Original Research Article

Distribution and Prevalence of Markers of Hepatitis B Virus Infection among HIV-Positive Patients attending Defence Healthcare Facility in Abuja, Nigeria

ABSTRACT

Aims: To determine the distribution and prevalence of markers of HBV infection among HIV-positive patients attending Defence healthcare facility for treatment in Abuja, Nigeria.

Study Design: A cross sectional study.

Place and Duration of Study: Defence Headquarters (DHQ) Medical Centre, Abuja, Nigeria, between February and October, 2019.

Methodology: Four mls of blood was collected from each of the 404 consenting HIV patients at the HIV clinic of DHQ Medical Centre and their socio-demographic information obtained using structured questionnaires. Plasmas were separated and screened for HBV infection serologic markers (HBsAg, HBsAb, HBeAg, HBeAb and HBcAb) using HBV combo 5-in-1 panel test kit (Royal Care Diagnostics Co. Ltd, Chennai, India). Data obtained were presented in Table and chart and analysed using Smith's Statistical Package (version 2.8, California, USA) and *P* value of ≤ 0.05 was considered statistically significant.

Results: Most of the recruited participants were married (256/404) females (264/404), aged 31-40 years (144/404) and civilians (376/404). Of these, 41(10.1%) were found to be positive for HBsAg, 189(46.8%) for HBsAb, 6(1.5%) for HBeAg, 20(5.0%) for HBeAb and 10(2.5%) for HBcAb. HBsAg which is the determinant of HBV infection was found to be higher among divorced (13.3%) females (11.4%), aged 31-40 years (16.0%) and civilians (10.6%). Only marital status was associated with prevalence of HBeAb ($P < 0.05$). However, there was no statistically significant difference between age, gender and rank with rates of markers of HBV infection in this study ($P > 0.05$).

Conclusion: This study reported high prevalence HBV infection serologic markers among the study participants. Hence, there is a need for integration of HBV interventions into HIV prevention and control programs including mass vaccination of HBV naïve HIV infected individuals.

Keywords: Hepatitis B virus; HIV-patients; Infection; Seromarkers; Abuja; Nigeria

1. INTRODUCTION

Human immunodeficiency virus (HIV) and hepatitis B virus (HBV) co-infection is common due to their shared transmission routes [1]. HIV and HBV are widespread in the developing countries and patients with dual infection with these viruses are increasingly being diagnosed among hospital patients [2]. Approximately, 10% of all HIV infected patients worldwide is estimated to have chronic HBV co-infection. However, wide regional variations are observed with prevalence rates estimated to be 5–10% in areas such as North America, Europe and Australia compared to higher prevalence rates of 20–30% in areas such as Sub-Saharan Africa and Asia [3]. These statistics are of significant importance in Sub-Saharan Africa where over 70% of the world's 36.9 million people infected with HIV live [3].

Although, the specific mechanisms by which HBV interacts with HIV to influence disease progression are not clearly understood. However, HIV/HBV co-infection has been identified to facilitate higher levels of HBV replication, decreased rates of spontaneous resolution of the HBV infection, and higher risk of reactivation of previous infections [4]. Subsequently, HIV infected individuals have been found to be about six times more likely to develop chronic HBV infection than their HIV negative counterparts [5]. Additionally, the progression rate and complications such as liver fibrosis, cirrhosis, end-stage liver disease, hepatocellular carcinoma (HCC) and mortality due to liver pathology arising from HBV infection are accelerated in patients with HIV co-infection [6].

The most common outcome after HBV infection is the expression of diverse serological markers of varying epidemiological and clinical significance including hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), hepatitis B envelope antigen (HBeAg), hepatitis B envelope antibody (HBeAb), hepatitis B core antigen (HBcAg) and hepatitis B core antibody (HBcAb) [7]. Symptomatic and asymptomatic forms of both acute and chronic infections may be discovered incidentally only through laboratory assay of these viral markers [8]. These markers may occur singly or in various combinations depending on the natural history of the infection and the patterns they present in individuals help to determine stages of HBV infection and plan better management strategies [7, 9].

Previous studies conducted on HIV/HBV co-infection in Nigeria yielded prevalence ranging between 10% and 70%, giving the widest variation in prevalence rates from studies emanating from any country all over the world [10-12]. An estimated 38.0 million people are infected with the HIV worldwide and more than 67% of this population are in sub-Saharan Africa [13]. In Nigeria, HIV prevalence among the general population is 2.8% with about 1.9 million people living with HIV and about 310,000 new infections occurring annually [13].

With the use of Highly Active Antiretroviral Therapy (HAART) in HIV-infected individuals in Nigeria with high HBV endemicity, it is likely that liver disease from chronic hepatitis B will emerge as an even greater problem in a foreseeable future. Therefore, it is important to estimate the national HIV/HBV co-infection prevalence in Nigeria with the view to further expand and streamline antiretroviral programs, especially in view of the implications of using HAART agents that also possess anti-HBV activity [14]. Hence, this study was conducted to determine the distribution and prevalence of markers of HBV infection among HIV-positive patients attending Defence healthcare facility in Abuja, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area

This research study was conducted in Defence Headquarters Medical Centre (DHQ MC) which is located in Mogadishu Cantonment Asokoro, Abuja, Nigeria. Abuja is Nigeria's Federal Capital Territory and an urban Centre. It is located between latitude $8^{o}25$ and $9^{o}20$ north of the equator and longitude $6^{o}45$ and $7^{o}39$ East of Greenwich Meridian. It is geographically located in the centre of the country and has a landmass of approximately 7,315 km^2 [15].

2.2 Study Population

The study population consist of male female HIV positive patients of all ages attending DHQ Medical Centre for treatment who agreed to participate in the study. The study ran from August through October, 2019. The socio-demographic information of the participants was obtained using a questionnaire while their clinical information was obtained from their hospital records.

2.3 Ethical Approval and Consent

Formal ethical approval to conduct this study (Ref: MODHREC/APP./0/3/8) was obtained from the Ministry of Defence Health Research Ethics Committee (MODHREC). In addition, All individuals included

in this study willingly completed and signed an informed consent form. Individual anonymity was treated with confidentiality and for the purpose of this study.

2.4 Determination of Sample Size

The sample size for this study was determined using the formula by Naing *et al.* [16] for sample size calculation a 0.05 level of precision;

$$\boldsymbol{n = \frac{Z^2 pq}{d^2}}$$

Where:

n = required sample size

Z = standard normal deviation at the required confidence interval (1.96) which corresponds to 95% confidence interval.

P = prevalence of HBV infection from previous study (14.0%) (0.14) [17].

Q = 1 – p = 0.9

d = degree of precision expected (0.05)

$$n = \frac{(1.96)^2(0.14)(0.9)}{(0.05)^2} = \frac{3.8416 \times 0.126}{0.0025} = \frac{0.4840}{0.0025} = 193.6$$

$$n = 194$$

This was however rounded up to 404 samples for minimum error

2.5 Collection, Processing and Storage of Samples

Four mls of blood sample was collected from each of the 404 consenting HIV patients from the HIV Clinic of DHQ Medical Centre by venepuncture and placed in an appropriately labelled 5ml EDTA (Ethylene diamine tetra acetic acid) tube. The collected blood samples were spun by centrifugation at 3000rpm (revolutions per minute) for 5 minutes. Plasmas harvested were stored at -20ºC and -80ºC for serological testing and for further molecular assay respectively at the Virology and Immunology Laboratory unit of Defence Reference Laboratory, Abuja, Nigeria.

2.6 Laboratory Analysis

2.6.1 Detection of HBV infection serologic markers

All collected samples were screened for HBV infection serologic markers (HBsAg, HBsAb, HBeAg, HBeAb and HBcAb) using the HBV combo 5-in-1 panel test kit (Royal Care Diagnostics Co. Ltd, Chennai, India). The tests procedure and results interpretation were done according to the instructions of the manufacturer.

2.7 Data Analysis

The obtained data were analyzed using Smith's Statistical Package (version 2.8, California, USA). Chi-square test was conducted at 95% confidence interval and *P* values ≤ 0.05 were considered statistically significant.

3. RESULTS AND DISCUSSION

HIV and HBV are widespread in the developing countries and patients with dual infection of HIV and HBV are increasingly being diagnosed among hospital patients [2]. This present study was conducted to determine the distribution and prevalence of markers of HBV infection among HIV-positive patients attending Defence healthcare facility in Abuja, Nigeria. A total of 404 participants were recruited among which most were married (256/404) females (264/404), aged 31-40 years (144/400) and civilians (376/404). They were all screened for HBV infection serologic markers for which 41(10.1%) were found to be positive for HBsAg, 189(46.8%) for HBsAb, 6(1.5%) for HBeAg, 20(5.0%) for HBeAb and 10(2.5%) for HBcAb (Figure 1).

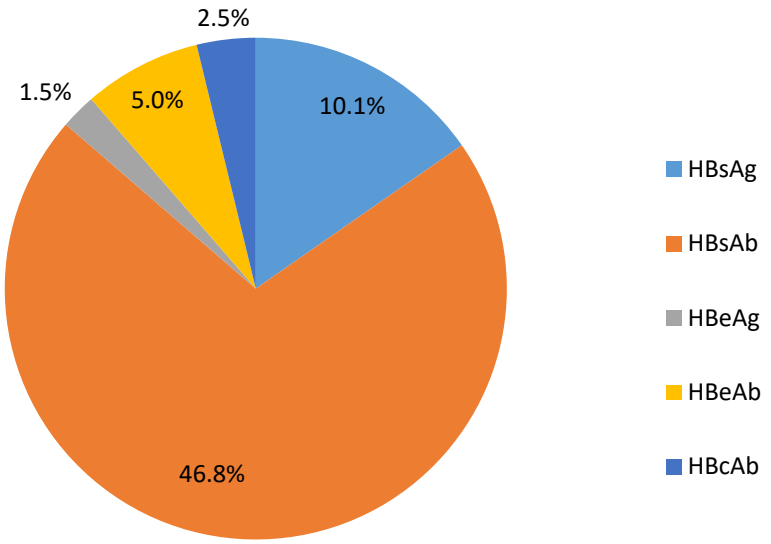

Figure 1: Prevalence of markers of HBV infection among HIV-positive patients attending Defence healthcare facility in Abuja, Nigeria.

The recorded seroprevalence of 10.1% for HBsAg in this study which is the most commonly used indicator for determining HBV infection [18] is regarded as high according to WHO's standard [19]. This recorded high prevalence is expected because of the similar mode of transmission of HBV with HIV and coupled with immunosuppressive effect of HIV which could not allow natural resolution of HBV infection [20]. Furthermore, other previous studies also reported higher prevalence of this marker among HIV positive patients in Nigeria [21-24] and other parts of the world [25-26].

The 46.8% seroprevalence of HBsAb recorded among the HIV patients in this study further indicated that some previously HBV infected individuals had it resolved naturally or as a result of vaccination [7, 27]. This result compares well with the 43.8% prevalence of natural HBsAb among blood donors in Central Nigeria [28], 40.2% among Surgeons in Lagos [29] and 37.5% among hospital personnel in Cairo, Egypt [30].

The presence of HBcAb which is the first antibody to appear in HBV infection [31] in 2.5% of the patients implies that 2.5% of them have had contact with the virus at one time or the other in their lives. Some researchers have previously reported higher rates of HBcAb. For instance, it was 58.1% among HIV individuals in Ogbomoso [32], 61.7% among Surgeons in Lagos [29] and 58.1% among pregnant Nigeria women [33]. However, a lower prevalence of HBcAb (11.4%) was also reported among infants in Benin [34]. The lower prevalence reported by Sadoh and Sadoh [34] may be because adults are more predisposed to the associating risk factors of HBV infection than infants.

Similarly, HBeAg which signifies the replicating phase of HBV occurred in 1.5% of the HIV patients. This rate is lower than the 19.2% reported among chronic HBV carriers [35], 6.5% among pregnant Nigerian women [33], 4.7% among individuals with HBsAg seropositivity in Benue State [9] and 32.1% among HIV-seropositive persons in the Eastern Region of Ghana [26]. However, a lower rate of 0.8% was reported among HIV-1-positive patients in Jos [36] and 0.0% was reported among HIV infected participants in Ogbomoso [32]. The reason for these differences may not be unrelated to the fact that the studies were

conducted in different populations. For instance, while Odimayo *et al.*[9] studied HBsAg seropositive individuals only, the current study included even those that were HBsAg negative. Notwithstanding, since the presence of HBeAg is associated with active HBV replication and transmission of infection, it means that these patients (1.5%) in this present study have high chances of transmitting the virus to other people [37].

HBeAb is produced by the body immune system against HBeAg and its presence indicates decreased infectivity and transmission of the virus [37]. Just like HBsAb, it may also imply recovery from HBV infection [38]. This study recorded 5.0% seroprevalence of HBeAb and it is lower than the 8.0% reported by Odimayo *et al.* [9] among HBsAg seropositive individuals in Makurdi, 13.0% by Mbaawuaga *et al.* [7] in Benue State and slightly higher than 4.6% reported by Isa *et al.* [39] in Northern Nigeria. This variation may be attributed to the differences in study population.

In most epidemiological studies carried out on HBV infection, there has been a link between age and prevalence of HBV infection 28, 40, 41]. In this present study however, there was no significant association between age and prevalence of HBV infection serologic markers ($p>0.05$) (Table 1). This result is similar to the reports of Mbaawuaga *et al.* [7] in Benue State and that of Alaku *et al.* [21] among HIV patients in Central Nigeria. Nevertheless, the age of peak infection in this study falls within the age range of greatest sexual activity (21-40 years), hence, supporting the role of sex in the viral transmission.

Table 1: Distribution and prevalence of markers of HBV infection in relation to socio-demographics among HIV-positive patients attending Defence healthcare facility in Abuja, Nigeria.

Socio-demographic	No. Screened	No. Positive (%)				
		HBsAg	HBsAb	HBeAg	HBeAb	HBcAb
Age (years)						
0-10	12	0(0.0)	5(33.0)	0(0.0)	0(0.0)	0(0.0)
11-20	21	1(4.8)	11(52.4)	0(0.0)	1(4.8)	1(4.8)
21-30	54	7(13.0)	24(44.4)	1(1.9)	4(7.4)	2(3.7)
31-40	144	23(16.0)	72(50.0)	3(2.1)	8(5.6)	5(3.5)
41-50	128	7(5.5)	55(43.0)	2(1.6)	5(3.9)	2(1.6)
≥ 51	45	3(6.7)	22(48.9)	0(0.0)	2(4.4)	0(0.0)
Total	**404**	**41(10.1)**	**189(46.8)**	**6(1.5)**	**20(5.0)**	**10(2.5)**
P-value		**0.0929**	**0.9828**	**0.9071**	**0.9009**	**0.6792**
Gender						
Male	140	11(7.9)	77(55.0)	2(1.4)	4(2.9)	2(1.4)

Female	264	30(11.4)	112(41.8)	4(1.5)	16(6.1)	8(3.0)
Total	**404**	**41(10.1)**	**189(46.8)**	**6(1.5)**	**20(5.0)**	**10(2.5)**
P-value		**0.3134**	**0.1516**	**0.9462**	**0.1768**	**0.3349**
Marital Status						
Single	133	12(9.0)	64(48.1)	1(0.8)	7(5.3)	3(2.3)
Married	256	27(10.5)	119(46.5)	5(23.0)	9(3.5)	6(2.3)
Divorced	15	2(13.3)	6(40.0)	0(0.0)	4(26.7)	1(6.7)
Total	**404**	**41(10.1)**	**189(46.8)**	**6(1.5)**	**20(5.0)**	**10(2.5)**
P-value		**0.8518**	**0.9309**	**0.5854**	**0.0021***	**0.5942**
Rank						
Officer	7	0(0.0)	1(14.3)	0(0.0)	0(0.0)	0(0.0)
NCO	21	1(4.8)	3(14.3)	0(0.0)	0(0.0)	0(0.0)
Civilian	376	40(10.6)	185(49.2)	6(1.6)	20(5.3)	10(2.7)
Total	**404**	**41(10.1)**	**189(46.8)**	**6(1.5)**	**20(5.0)**	**10(2.5)**
P-value		**0.50564**	**0.05378**	**0.7999**	**0.4761**	**0.6896**

Statistically Significant (p<0.05)
NCO: Non Commissioned Officer

There was no significant association between gender and prevalence of HBV infection serologic markers in this study (p>0.05). Although HBsAg, HBeAg, HBeAb and HBcAb were more prevalent among females than their male counterparts. Surprisingly however, most previous studies reported higher prevalence of HBV infection among males than females [8, 21, 28, 42] and connected this to the higher rate of promiscuity among males than females particularly in Nigeria [43]. The higher prevalence of the viral markers among females than males in this present study may be an indication that the females contracted the virus through other risk factors that are not obvious.

Similarly, infection with HBV was not significantly associated with marital status in this study (p>0.05). However, findings from this study also show similar prevalence of HBV infection in relation to marital status with the work carried out by Aminu *et al*. [44] and recorded higher seroprevalence of HBsAg in married (10.5%) than the unmarried participants (9.0%) although those divorced had the highest rate (13.3%). The higher prevalence recorded among the married and divorced patients may be due to the risk of exposure from their current and/or previous spouses.

4. CONCLUSION

This study reported high prevalence HBV infection serologic markers among HIV-positive patients attending Defence healthcare facility in Abuja, Nigeria. This is not surprising because of the similar mode

of transmission of HBV with HIV and coupled with immunosuppressive effect of HIV which could not allow natural resolution of HBV infection. It however calls for concern because there is likeness for chronic HBV to advances faster to cirrhosis, end-stage liver disease, hepatocellular carcinoma and high mortality rate in people with HBV/HIV co-infection.

CONSENT

All authors declare that written informed consent was obtained from each participant (or other approved parties) for publication of this research work and accompanying images. A copy of the written informed consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1975 Declaration of Helsinki.3

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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