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Full Length Research Paper

Hepatitis B and C virus Co-Infection in Pregnancy at a Tertiary Hospital, Yenagoa, Bayelsa State, Nigeria

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Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a reasonable proportion of liver diseases worldwide. Co-infection with the two viruses is not uncommon because the two viruses share similar modes of transmission. The primary concern with HBV/HCV co-infection is that it can lead to more severe liver disease and an increased risk for progression to Hepatocellular cancer. The objective is to determine the Hepatitis B and C virus co-infection in pregnancy, their seroprevalence and clinico-epidemiological correlates. This is a descriptive cross sectional study. Two hundred and twenty (220) consecutive healthy pregnant women attending the antenatal booking clinic of the hospital who met the inclusion criteria were recruited into this study after pretest counselling and obtaining consent from them. This was tested for both HBsAg and anti-HCV antibodies with commercially available in vitro diagnostic kits (one step test strips). Data was collected via a questionnaire. Data entry and analysis was done using SPSS (statistical package for social sciences) 22 statistical package (SPSS Inc., Illinois, U.S.A). P value less than 0.05 was taken as being significant. The mean age of the pregnant women studied was 28.8 years ± 5.2 while the mean parity was 1.20 ± 1.16. Of the 220 recruited pregnant women, 4.6% (n=10) were seropositive for hepatitis B surface antigen (HBsAg) while 2.7% (n=6) were seropositive for hepatitis C viral (anti-HCV) antibodies. There was 0% Hepatitis B and C virus co-infection in pregnancy. Multiple sexual partners and Female circumcision were the significant risk factors for HBsAg seropositivity (p<0.05). None of the risk factors were significantly associated with hepatitis C viral antibody seropositivity. Hepatitis B and C virus co-infection rate in pregnancy is infinitesimal in our obstetrics population. Routine screening for Hepatitis B virus infection and advocacy for active and passive immunization to infants of seropositive pregnant women is however recommended.

Keywords: Hepatitis B virus, Hepatitis C virus, Hepatitis in pregnancy

INTRODUCTION

Globally, Hepatitis B and C virus infections are considered a major public health problem. During their acute phase they are often clinically similar. Chronic hepatitis is by far the most common complication of hepatitis B and C (Cunningham et al., 2005; Richard et al., 2005).

Infections by Hepatitis B or C viruses can be acute or chronic. When it is acute, recovery usually occurs (Awole and Gebre-selassie, 2005) or recovery may follow supportive therapy but when these do not completely occur, it becomes chronic. Infections by these two (2)

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viruses tend to follow a chronic course than any other hepatitis virus (Cunningham et al., 2005) and in this regard the morbidity and mortality caused by Hepatitis C virus far outweighs that of its Hepatitis B virus counterpart (Cunningham et al., 2005; Kumar et al., 2007).

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a reasonable proportion of liver diseases worldwide. Co-infection with the two viruses is not uncommon because the two viruses share similar modes of transmission. The exact number of patients co-infected with HCV and HBV is unknown. The primary concern with HBV/HCV co-infection is that it can lead to more severe liver disease and an increased risk for progression to Hepatocellular cancer (Seth and Emmet, 2005).

Viral Hepatitis complicates 0.2% of all pregnancies in the United States (Guberman et al., 2007). Atanosova et al (Atanasova et al., 2004) in Bulgaria (Eastern European study) reported an incidence of 0.68% of co-infection of HBV and HCV in a randomly selected healthy population of over 2200 individuals (Guberman et al., 2007). In patients with chronic Hepatitis B, estimates of the rates of HCV co-infection vary from 9-30%, depending on the geographic region (Lin et al., 2003). One Italian study found that rates of dual infection increased with age, and was more common in patients over 50 years of age (Gaeta et al., 2003). These numbers may underestimate the true number of patients with both viral infections because no large-scale studies have been performed, and there is a well-described phenomenon of "serologically silent" occult HBV infection (i.e. patients with negative hepatitis B surface antigen [HBsAg] but detectable serum HBV DNA) in patients with chronic Hepatitis C (Richard et al., 2005).

Furthermore, it is on record that perinatal transmission of hepatitis B virus (HBV) and hepatitis C virus (HCV) account for majority of chronic infections worldwide, the risk of perinatal transmission being highest in women with high levels of viraemia. Modalities to reduce HBV and HCV burden should include methods to decrease this mode of acquisition. Many women chronically infected with these viruses are of child bearing age, minority however, have serious liver disease requiring intervention during pregnancy.

The basic clinico-epidemiological data for these viruses might be of great importance to program managers and health planners so as to initiate screening packages in antenatal care clinics (Rasha et al., 2007). Consequently, selective screening based on the identification of risk factors has been advocated for hepatitis C during the antenatal period (Obi et al., 2006). Screening pregnant women for hepatitis B infection on the basis of the presence of risk factors may not be effective. Universal antenatal screening for HBsAg, health education aimed at reducing risk factors and immunisation of all new born and those at risk of hepatitis B is advocated (Araoye, 2003) and this has been adopted by some centres in the developed world.

This study therefore proposes to determine the hepatitis B and hepatitis C viral co-infection in pregnancy in Yenagoa. Since detection of HBsAg and HCV antibodies in the serum are indicative of either acute or chronic phase of HBV and HCV infection respectively, these investigations will be carried out to detect the prevalence of HBsAg and HCV antibodies in the sera of pregnant women attending booking antenatal clinic at the Federal Medical Centre, Yenagoa.

Objectives

The objective is to determine the Hepatitis B and C virus co-infection in pregnancy, their seroprevalence and clinico-epidemiological correlates.

METHODOLOGY

Study Area

This study was carried out at the Antenatal clinic of the Federal Medical Centre, Yenagoa, Bayelsa state in the South-south region of Nigeria between 4th September to 28th October, 2016.

Study Design

A descriptive cross sectional study.

Inclusion Criteria

This included all pregnant women who presented for booking at the antenatal clinic of FMC Yenagoa and gave consent.

Exclusion Criteria

- This included all pregnant women who declined to participate.
- Patients who withheld their consent for inclusion in the study.
- Those immunised within the last six (6) months

Sample Size

The sample size was calculated using the statistical formula (Araoye, 2003) based on reported prevalence rates of hepatitis B and C virus of 13.3% (Jatau and Yabaya, 2009) and 1.86% (Onakewhor and Okonofua, 2009) respectively from previous studies and a confidence interval of 95%.

Study Population

The minimum sample size was thus calculated to be 177 and 28 for HBsAg and anti-HCV respectively. However, a total of 220 consecutive healthy pregnant women attending the antenatal booking clinic of the hospital who met the inclusion criteria were recruited into this study after pre test counselling and obtaining consent from them. These were tested for both HBsAg and anti-HCV antibodies.

Sample Collection and Processing

Five millilitres (5ml) of peripheral venous blood was collected from consecutive subjects in the antenatal booking clinic into plain sterile bottles. Blood samples were centrifuged for ten minutes at 6,000 rpm, serum was obtained and stored at -20OC until used. Samples were analyzed in batches with commercially available in vitro diagnostic kits (one step test strips). The kits utilize immunochromatographic methods to assay for antibodies to hepatitis C virus (one step HCV test strip, SPODEX Diagnostics U.S.A) and HBsAg (one step HBsAg test strip, SPODEX Diagnostics, U.S.A). Using the in vitro diagnostic test kits, the detection of anti-HCV antibodies and HBsAg was done by dipping into each serum sample a strip of the kit and allowing 10-15 seconds for it to react ensuring that the maximum line of the strip will not be exceeded. The strip was then removed and allowed to stand for 15 minutes at room temperature after which the result was read and interpreted according to the manufacturer's instructions.

The HBsAg one step test is a rapid lateral flow immunoassay which qualitatively detects the presence of HBsAg in serum utilizing a combination of monoclonal and polyclonal antibodies to selectively detect elevated levels of HBsAg in serum. The membrane is percolated with anti- HBsAg antibodies on the test line region of the strip. During testing, the serum specimen reacts with the particles coated with anti- HBsAg antibody. The mixture migrates upward on the membrane chromatographically by capillary action to react with anti- HBsAg antibodies on the membrane and generate a coloured line in the test region.

The HCV one step test is a qualitative membrane based immunoassay for the detection of antibodies to HCV in serum. The membrane is coated with recombinant HCV antigen on the test line region of the strip. During testing, the serum specimen reacts with the protein A coated particles. The mixture migrates upward on the membrane chromatographically by capillary action to react with recombinant HCV antigen on the membrane and generate a coloured line. Presence of this coloured line indicates a positive result while its absence indicates a negative result.

To serve as procedural control (in both the HBsAg one step test strip and HCV one step test strip), a coloured line always appeared at the control line region indicating that proper volume of specimen had been added and membrane wicking had occurred. Tests in which two distinct red lines appeared, one in the control region and another in the test region, was regarded as positive. Tests in which only the control line was distinctly coloured red was recorded as negative while tests in which the control line fails to appear was regarded as invalid and was repeated.

Each sero-positive woman for HBsAg and anti-HCV antibodies had a liver enzyme assay done particularly the serum transaminases (alanine and aspartate transaminase), as these have been shown to increase in active liver disease. The Randox test kit by RANDOX Laboratories Ltd., United Kingdom was used. Levels above 12 U/L were regarded as elevated for both AST and ALT.

Questionnaire

Women were enrolled and underwent pretest counselling and were administered a structured interviewer-administered questionnaire consisting of three sections.

Data Analysis

Data was analysed using SPSS (statistical package for social sciences) 22 statistical package (SPSS Inc., Illinois, U.S.A). Univariate analysis for categorical variables was performed using chi-square. P value less than 0.05 was taken as being significant.

Ethical Considerations

Approval for the study was obtained from the ethical committee of the FMC Yenagoa. The study was carefully explained to the patients and their informed consent obtained before being recruited into the study.

RESULTS

A total of two hundred and twenty (220) pregnant women were interviewed.

The predominant age group was 20-29 years (50.0%). The mean age is 28.8 years ± 5.2. Majority (50.0%) of the respondents were from the Ijaw ethnic group and it is followed closely by the Igbo ethnic group (28.2%). Most (96.8%) of the respondents were Christians. Majority (41.8%) of the respondents were involved in doing business as an occupation. Majority (91.8%) also, of the respondents were married, and most of the marriages were of the polygamous type or setting (83.7%). Most (77.8%) had a secondary education.

Table 1. The seroprevalence of Hepatitis B and C amongst the different age groups of respondents.

Variables	Frequency (%)			
HBsAg			HCV	
	Reactive	Non reactive	Reactive	Non reactive
Age at last birthday (years)				
10 – 19	0 (0)	8 (3.8)	0 (0)	8 (3.7)
20 – 29	2 (20.0)	108 (51.4)	6 (100.0)	104 (48.6)
30 – 39	7 (70.0)	86 (40.9)	0 (0)	93 (43.5)
40 – 49	1 (10.0)	8 (3.8)	0 (0)	9 (4.2)
Total	**10 (100.0)**	**210 (100.0)**	**6 (100.0)**	**214 (100.0)**

The prevalence of Hepatitis B was found to be highest amongst the 30 – 39 age group with 70.0% prevalence as compared with the other age groups. While, all the six reactive cases of HCV was from the 20 – 29 age group with a 100% prevalence in this group.

Table 2. The seroprevalence of Hepatitis B and C amongst the different parity groups.

Variables	Frequency (%)			
HBsAg			HCV	
	Reactive	Non reactive	Reactive	Non reactive
Parity				
Para 0-1	5 (50.0)	118 (56.2)	5 (83.3)	118 (55.1)
Para 2-3	3 (30.0)	50 (23.8)	0 (0)	53 (24.8)
Para 4-5	2 (20.0)	23 (11.0)	1 (16.7)	24 (11.2)
Para 6-7	0 (0)	12 (5.7)	0 (0)	12 (5.6)
Para 8-9	0 (0)	7 (3.3)	0 (0)	7(3.3)
Total	**10 (100.0)**	**210 (100.0)**	**6 (100.0)**	**214 (100.0)**

From the table above, the mean parity is 1.20 ± 1.16. It was observed that respondents with parity of 0-1 had the highest 5 (50.0%) reactive HBsAg result; and also HCV reactive results were 5 (83.3%) and consequently, this group had the highest prevalence of 50.0% for Hepatitis B and 83.3% for Hepatitis C respectively.

Table 3. The seroprevalence of Hepatitis B and C amongst the different Gestational Age groups.

Variables	Frequency (%)			
HBsAg			HCV	
	Reactive	Non reactive	Reactive	Non reactive
GA (In weeks)				
1 – 12	4 (40.0)	34 (16.2)	4 (66.7)	34 (15.9)
13– 24	2 (20.0)	89 (42.4)	0 (0)	91 (42.5)
25 - 40	4 (40.0)	87 (41.4)	2 (33.3)	89 (41.6)
Total	**10 (100.0)**	**210 (100.0)**	**6 (100.0)**	**214 (100.0)**

Those respondents with a booking gestational age of between one week and twelve weeks (1 – 12), i.e. the first trimester; and those above twenty five weeks gestation i.e. those in third trimester gestation, were both found to be 40.0% reactive to HBsAg. Hence, the prevalence of hepatitis B was equal in respondents of both the first trimester and third trimester.

Those respondents with a booking gestational age of between 1 – 12 weeks (First trimester gestation), had the highest 4 (66.7%) reactive results to HCV, hence they had the highest prevalence of HCV.

Table 4. The relationship between having more than one sexual partner and the seroprevalence of Hepatitis B and C viral infection.

Variables	Having more than one sexual partner		Total	Test/p -value
	Yes (%)	No (%)		
HBsAg				
Reactive	4 (40.0)	6 (60.0)	10 (4.6)	X^2= 5.59
Non- reactive	155 (74.2)	54 (25.8)	209 (95.4)	df = 1
Total	**159 (72.6)**	**60 (27.4)**	**219 (100.0)**	**p<0.05**
HCV				
Reactive	4 (66.7)	2 (33.3)	6 (2.7)	X^2= 0.11
Non- reactive	155 (72.8)	58 (27.2)	213 (97.4)	df = 1
Total	**159 (72.6)**	**60 (27.4)**	**219 (100.0)**	**p>0.05**

The table above shows that there is a statistically significant association between respondents with more than one sexual partner and Seroprevalence of Hepatitis B Infection (P < 0.05). There was no association between respondents with more than one sexual partner and Seroprevalence of Hepatitis C viral infection.

Table 5. The seroprevalence of Hepatitis B and C amongst those with history of tattoos/scarifications, and circumcision.

Variables	Frequency (%)			
HBsAg			**HCV**	
	Reactive	**Non reactive**	**Reactive**	**Non reactive**
Presence of tattoo/scarifications				
Yes	0 (0)	2 (1.0)	0 (0)	2 (1.0)
No	10 (100.0)	203 (99.0)	6 (100.0)	207 (99.0)
Total	**10 (100.0)**	**205 (100.0)**	**6 (100.0)**	**209 (100.0)**
History of Circumcision				
Yes	4 (40.0)	19 (9.0)	1 (16.7)	22 (10.3)
No	6 (60.0)	191 (91.0)	5 (83.3)	192 (89.7)
Total	**10 (100.0)**	**210 (100.0)**	**6 (100.0)**	**214 (100.0)**

From the table above, there was zero percent reactive results for both HBsAg test and HCV test amongst the respondents that had tattoos/scarifications.

Amongst those that were circumcised, 40.0% had positive HBsAg test; and 16.7% had positive HCV test.

Table 6. Results of Laboratory Investigations.

Variables	Frequency (%)		Total
	Reactive	**Non reactive**	
Result of HBsAg	10 (4.6)	213 (96.8)	220 (100.0)
Result of HCV antibodies	6 (2.7)	214 (97.3)	220 (100.0)

Four point six percent (4.6%) of the respondents were reactive to HBsAg. While for Hepatitis C 2.7% were reactive.

Table 7. Results of Hepatitis B and C virus co-infection. (N = 220)

Variables	HBsAg Frequency (%)		Total
	Reactive	**Non reactive**	
HCV Reactive	0 (0)	6 (2.7)	6 (2.7)
Non-reactive	7 (3.1)	207 (94.1)	214 (97.3)

The result above shows that there was 0% Hepatitis B and C co-infections.

All HBsAg and anti-HCV antibody seropositive pregnant women had normal serum aspartate aminotransferase (AST: normal <12U/L), alanine aminotransferase (ALT: normal <12U/L), and alkaline phosphatase values (ALP: normal, 9-35U/L).

DISCUSION

This is a hospital based study to determine the Hepatitis B and C virus co-infection in pregnancy, their seroprevalence and clinico-epidemiological correlates.

The seroprevalence rates were highest among the Ijaw women. This is due to the fact that majority (50.0%) of the subjects were from the Ijaw ethnicity which is the major ethnic group in Bayelsa. The prevalence of anti-HCV antibodies and HBsAg was more in nulliparous and primiparous females with a mean parity of 1.20 ± 1.16 in this study. This can be explained by the increased rate of multiple sexual partners (72.5%) in the past seen in our nulliparous and primiparous women as compared to our multiparous women. Alegbeleye et al in Port Harcourt (Alegbeleye et al., 2013) reported similar finding. It may be easy to think that HBsAg and anti-HCV prevalence would have been higher in multiparous women because of repeated risk of exposure to contaminated surfaces and instruments during delivery (Aigere et al., 2013; Okusanya et al., 2013; Lilavati et al., 2004; Pennap et al., 2011). In contrast to that, the prevalence is higher in our nulliparous and primiparous women.

The highest prevalence rate for anti-HCV antibodies was in the first trimester. That for HBsAg was however in the first and third trimesters. This was comparable with findings in studies done in Nigeria (Aigere et al., 2013) and India (Lilavati et al., 2004) where it was observed that the third trimester in pregnant women had the highest prevalence rate. However, in this study, first trimester also topped the highest prevalence equally with third trimester.

Moreover, in this study, outstanding risk factors, for example, intravenous drug use, blood transfusion, liver disease in our nulliparous and primiparous women respectively, were not associated with either HBV or HCV. None of the seropositive subjects had a history of blood transfusion. This may have been due to the aversion to receiving blood among our people. In Nigeria, illicit (hard) drugs including opiates are under control and draw in serious punishments hence restricting accessibility or potential availability. This is why it's not surprising that as low as 1.4% of the women alluded to have taken illicit drugs in this study. Also, the poor economic situation may preclude the majority of our women of reproductive age from having access to these drugs even if they will dare the law (Pennap et al., 2011). Tattooing/scarifications (0.9%) did not also contribute to HBsAg and anti-HCV antibody seropositivity. This was not shocking as it is a traditional practice looking out bit by bit. Amongst the surgical risk factors, female circumcision (40%) even though a harmful traditional practice, posed a higher risk to HBsAg seropositivity than caesarean section (20%) and appendectomy (20%). There was no surgical risk factor to anti-HCV antibody seropositivity in this study.

Previous studies have shown an inverse relationship between educational status and HbsAg positivity with less educated women showing the highest positivity (Pennap et al., 2011; Ndams et al., 2008; Ojo et al., 2009). However, in this study, educational level was not found to statistically, significantly influence knowledge of hepatitis B and C viral infections ($p > 0.05$). Educational level was not also found to significantly influence both knowledge of virus/infection transmission from person to person and having more than one sexual partner in life ($p > 0.05$).

Education has been shown to play key roles in the level of Hepatitis infection in pregnant women. This was not reflected in our study. Perhaps due to the declining exposure to harmful traditional and cultural practices in our environment. This finding is similar to the study in Port Harcourt (Alegbeleye et al., 2013) and Akure (Ojo et al., 2009).

Majority (72.5%) of the obstetric women has had a history of multiple sexual partners in their life and in addition, most (85.3%) of them did not know if their spouses had other sexual partners. Of the HBsAg seropositive women, 40% had history of multiple sexual partners and there was a significant association between the history of multiple sexual partners and seropositivity for HBsAg. There was a significant association between the history of multiple sexual partner and seropositivity for HBsAg. Dilatation and Curretage was not found to statistically, significantly influence Hepatitis B and C viral infections ($p > 0.05$). This could be because most of the D and C was done in the hospital and the instruments used could have been well sterilized. These findings were similar to reports in Irrua (Aigere et al., 2013; Okusanya et al., 2013). However, it was found in their study that Dilatation and curettage had a significant contribution to HBsAg seropositivity.

Interestingly, in this study, there was 0% hepatitis B and C virus co-infection, despite the fact that the seroprevalence of hepatitis B surface antigen was 4.6% and that for anti-HCV antibody was 2.7%. This may have occurred by chance and/ or relatively moderate sample size in our study. This was far from the 9-30% HBV/HCV co-infection (Lin et al., 2003) found in the literature. The primary concern with HBV/HCV co-infection is that it can lead to more severe liver disease and an increased risk for progression to liver cancer (Guberman et al., 2007; Donato et al., 1998; Shi et al., 2005; Cho et al., 2011). Meaning seropositive patients to either HBV or HCV infection in pregnancy may be at reduced risk of more severe liver disease and fast progression to liver cancer.

CONCLUSION

Hepatitis B and C virus co-infection rate in pregnancy is infinitesimal in our obstetrics population. Routine screening for Hepatitis B virus infection and advocacy for active and passive immunization to infants of seropositive pregnant women is however recommended.

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