9-1-2014

Effects of Chronic Hepatitis B Infection on Pregnancy and Birth Outcomes in Ghana

Mate Siakwa
University of Cape Coast, Ghana

Dzigbodi Kpikpitse
Garden City University College

Amandus Ankobil
University of Cape Coast, Ghana

Sylvia C. Mupepi
Grand Valley State University, mupepis@gvsu.edu

Mildred John
University of Calabar, Nigeria

See next page for additional authors

Authors
Mate Siakwa, Dzigbodi Kpikpitse, Amandus Ankobil, Sylvia C. Mupepi, Mildred John, Patience Doe, Nancy Ebu, Shadrach Dare, and E Hansen Owoo

Sept. 2014. Vol. 4, No.5 ISSN 2307-2083
International Journal of Research In Medical and Health Sciences

http://www.ijsk.org/ijrmhs.html

EFFECTS OF CHRONIC HEPATITIS B INFECTION ON PREGNANCY AND BIRTH OUTCOMES IN GHANA

[1*]MATE SIAKWA, [2]DZIGBODI KPIKPITSE, [1]AMANDUS ANKOBIL, [3]SYLVIA MUPEPI [4]MILDRED E JOHN, [1]PATIENCE F DOE, [1]EBU I NANCY, [1]SHADRACH DARE, [5]E HANSEN-OWOO

[1.] School of Nursing, University of Cape Coast, Cape Coast, Ghana.
[2.] School of Nursing, Garden City University College, Kumasi, Ghana.
[3.] Kirkhoff College of Nursing, Grand Valley State University, USA.
[4.] University of Calabar, Calabar, Cross River State, Nigeria.
[5.] Cape Coast Teaching Hospital, Cape Coast, Ghana.
***Correspondence:** msiakwa@ yahoo.co.uk

ABSTRACT

Ghana is a known endemic area for hepatitis B virus (HBV) infections, yet the consequences of HBV infection on pregnancy outcomes are unknown. This prospective cohort study was thus conducted among 512 pregnant women attending antenatal clinic in the Cape Coast Teaching Hospital, Ghana, between January, 2011 and December, 2013 to determine the effects of hepatitis B during pregnancy on birth outcomes in Ghana. The HBsAg status of all pregnant women was determined by the latex agglutination test while a researcher administered semi-structured checklist was used to collect demographic/obstetric/medical data of respondents. We obtained 262 HBsAg positive and 250 HBsAg negative women most of whom were aged 20-29 (40%), classified themselves as low income earners (50%), and had attained primary education (42%). Logistic regression analysis showed that pregnant women who had chronic hepatitis B were more likely to develop PROM (p=0.008) and foul smelling liquor (p=0.024) at delivery. Moreover, neonatal consequences for chronic hepatitis B were; preterm babies (p=0.002), underweight (p<0.001), Apgar score lower than 7 (p<0.001), asphyxia at birth (p=0.006) and still birth (p=0.04). We conclude that babies born to mothers with positive HBsAg status have a higher risk for vertical transmission as well as adverse neonatal consequences.

Keywords; Hepatitis B, neonatal outcome, pregnancy outcome, Ghana

INTRODUCTION

Hepatitis B virus (HBV) infection in pregnancy is an important public health issue, particularly in developing countries. Hepatitis B virus is a DNA virus that could be transmitted percutaneously, sexually, or perinatally and over 350 million individuals around the world are chronic carriers (Deinstag, 2008 and WHO, 2000). Majority of the world's chronic HBV infection carriers, especially children, acquire this infection via the perinatal route (Jonas, 2009 and Lavancy, 2004). Compared to the adult, a child who develops HBV infection at an early age has about 80-90% greater chance of progressing into a chronic state and thus hepatic failure (Chang, 2000). Fifteen to 40% of HBV infected persons would develop cirrhosis of the liver, liver failure or hepatocellular carcinoma (Lok, 2002), and 500,000 – 1.2 million people die of HBV infection annually (Lee, 1997 and Mahoney, 1999). Sub Saharan Africa remains one of the highest endemic regions for HBV infection (WHO, 2000). An estimated 50 million cases of chronic HBV infection live in Africa (Blankson et al., 2005). In Ghana, sero-prevalence rate of HBV infection ranges from 6.7% to 10% in blood donors (Acquaye, 1991), 15.6% in children (Martinson et al., 1996), and 10.5% in pregnant women (Cho et al., 2012).

Acute hepatitis B may present as asymptomatic or with unspecific symptoms that make diagnosis challenging. Common signs associated with HBV infection include nausea, vomiting, anorexia, mild diarrhoea, malaise and pain over the abdomen. In the empty uterus these signs are similar to influenza but in the gravid uterus these signs could mimic signs of pregnancy and this may present a 'unique challenge' to diagnosis of HBV infection during pregnancy (Fraser et al., 2003). Thus the presence of hepatitis B surface antigen (HBsAg) in the bloodstream remains the serological hallmark for diagnosis (Fraser et al., 2003). In resource poor regions however, the facilities to conduct this test may not be readily available to the entire population so that the HBsAg status of the pregnant woman may not be known prior to labour. The practices of women in developing countries tend to increase their chance of contracting HBV infections. For instance, most women in developing countries, unfortunately, have insufficient knowledge regarding mode of transmission of hepatitis B (80%) and less than 10% of women of childbearing age are fully immunised against HBV infection (Sharma et al., 1996).

The relationship between HBV infection and pregnancy is complex and incompletely understood. While most authors agree that pregnancy does not necessarily worsen liver function, other authors suggest there may be a change in liver size and blood flow in pregnancy (Fraser et al., 2003; Nguyen et al., 2009). In addition, the rare occurrence of intrahepatic cholestasis of pregnancy (ICP) have caused some authors to call careful interpretation of laboratory results in pregnancy and also for further studies into hepatic changes in pregnancy (Fraser et al., 2003; Nguyen et al., 2009 and Potthoff et al., 2009). Normal pregnancy is associated with high levels of adreno-corticosteroids, alanine aminotransferase (ALT) and oestrogen hormones resulting in increased HBV viremia (ter Borg et al., 2008). These hormonal and cytokine changes could also lead to fluctuations in liver function tests.

Literature regarding the effects of Hepatitis B virus infection on pregnancy is sparse and results from these studies have found conflicting results. The few studies published on the subject have also been based predominantly in the Eastern and far Eastern countries. While some authors suggest that maternal HBV infection may be associated with adverse pregnancy outcomes like gestational diabetes, antepartum haemorrhage, birth defects, still births and preterm birth (Shepard, 1998; Ka, Lai and Terence, 2005; Gambarin-Gelwan, 2007; Safir et al., 2010; Elefsiniotis et al., 2010; Aghamohammadi and Nooritajer, 2011; and Borgia et al., 2012), other studies have suggested that acute HBV infection in pregnancy has no teratogenic effects (Jonas, 2009; Wong et al., 1999; To et al., 2003; and Lobstein et al., 2011). Such conflicting results have been largely influenced by the research setting in which these studies were conducted. Studies conducted in high prevalence regions like Asia were more likely to report significant associations, compared to studies in low endemic areas like the United Kingdom (Ma and Bauman, 1996; Chen et al., 2000; and Kawsar and Goh, 2002). On the contrary, other studies conducted in low endemic regions that have reported high incidence of adverse pregnancy outcomes among pregnant women born in high endemic regions (Von Katterfield et al., 2011). The authors, unfortunately, did not measure the HBV status of pregnant women (Von Katterfield et al., 2011). A suggestion that these excess deaths in women of high endemic regions may be related to their HBV statuses, however, may not be misplaced.

Birth weight is perhaps the only pregnancy outcome that has been studied extensively with regards to its relationship with maternal HBsAg status. Yet the results of several studies have not been consistent. Many studies have found a significant positive relationship between a positive maternal HBsAg status and infant birth weight, despite no differences in obstetric complications (Lao et al., 2012) and others have found negative associations (Shepard, 1998). In a large retrospective cohort study in China, Lao et al. found that HBsAg status was significantly associated with marcrosomic infants after adjusting for sex, BMI, age and gestational diabetes mellitus (OR; 1.11), but significant associations were observed for the male gender. Although in some medical literature, a positive association between infant macrosomia (birth weight >4kg) and gestational diabetes mellitus has been recorded (Lao et al., 2012 and Gambarin-Gelwan, 2007), other studies have reported the opposite (Tse et al., 2005; and Lao

et al., 2007). This contrary observation has made interpretation of the effects of infant macrosomia associated with positive maternal HBsAg status challenging. On one hand, if maternal HBV infection increases foetal growth and size, then this could be beneficial as low birth weight is associated with future cardiovascular complications (Saleh-Gargari et al., 2009; Mi et al., 2000; Hardy et al., 2005; and Whincup et al., 2008). On the other hand, however, infant macrosomia could be a risk factor for adolescent obesity, diabetes mellitus and cancer (Okasha et al., 2002; Hjalgrim et al., 2004; and Fomulu et al., 2013). Clarification of the effects of maternal HBV infection on pregnancy outcomes is thus very important especially in endemic regions.

MATERIALS AND METHODS

Research design

This was a prospective cohort study conducted among pregnant women attending antenatal clinic in the Cape Coast Teaching Hospital, Ghana between January 2011 and December 2013. These pregnant women were followed over the study period, from the time of recruitment at antenatal clinic until they were delivered. Demographic, medical and obstetric data of the pregnant women were taken at recruitment and data on the characteristics of their babies, birth outcomes and mode of deliveries were collected at the end of the study. Informed consent was obtained from the pregnant women prior to data collection. The authors also obtained ethical clearance from the Institutional Review Boards of the University of Cape Coast and the Cape Coast Teaching Hospital, Ghana.

Demographic, obstetric and medical data collected from pregnant women were; age, education, employment status, parity, premature rupture of membranes (PROM), antenatal attendance, mode of delivery, maternal urinary tract infection/sexually transmitted infections (UTI/STI), bleeding during pregnancy/APH, history of previous abortion, pregnancy-induced hypertension (PIH), foul smelling liquor, and prolonged labour. Characteristics of babies born to the pregnant women included in this study were; sex, gestational age, birth weight, Apgar score at minute one and five, birth outcome and level of oxygenation at birth.

At recruitment, the pregnant women were categorized into exposed and not-exposed groups based on their HBsAg status. In Ghana, all pregnant women undergo medical screening during the antenatal period and this includes a test for the hepatitis B status. The HBsAg status of all pregnant women included in the study was thus checked from patient's folder and confirmed by the latex agglutination test, a serological test for HBsAg done by a registered biomedical scientist according to the standard protocols of the Ghana Health Service. An exposed group was determined as a pregnant woman who had seroconverted for HBsAg for six months or more. An internal comparison group of pregnant women who had not seroconverted for HBsAg was selected as a not-exposed group. A cohort study, using an internal comparison group, was preferred because the incidence of hepatitis B among pregnant women in Ghana, though not known by certainty, is perceived to be small as in neighbouring African countries of similar demographics (Fomulu et al., 2013). For the purpose of this study, a pregnant woman in the exposed group, i.e. with Hepatitis B, would be referred to as case and a pregnant woman without hepatitis B would be referred to as control.

A researcher developed semi-structured checklist was developed as the main instrument for data collection. The contents of the checklist were based on hypothesised demographic, medical, obstetric and neonatal characteristics likely to be influenced by chronic Hepatitis B infection. The checklist was pretested in a pilot study before its use in the present study. Research assistants, mostly midwives, were specially trained on the use of the instrument so they could administer the checklist.

Conceptual definitions

Premature infant: a live born infant delivered before 37 weeks of pregnancy (based on the Ballard score or from first day of last menstrual period).

Low birth weight: A neonate whose birth weight is <2.5 kilograms. Birth weight was determined

at birth for each neonate using a standardised and calibrated infant weighing scale. The neonate was undressed and put on the scale in a ventral position.

Premature rupture of membranes (PROM): the time from membranes' rupture to onset of delivery more than 18 hours.

Meconium stained amniotic fluid (MSAF): was considered if the amniotic fluid was green in colour or mixed with meconium, or appears meconium stained in the baby.

Asphyxia: Apgar score less than 3 in the first 5 minutes from delivery.

Statistical analysis

Data from the checklist were processed and analysed using computer assisted Statistical Package for Social Sciences Version 20.32 (SPSS ver. 20.32). Pearson's chi-squared was used to determine significant differences, if any, between cases and controls with respect to the several outcome or dependent variables included in this study. Thus significant associations between dependent maternal and neonatal characteristics and the independent variable, HBsAg status, of the mothers were determined. Logistic regression analyses were used to determine the risk of maternal hepatitis B infection for maternal and neonatal outcomes, compared to a reference parameter of a variable. Mean differences were considered statistical significant a p-value <0.05.

RESULTS

The study comprised 512 mothers and their respective babies. The average age of mothers in this study was 20-29 years, considered herself of low income earning status, had attained a primary education, and lived in a rural setting. Table 1 shows the distribution of the demographic characteristics of cases and controls. It is clear there was no statistically significant difference between the case and control groups in terms of age (p=0.683), income (p=0.329), educational level (p=0.339), and residence (p=0.326). The groups were thus comparable.

Table 1: Socio-demographic Characteristics of Respondents

Parameters	Variables	Case (n=262)	Control (n=250)	X^2	p-value
Age	<20 20 – 29 30 – 39 ≥ 40	54 104 72 32	50 102 60 38	1.498	0.683
Income	Low Medium High	124 90 48	132 71 47	2.223	0.329
Educational Level	Illiterate Primary Secondary Tertiary	91 101 42 18	92 112 28 18	3.366	0.339
Residence	Rural Urban	160 102	142 108	0.964	0.326

Table 2 presents the maternal obstetric characteristics of the mothers who participated in this study. Majority of the mothers had one child (77%), did not have history of premature rupture of membranes, PROM (73%), did not have PIH (75%), and did not have history of foul smelling liquor (85%), no history of previous abortion or history of UTI/STI (79%). Results of chi squared analysis showed significant differences between cases and controls in terms of parity (p=0.001),

PROM (p=0.008), foul smelling liquor (p=0.024), and maternal history of UTI/STI (p=0.005). Compared to mothers who had one child, mothers with hepatitis B were less likely to two children (OR= 0.315; 95% CI: 0.13-0.68) but more likely to have three or more children (OR= 1.54; 95% CI: 0.95-2.5). The study also observed that mothers with positive HBsAg status were more likely to have PROM (OR=1.71 95% CI: 1.151 – 2.556), foul smelling liquor (OR= 2.023 95% CI: 1.093 – 3.889), and HO/UTI/STI (OR= 1.854 95% CI: 1.198 – 2.902). There were no significant differences between the case and control groups in terms of PIH and previous abortions and the confidence interval for the association between Hepatitis B in the mother and parity overlapped 1. Therefore it is likely the result happened by chance.

Table 2: Maternal Obstetric Characteristics of Respondents

Parameters	Variables	Case (n=262)	Control (n=250)	X^2	P-Values	Odd Ratio	CI	
							Lower	Upper
Parity	1	201	192	13.294	0.001			
	2	27	8			0.315	0.130	0.684
	≥ 3	34	50			1.536	0.954	2.499
PROM	Present	84	54	7.111	0.008	1.710	1.151	2.556
	Absent	178	196					
PIH	Present	71	55	1.793	0.181	1.317	0.879	1.980
	Absent	191	195					
Foul Smelling Liquor	Present	32	16	5.089	0.024	2.023	1.093	3.889
	Absent	230	234					
Previous Abortion	Present	43	36	0.397	0.529	1.166	0.720	1.897
	Absent	219	214					
HO/UTI/STI	Present	67	39	7.750	0.005	1.854	1.198	2.902
	Absent	195	211			1.143		

Table 3 shows foetal birth outcomes of mothers with and without Hepatitis B. The differences in the distributions of gestational age, birth weight, Apgar score at first minute, Apgar score at fifth minute, birth outcome, and asphyxia is shown by chi squared analysis and the risk of outcome in the case and control groups is shown by odds ratios of the logistic regression analysis. Results of chi-squared analyses reveal significant differences in gestational age (0.002), birth weight (<0.001), Apgar scores at first (<0.001) and fifth minute (<0.001), birth outcome (0.04), and asphyxia status at birth (0.006). Cases were significantly more likely to have preterm babies than controls (27% vs 16%), more likely to have children of low birth weight than controls (29% vs 16%), more likely to have children of Apgar scores less than 7 than controls (26% vs 9%), more likely to have children still birth than controls (4% vs 1%) and more likely to have asphyxiated babies than controls (11% vs 9%).

Results of logistic regression analysis showed that mothers with hepatitis B were about twice more likely to have preterm babies [1.98 (1.29-3.08)], deliver babies with low birth weight [2.2 (1.44-3.43)] and babies with Apgar score less than 7 in the first minute [2.03 (1.38-3.01)]. Mothers with hepatitis B were 70% less likely than mothers without hepatitis B to have babies born alive [0.29 (0.062-0.95)]. Mothers with hepatitis B were again more likely to have babies born asphyxiated, however the confidence interval overlapped 1[1.23 (0.69-2.21)], thus the possibility that this result occurred by chance cannot be ruled out.

Sept. 2014. Vol. 4, No.5 ISSN 2307-2083
International Journal of Research In Medical and Health Sciences

http://www.ijsk.org/ijrmhs.html

Table: 3 Neonatal Characteristics of Infant Born to Respondent

Parameters	Variables	Case (n=262)	Control (n=250)	Chi-Square	P-Values	Odd Ratio	CI	
							Lower	Upper
Gestational Age	Preterm Term	72 190	40 210	9.867	0.002	1.984	1.291	3.084
Birth Weight	<2500g ≥2500g	76 186	39 211	13.205	<0.001	2.204	1.435	3.428
Apgar Score at 1 min	< 7 ≥ 7	97 165	56 194	13.055	<0.001	2.032	1.380	3.012
Apgar Score at 5 min	< 7 ≥ 7	68 194	22 228	25.983	<0.001	3.608	2.180	6.186
Birth Outcome	Live Still Birth	251 11	247 3	4.325	0.038	0.288	0.062	0.951
Asphyxia	Present Absent	29 233	23 227	7.461	0.006	1.226	0.688	2.208

DISCUSSION

This study is first to investigate the consequences of chronic hepatitis B virus infection among pregnant women on the outcome of pregnancy in Ghana. The study included a total of 512 pregnant women; 262 classified as HBsAg positive and 250 as HBsAg negative. Although the study methodology employed in this study does not allow us to determine the prevalence of hepatitis B among pregnant women in Ghana, it could be said that pregnant women aged between 20-29 years, of low income status, had attained a maximum of primary education and lived in a rural setting were overrepresented in the sample of pregnant women with hepatitis B. Many studies published on the prevalence of hepatitis B among pregnant women or women for that matter concur that women aged less than 30 and of less socioeconomic status are at higher risk for contracting Hepatitis B (El-Shabrawi et al., 2013 and Esan et al., 2014). Medical literature on the lifestyle practices which influence HBV infection is not lacking (Lewis et al., 2014; Wong et al., 2006). All these studies agree that factors that predispose women to sexually transmitted infections in general-multiple sex partners, multiple STIs, sharing of sharps- also predispose women to contracting hepatitis B. Women who live in rural settings and are of lower income status are likely to engage in these 'risky' behaviours. Other studies have also identified that women in rural settings and of lesser education had insufficient knowledge regarding HBV infection and its mode of transmission (Sharma et al., 1996 and Chandan et al., 2012).

Neonatal Consequences

Many authors agree that the presence of hepatitis B infection during pregnancy has more detrimental effects for the foetus and neonate than the mother (Fraser et al., 2003 and Wong et al., 2006). It is established that neonates born to mothers with hepatitis B stand a greater chance, about 90%, of acquiring HBV infection at birth (Chang, 2000). Without immunisation, or if immunisation is unable to clear the infection, neonates who acquire infections at an early age are at an increased risk of progressing to chronicity or hepatocellular carcinoma in the worst situation (Chang, 2000). This study observed that babies born to mothers with chronic hepatitis B infection have higher risk for

preterm birth, low birth weight, lower APGAR score at birth (<7) and neonatal asphyxia at birth. Studies on the effects of hepatitis B infection in mothers on neonatal outcomes is insufficient, however literature on the effects of neonatal sepsis on neonatal outcomes is not lacking (Chandan et al., 2012 and West and Tabansi, 2012). Most of these studies on the effects of neonatal sepsis on neonatal outcomes have maintained the classical definition for defining neonatal sepsis as an infection occurring within 28 days of birth. Thus by this definition, a neonate who acquires hepatitis B infection at birth may be classified as having neonatal sepsis. Yet it is known that almost all (9 out of 10) babies born to mothers with hepatitis B would acquire the infection (Chang, 2000). Unfortunately, previous studies on the effects of neonatal sepsis on neonatal outcome did not adjust for maternal hepatitis B, thus it is not out of place to suggest that studies that found positive relationships between neonatal sepsis on neonatal outcomes could apply to neonatal hepatitis B infection. When findings of the current study are viewed in the lens that neonates born to mothers with HBV infections had the infection, it would then follow the biological mechanism that neonates with sepsis, in

this case HBV infection, would have weak defences for extra uterine life, thus the adverse consequences observed (Shah et al., 2006 and Al-Dasoky et al., 2005). We however, explain these findings with caution, as we were unable to determine the hepatitis B status of neonates born to HBsAg positive mothers in the present study. Neither could we adjust for some characteristics, maternal demographics for example, thus an alternative explanation of confounding may not be easily dispelled (Webb and Bain, 2011).

The few studies published on the neonatal consequences of maternal hepatitis B infection in pregnancy have concentrated on infant birth weight, but results from these studies is not consistent (Shepard, 1998; Wong et al., 2003; Lao et al., 2012). In a recent Chinese study on the effect of maternal hepatitis B infection on infant size, Lao et al. found a positive maternal HBsAg status to be associated with high birth weight. Other studies however, have found no association between maternal HBsAg status and infant size (Wong et al., 2003). Lao et al., suggests that since maternal hepatitis B status is associated with gestational diabetes (Tse et al., 2005), and gestational diabetes is associated with infant marcosomia, therefore, it is not surprising that maternal hepatitis B may be associated with high birth weight. It is however, not known whether an increased birth weight for babies born of mothers with Hepatitis B may be beneficial or would have long term detrimental consequences, especially in developing countries. This study supports previous findings which found a negative association between a mother with chronic hepatitis B and infant size (Wong et al., 2003). In the current study, babies who weighed less than 2.5kg at birth were about 2 times more likely to have mothers who had positive HBsAg status during pregnancy. This association could be due to the observation that mothers with hepatitis B in this study were more likely to be of low socio economic status, gained less education and lived in rural settings. These factors, unfortunately, are also associated with low birth weight. Given contrasting evidence from this study and previous ones regarding the effect of maternal hepatitis B infection on birth weight, it would have been ideal to determine which of the two, an increase birth weight or low birth weight would have detrimental effects on the health of the neonate. This is however, beyond the scope of the current study, thus further studies are recommended.

This study agrees with former studies that found that maternal HBsAg status was associated with preterm birth. The possible theory underlying this relationship could be the general effects of neonatal infections on birth outcome (Nithin et al., 2009). The significant increase in pro inflammatory cytokines among pregnant women with chronic hepatitis B (Sheron et al., 1991; Bozkaya et al., 2000 and Luppi et al., 2002) could be an alternative explanation to the significant number of preterm births among mothers with chronic hepatitis B infection in this study. Mothers with a positive HBsAg status were found to be more likely to have neonates with low APGAR scores at birth and neonatal asphyxia compared to women with a negative HBsAg status. Previous studies on these variables are rare.

Maternal Consequences

To date only a few of studies have sought to determine the effects of chronic HBV infection on pregnancy outcomes. A few of these studies focusing on maternal HBsAg carrier status and pregnancy outcome have reported that, HBsAg positive mothers have an increased risk for adverse pregnancy outcomes including maternal complications (Ka et al., 2005; Gambarin-Gelwan, 2007; and Aghamohammadi and Nooritajer, 2011). Results of this study showed significant positive relationship between a positive HBsAg status of mother in pregnancy and PROM and foul smelling liquor. There was however no association between pregnancy-induced hypertension (PIH) and previous abortions and HBsAg carrier status.

It remains true that scientific evidence regarding the effects of chronic hepatitis B infection of mother in pregnancy on maternal outcomes in pregnancy is inadequate. It is not clear whether indeed studies regarding this area are yet to be published or it is due to the possibility of publication bias, where studies that found insignificant relationships were not published. Another alternative explanation could be that scientists are yet to develop interest for this area of research. But this is unlikely, as earlier studies regarding hepatitis B have been published over two decades. The inherent methodological challenge associated with investigating the effects of a disease on pregnancy outcomes could be another challenge. This is because a cohort study, at best, may be the highest form of evidence or most rigorous study that may answer such research questions as it would be unethical to use an experimental design, a randomised controlled trial for example (Carneiro and Howard, 2011). Observational studies, including cohort studies, have serious limitations- residual confounding for example which limits an inference for a causal relationship.

Biological explanations to the possible mechanism underlying the relationship between hepatitis B and pregnancy outcomes are not convincing. However, Luppi et al. believes that the increase in pro inflammatory cytokines associated with chronic hepatitis B infection in pregnancy may be responsible for the heightened adverse outcomes observed in positive HBsAg mothers. This belief may be supported by the clear evidence of the effects of liver cirrhosis, a possible end stage of chronic hepatitis B, on pregnancy outcomes. Many studies agree that liver cirrhosis during pregnancy has detrimental consequences for the mother (Tan et al., 2008; Shaheen and Nyers, 2010; and DegliEsposti and Shah, 2011).

Significant positive relationship observed between a positive HBsAg status of mother in pregnancy and PROM and foul smelling liquor in this study is not surprising. Earlier studies have identified PROM (Vinodkumar et al., 2009; Giogiana et al., 2010; and West and Tabansi, 2012), maternal UTI/STI (Webb and Bain, 2011) and foul smelling liquor (Shah et al., 2006 and West and Tabansi, 2012) as significant risk factors for neonatal sepsis. The risk for vertical transmission of HBV infection to neonates born to HBsAg positive mothers has been discussed earlier. It therefore makes sense that PROM and foul smelling liquor were identified as consequences of chronic HBV infection in pregnancy. This argument may validated by the fact that this study did not observe PIH or history of previous abortions as consequences of chronic HBV infection in pregnancy as none of these are risk factors for HBV infections. The authors suggest further studies to investigate this.

CONCLUSION

Babies born to mothers with positive HBsAg status have higher risk for vertical transmission as well as adverse neonatal consequences. Mothers with positive HBsAg during pregnancy are also likely to suffer some adverse outcomes. It is recommend that mothers with positive HBsAg status receive immunoprophylaxis and immunisations for HBV infection for babies be completed for all children. Further studies regarding long term consequences of HBV infection in pregnancy is recommended.

STRENGHTS AND LIMITATIONS

The main strength of this study is that it is the first study in Ghana, as far as the authors are concerned, to have investigated the consequences for Hepatitis B in pregnancy. Previous attempts to document on this subject focused on Hepatitis E rather than Hepatitis B (Bonney et al., 2012). Another, strength of this study which distinguishes it from previous

studies is the rigorous methodology employed. Unlike a previous study which was a case report on 3 people (Bonney et al., 2012), this study had a large sample size which increased the power of the study, a longitudinal study design and a population wide study. Classification of exposure status, hepatitis B status of pregnant women, was also based on biochemical tests rather than self-reportage which although would have made study cheaper yet would not be devoid of information bias.

The main outcome measure in this study was the odds ratio of outcome (dependent variables), which was estimated as the odds of outcome in cases divided by the odds of outcome in the controls (Carneiro and Howard, 2011). Unfortunately, pregnant women selected for this study was based on their HBsAg status, rather than a random sample from a population of pregnant women. Thus while we acknowledge that this study could not determine, directly, the prevalence or incidence of hepatitis B among pregnant women in the general population, the odds ratio of outcome as determined in this study provided good information on the possible effects of perinatal hepatitis B on pregnancy outcomes.

The last methodological challenge facing this study is that the authors reported unadjusted odds ratios as measure of association. While the use of odds ratios to measure associations is justified, the inability to adjust for possible confounding factors make an alternative explanation in favour of confounding factors plausible. Again, the use of an observational design means the authors cannot infer a causal relationship for results observed. An observational study, however, seem the best approach to investigate the consequence of chronic hepatitis B virus infection on pregnancy, as an experimental approach would not pass ethical approval!

REFERENCES

1. Acquaye JK (1991). Hepatitis Bs Antigen Carrier status among Ghanaian blood donors. Ghana Med. J. 25: 366 - 368.
2. Al- Dasoky AH, Faten Al- Awasheh NF, Kaplan MN, Hanadi A, Al- Rimawi AH, Aga MR, Abu-Setteh HM (2005). Risk Factors for Neonatal Sepsis in Tertiary Hospital in Jordan. J. Royal Med. Serv. 16.
3. Aghamohammadi A, Nooritajer M: Maternal HbsAg carrier and pregnancy outcome. Australian Journal of Basic and Applied Sciences 2011, 5(31): 607 - 610.
4. Blankson A, Wiredu EK, Gyasi RK, Adjei A, Tettey Y (2005). Seropevalence of hepatitis B and C virus in cirrhosis of the liver in Accra, Ghana. Ghana Med. J. 39(4): 134 – 137.
5. Bonney JHK, Kwame-Aryee RA, Obed S, Tamatey AA, Barnor JS, Armah NB, Oppong SA, Osei-Kwesi M (2012). Fatal hepatitis E viral infection in pregnant women in Ghana: a case series. BMC Research Notes. 5: 478.
6. Borgia G, Carleo MA, Gaeta GB, Gentile I (2012). Hepatitis B in pregnancy. World J. Gastroenterol. 18(34): 4677 - 4683.
7. Bozkaya H, Bozdayi M, Turkyilmaz R, Sarioglu M, Cetinkaya H, Cinar K (2000). Circulating IL – 2, IL – 10 and TNF- alpha in chronic hepatitis B: their relations to HBeAg status and the activity of liver disease. Hepatogastroenterology. 47: 1675-1679.
8. Cameroon: is perinatal transmission of HBV neglected in Cameroon? BMC Pregnancy and Childbirth. 13:158.
9. Carneiro I, Howard N (2011). Introduction to Epidemiology. 2nd edition. Open University Press. UK.
10. Chandan KS, Sanjoy KD, Kamrul HS, Jubair C, Mannan AM, Jashimuddin MD, Tariqul IMD, Mohammod S (2012). Neonatal Sepsis: A Review. Bangladesh J. Child Health. 36(2): 82 - 89.
11. Chang MH (2000). Natural history of hepatitis B virus infection in children. J. Gastroenterol. Hepatol. 15 suppl E: 16–19.
12. Chen CJ, Wang LY, Yu MW (2000). Epidemiology of hepatitis B virus infection in the Asia-Pacific region. J. Gastroenterol. Hepatol. suppl:E3-6.

13. Cho Y, Bonsu G, Akoto Ampaw A, Nkrumah- Mills G, Nimo JJA, Park JK, Ki M (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. DegliEsposti S, Shah D (2011). Hepatitis B in pregnancy: challenges and treatment. Gastroenterol. Clin. North Am. 2011. 40: 355–372.
15. Deinstag DL (2008). Hepatitis B virus infection. N. Engl. J. Med. 359: 1486-1500.
16. 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.
17. Esan AJ, Omisakin CT, Ojo-Bola T, Owoseni MF, Fasakin KA, Ogunleye AA (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.
18. Fomulu NJ, Morfaw FL, Torimiro JN, Nana, P, Koh MV, William T (2013). Prevalence, correlates and pattern of Hepatitis B among antenatal clinic attenders in Yaounde-Cameroon: is perinatal transmission of HBV neglected in Cameroon? BMC Preg. And Childbirth. 13: 158.
19. Fraser DM, Cooper AM, Nolte AGW (2003). Myles Textbook for Midwives. African Edition. Elsevier Publishers. UK.
20. Giogiana FB, Ioan S, Ioan M, Marioara B, Elena P, Calin P, Nilima K (2010). Sepsis in newborns. TMI. 60 (4).
21. Hardy R, Sovio U, King VJ, et al. (2005). Birth weight and blood pressure in five European birth cohort studies; an investigation of confounding factors. Eur. J. Pub. Health. 16: 21 - 30.
22. Hjalgrim LI, Rostgaard K, Hjalgrim H, et al. (2004). Birth weight and risk for childhood leukemia in Denmark, Sweden, Norway, and Iceland. J. Nati. Cancer Inst. 96: 1549 - 1556.
23. Jonas MM (2009). Hepatitis B and Pregnancy: an underestimated issue. Liver Int. 29 suppl 1:133-139.
24. Ka YT, Lai FH, Terence L (2005). The impact of maternal HBsAg carrier status on pregnancy outcomes. A case- control study. J. Hepatology. 43:771 - 775.
25. Kawsar M, Goh BT (2002). Hepatitis B virus infection among Chinese residents in the United Kingdom. Sex. Transm. Infect. 78:166 - 168.
26. Lao TT, Sahota DS, Suen SSH, Law LW, Leung TY (2012). Maternal HBsAg status and infant size – a Faustian bargain? J. Viral Hep. 19:519-524.
27. Lavanchy D (2004). Hepatitis B virus epidemiology, disease, burden, treatment, and current emerging prevention and control measures. J Viral. Hepat. 11:97-107.
28. Lee WM (1997). Chronic hepatitis B. N. Engl. J. Med. 337:1733-1745
29. Lewis S, Dirksen SR, Heitkemper MM, Bucher L. (2014). Medical Surgical Nursing. Eighth edition. Elseivier. USA.
30. Lok AS (2002). Chronic hepatitis B. N. Engl. J. Med. 346:1683-1683
31. Luppi P, Haluszczak C, Trucco M, Deloia JA (2002). Normal pregnancy is associated with peripheral leukocyte activation. Am. J. Reprod. Immunol. 47: 72 - 81.
32. Mahoney FJ (1999). Update on diagnosis, management, and prevention of hepatitis B virus infection. Clin. Microbiol. 12:351-366.
33. Martinson FE, Weigle KA, Mushawar IK, Weber DJ, Royce R, Lemon SM (1996). Seroepidemiology survey of hepatitis B and C virus infections in Ghanaian children. J. Med. Virol. 48:278 - 283.
34. Nguyen G, Garcia RT, Nguyen N, Trinh H, Keeffe EB, Nguyen MH (2009). Clinical course of hepatitis B virus infection during pregnancy. Aliment. Pharmacol. Ther. 29: 755 - 764.
35. Potthoff A, Rifai K, Wedemeyer H et al. (2009). Successful treatment of fulminant hepatitis B during pregnancy. Z. Gastroenterol. 47:667 - 670.
36. ter Borg MJ, Leemans WF, de Man RA, Janssen HL (2008). Exacerbation of

chronic hepatitis B infection after delivery. J. Viral Hepat. 15:37 - 41.
37. Shepard TH (1998). Catalog of Teratogenic Agents. Baltimore John Hopkins University Press.
38. Gambarin-Gelwan MB (2007). Hepatitis B in pregnancy. Clin. Liver Dis. 11(4):945 -963.
39. 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.
40. Elefsiniotis T, Tsoumakas K, Vezali E, Glynou I, Drakoulis N, Saroglou G (2010). Spontaneous Preterm Birth in Women with Chronic Hepatitis B Virus Infection. Int. J. Gynecol. Obstet. 110:240 – 244.
41. Lobstein S, Faber R, Tillmann HL (2011). Prevalence of hepatitis B and its impact on pregnancy and newborn complications at a tertiary hospital in the Eastern part of Germany. Digestion. 83: 76 - 82.
42. Ma J, Bauman A (1996). Obstetric profiles and pregnancy outcomes of Immigrant women in New South Wales. Aust. N. Z. J. Obstet. Gynaecol. 36:119 – 125.
43. Von Katterfield B, Li J, McNamara B, Langridge AT (2011). Obstetric profiles of foreign- born women in Western Australia using data linkages 1998-2006. Aust. N. Z. J. Obstet. Gynaecol. 51: 225 - 232.
44. Sharma R, Malik A, Rattan A, Iraqi A, Maheshwari V, Dhawan R (1996). Hepatitis B virus infection in pregnant women and its transmission to infants. J. Trop. Ped. 42(6):352 - 354.
45. Saleh-Gargari S, Hantoushzadeh S, Zendehdel N, Jamal A, Aghdam H (2009). The association of maternal HBsAg carrier status and perinatal outcome. J. Hep. 9(3): 180 - 184.
46. To WW, Cheung W, Mok KM (2003). Hepatitis B surface antigen carrier status and its correlation to gestational hypertension. Aust. N. Z. J. Obstet. Gynaecol. 43:110-122.
47. Tse KY, Ho LF, Lao T (2005). The impact of maternal HBsAg carrier status on pregnancy outcomes: a case- control study. J. Hepatol. 43:771-775.
48. Lao TT, Chan BC, Leung WC, Ho LF, Tse KY (2007). Maternal Hepatitis B infection and gestational diabetes mellitus. J. Hepatol. 47: 46 - 50.
49. Mi J, Law C, Zhang KI, Osmond C, Stein C, Barker D (2000). Effects of infant birth weight and maternal body mass index in pregnancy on components of the insulin resistance syndrome in China. Ann. Intern. Med. 132: 253 - 260.
50. Nithin J, Nithin H, Nitha J (2009). Risk Factors of Neonatal Sepsis in Trivandrum, Kerala. Retrieved from http://w.w.w.scribe.com>School Work>Essays & Theses. accessed 28/04/2013@10:50am.
51. Okasha M, Gunnell D, Holly J, Smith GD (2002). Childhood growth and adult cancer. Best Pract. Res. Clin. Endocrinal. Metab. 16:225 - 241.
52. Shah GS, Budhathoki S, Das BK, Mandal RN (2006). Risk factors in early neonatal sepsis. Kathmandu Uni. Med. J. 4(14): 187 - 191.
53. Shaheen AAM & Myers RP (2010). The outcomes of pregnancy in patients with cirrhosis: a population-based study. Liver Int. 30: 275 – 83.
54. Sheron N, Lau J, Daniels H, Goka J, Eddleston A, Alexander GJM (1991). Increased production of tumor necrosis factor alpha in chronic hepatitis B virus infection. J. Hepatol. 12:241-245.
55. Tan J, Surti B, Saab S (2008). Pregnancy and cirrhosis. Liver Transpl. 14:1081–91.
56. Vinodkumar CS, Neelagund YF, Kalsurmath S, Banapurmath S, Kalappannavar NK, Basavarajappa KG (2009). Perinatal Risk factors and microbial profile of neonatal septicemia: A multicentred study. J. Obst. and Gynecol. of India. 58: 32 - 40.
57. Webb P, Bain C (2011). Essential Epidemiology. Second edition. UK: Cambridge publishers.

58. West B, Tabansi PN (2012). Clinico-Bacterial profile of early and late onset sepsis in a tertiary hospital in Nigeria. J. Medic. and Med. Sci. 3(2): 107-111. Available online at http://w.w.w.interesjournals.org/JMMS.
59. West B, Tabansi PN (2012). Clinico-Bacterial profile of early and late onset sepsis in a tertiary hospital in Nigeria. J. Medic. and Med. Sci. 3(2): 107-111. Available online at http://w.w.w.interesjournals.org/JMMS.
60. Whincup PH, Kaye SJ, Owen CG, et al. (2008). Birth weight and risk of type 2 diabetes. A systematic review. JAMA. 300: 2886 - 2897.
61. Wong S, Chan LY, Yu V, Ho L (1999). Hepatitis B Carrier and Perinatal Outcome in Singleton Pregnancy. Am. J. Perinatol. 16: 485 - 488.
62. Wong DL, Perry S, Hockenberry MJ, Lowdermilk LD, Wilson D (2006). Maternal Child Nursing Care. 3rd edition. Mosby Elsevier. USA.
63. World Health Organization (2000). Hepatitis B. Retrieved: August 23, 2013 from http:// wwwwho.int/media centre/factsheets/fs 204/en/.