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Abstract

Introduction: HIV, hepatitis B and hepatitis C pose a public health challenge in sub-Saharan Africa and there are only few studies on co-infection of these viruses done in rural areas in Northern Nigeria. This study provides a rural perspective on HIV-Hepatitis co-infection in a Northern Nigerian community.

Methods: this cross-sectional study was carried out amongst PLWHA in a rural community hospital over a three-month period. Socio-demographic data and other relevant information were obtained from the participants and case notes using an interviewer-administered questionnaire. Hepatitis B surface antigen and antibody to Hepatitis C virus were assayed from serum using enzyme-linked immunosorbent assay (ELISA) kits developed by LabACON®. Chi-square test was used to compare categorical variables and logistic regression modelling was used to determine correlates of co-infection in the population.

Results: a total of 281 individuals participated in the study. The prevalence of Hepatitis B co-infection, Hepatitis C co-infection and triple infection was 6.0%, 14.6% and 1.1% respectively. Using Chi-square test, none of the socio-demographic characteristics, WHO Clinical Stage, viral suppression had significant association with Hepatitis B co-infection, however marital status was significantly associated with Hepatitis C co-infection and level of education was significantly associated with triple infection (p < 0.05). Logistic regression modelling generated no significant results.

Conclusion: co-infection of viral hepatitis (particularly Hepatitis C) in PLWHA is common in rural Northern Nigeria, and significant correlates include lack of formal education and being married. There is need for provider-initiated routine counselling and screening of PLWHA for viral hepatitis, with adequate follow-up and treatment of co-infected individuals and Hepatitis B vaccination for those without co-infection.

Introduction

Human Immunodeficiency Virus (HIV) infection and chronic viral hepatitis (Hepatitis B and C virus infection) are global health problems that are of concern particularly to the African people, as the prevalence of these chronic illnesses remain high in the continent, particularly the Sub-Saharan region [1-3]. About 37 million individuals are infected with HIV globally, out of which 5-20% are also co-infected with Hepatitis B virus (HBV) [4]. Chronic viral hepatitis affects about 70 million people in Africa (60 million with Hepatitis B and 10 million with Hepatitis C) [5]. Co-infection of any of these hepatotropic viruses with HIV hastens the progression of liver disease in these patients [6,7].

Nigeria, a country with a population of about 200 million people is known to have the second highest prevalence of HIV/AIDS in the world, recently pegged at 1.4% in 2019, an improvement from previous years [8]. The prevalence of HBV infection in Nigeria is between 12.2-14%, while the prevalence of Hepatitis C virus (HCV) infection ranges from 2.8 to 24.2% amongst adults from different sub-regions of the country [9-12]. Nasarawa state, a state in the North-central part of the country is home to many viruses, as high prevalence rates of HIV, Hepatitis B and Hepatitis C have been documented in the state. A recent update by the National Agency for the Control of AIDS (NACA) placed the state in the top ten list of states with the highest prevalence of HIV in Nigeria, with prevalence rate of 1.9%. Prevalence of Hepatitis B in Nasarawa state ranges between
quoted at around 13.2% to 24.2% [9,15]. Co-infection of one or more of the Hepatitis viruses with HIV is not uncommon, as these viruses all share similar routes of transmission including unsafe sexual practices, mother-to-child transmission, unsafe blood transfusion, injection with contaminated sharps in the healthcare setting, traditional tattooing and scarification to mention a few. Recent studies in the state have shown HIV-HBV co-infection rates to be about 11%, while HIV-HCV co-infection rates were about 13.5% and 5% of the HIV positive individuals had both HBV and HCV in a particular study [14]. This implies a higher risk of progression of liver disease to liver cirrhosis and hepatocellular carcinoma amongst co-infected individuals [16,17].

Studies providing information on the state of HIV-hepatitis co-infection in rural Nigeria, including the current screening practices for these viruses are lacking. This study will fill a gap in knowledge on this subject, providing information relevant for a region with high prevalence rates of HIV, Hepatitis B and Hepatitis C. This study will also inform hospital practices and policies as regards serological screening practices in HIV positive individuals who present to the hospital for medical care. The objectives of this study were to determine the prevalence of Hepatitis-Hepatitis co-infection (HIV-Hepatitis B co-infection, Hepatitis C co-infection and HIV-Hepatitis B-Hepatitis C co-infection /Triple infection), and ascertain factors associated with HIV-Hepatitis co-infection, as well as correlates of HIV-Hepatitis co-infection among people living with HIV/AIDS (PLWHA) in a Northern Nigerian community.

Methods

Study area: the study was carried out in a secondary healthcare centre located in Garaku (General Hospital, Garaku), the local government headquarters of Kokona Local Government Area in Nasarawa State. This hospital, which is the only secondary healthcare facility serving the area, provides healthcare to indigenes of the town, as well as other smaller villages in the local government. The hospital provides care to PLWHA in collaboration with the Institute of Human Virology Nigeria (IHVN), Garaku, by running an anti-retroviral therapy (ART) clinic, providing HIV Voluntary Counselling and Testing (VCT), Provider-initiated testing, treatment and follow-up, and management of complications.

Study population: the target population for this study was all HIV positive individuals who presented to the ART clinic during the study period, who were not known to have Hepatitis B or Hepatitis C, and had not been screened for Hepatitis B and Hepatitis C in the last 6 months. All those who had been previously diagnosed with Hepatitis B or Hepatitis C, or who had been screened for any of two viruses within the last 6 months were excluded.

Study design: the study was a descriptive cross-sectional study, carried out over a three-month period, from December 2019 to February 2020. Data was obtained from the participants and from their case notes using an interviewer-administered questionnaire, which was applied by trained research assistants. The age, gender, occupation (grouped according to the International Standard Classification of Occupations) [18], level of education, marital status, viral suppression (HIV RNA <1000 copies per millilitre) [19] and current WHO clinical stage were obtained and documented. Blood samples (5 millilitres) were obtained by venepuncture from the antecubital fossa and centrifuged to separate serum from packed cells. Hepatitis B surface antigen (HBSAg) and antibody to Hepatitis C virus (anti-HCV) were assayed using enzyme-linked immunosorbent assay (ELISA) kits developed by LabACON® (Hangzhou Biotest Biotech Co., Ltd, China). The manufacturer’s instructions on the use of the kits were strictly adhered to.
Sample size determination: the minimum sample size was determined using the Kish formula \((n = Z^2pq/d^2)\) where \(n = \) sample size, \(p = \) prevalence, \(q = 1-p\), \(d = \) absolute precision \([20]\) to be approximately 260, after finite population correction, assuming a confidence interval of 95% and 5% absolute precision, with a prevalence of 28.4% from a previous study\([21]\).

**Sampling technique:** a multistage sampling technique was employed. The sample size (260) was divided into three strata, based on the month of ART clinic appointments for the clients (December, January, February), with at least 87 participants allotted to each stratum. Since each month (stratum) had 8 clinic days on average, at least 11 participants were randomly selected on each clinic day throughout the study period, until the minimum sample size was reached.

**Data collection and analysis:** data was entered into the IBM Statistical Package for Social Sciences (SPSS) Version 22 (Chicago, IL, USA) and summary statistics were generated. Chi-square test was used to compare categorical variables, while univariate/multivariate logistic regression was used to model the relationship between sociodemographic variables and HIV-Hepatitis co-infection in the population. Unadjusted odds ratio (OR) and adjusted odds ratio (aOR) were generated for the univariate and multivariate logistic regression models respectively, and their associated 95% confidence intervals computed. Age, gender, level of education, occupation, marital status, WHO clinical stage and viral suppression were used as sociodemographic (independent) variables, while HIV-Hepatitis B co-infection, HIV-Hepatitis C co-infection and HIV-Hepatitis B-Hepatitis C co-infection (triple infection) each served as the dependent variables.

Level of significance was set at \(p < 0.05\).

**Ethical considerations:** ethical approval was obtained from the ethics review committee of the Federal Medical Centre, Keffi, Nasarawa state, Nigeria, with registration number NHREC/21/12/2012. Written informed consent was obtained from study participants.

### Results

**Sociodemographic characteristics of respondents:** a total of 281 respondents were sampled, 79.7% of whom were female while 20.3% were male. The mean age of respondents was 37.1±9.5, with the age of respondents ranging between 7 and 68 years. Most respondents (43.8%) were however within the 31-40 age group\((\text{Table 1}, \text{Table 1(suite)})\). Majority of the participants (43.4%) had no prior formal education, whereas 23.5% had primary, 25.3% had secondary and 7.8% had tertiary education. Two hundred and forty four (86.8%) of the respondents were married, while 24 (8.5%) and 13 (4.6%) respondents were single and divorced/separated respectively. The occupations of the respondents are classified in line with the International Standard Classification of Occupations\((\text{Table 1}, \text{Table 1(suite)})\).

**HIV status and co-infection with viral hepatitis:** all of the respondents had been previously diagnosed with HIV and commenced on Highly Active Anti-Retroviral Therapy (HAART). Two hundred and seventy five (97.9%) of the study participants were in WHO clinical stage 1, while 5 (1.8%) were in stage 2 and 1 (0.4%) in stage 3. Two hundred and fifty participants (89%) had achieved HIV viral suppression (defined as viral load <1000 copies per ml)\([19]\), while 11% had not achieved HIV viral suppression, as documented in their case notes. However, only 224 (80.4%) of the respondents had their most recent viral load tests done within the last 12 months; 54 (19.2%) had their viral load checked within the last 24 months while 1 participant’s result was from the last 36 months. Seventeen participants (6.0%) had Hepatitis B Co-infection, while 41 participants (14.6%) had Hepatitis C co-infection. Three individuals...
Our study also showed that majority of those who had Hepatitis B co-infection, Hepatitis C co-infection and triple infection were between 31 and 40 years of age, female, skilled agricultural workers, though the occupation of those with triple infection was evenly distributed between civil servants, professionals and the unemployed (Table 2, Table 2 (suite), Table 2 (suite 1)). While most of the respondents who had Hepatitis B and C co-infection were uneducated, two-third of those with triple infection had tertiary education. Furthermore, majority of the respondents with Hepatitis B co-infection, Hepatitis C co-infection and triple infection were married, in WHO clinical stage 1 and had achieved HIV viral suppression (Table 2, Table 2 (suite), Table 2 (suite 1)).

There was no statistically significant association between the sociodemographic characteristics, WHO Clinical Stage, HIV viral suppression and Hepatitis B co-infection using Chi-square test (p > 0.05) (Table 2, Table 2 (suite), Table 2 (suite 1)). However, marital status was significantly associated with Hepatitis C co-infection (p < 0.05), as 97.6% of those who had Hepatitis C co-infection were married (Table 2, Table 2 (suite), Table 2 (suite 1)). Other sociodemographic characteristics, along with WHO clinical stage and HIV viral suppression had no association with Hepatitis C co-infection (p > 0.05) (Table 2, Table 2 (suite), Table 2 (suite 1)). Only level of education had a significant association with HIV-Hepatitis B-Hepatitis C (triple) infection (p < 0.05) with two-third (66.7%) of those that had triple infection having tertiary education (Table 2, Table 2 (suite), Table 2 (suite 1)). Results of logistic regression analyses for the HIV-Hepatitis B co-infection model, after systematic removal of variables with extremely high or low odds ratio (unadjusted and adjusted odds ratios) indicated that the generated models were no different from null models, suggesting that none of the independent variables were sufficiently correlated with HIV-Hepatitis B co-infection. A similar finding was obtained when HIV-Hepatitis C and Triple infection were set as the dependent variable.

Discussion

The goal of the study was to establish the prevalence and factors associated with Hepatitis co-infection in a rural population of PLWHA in Nigeria. It was found that most of the study participants were aged 31-40 years. This finding is in agreement with recent national statistics that indicate that the burden of HIV infection in Nigeria is highest in individuals aged 15-49 years (about 75% of all PLWHA) [22]. More women (randomly selected) were found to have participated in this study, which may suggest that more women attended the ART clinic during the study period. This is generally in keeping with national statistics that reports over half of PLWHA in Nigeria to be females, in both rural and urban areas [22-24]. A study conducted in Keffi, a town not far from the study location also yielded similar male-female distribution, while another report from a study conducted six years prior, in the same hospital, confirmed the pattern [14,25]. On another note, this finding may also suggest a higher clinic attendance and health-seeking behaviour in women, though this was not an objective of the study and hence was not properly assessed. The above referenced report by the National Agency for the Control of AIDS (NACA) also shows that females with HIV had a higher incidence of sexually transmitted infections, a report which is in tandem with our findings, which showed that females had a proportionately higher prevalence of Hepatitis B co-infection, Hepatitis C co-infection and HIV-Hepatitis B-Hepatitis C triple infection [22,24].
co-existing with HIV, which is similar to previous studies conducted in the same region of Northern Nigeria[14,25]. However, studies in South-east and Southwest Nigeria found males to be more likely to have co-infection with the Hepatitis viruses [26,27]. Our report also shows that the burden of HIV-Hepatitis co-infection is higher in middle aged individuals than in any other age bracket, especially in those aged 31-40 years, similar to what was found six years prior in the same study population [25]. The prevalence of Hepatitis B co-infection, Hepatitis C co-infection and triple infection was 6%, 14.6% and 1.1% respectively. This prevalence rate for Hepatitis B co-infection is much less than the 13% reported in the same community (Garaku) years ago, and the other higher rates reported in the state, as well as the national average [13-15, 25]. The story is however different for Hepatitis C co-infection rates which are notably higher than Hepatitis B co-infection both in our study and the above mentioned Keffi study [14]. Varying co-infection rates have also been reported in different parts of the country, from 1.9% in Ekiti and 3% in Ibadan, to 23.5% in Abeokuta [27-29]. Prevalence of viral hepatitis is generally noted to be comparatively higher in Northern Nigeria than the Southern parts of the country [30]. Education and occupation could be likely drivers of this problem, as most of our respondents who had co-infection (particularly Hepatitis B and Hepatitis C) were uneducated agricultural workers, though most of those who had triple infection had tertiary education. This finding of education affecting co-infection in general is not alarming, as the study was carried out in a rural community where lack of formal education is commonplace. It is possible that a lack of formal education could preclude some individuals from utilizing their clinic visits to the utmost, by obtaining all needed information from the healthcare givers. It is also possible for a lack of formal education to favour poor health-seeking behaviours. This hence suggests the need for healthcare workers, particularly those caring for PLWHA in rural settings to give voluntary counselling and screening for Hepatitis B and Hepatitis C to PLWHA.

Worthy of note is the fact that a large majority of our respondents with co-infection were married. This suggests the perpetuation of co-infection within married couples, and possible transmission to their offspring, more so in a culture that permits polygamy. This assumption is however subject to confounding by other variables such as the presence or absence of extramarital sexual relations, one partner being a chronic carrier prior to marriage and other known risk factors for HIV, Hepatitis B and Hepatitis C infection. This finding however raises questions on why there are more married PLWHA who are co-infected. Interestingly, most of our respondents were in WHO clinical stage 1 and had achieved viral suppression (< 1000 RNA copies/ml), an acceptable cut-off in the developing world. This was a noteworthy observation, and is indicative of efforts of the caregivers in encouraging drug compliance, as well as the patients’ willingness to adhere to the anti-retroviral medications. It is however not yet common practice for healthcare providers to request routine viral hepatitis screening for PLWHA in Nigeria. A similar study in Jos however found that most of their respondents who had Hepatitis B co-infection and triple infection had higher HIV RNA loads and had more severe immunosuppression prior to the initiation of HAART [31]. Some of the limitations of this study include the fact that we did not evaluate the presence of risk factors (modes of transmission) for hepatitis B and Hepatitis C, though this may have aided in the establishment of some associations. We were also unable to run other viral markers such as Hepatitis B core antigen, which would have provided further details on the serostatus of the participants, as it relates to chronic carriage and infectivity. This was due to the limited resources available for the study.

Conclusion
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This study found a higher Hepatitis C co-infection rate relative to Hepatitis B co-infection rate, and a low rate of triple infection. Lack of formal education, as well as being married were significant correlates of triple infection and HIV-Hepatitis C co-infection respectively, from this study. The authors recommend that healthcare providers for PLWHA be aware of the risk of their patients contracting Hepatitis B and Hepatitis C, particularly those living in the Northern part of Nigeria where there is a high prevalence of HIV, Hepatitis B and Hepatitis C, and hence provide annual or biannual routine voluntary counselling and screening for them, to possibly correspond with the routine viral load checks.

What is known about this topic

- It is known that HIV, Hepatitis B and Hepatitis C are prevalent in Sub-Saharan Africa, more so in Nigeria, and co-infection of these viruses in an individual is inevitable.

What this study adds

- This study gives a snapshot of the situation in a rural community in Northern Nigeria, where the prevalence of HIV, Hepatitis B and Hepatitis C are known to be high;
- It gives the prevalence rates of co-infection for an entire local government and also identifies significant correlates of Hepatitis B and Hepatitis C co-infection amongst PLWHA in a rural community which include lack of formal education and marital status (being married).

Competing interests

The authors declare no competing interests.

Authors’ contributions

Oluwaseyitan Andrew Adesegun was the principal investigator, involved in the conceptualization, design, implementation of the research protocol and drafting of the manuscript. Olabiyi Hezekiah Olaniran and Emmanuel Bamidele were involved in the design of the study as well as drafting and critical review of the manuscript. Joseph Nicholas Inyang and Michael Adegbe were involved in the implementation of the research protocol as well as review of the manuscript. Tolulope Oyinloluwa Binuyo, Osaze Ehiohgae, Oluwafumilola Adeyemi, Oyekunle Oyebisi, Akolade Olukorede Idowu and Oluwafemi Ajose were instrumental in the critical review of the manuscript, and provided editorial oversight to the project.

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Tables

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Table 1: socio-demographic characteristics of study participants

Table 2: association between sociodemographics and co-infection

Table 2(suite): association between sociodemographics and co-infection

Table 2(suite 1): association between sociodemographics and co-infection

References


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