



Burden and Determinants of Hepatitis B Virus Co-infection in a Cohort of HIV Positive Pregnant Women in Jos, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author FNO designed the study, wrote the protocol and performed the statistical analysis while author ASA wrote the first draft of the manuscript. Authors ASA, ANO, JM and ASS managed the analyses of the study as well as the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2015/18458

Editor(s):

(1) William Ebomoyi, Department of Health Studies, College of Health Sciences, Chicago State University, USA.

Reviewers:

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(2) Anonymous, University of Maiduguri, Nigeria.

(3) Anonymous, University Sains Malaysia, Malaysia.

(4) Mathew Folaranmi Olaniyan, Department of Medical Laboratory Science, Achievers University, Nigeria.

Complete Peer review History: <http://sciencedomain.org/review-history/9774>

Original Research Article

Received 23rd April 2015
Accepted 3rd June 2015
Published 15th June 2015

ABSTRACT

Background: Human immunodeficiency virus (HIV) infected pregnant women represent a unique population and co-infection with hepatitis B Virus (HBV) is considered a major health problem worldwide.

Aims: This study was undertaken to determine the prevalence and determinants of hepatitis B infection among a group of HIV positive pregnant women in Jos, Nigeria.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Department of Obstetrics and Gynaecology, Jos University Teaching Hospital, Jos, between December 2011 and May, 2012.

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Methodology: A cross sectional study among consecutive HIV positive pregnant women at the antenatal clinic of the Jos University Teaching Hospital (JUTH), Jos, over a 5-month period. Hepatitis B surface antigen (HBsAg) detection was done using in vitro diagnostic kit. Reactive samples were confirmed by Enzyme Linked Immunosorbent assay (ELISA) kit. Information on socio-demographic characteristics and other risk factors associated with the prevalence of HBsAg among HIV positive pregnant women were obtained from participants using pre-tested questionnaires. Data was analyzed using Epi info statistical software version 3.5.1 (CDC, Atlanta Georgia, USA).

Results: Among the 124 HIV positive pregnant women studied, 15 (12.1%) were positive for HBsAg. HIV/ HBV co-infection rates were highest among the age group 31–40 years, unmarried, uneducated, multigravidae, those at third trimester of pregnancies, with multiple sex partners, and those with history of STI, low CD4 count and high viral load. Statistical analysis showed significant association between multiple sex partners ($P = 0.017$), history of jaundice ($P = 0.001$), low CD4 count ($P = 0.006$), high HIV viral load ($P = 0.001$) and hepatitis B infection among the study population.

Conclusion: Prevalence of hepatitis B virus infection among HIV positive pregnant women among this group of Nigerian women is high. Intensive free hepatitis B screening among HIV positive pregnant women attending ante-natal clinics as a policy especially those with history of multiple sexual partners, jaundice, low CD4 count and high viral load is recommended so as to immunize those without HBV infection.

Keywords: HBsAg; HBV; HIV positive pregnant women; Nigeria.

1. INTRODUCTION

Hepatitis B Virus and HIV infections have emerged as major global public health concern because of their worldwide distribution and significant cause of morbidity and mortality [1]. There are approximately 400 million chronic hepatitis B virus (HBV) carriers and 42 million people with HIV infection worldwide, most of which are in Asia and sub-Saharan Africa [1-3].

The adverse impacts of increasing HIV pandemic in sub-Sahara Africa on this endemic hepatitis have become a significant clinical and public health concern with respect to control and treatment of both infections. In Europe and USA, the prevalence of HBV infection is 10-27 folds higher in HIV positive individuals than the normal population [2,4]. This high risk of co-infection is being attributed to shared sexual and parenteral routes of HBV and HIV transmission and there is also evidence that HIV infection may be a cofactor for heterosexual transmission of HBV infection [5–7].

HBV in infected pregnant women serves as health hazards not only to the health workers and other women in labour but also to the baby as seen also in HIV infection. There have been documented evidences of mother-to-child transmission of HBV through the vertical route with rate of between 5 - 11.1% [8]. There are convincing evidences that HIV infection significantly increases the infectivity of HBV and

predisposes to drug hepatotoxicity thereby complicating the delivery of anti-retroviral drugs [9,10]. Also patients who are co-infected with this virus appear to have a more rapid progression to chronic hepatitis and liver cirrhosis [11]. Similarly, immune suppression due to HIV infection may cause reactivation or re-infection in individuals previously exposed to HBV [3,4].

Although a number of prevalence studies of HIV/HBV co-infection among pregnant women have been reported from Africa, differing results have been observed. In a study carried out among HIV infected in Southern Tanzania, the prevalence of HBV was 6.3% [8]. In the West African sub-region, a prevalence of 9.8% of HBV was demonstrated among HIV positive pregnant women in Ouagadougou, Burkina Faso while a figure of 9.0% was reported in Abidjan, Cote d'Ivoire [12,13]. In both studies, the prevalence of HBV was significantly higher in HIV positive than in HIV-negative pregnant women. In Zaria, Nigeria [14], a prevalence of 8.3% of HBV infection was reported among pregnant women while prevalence rates of 11.6% and 2.2% were reported in Maiduguri and Benin respectively [15,16]. A prevalence of 9.3% of HBV was reported among pregnant women in Anambra State and 0.7% of the women had HIV and HBV co-infection [17].

Despite the fact that Hepatitis B viral infection among HIV infected pregnant women has

potential for maternal-fetal transmission, maternal morbidity and mortality as well as transmission to health workers, pregnant women attending antenatal clinics in Nigeria are not routinely screened for HBsAg. There have been limited reports from Jos on HBV co-infections among HIV infected pregnant women. Hence we sought to determine the prevalence and risk factors for HBV co-infection among HIV-infected pregnant women in Jos, Nigeria.

2. MATERIALS AND METHODS

This was a cross-sectional study conducted among consecutive HIV positive pregnant women attending antenatal care between December 2011 and May 2012, at the department of Obstetrics and Gynaecology, Jos University Teaching Hospital, Jos, Nigeria. The department also offers services relating to the prevention of mother to child transmission of HIV/AIDS (PMTCT), supported by the APIN/PEPFAR project. HIV positive pregnant women with unknown HBV status who consented were included in the study. Women with known positive HBV status and those with history of previous hepatitis B immunization were excluded.

The sample size used for the study involved a frequency of 113 and the formula employed is as follows; $n = Z^2pq/d^2$ and a prevalence rate of 8.3% reported from Zaria was used [14]. However, a total of 124 patients were recruited to guard against possible attrition. Information was collected from each patient and documented on a structured proforma developed by the researchers as well as the laboratory results. HIV rapid test screening method is offered routinely to all pregnant women by the AIDS Prevention Initiative in Nigeria (APIN) in the hospital, with the option to opt-out. HIV positive pregnant women who presented to the antenatal clinic with evidence of their status were recruited into the study. The CD4 count and viral load of eligible women were also ascertained.

Blood samples were collected aseptically by venepuncture from the eligible HIV positive pregnant women using sterile 5 ml disposable hypodermic syringes and needles. The blood samples collected were dispensed into pre-coded specimen bottles. The samples were allowed to clot and centrifuged at 3,000 rpm for 5 minutes to separate the sera. The sera were then extracted using micropipette.

Hepatitis B surface antigen (HBsAg) detection was done using in vitro diagnostic kit manufactured by ACON Laboratories, Inc. 4108 Sorrento Valley Blvd., San Diego, CA 92121, USA. The test kit (dipsticks) is a rapid immunochromatographic assay designed for qualitative determination of HBsAg in human serum or plasma. The test strips were immersed into serum samples and taken out after about 10 seconds and placed on a clean, dry, non-absorbent surface. The results were read after 10 minutes post immersion. Positive samples generated a colour band in the test (T) region of the strips and another in the control (C) region while negative samples had a colour band in the control (C) region only. Positive samples were stored at -20°C and were later confirmed by using a commercially available Enzyme Linked Immunosorbent Assay (ELISA) Kit (Bio Rad, France).

The data was analyzed using the Epi info statistical software version 3.5.1 (CDC, Atlanta Georgia, USA). Descriptive statistics was done and test of association between categorical variables were carried out using chi square test or Fisher exact test where applicable. A $P < 0.05$ was accepted as significant. Ethical approval was sought and obtained from the ethical committee of Jos University Teaching Hospital, Jos, Nigeria. An informed consent was obtained from each patient before recruitment into the study.

3. RESULTS

A total of one hundred and fifty (150) HIV positive pregnant women were approached during the study period. Twenty six of them declined consent or opted out mid-way into the interview. A total of 124 respondents who met the eligibility criteria were studied. The mean age of the women was 28.5 ± 5.4 years. Majority were aged between 31-40 years [70 (56.5%)], Christians [97 (78.2%)], married [121 (97.6%)], completed secondary education [57 (46.0%)], and were multigravidae [102 (82.3%)]. Most of them were from the various ethnic groups in Plateau State [64 (51.6%)], while Hausa/Fulani, Yoruba and Igbo were [48 (38.7%)]. Most of the women were self-employed [70 (56.4%)] (Table 1).

The prevalence of HBV infection among the study population was 12.1% (15/124). The highest prevalence [9 (12.9%)] was recorded among the age group 31-40 years and those with no formal education [2 (33.3%)]. HBV infection

was found in 14 (11.6%) married women while one case was noted in a single woman (33.3%). Statistical analysis showed no significant association between the age groups, marital status, educational level, occupation, ethnicity, religion and prevalence of HBsAg among the subjects ($P > 0.05$) (Table 1).

Of the 124 women studied, 114 (91.9%) had been on highly active antiretroviral therapy (HAART) and the remaining 10 (8.1%) were newly diagnosed as HIV positive after voluntary counseling and testing (VCT). Most of the respondents had no previous blood transfusion 103 (83.1%), never smoked 123 (99.2%), never used intravenous drugs 122 (98.4%) and had no previous history of jaundice 118 (95.2%). Seventy two (58.1%) of the women had multiple sexual partners and 68 (54.8%) had history of

sexually transmitted infections. However, among the study population, 13 (12.7) multigravidae had HIV/HBV co-infection. The co-infection rate was higher among subjects that admitted to multiple sexual partners [13 (18.1%)] than those without multiple sex partners [2 (3.8%)]. Also the co-infection rates were higher in women with history of sexually transmitted infections as well as those with history of jaundice and blood transfusion. Table 2 shows the prevalence rates of HBV/HIV co-infection among subgroups within the study population.

Table 2 also depicts other determinants of HBV/HIV co-infection in the study population. Women with history of multiple sexual partners, jaundice as well as those with low CD4 count and high viral load were at increased risk of having HIV/HBV co-infection among the women.

Table 1. Socio-demographic characteristics of the study population and their impacts on HIV/HBV infection

Socio-demographic characteristics	Number tested	HBsAg negative no (%)	HBsAg positive no (%)
Age group			
21-30	51	45(88.2)	6(11.8)
31-40	70	61(87.1)	9(12.9)
41-50	3	3(100)	0(0.0)
Marital status			
Married	121	107(88.4)	14(11.6)
Single	3	2(66.7)	1(33.3)
Educational level			
None	6	4(66.7)	2(33.3)
Primary	28	23(82.1)	5(17.9)
Secondary	57	50(87.7)	7(12.3)
Tertiary	33	32(97.0)	1(3.0)
Occupation			
Civil servant	31	27(87.1)	4(12.9)
Self employed	70	62(88.6)	8(11.4)
Students	6	5(83.3)	1(16.7)
Unemployed	17	15(88.2)	2(11.8)
Religion			
Christianity	97	84(86.6)	13(13.4)
Islam	27	25(92.6)	2(7.4)
Ethnicity			
Berom	44	39(88.6)	5(11.4)
Yoruba	20	19(95.0)	1(5.0)
Hausa/Fulani	11	9(81.8)	2(18.2)
Igbo	17	15(88.2)	2(11.8)
Ngas	20	18(90.0)	2(10.0)
Others	12	9(75.0)	3(25.0)

Table 2. Determinants of HIV/HBV co-infection in the study population

Risk factors	Number screened	Number of HBsAg positive (%)	Number of HBsAg negative (%)	P-value
Parity				
Primigravidae	22	2 (9.1)	20 (90.9)	0.634 [‡]
Multigravidae	102	13 (12.7)	89 (87.3)	
Multiple sexual partners				
Yes	72	13 (18.1)	59 (81.9)	0.017 [‡]
No	52	2 (3.8)	50 (96.2)	
History of jaundice				
Yes	6	4 (66.7)	2 (33.3)	0.001 [‡]
No	118	1 (9.3)	107 (90.7)	
History STIs*				
Yes	68	10 (14.7)	58 (85.3)	0.326
No	56	5 (8.9)	51 (91.1)	
History of blood transfusion				
Yes	21	3 (14.3)	18 (85.7)	0.736 [‡]
No	103	12 (11.7)	91 (88.3)	
Alcohol consumption				
Yes	13	1 (7.7)	12 (92.3)	0.607 [‡]
No	111	14 (12.6)	97 (87.4)	
Intravenous drug use				
Yes	2	0 (0.0)	2 (100.0)	0.597 [‡]
No	122	15 (12.3)	107 (87.7)	
History of smoking				
Yes	1	0 (0.0)	1 (100)	0.710 [‡]
No	123	15 (12.2)	108 (87.8)	
CD4 count level				
≤ 350	45	10 (22.2)	35 (77.8)	0.006
> 350	79	5 (6.3)	74 (93.7)	
Viral load				
> 1000	47	12 (25.5)	35 (74.5)	0.001 [‡]
200 - 1000	77	3 (3.9)	74 (96.1)	

STIs* – Sexually transmitted infections ‡ - Fisher exact test

4. DISCUSSION

In this study, prevalence of HBV among HIV positive pregnant women was 12.1% and this high prevalence rate suggests that Jos like other areas in Nigeria is endemic for HBV infection. This result is in conformity with earlier reports that sub-Saharan Africa has HBV carrier rate of 9 – 20% [18,19]. The prevalence of 12.1% is similar to findings from previous studies from Cote d' Ivoire, Congo, and Burkina Faso [13,20,21]. It is however, much higher than the reported prevalence rates among HIV positive pregnant women in other parts of Nigeria [17, 22–24]. Variations in prevalence rates may be due to differences in methodology, sample size, sensitivity and specificity of various screening kits. Also, since the two infections share same routes of transmission, the higher prevalence suggest that Jos might also be an area of high HBV transmission as HIV prevalence is higher in

Jos compared to other parts of the country. Incessant crisis (civil unrest) in Jos for over a decade now may have equally contributed to increase in risky sexual behavior including rape with resultant rise in HIV/HBV co-infection.

Epidemiological studies suggest that age is an important risk factor and the age of acquiring infection is the major determinant of the incidence and prevalence rates [17,19]. In this study, the differences in prevalence rates of HBsAg among HIV positive pregnant respondents in various age groups indicate that this factor plays an important role in the prevalence of HBV. The age group 31-40 years had the highest prevalence of HIV/HBV co-infection (12.9%) followed by 21-30 years (11.8%). This is consistent with other studies [19,23,25]. This could be as a result of the fact that these age brackets are at the peak of sexual activities, supporting the role of sexual

intercourse in the transmission of HBV [23]. The high prevalence of HIV/HBV co-infection among these age groups is in line with the report that persons within the ages of 25 to 35 years are mostly infected with HIV/AIDS [17,25]. The Center for Disease Control (CDC) reported that at least 38% of women infected with HIV are through heterosexual contact with HIV positive partners [26]. Since HBV has similar routes of transmission and risk factors as HIV, increased prevalence of HIV will translate to increase in HBV prevalence. Many of these women are involved in illicit and unprotected sex with men, who entice them with money [17].

However, in relation to marital status, single subjects in this study had higher prevalence of HIV/HBV co-infection than married subjects. The finding in this study is in agreement with previous studies reported from Anambra state and Jos [17,27], where single women had higher prevalence of HIV/HBV co-infection than married women. The finding however, is at variance with a study from Enugu, Nigeria [24] where married women recorded the highest prevalence. The higher prevalence among single women in comparison with those that are married as found in this study may be due to the fact that they are un-married/un-attached and thus are more likely to indulge in unsafe sexual activity [17].

Another important factor in the study was the level of education. Prevalence of HIV/HBV co-infection was inversely associated with increasing educational status. Thus, the less educated women had the highest prevalence rates indicating a possible influence of education and public enlightenment/awareness on the carrier rates of these infections. Among the occupational groups, students had the highest co-infection rates with HIV/HBV. This finding is consistent with a previous report [17], and this confirms the finding that, even though Nigerian students studied and were knowledgeable about the routes of HIV/AIDS transmission, they were not deterred from engaging in risky unprotected sexual intercourse [17,28].

The prevalence of HIV/HBV co-infection was higher among subjects with positive history of multiple sex partners compared to those without such history. This finding is consistent with a previous report [19]. This supports the role of sexual intercourse in transmission of HIV and HBV infections. In this study, the carrier rate for HBsAg was higher among multigravidae compared with the primigravidae. This is similar

to the findings in a study from Port Harcourt, Nigeria [23]. This may be attributable to previous multiple deliveries which could be fraught with the risk of exposure to contaminated birth instruments. Subjects with history of sexually transmitted infections (STI) in this study had higher prevalence rate of HIV/HBV co-infection than those without previous STI, although there is no significant association. This finding is similar to the study from Ethiopia [29].

The findings also showed that women with history of jaundice were more likely to have HIV/HBV co-infection which may be a pointer to previous exposure to HBV during the episode of jaundice. Superimposed HIV infection in these individuals is associated with HBV re-infection and reactivation, increased progression to HBV chronic carrier state, reduced persistence of anti-HBs antibodies in naturally infected and vaccinated individuals, and an increased HBV infectivity rate [6,20]. Thus, it is clear that HIV immunosuppression facilitates transmission of HBV [3,6,20]. There were no associations between alcohol consumption, smoking and HBsAg positivity. This could be attributed to the fact that smoking and alcohol consumption are not common among pregnant women in our environment. Subjects in this study with history of blood transfusion as in other studies [30,31] had a higher prevalence of HIV/HBV co-infection, though it was not statistically significant. However, HBV has been reported to spread primarily by blood and blood products. Blood transfusion still remains a main source of HBV transmission in developing countries [2,32]. This study found no association between intravenous drug use and HBsAg positivity. This could be attributed to the fact that intravenous drug use may not be common among our female population.

Prevalence of HBsAg among HIV infected pregnant women was higher in those with lower CD4 cell count and high HIV viral loads. This is similar to findings from previous studies [5-7,20,33]. This finding may be due to reactivation of previous HBV infection or inability to clear a subsequent HBV infection. Support for the latter is given by a study which found that lower mean CD4 counts (as found in more advanced HIV infections) at the time of acute HBV infection are significantly associated with progression to chronic carrier state [20]. As seen in progression to chronic carrier status, the degree of HIV immunosuppression is related to the degree of HBV infectivity [20]. More recently, a

retrospective study on the effect of HBV on the course of HIV infection in 458 HIV-positive patients revealed that HIV viral loads were lower over time in HBsAg-positive patients [20]. However, extensive research has shown that there is no convincing evidence that HBV hastens progression to AIDS [4,20] in HIV/HBV-co-infected patients.

The major limitation of this study was that other serological markers of HBV infection such as HBeAg, anti-HBs, anti-HBc and HBV DNA were not assayed for. Therefore this study was unable to investigate serological evidence of past infection or prior immunization. If these markers were assayed for, the actual co-infection rate would most probably be much higher than the reported figure. The relative small sample size may have made it difficult to ascertain significant associations between many risk factors and development of HBV/HIV co-infection.

5. CONCLUSION

Burden of HBV infection (12.1%) among HIV positive pregnant women is quite high and this constitutes a serious public health problem. There is need for this problem to be addressed in the antenatal clinic through routine screening of all HIV positive pregnant women especially those with history of multiple sexual partners, jaundice and those with low CD4 count and high viral load.

6. RECOMMENDATIONS

All pregnant women especially HIV infected women should be screened routinely for HBV co-infection and those found negative should be immunized against hepatitis B virus. Also, this would guide correct choice of antiretroviral drugs that are also effective against HBV as well as reduce morbidity and mortality from drug induced hepatotoxicity.

CONSENT

Informed consent was obtained from each subject before enrolment into the study.

ETHICAL APPROVAL

Ethical approval was sought and granted by the ethical committee of Jos University Teaching Hospital, Jos, Nigeria with ethical approval number JUTH/DCS/ADM/127/XIX/2957.

ACKNOWLEDGEMENTS

We wish to appreciate the staff of PMTCT- APIN and Immunology laboratory of Jos University Teaching Hospital for their cooperation and assistance during analysis of the blood samples in the laboratory.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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The peer review history for this paper can be accessed here:
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