.A.M., & Myers, R.P. 2010. The outcomes of pregnancy in patients with cirrhosis: a population-based study. *Liver Int*., 30: 275 – 83

Sharma R, Malik A, Rattan A *et al*. 1996. Hepatitis B virus infection in pregnant women and its transmission to infants. *J. Trop. Ped*., 42(6):352 - 354.

Shui-Lam, M. A. K., & Kwok-Yin, L. 2013. Hepatitis B Carriers in Hong Kong: Prevalence and Pregnancy Outcomes. *Hong Kong J GynaecolObstet Midwifery* 13(1):67-73 retrieved at http://hkjgom.org/sites/default/files/pdf/v13-p67-hepatitis.pdf

Siakwa, M., Kpikpitse, D., Ankobil, A. *et al*. 2014. Effects of Chronic Hepatitis B Infection on Pregnancy And Birth Outcomes In Ghana.*Int. J Res Med HealthSci.,* 4(5):1-12 http://ijsk.org/uploads/3/1/1/7/3117743/1_chronic_hepatitis_b.pdf

Singh AE, Plitt SS, Oslowy L *et al*. 2011. Factors associated with vaccine failure and vertical transmission of hepatitis among a cohort of Canadian mothers and infants. *J VirHepat,* 18:468-473.

Wiseman E, Fraser MA, Holden S *et al*. 2009. Perinatal transmission of hepatitis of virus: an Australian experience. *Med J Australia*, 190:489-92

World Health Organization 2015. Guidelines for the prevention, care and treatment of persons living with chronic hepatitis B infection. Retrieved on 15/10/2015 at http://www.who.int/mediacentre/factsheets/fs204/en/

Xu DZ, Yan YP, Choi BC *et al*. 2002. Risk factor and mechanism of transplacental transmission of hepatitis B virus: A case control study. *J Med Virol.,* 67:20-26

Xu H, Zong T, Lui JY *et al*. 2014. Measures to reduce MTCT of hepatitis B virus a Chinese meta analysis. *Dig Dis Sci.,* 59(2)242-258

Xu WM, Cui YT, Wang *et al*. 2009. Lamivudine in late pregnancy to prevent perinatal transmission of Hepatitis B viral infection; a multicenter randomized double blind placebo controlled study. *J virHepat.,* 16:94-103

Zhu Q, Yu G, Yu H *et al*. 2003. A randomized control trial on interruption of HBV transmission in uterus. *Chinese Med J.* (*Engl*), 116:685-7

Zou H, Chen H, Duan Z *et al*. 2011. Virologic factors associated with failure of passive-active immunoprophylaxis in infant born to HBsAg positive mothers. *J VirHepat.,* (E Pub, ahead of Print).

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