ORIGINAL ARTICLE

Prevalence of hepatitis B surface antigen seropositivity among HIV-infected and non-infected individuals in Nnewi, Nigeria

E. C. Okocha, O. C. Oguejiofor[1], C. U. Odenigbo[1], U. C. Okonkwo[1], L. Asomugha[1]

Departments of Haematology, [1]Medicine, Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Nigeria

ABSTRACT

Background: Co-infection of human immunodeficiency virus (HIV) and hepatitis B virus (HBV) is common as both viruses share common routes of transmission. HIV significantly affects the natural history of HBV, hence the need to determine the prevalence of co-infection. **Materials and Methods:** This was a retrospective study between 2005 and 2009, in which is a total of 2018 subjects who reported at our University Teaching Hospital blood bank and human immunodeficiency virus clinic were studied. Hepatitis B surface antigen (HBsAg) was tested for using a one step lateral flow rapid chromatographic immunoassay (Acumen labs and diagnostic centre, Bangalore, India) and HIV 1/2 was tested using two kits, Determine (made by Abbot, Japan for Inverness Medical, Japan). **Results:** A total of 2018 subjects were studied out of which 1176 were HIV positive (964 males and 212 females) and 842 (334 males and 508 females) were negative. The prevalence of HBsAg positivity in the study population was 5.9%. It was 6.3% and 5.6% in the HIV-infected and un-infected population, respectively. Although the prevalence was higher in those who are HIV infected, the difference was not statistically significant (P=0.52). Males who were HIV positive were found to be more likely to have co-infection than females (8.7% vs. 4.2%, P=0.02, OR=1.917). **Conclusion:** This study showed that in south-eastern Nigeria, infection with HBV is relatively common in both HIV-infected and un-infected individuals. Routine screening for HBV should be done for all HIV positive individuals.

Key words: Hepatitis B virus, human immunodeficiency virus, Nnewi, south-eastern Nigeria

Address for correspondence:
Dr. E. C. Okocha, Department of Haematology, Nnamdi Azikiwe University Teaching Hospital, P.O. Box 910, Nnewi, Anambra State, Nigeria.
E-mail: onyichideokocha@yahoo.com

INTRODUCTION

Human immunodeficiency virus (HIV) and hepatitis B virus (HBV) infection have a worldwide distribution. However, prevalence of both infections is greater in the developing world especially Africa and Asia. In sub-Saharan Africa, it is estimated that 25 million people are infected with the HIV virus, and another 50 million people are HBV positive.[1] Despite this alarming statistics, data on prevalence of co-infection of these two viruses in African subjects is sparse or even non-existent in many parts.[1]

Co-infection with HIV has a major impact on the natural history, diagnosis, progression, morbidity, and mortality of HBV infection.[2] In addition, the presence of chronic hepatitis B leads to an increased risk of hepatotoxicity related to administration of Highly Active Anti-Retroviral Therapy (HAART).[3] With the present availability of HAART and so improved longevity of subjects, co-infected patients have a higher chance of death from liver-related causes.[1]

The diagnosis of chronic HBV infection in HIV-infected patients is same as in HIV seronegative patients. HBsAg is the serological hallmark of HBV infection and appears in serum 1-10 weeks after acute exposure to HBV.[2] Persistence of HBsAg for more than 6 months implies chronic infection, which is associated with the presence of viraemia as measured by HBV DNA.

Because of the similarity in routes of transmission and socioeconomic factors, HIV and HBV infection often coexist in the same patient. Worldwide, chronic HBV infection affects about 10% of HIV-infected patients.[4] However, regional differences exist in the prevalence of this co-infection. The highest rates also occur in sub-Saharan Africa and Asia.[2] Some studies observed a higher prevalence of this co-infection in men who have sex with men and injection drug users.[5,6]

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Epidemiological data suggests that HBV DNA levels and reactivation rates are higher in HIV-infected patients than those with HBV alone and end stage liver disease is an important cause of death among patients with co-infection.[7] Secondly, reappearance of HBsAg and HBV viremia has been documented in HIV/HBV co-infected patients, whose markers had previously disappeared and HIV-infected patients have lower rates of spontaneous clearance of HBeAg.[8-10]

Other studies have also shown a tendency for HIV-infected patients to develop chronic infection after exposure to HBV infection.[11] Some early observations noted an accelerated course of HIV progression in co-infected individuals,[12] which is disputed by other researchers.[13]

This work is intended to compare the prevalence of hepatitis B infection in HIV-infected patients with that of non-infected subjects in Nnewi, a commercial metropolitan town in south-eastern Nigeria.

MATERIALS AND METHODS

Patient

This was a retrospective study between 2005 and 2009, in which a total of 2018 subjects who reported at our University Teaching Hospital blood bank and human immunodeficiency virus clinic were studied. The hospital is a 250 bed hospital located in the south-east of Nigeria. Donors and HIV positive subjects who reported within this period and had complete data were included in the study. A total of 842 HIV positive subjects with age ranging from 3 to 88 years were studied. Their mean age was 35 ± 10.2 years and the median age was 34 years. For the HIV negative cohort, 1176 subjects were recruited; age range 18-70 years [Table 1], with a mean age of 30 ± 8.5 years and a median age of 28 years. Male:Female (M:F) ratio for the entire group was 1.8:1. Ethical approval was obtained from the University Teaching Hospital Ethics Committee.

Laboratory analysis

Blood was collected by routine phlebotomy and tested for hepatitis B surface antigen (HBsAg) using a one step lateral flow rapid chromatographic immunoassay that qualitatively detects HBsAg. Antibodies used were developed against whole hepatitis B antigen isolated from HBV (Acumen labs and diagnostic centre, Bangalore, India) and has a relative sensitivity greater than 99.0%, relative specificity is 97.0%, and accuracy of 98.5%. A procedural control is built into each test.

HIV 1/2 was tested for using two kits. Determine (Abbot, Japan for Inverness Medical, Japan), which is a qualitative immunochromatographic assay that detects HIV 1 and 2 antibodies using recombinant antigens and synthetic peptides; and HIV 1/2 stat pack (Chember diagnostic system Inc, 3661 Horseblock road, Medford, NY, 11763, USA). Subjects were labelled HIV positive, if they tested positive to both kits.

The statistical analysis was done with the Statistical Package for Social Sciences (SPSS) version 15. Normally distributed variables were expressed as mean ± standard deviation (SD). The Students *t*-test and Chi square were used to test for significance for continuous and categorical variables, respectively. Unadjusted Odds ratio (OR) was used to calculate the relative risk and *P* values <0.05 were accepted as significant.

RESULTS

A total of 2018 subjects were studied. Among them, 1176 were HIV non-infected and 842 were HIV infected. There were 1298 males and 720 females out of which 334 (25.7%) males were HIV positive and 964 (74.2%) were HIV negative. The corresponding figures for females are 212 (29.4%) and 508 (70.5%) for HIV-infected and non-infected persons, respectively. Those aged 20-29 years constituted 43.6% of the subjects followed by those aged 30-39 years (31.5%). The age group 40-49 years constituted 16.1%, followed by those aged 50 years and above (5.7%) and those less than 20 (3.1%) [Table 2].

The prevalence of HBsAg positivity in the study population was 5.9% (119/2018). Among the HIV-infected population, the prevalence was 6.3% (53/842) and 5.6% (66/1176) in the HIV negative population. Though the prevalence was higher in those who are HIV infected, the difference was not statistically significant (*P*=0.52) [Table 3].

Our result showed that the prevalence of HBsAg positivity was higher in males who are HIV infected than females of same status. The percentages are 8.7% versus 4.7%, which was statistically significant (*P*=0.02). OR showed that males who were HIV positive are two times more likely to be HBsAg positive than their female counterparts (OR=1.917 (1.096-3.355)).

Table 1: Age and sex distribution of the HIV negative cohort

Gender (%)	Age (Years)					Total
	<20	20-29	30-39	40-49	≥50	
Male	34 (79.1)	497 (79.8)	258 (82.4)	143 (88.3)	32 (91.4)	942 (82)
Female	9 (20.9)	126 (20.2)	55 (17.6)	19 (11.7)	3 (8.6)	212 (18)
Total	43 (3.7)	623 (53)	313 (26.6)	162 (13.8)	35 (3)	1176 (100)

Chi square=8.79. *P*=0.06, NB – HIV negative cohorts were drawn from blood donors who were HIV negative and persons presenting to the HIV clinic who were found to be HIV negative. They are therefore not representative of the donor population in the hospital. HIV – Human immunodeficiency virus

The pattern in the HIV negative population was completely different. The prevalence of HBsAg in males and females was 5% versus 8.5%. This difference was also statistically significant (*P*=0.04). OR showed that males who were HIV negative are 0.5 times less likely to be HBsAg positive than females (OR=0.565 (0.322-0.922) [Table 4].

Among the HIV non-infected population, there appeared to be a reduction in the prevalence of HBsAg with advancing age. It was highest (18.6%) in those aged <20 years and lowest (2.9%) in those aged 50 years and above. This relationship was found to be statistically significant (*P*=0.005). In the HIV-infected population, the association between age and HBsAg positivity was not statistically significant (*P*=0.8). There was a relatively high prevalence rate in all age groups. The highest (8.4%) was recorded in those aged 40 years and above and the lowest prevalence (6%) was recorded in those aged 30-39 years [Table 2].

DISCUSSION

The overall prevalence of HBsAg positivity in our study population involving both HIV-infected and un-infected subjects was 5.9%. Imoru *et al.*[14] from North Central Nigeria, reported a HBsAg prevalence rate of 10.7% among 2288 apparently healthy male blood donors in Kano, Abiodun *et al.*[15] found a prevalence of 10.4% among blood donors in Benin City, south-west Nigeria while a prevalence rate of 4.98% was documented in Portharcourt, South-south Nigeria.[16] These findings are in keeping with previous observation that in Nigeria, the prevalence of HBsAg increases as one migrates from the South to the North though the reason is yet to be clearly elucidated.[17]

Regarding the prevalence of HBsAg positivity among the HIV positive and HIV negative cohorts, our study found prevalence rates of 6.3% and 5.6%, respectively, with the difference in the prevalence of HBsAg positivity in both cohorts not being statistically significant (*P*=0.52). Nakwagala and Kagimu,[18] reported similar findings when they compared frequency of exposure to hepatitis B infection among 129 HIV seropositive and 129 HIV seronegative medical outpatients in a case control study in Mulago hospital, Uganda. They found no significant difference in the frequency of HBsAg serpositivity among both study populations.

Table 2: Relationship between HBsAg and age among HIV positive and negative cohorts

HBsAg	Years					χ^2	*P* value
	<20	20-29	30-39	40-49	50-59		
HIV positive						1.192	0.88
Positive	1 (6.7)	16 (8)	17 (6)	12 (8.4)	6 (8.3)		
Negative	14 (93.3)	184 (92)	265 (94)	131 (91.6)	66 (91.7)		
Total	15 (100)	200 (100)	282 (100)	143 (100)	72 (100)		
HIV negative						14.99	0.005
Positive	8 (18.6)	32 (5.1)	18 (5.8)	7 (4.3)	1 (2.9)		
Negative	35 (81.4)	591 (94.1)	295 (94.2)	155 (95.7)	34 (97.1)		
Total	43 (100)	623 (100)	313 (100)	162 (100)	35 (100)		

HBsAg – Hepatitis B surface antigen; HIV – Human immunodeficiency virus

Table 3: Prevalence of HBsAg infection among HIV-infected and non-infected cohorts

HIV status	HBsAg status		Total	χ^2	*P* value
	Positive	Negative			
Positive	53 (6.3)	789 (93.7)	842 (41.7)	0.412	0.52
Negative	66 (5.6)	1110 (94.4)	1176 (58.3)		
Total	119 (5.9)	1899 (94.1)	2018 (100)		

HBsAg – Hepatitis B surface antigen; HIV – Human immunodeficiency virus

Table 4: Prevalence of HBsAg infection according to sex in HIV infected and non-infected population

HIV status	HBsAg status		Total	Odds ratio	χ^2	*P* value
	Positive	Negative				
HIV positive					5.353	0.02
Males	29 (8.7)	305 (91.3)	334 (100)	1.92 (1.09-3.35)		
Females	24 (4.7)	484 (95.3)	585 (100)			
HIV negative					4.045	0.04
Males	48 (5)	916 (95)	964 (100)	0.56 (0.32-0.92)		
Females	18 (8.5)	194 (91.5)	212 (100)			

HBsAg – Hepatitis B surface antigen; HIV – Human immunodeficiency virus

Burden of co-infection is expected to be greater in areas of the world with high HBV endemicity,[19] but in our data set, we have found a lower rate of coinfection compared with regions of the world with lower HBV endemicity. Puoti *et al*.[20] and Chomann *et al*.[21] reported that chronic hepatitis B (CHB) virus infection affects about 10% of HIV-infected patients in western countries. This discrepancy may be explained by the fact that in countries not endemic for HBV, most HBV infections are acquired in adolescence through sexual transmission and therefore HIV and HBV share a common route of transmission and the prevalence of co-infection is higher than what is found in the general population unlike in HBV endemic areas including Nigeria, most HBV infection are acquired in childhood through horizontal and vertical transmission and therefore its prevalence in HIV-infected population mirrors what is observed in the general population.[22]

Our prevalence finding of 6.3% HBsAg positivity among HIV positive cohorts agrees with reports from several other studies. Christian *et al*.[23] reported a 6.5% prevalence of HIV/HBV co-infection from Tanzania, Ramia *et al*. 6.9%[24] among a Lebanese cohort and Shire *et al*. 7.1%[25] among an American cohort. These reports show that co-infection with HBV is prevalent among HIV-infected individuals. Among HIV non-infected individuals, prevalence of HBV infection is equally significant. We found an infection rate of 5.6% in this cohort, which was similar to the 5.0% prevalence reported by Anna[26] among the non-HIV infected population. The difference in HBsAg positivity among the HIV positive cohort (6.3%) and HIV negative cohort (5.6%) was not statistically significant (P=0.52).

Gender wise, among the HIV positive cohort, co-infection was significantly higher among HIV positive males compared with females (8.7% vs. 4.7%; P=0.021), with HIV positive males being twice more likely to be HBsAg positive than their female counterparts (OR=1.917). This is very similar to the report of Otegbayo *et al*.[27] They studied the prevalence of hepatitis B and C seropositivity in a Nigerian cohort of HIV-infected patients and found a higher rate of HBV co-infection among males than females (17.9% vs. 10.7%), with male gender being associated with HBV co-infection on logistic regression (OR 1.786). We hypothesize that male preponderance in HBV/HIV co-infection probably result from the fact that generally, boys are more prone to aggressive sports and plays that may result in injury with bleeding, predisposing them more to horizontal HBV transmission.[28] By adulthood, permissive societal attitude to multiple sexual partners for men further contributes to the risk for co-infection with both viruses in the male gender.

The effect of age on prevalence of co-infection was also remarkably different in both study cohorts. Among the HIV non-infected population, we found a decreasing prevalence of HBsAg positivity with age with a statistically significant P trend (P=0.005). This is likely due to many routes of transmission, which operate in the younger age groups; such as use of un-sterile instruments for circumcision, ear piecing, tribal marks, and ritual scarification.[29] In the older age groups, most of the individuals have cleared the infection or died, leaving just 10% as chronic carriers. This pattern was not seen in the HIV positive population (P=0.88), where relatively high prevalence rates obtained in all age groups.

In conclusion, HBsAg positivity is relatively prevalent among both HIV-infected and un-infected adults in Nigeria. Among the HIV-infected population, co-infection is more prevalent in males compared with female and prevalence is relatively high in all age groups. This finding underscores the need to routinely screen for HBV in all HIV-infected persons in our environment, especially males.

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