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Sero-Prevalence of Hepatitis B and C Co-Infection among HIV Patients attending Lapai General Hospital, Niger State, Nigeria

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Abstract

Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are blood borne pathogens that are continued to be globally significant as a public health problem. This study aimed at determining the prevalence of Hepatitis B and C co-infections among HIV patients accessing healthcare in Lapai General Hospital. The investigation was carried out between March and June 2019. A total of one hundred and one (101) HIV patients participated in the study conducted at the Anti-retroviral therapy (ART) clinic. Five milliliter of blood samples each collected from participants were screened for the presence of HBV and HCV. Socio-demographic information was collected by the use of a structured health-based questionnaire. The study population comprised 44 (43.6%) males and 57 (56.4%) females. The findings from the study revealed that 10.89% were positive for HBV and 13.86% were positive for HCV. The results also showed that 1 (0.99%) were positive for both HBV and HCV. Twenty-five (25) of the participants constitute the majority (24.75%) and within age group of 25-29 years. Similarly, the age group (55-59; >60 years) had one (0.99%) participant. The prevalence rates of HBV (10.89%) and HCV (13.86%) co-infections are increasing in these HIV patients. The presence of viral hepatitis in this study among HIV infected patients may also alleviate the action of drug treatment. This study therefore recommends that treatment option for viral hepatitis should be considered as a mainstream plan in HIV care and management.

Keywords: Anti-retroviral, Co-infection, Hepatitis B Virus, Hepatitis C Virus, Human Immunodeficiency Virus

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INTRODUCTION

Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are blood borne pathogens that continued to be globally significant public health problem (UNAIDS, 2017; WHO, 2017). It is estimated globally that almost 37 million people are living or infected with HIV and roughly about two thirds of the infected individuals reside in Sub-Saharan Africa (UNAIDS, 2017); over 250 million and 70 million persons are also estimated to be chronically infected and living with HBV and HCV respectively (WHO, 2017). In 2017, it was estimated that 940,000 deaths of the global HIV infected individuals occurred due to opportunistic or AIDS-related illnesses (UNAIDS, 2017).

The treatment introduction of antiretroviral therapy (ART) has significantly reduced opportunistic and HIV/AIDS-related morbidity and mortality (Obiri-Yeboah *et al.,* 2018). Nevertheless, deaths resulting from opportunistic or non-AIDS-related illnesses have been on the boost. Globally, a high number of People Living with HIV (PLHIV) die from opportunistic or non-AIDS illnesses including liver diseases (Farahani *et al.,* 2017). The high rate of morbidity and mortality associated with liver diseases among PLHIV is partly because of co-infection with HBV and or HCV (WHO, 2017) and other non-infectious agents. Therefore, the worldwide prevalence of viral hepatitis B and C among PLHIV is 7.4 and 1.0% respectively (WHO, 2017).

Viral hepatitis B infection primarily affects the liver cells. Although, it is transmitted through sexual intercourse, neonates of infected mothers got infected through breastfeeding and the placenta during childbirth. Other means of infection of viral hepatitis are also by exchange of saliva or other mucosal fluids during kissing with an infected person (Krajden *et al.,* 2005). Globally, there are more than 350 million chronic carriers of HBV and the prevalence ranges from 1% in some developed countries to 15% in developing countries (Bertolini, 2006). This virus is an enveloped DNA that has the ability to infect the human liver cells which can result in inflammation, hepatocellular necrosis and other liver challenges. This virus is seen as potential life-threatening cause of liver diseases globally that can either be acute or chronic; which may range from showing no symptom of disease or mild disease to prone symptomatic or greatly fulminant inflammation (Doo and Ghany, 2010). The acute or chronic hepatitis B virus infection is usually a self-limiting infection known to cause hepatocellular necrosis and mild inflammation with a case mortality rate between 0.5 to 1% (Lavanchy, 2004).

Viral hepatitis C is spherical, single stranded RNA virus (Ferr, 2015). It is one of the hepatotropic virus which belongs to the Flaviviridae family, genus Hepacivirus and has ability to cause chronic hepatitis, hepatocellular carcinoma (HCC) and cirrhosis (Rusyn and Lemon, 2014). It also belongs to group of pathogens that causes the disease referred to as transfusion transmissible infections (TTIs) (Zerihun *et al.,* 2018). This viral hepatitis C was recently been enlace in the pathogenesis of non-Hodgkin's lymphoma (Khaled *et al.,* 2017; Rattotti *et al.,* 2019). Over 170 million people reacted or positive to hepatitis C virus antibodies globally with estimated prevalence rate of 1-2% in most populations (Petruzziello *et al.,* 2016). It has approximately 80%-85% rate of persistence with only 15%-20% of hepatitis C virus cases that could be sero-converted and resolved (Petruzziello *et al.,* 2016). The public health importance of this viral agent is owing to its persistence in about 85% of individuals infected and the consequential risk of causing irrevocable liver cirrhosis and damage (Moradpour *et al.,* 2016).

One of significant issue is the interaction between HIV and viral hepatitis B or C. HIV/viral hepatitis B and HIV/ viral hepatitis C co-infection have a negative impact on liver infection caused by these viruses (Benhamou *et al.,* 1999; Feld *et al.,* 2005). For instance, viral hepatitis C accelerates the evolution and progression of liver infection in HIV-infected persons (Benhamou *et al.,* 1999; Rockstroh, 2006). HIV/viral hepatitis B co-infected persons are at most increased risk of developing cirrhosis, having lower rates of spontaneous resolution of the viral hepatitis B infection., Viral hepatitis B replication and has a higher risk of reactivation of previous infections (Gilson *et al.,* 1997; Kellerman *et al.,* 2003; Feld *et al.,* 2005). Viral hepatitis B and C infections also have capabilities to increase the toxicity of antiretroviral medications (Feld *et al.,* 2005).

Most studies showed increase access to ART and thus, the saddle of viral hepatitis infection in limited resource settings like Nigeria is expected to increase similar to reported cases in Europe and North America (Milazzo and Antinori, 2014; Xie *et al.,* 2016). Based on the overall national prevalence of 1.4% reported by UNAIDS in 2019 in Nigeria. UNAIDS welcomes the new survey findings and calls for better and improve prevention, treatment and care services to the people living with HIV (UNAIDS, 2019). It is therefore, of paramount important to address challenges relating to viral hepatitis problems that may cramp the success of ART programs in developing countries (Xie *et al.,* 2016). Understanding the prevalence and disease characteristics of viral hepatitis co-infection with HIV is thus significant (Matthews *et al.,* 2015). Guidelines for the clinical management of HIV infected persons recommends screening for viral hepatitis but regrettably this is not an acceptable practice in Nigeria, because it is not included in the recommended package for baseline commencement laboratory tests and ART initiation.

Contemptuousness widespread proof that suggests increasing prevalence of viral hepatitis B/HIV and viral hepatitis C/HIV co-infections, there has been no published document about the prevalence of viral hepatitis B and C in HIV infected patients in Lapai General Hospital which is one of HIV treatment centre in Niger State, Nigeria. The aim of this study is to determine the prevalence of serologic evidence of viral hepatitis B and C infection among HIV infected patients accessing care and support in this treatment centre. This will help in ascertaining the base line information on disease burden among the population of HIV infected patients.

MATERIALS AND METHODS

Study Area

The study area for this research was Lapai General Hospital., the headquarters of Lapai Local Government Area (LGA) in Niger State, Nigeria., and adjoining the Federal Capital Territory. It is located in the southern part of the State headquarters Minna, in the North by Paikoro LGA, in the South West by Agaie LGA, and in the East by Gurara LGA. Lapai LGA populace is mostly farmers and fishermen that lives in rural settings, lying at latitude 9°03′00″ north of the equator and longitude 6°34′00″ east of Greenwich Meridian. It has a landmass of approximately 3,051 km² with population of 110,127 at the 2006 census (NPC, 2008).

Ethical Considerations

Ethical clearance and approval for this study was sought from the Niger State Hospital Management Board, Minna in accordance with the code of ethics for biomedical research

involving human subjects. The study participants were enrolled after they were adequately counselled and each signed a consent form with the assurance that all information would be treated with utmost confidentiality.

Study Design

This research work was a cross-sectional survey carried out at General Hospital Lapai, Niger State, Nigeria involving one hundred and one (101) participants within age group of 19 years and above between March 2019 and June 2019. Prior to the recruitment, participants were given health talk on HIV/AIDS and its co-infection with viral hepatitis infections; they were also informed on the need of knowing their status. The recruitment of the study participants was non-randomized, and recruited into the study when found to be HIV positive and or on ART. The consent of the participate were sought and consent agreement form signed. The participants were assured of all information would be treated with utmost confidentiality. Questionnaire was administered on each participant to collect socio-demographic information. The participants were screened for viral hepatitis B and C antibodies using hepatitis B surface antigen (HBsAg) ELISA rapid test kit (ACON, USA) for HBV and HCV using rapid ELISA HCV kit ACON (ACON laboratory INC.) test strips, the positive samples were further confirmed using rapid third generation enzyme linked immunosorbent assay (ELISA) system for HBV using rapid ELISA HBV kit (ABON, Abon Biopharm Hangzhou Co., Ltd) and for HCV using rapid ELISA kit ORTHO HCV ELISA (Ortho-Clinical Diagnostics, Raritan, NJ).

Study Population

A total of one hundred and one (101) venous blood of adults living with HIV/AIDS consisting of both males and females of age group 19 - 60 years presented at the ART clinics in General Hospital Lapai, who agreed to participate in the study were included for the study. The age bracket considered were 19-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59 and >60.

Inclusion Criteria

The study included adults both males and females of various age brackets of 19-60years who were HIV infected, attended ART clinic in General Hospital Lapai.

Exclusion Criteria

The study excluded adults both males and females of various age below 19 and greater than 60 years, HIV sero-negative patients, not attending ART clinic in General Hospital Lapai.

Sample Collection and Processing

Five milliliters (5mL) of venous blood were carefully drawn from the veins of each participant into a well labeled sterile EDTA Vacutainer® blood sample tube for serological analysis for HIV, HBV and HCV. The blood samples were each centrifuged at 4,000 rotations per minute (rpm) for 10 minutes and the recovered plasma was aliquoted in the well-labeled cryovials, and kept into -40^{o}C freezer until further use.

Serological Screening

HIV infected patients that are recruited for the study were screened for confirmation of their HIV status using standard protocol for the serology according to WHO. 2006 strategy II HIV testing algorithm prior to their screening for viral hepatitis B and C. Two HIV screening test kits were used for the test, but a non-reactive result on the first ending of the testing is

reported as negative, while positive result on the first test requires that the sample is tested by a second test. Therefore, all the one hundred and one (101) aliquoted HIV infected patient samples were re-tested for HIV-1 antibody using determine HIV test kit and those that were reactive with the first kits are repeated using Uni-gold HIV-1/2 antibody test kit according to manufacturer's specifications.

All the aliquoted plasma samples of confirmed HIV sero-positive samples in the study were screened for HBV using the hepatitis B surface antigen (HBsAg) ELISA rapid test kit (ACON, USA) and ELISA positive samples were further subjected to another rapid ELISA kit (ABON, Abon Biopharm Hangzhou Co., Ltd) for confirmation according to the manufacturer's instructions.

The aliquoted plasma samples of sero-positive HIV infected patient samples in the study were also screened for antibodies against Hepatitis C virus (HCV) by rapid ELISA HCV kit ACON (ACON laboratory INC.) and ELISA positive samples were further subjected to third generation rapid ELISA HCV kit ORTHO HCV ELISA (Ortho-Clinical Diagnostics, Raritan, NJ) for confirmation according to the manufacturer's instructions.

Data analysis

The data obtained from the study was analyzed using Statistical Package for Social Sciences (SPSS version 20.0) and the descriptive statistics were obtained and presented in Tables. The level of association of the prevalence of HBV/HCV co-infection among HIV infected patients with respect to sex, age, marital status and occupation was determine using Chi-square (x^2). Values obtained were considered statistically significant at $p \leq 0.05$ at 95% Confidence interval.

RESULTS

Among the 101 samples collected, 44 (43.6%) males and 57 (56.4%) females were obtained as presented in Table 1. More so, the socio-demographic characteristics of the studied HIV infected patients; educational attainment status, marital status, occupational status, risk factors and others are presented, 25 (24.75%) of the participants were within the age group 25 - 29 years and least 1 (0.99%) each in age group 55 – 59 and >60 years respectively. Most of the participants were married 37 (64.91%), follow by those that were single 11 (19.30%), closely followed 6 (10.53%) were those married before but separated (divorced) and least participants are widow/widower 3 (5.26%). The educational status included 38 (37.62%) had at least a primary education and followed by no formal education with 29 (28.71%) while 13 (12.87%) of the participants had various tertiary education. About 22.77% of the participants were self-employed. Looking at the occupational status of participants, majority of them were unemployed 29.71%, 23.77% were self-employed, 23.77% were businessmen, 18.81% were civil servants while 5.94% were students. Risk factors in relation to viral transmitted infections, it was observed that 11 (10.89%) of the participants had unprotected sex and 6 (5.94%) participants had blood transfusion.

The participants (n =101) were disaggregated by sex and age (Table 2). The prevalence of HBV were higher among the females (6.93%) compare to the males (3.96%) and same for HCV were 7.92% of females were positive and 5.94% of the males were positive. There was no significant association ($p>0.05$) between sex and HBV or HCV status, despite more females were infected than males.

Considering age group, the HBV prevalence of 2.97% were observed at 19-24, 25-29 and 35-39 years each followed by those in the age group of 30 – 34 and 40 - 44 years with prevalence of 0.99% each. The HCV prevalence of 5.94% were observed in the age group of 25-29 years closely followed by those within the age group of 30 – 34 with prevalence of 3.96% while 0.99% were observed each in the age group 19 – 24, 35 – 39, 40 – 44 and 45 – 49 years. The HBV and HCV co-infection of 0.99% were observed in the age group of 40 – 44 years. Analysis showed that there is no significant difference between prevalence of HBV and HCV in the age group ($p > 0.05$) (Table 2). Generally, the prevalence of HBV was 10.89%, HCV was 13.86% while HBV/HCV co-infection was 0.99%.

Table1: Socio-demographic characteristics of the study participants.

Variable	Total Number (%)
Sex	
Male	44 (43.6)
Female	57 (56.4)
Age Group	
19 – 24	20 (19.80)
25 – 29	25 (24.75)
30 – 34	23 (22.77)
35- 39	15 (14.86)
40 – 44	8 (7.92)
45 – 49	5 (4.95)
50 – 54	3 (2.97)
55 – 59	1 (0.99)
>60	1 (0.99)
Marital Status	
Single	6 (10.53)
Married	37 (64.91)
Divorce	11 (19.30)
Widow/Widower	3 (5.26)
Educational Status	
No formal	29 (28.71)
Primary	38 (37.62)
Secondary	21 (20.80)
Tertiary	13 (12.87)
Occupational Status	
Unemployed	30 (29.71)
Self employed	23 (22.77)
Civil Servant	19 (18.81)
Business	23 (22.77)
Students	6 (5.94)
Risk Factors	
Unprotected sex	11 (10.89)
Blood transfusion	6 (5.94)
Scarification marks	3 (2.97)

Table 2: Age and Sex distribution of HIV infected patients with HBV and HCV.

Age Group	A (%)	B (%)	C (%)	D (%)	E (%)	F (%)	G (%)	H (%)	I (%)
19 – 24	3 (2.97)	1 (0.99)	2 (1.98)	1 (0.99)	0	1 (0.99)	0	0	0
25 – 29	3 (2.97)	0	3 (2.97)	6 (5.94)	3 (2.97)	0	0	0	0
30 – 34	1 (0.99)	0	0	4 (3.96)	2 (1.98)	3 (2.97)	0	0	0
35 – 39	3 (2.97)	1 (0.99)	1 (0.99)	1 (0.99)	0	0	0	0	0
40 – 44	1 (0.99)	0	1 (0.99)	1 (0.99)	0	2 (1.98)	1 (0.99)	0	1 (0.99)
45 – 49	0	2 (1.98)	0	1 (0.99)	1 (0.99)	1 (0.99)	0	0	0
50 – 54	0	0	0	0	0	0	0	0	0
55 – 59	0	0	0	0	0	1 (0.99)	0	0	0
>60		0				0			
Total	11 (10.89)	4 (3.96)	7 (6.93)	14 (13.86)	6 (5.94)	8 (7.92)	1 (0.99)	0	1 (0.99)

Key: A = HBV positive patients; B = HBV positive male; C = HBV positive female; D = HCV positive patients; E = HCV positive male; F = HCV positive female; G = HBV/HCV positive patients; H = HBV/HCV positive male; I = HBV/HCV positive

DISCUSSION

The serological screening of asymptomatic persons is an important detection of any infection, prompt diagnosis and intervention especially in infections like HBV and HCV would help in resolving problems caused by those infected. In HIV infected persons, HBV or HCV co-infection had been associated with increased morbidity and mortality rate (WHO, 2014). The increased risk of HBV or HCV in advanced related liver diseases of persons with HIV infection makes early HBV/HCV diagnosis and treatment utmost priority (WHO, 2014); but in Nigeria this is not the case since diagnosis and treatment is not given its desired preference, thus making the clinical care and management complicated for HIV infected persons.

The use of rapid Hepatitis surface B antigen (HBsAg) and anti HCV antibody tests can be a powerful tool for screening at the point of care. The test pinpoint persons infected with these viruses so that preventive, care and treatment services can be given as soon as possible. Persons tested are therefore immediately told of their results and are advised accordingly regarding measures to be taken about medical care and options for treatment (CDC, 2013). Although, sensitivity of rapid testing has been questioned by some scientists (Hoffmann *et al.,* 2008). However, it was reported in study carried out by Franzeck *et al.* (2013) that viral hepatitis rapid diagnostic testing has ability to give accurate assay result for serological testing of viral hepatitis in HIV infected patients in a Sub Saharan African setting.

This study established the seroprevalence of HBV and HCV co-infection among HIV infected patients and the observed positivity rate of 10.89%, 13.86% and 0.99% for HBV,

HCV and co-infection respectively. The prevalence rates of HBV and HCV among these infected patients are similar with reports in north central Nigeria by Forbi *et al.* (2007), in North East of Nigeria by Ameh *et al.* (2012), in South African cohort by Parboosing *et al.* (2008) and in Senegal by Diop-Ndaiye *et al.* (2008). The prevalence rates of HBV (10.89%) obtained in this study is not comparable with the previous reports of high prevalence in different parts of Nigeria; Keffi (20.6%) (Forbi *et al*., 2007), Jos (28.7%) (Irisena *et al*., 2002), Ilorin (30.4%) (Olatunji *et al*., 2008), Kano (70.5%) (Nwokedi *et al*., 2006) and India (33.8%) (Stud *et al*., 2001).

The prevalence of HBV, HCV and HBV/HCV in this study was found to be 10.89%, 13.86% and 0.99% respectively. Co-infection of the viral hepatitis in this study, however showed no significant difference (P>0.05) statistically between the two genders. This simply depicts that hepatitis B and C have no host preference as both sexes are susceptible to it (Table 2).

The findings from this research work also brought to light the presence of HBV and HCV co-infection among HIV persons, with the prevalence of HBV, HCV and co-infection been 10.89%, 13.86% and 0.99% respectively was established from this study. These viral hepatitis results may pose an endemic outbreak in this country. The prevalence of HBV (10.89%) observed among the HIV infected participants showed high endemicity based on WHO criteria (WHO, 1999). This finding is also in agreement with that reported by WHO in the year 1990 for Nigeria as being highly endemic for HBV with prevalence greater than 8% (WHO, 1990).

The prevalence of HBV (10.89%) obtained in this study is comparable to the findings obtained from studies in Thailand (8.7%) (Sungkanuparph *et al.,* 2004) but slightly comparable with previous studies reported in different parts of Nigeria; Lagos (9.2%) reported by Lesi *et al.* (2007) and Niger-Delta (9.7%) reported by Ejele *et al.* (2004). These variations may be because of the distribution of risk factors and geographic location of the studied participants.

The prevalence of HCV (13.86%) in this study; was not concordance with study of Adewole *et al.* (2009) who observed prevalence of 2.3% and also to the prevalence of HIV/HCV co-infection observed in 1000 individuals with reported prevalence of 2.9% in Nigerian population (Koate *et al.,* 2005). This prevalence (13.86%) in this study was however higher than 4.7% obtained in North Central, Nigeria (Ya'aba *et al.,* 2016).

A common finding with these highlighted studies is that the prevalence of HCV (13.86%) is higher than that of HBV (10.89%). This is in concordance to studies carried out in Nigeria by Haliru and Ajayi (2000) reporting lower prevalence (12.3%) of HCV. The higher prevalence rate of HCV in HIV infected persons in this study as compared to the rate for HBV in HIV infected persons could be attributed to distinct factors specifically due to lack of vaccines for HCV infection to the existence of vaccines for HBV infection. Also, sexual transmission of viral hepatitis C is lower in comparison to viral hepatitis B, this virus is mostly transmitted via infection specifically in drug addiction (Alter, 2002). Although, many research works have been done in this area and most of the findings showed high rates for these viruses in HIV infected persons because of aforementioned factors above. Most of HIV infected persons are presently co-infected with the three viruses (HIV, HBV and HCV) due to their shared mode of transmission and risk factors. Thus, co-infection with the three viruses (HIV, HBV and HCV) will increase the risk of liver diseases such as cirrhosis and mortalities in

comparison to when a patient is mono-infected with only one of the viruses. Therefore, diagnosing HBV and HCV in HIV infected persons is of paramount important in order to commence care and management (Salmon-ceron *et al.,* 2003).

In this study, there was no significant difference (P>0.05) between prevalence of HBV and HCV with respect to sex. This observation depicts that hepatitis B and C had no host preference and both sexes are susceptible to the viral hepatitis infection. The observed in this study may be related to the peculiarities on the methods of transmissions of HBV or anti-HCV dictated by socio-cultural practices and geographical related factors. The co-infection prevalence (0.99%) in this study is non-negligible, thus, these patients should receive special attention and care, as it is known that viral hepatitis infection increases morbidity and mortality in HIV infected persons (Chen *et al.,* 2009; WHO, 2014).

From this study, the risk factors in relation to viral transmitted infections, it was observed that 11 (10.89%) of the participants had unprotected sex and 6 (5.94%) participants had blood transfusion. Thus, it may be presumed that one of the modes of acquiring these viral hepatitis B and C in this study is most likely to be through unprotected sex.

CONCLUSION

The overall prevalence of HIV/HBV (10.89%), HIV/HCV (13.86%) and HIV/HBV/HCV (0.99%) co-infections have been established in this study and should be taken into account by clinicians when treating HIV/hepatitis co-infected patients as drug toxicity and interactions can increase morbidity in this population.

RECOMMENDATIONS

We recommend that viral hepatitis B and C screening should be included as part of routine test for diagnosis and treatment of HIV and campaign be intensified on the implication of viral hepatitis infections either alone or with HIV, since they both share the same mode of transmission in the country.

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