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## HEPATITIS B AND C COINFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS IN A TERTIARY CENTRE IN JOS, NORTH CENTRAL, NIGERIA

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1. Chima AA George – conceptualisation of study and design, data analysis, protocol and manuscript writing and editing.
2. Adetutu OJ – Data collation and study protocol implementation
3. Oseni – Momodu E. – Protocol implementation and editing.

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### ABSTRACT

**Background:** Human immunodeficiency virus HIV, hepatitis B and hepatitis C co-infection have become a global health challenge. The situation is made worse by the fact that they share the same route of transmission and co-infection increase's progression, complications and outcome illness. Prompt recognition of the co-infections leads to a well-timed early treatment with better outcome. Lack of funding prevented Hepatitis B and C routine screening among HIV positive clients at the inception of the HIV/AIDS programme in our facility. Our aim was to discover the baseline data in our local populace to enable us understand the magnitude of the problem in our facility and Jos metropolis in particular.

**Materials and Methods:** A 5-year retrospective review (from January 1<sup>st</sup>, 2009 to December 31<sup>st</sup>, 2013) was carried out. Subjects who previously tested positive to HIV and were on highly active anti-retroviral therapy in Bingham University Teaching Hospital (BHUTH), Jos were recruited into the study. The subjects' were then tested for Hepatitis B surface antigen (HBsAg) and the anti-HCV antibody. All data were collated and analysed with SPSS version 22.

**Results:** A total of 2,224 subjects were tested for hepatitis B and C viral presence. Females were 1,527 (68.7%) while 697 (31.7%) were males, giving a male: female ratio of 1:2.2.

Out of the 2,224 screened, 297 were HBV positive, 95 had HCV infection while 7 of the subjects had both HBV and HCV coexisting with HIV. The prevalence of HbsAg was 13.4% while the prevalence of HCV was 4.3% whereas only 0.31% the three infections coexisting.

**Conclusion:** Co-infection of HIV with Hepatitis B and or C infection in our environment is significant, making it imperative that HBV and HCV screening be carried out among HIV positive clients routinely to enhance early treatment and better quality of care.

### INTRODUCTION

Nigeria has the second largest number of persons living with HIV/AIDS in the world, after South Africa.<sup>1</sup> Hepatitis B is known to be a major cause of liver morbidity and mortality globally.<sup>2,3</sup> It accounts for more than 360 million cases of chronic hepatitis and 620, 000 deaths per annum.<sup>2</sup> In Sub – Saharan Africa there is hyper-endemicity hepatitis B virus infection, accounting for greater than 8% of the affected population.<sup>2</sup>

In Nigeria the prevalence of HIV is about 3% with about 3 million Nigerians living with HIV with a record of 300,000 new infections yearly.<sup>2,3</sup>

Similar routes of transmission make HIV, hepatitis B and hepatitis C co-infection a common experience.<sup>1</sup> Hepatitis B and C viral infections are known to cause chronic hepatitis, liver cirrhosis and hepatocellular carcinoma; altogether these are of grave public health concern.<sup>4</sup>

On the other hand heavy burden of HIV-HBV and HCV co-infections in several areas of the emerging world, including Nigeria have been noted and is worrisome.<sup>4</sup> Studies have shown that 15 – 60% of the usual people in several African countries may well be positive for one or more serological indicators of hepatitis B virus and this have been attributed to horizontal spreads through childhood.<sup>2,4</sup> When HIV-HBV co-exists, there is increased risk of chronic hepatitis B and liver related morbidity and mortality.<sup>2,4</sup> Hepatitis C virus is a major contributor to Non A, non B hepatitis globally.<sup>4</sup>

Hepatitis B - HIV co-infection is common and this relationship is associated with increased mortality and renal morbidity.<sup>2,4</sup> The same result is obtained for individuals with HIV-HCV infections<sup>2,4</sup>

The prevalence of HCV co-infections with HIV have been variously put at about 50% in the US.<sup>4</sup> Rapid

decline in CD4, rapid progression of HIV infection with increased morbidity and mortality as well as increased risk of antiretroviral drug related hepatotoxicity have been observed among people with HIV and HCV co-infection.<sup>2,4</sup>

Thus the presence of HIV infection in a patient therefore warrants the search for other blood-borne infections, topmost of which is hepatitis B and C infections.

Hepatitis B virus (HBV) remains endemic in many parts of the world and continues to pose a serious threat to public health.<sup>5</sup>

Hepatitis B virus (HBV) and HIV are blood borne viruses transmitted primarily through sexual contact and injection drug use. As a result of the shared routes of transmission, people at risk for HIV infection are also at risk for HBV infection.<sup>6,8</sup> Hepatitis C viruses (HCV) is a blood borne virus transmitted through direct contact with the blood of an infected person. It is estimated that HCV affects 2–15% of people living with HIV worldwide (and up to 90% of those are people who inject drugs (PWID)) and that chronic HBV infection affects an estimated 5–20% of people living with HIV.<sup>6,8</sup>

As hepatitis B virus (HBV) and HIV share routes of transmission, co-infection has become a frequent problem, with up to 9% of HIV patients from industrialized countries carrying hepatitis B surface antigen (HBsAg)<sup>1,6-8</sup>

The global estimate of burden of HIV-HCV co-infection is 2.75 million of whom, 1.3 million are people who inject drugs (PWID), and for HBV-HCV co-infection of 2.6 million. The burden of these co-infections is greatest in the African and South East Asia Regions.<sup>6</sup>

HIV-positive persons who become infected with HBV or HCV are at increased risk for developing chronic hepatitis. In addition, persons who are co-infected with HIV and hepatitis can have serious medical complications, including an increased risk for liver-related morbidity and mortality.<sup>6,8</sup>

Therefore, chronic HBV infection occurs in 5-10% of HIV-infected individuals who are exposed to HBV, a rate 10 times higher than that for the general population.<sup>7</sup>

Viral hepatitis progresses faster and causes more liver-related health problems among people with HIV than among those who do not have HIV.<sup>8</sup> Although drug therapy has extended the life

expectancy of people with HIV and liver diseases most of which are related with HCV and HBV and has become the leading cause of non – AIDS related deaths.<sup>3</sup> HIV co-infection more than triples the risk for liver disease, liver failure, and liver-related death from HCV.<sup>8</sup>

As a result of the above, anyone living with HIV should be tested for HBV and HCV, since HIV co-infection with hepatitis infection can significantly affect the morbidity and mortality pattern as well as the management of the individual affected.<sup>4,8</sup>

To help us understand the magnitude of HIV, HBV and HCV co-infection among the HIV positive clients of BHUTH we therefore decided to determine the prevalence of these disease relationships amongst our clients. We hope that the outcome of this study will provide the basis for future studies.

#### **MATERIALS AND METHODS:**

This study was conducted in BHUTH, Jos, Plateau State; Nigeria, a 250 bedded hospital with comprehensive care and treatment for people living with HIV and for over 10 years, BHUTH have cumulatively managed over 10,000 patients both in care and on treatment and are currently practicing the new standard of care which is test and treat modality irrespective of CD4 counts.

We embarked upon this study after obtaining ethical clearance from BHUTH Health Research Ethics Committee. The study population was adult Nigerians of different tribes represented in Jos metropolis that had earlier on been screened and found to be positive for HIV and has been on antiretroviral therapy.

These subjects who could not be screened for HBV and HCV infections at baseline, due to lack of fund were subsequently screened for hepatitis B and hepatitis C viral infections respectively. Informed consent was obtained from the study subjects as part of the encounter form protocol at first patient encounter and documented that the information being obtained from them were confidential but can be used for study purposes and can be published while still maintaining their anonymity by removing all identifiers.

They were however given the option of opting out of the study with no penalty attached while still receiving the full standard of care.

At baseline of recruitment into the HIV treatment programme of BHUTH, positivity for HIV was made by use of WHO approved rapid test kits, following

the Nigerian national algorithm for HIV diagnosis. The rapid test kits had 99.6% specificity and 100% sensitivity.

The blood sample collected from each client at the time of this study was analysed for the presence of HBsAg and anti-HCV antibody via a commercially existing Enzyme linked Immuno Assay (ELISA) kits Dialab Austria with 99.8% specificity and 100% sensitivity. The data resulting from the tests were computed unto the statistical package for social sciences (SPSS) version 22 and analysed with the same version of SPSS.

### RESULTS AND ANALYSIS

Between the first of January; 2012 and 31<sup>st</sup> of December; 2016 2,750 adult clients who had been confirmed to have HIV infection and had been initiated on highly active antiretroviral therapy were recruited into the study. This study subjects also included those who were newly diagnosed and had qualified for highly active antiretroviral therapy. The entry points for all the subjects were various care providers with BHUTH and also from the community based HIV awareness unit of ECWA (Evangelical Church Winning All); called The ECWA AIDS Ministry (Spring of Life).

Within the period of study 2,224 were found to be either HIV positive or HIV co-infected with HBV, HCV or with both HBV and HCV. These comprised of 697 males (31.3% of 2,224) and 1,527 (68.7%) females with male: female ratio of 1:2.2.

Of the 2,224 subjects that tested positive for HIV, 297 (13.4% of 2,224) had hepatitis B as well while 95 (4.3% of 2,224) had hepatitis C viral co-infection with HIV. The total numbers of clients who tested positive for HIV and had either hepatitis B or C 392 (17.6% of 2,224). Those that had HIV and also had hepatitis B and C coexisting with the HIV were only 7 (0.31% of 2,224).

The age range of the subjects was between 10 years and 80 years of age. While most of the subjects fell within the age range 31 – 40 (38.6%) years, followed by 41 – 50 (34.2%) years, the least age group affected by HIV in the study were those that fell into the age range 10 – 20 which accounted for 0.3% of the subjects followed by 71 – 80 years age group, which accounted for 0.8% of the subjects studied. The table below shows the gender distribution, HIV positivity with the various hepatitis viral co – infections identified:

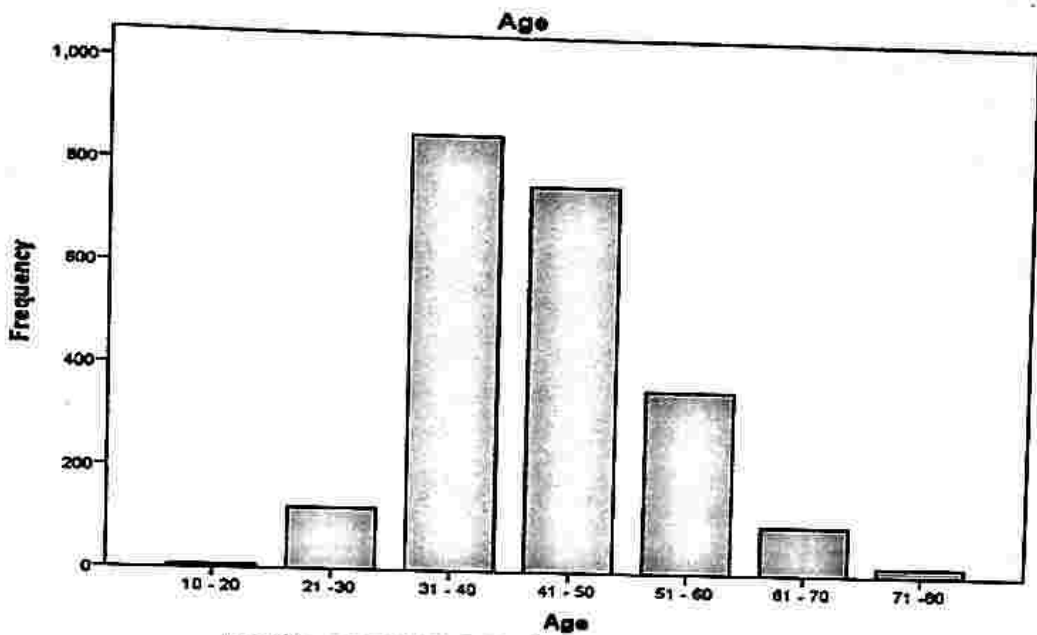
**Table Showing Gender, HIV, HIV – HBV, HIV – HCV and HIV – HBV – HCV co-infection Distribution**

TEST	Total	Males	Females	M:F Ratio
HIV	2,224	697 (31.3%)	1527 (68.7%)	1:2.2
HIV+HBV	297	112 (37.7%)	185 (62.3%)	1:1.7
HIV+HCV	95	37 (38.9%)	58 (61.1%)	1:1.6
HIV+HBV+HCV	7	2 (28.6%)	5 (71.4%)	1:2.5

The above table shows that there were more females who were HIV positive 68.7%, probably leading to more females having HBV and or HCV infection co-

existing with HIV respectively. Seven out of the 2,224 clients screened, had HBV and HCV infection co-existing with HIV infection.

Bar-Chart 1 of Age Distribution



Bar Chart 2 HIV Co-Infection with HBV and HCV

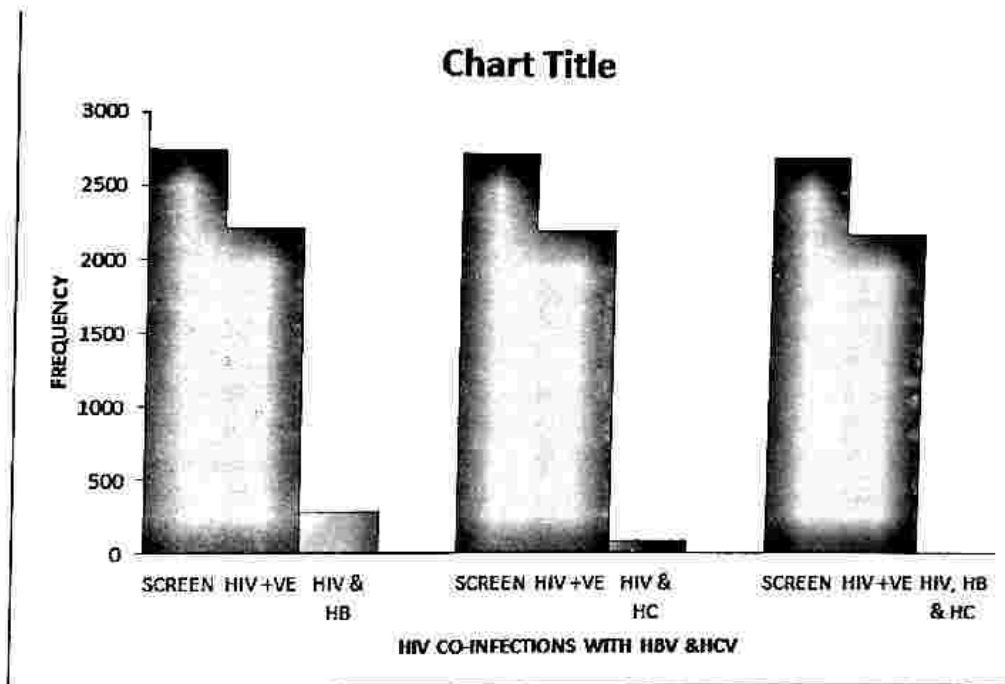


Chart showing HIV co-infections with HBV, HCV and HBV + HCV respectively

## DISCUSSION

Nigeria still maintains the second place in terms of the burden of people living with HIV after South Africa.<sup>1</sup> Since HIV shares the same routes of transmission with HBV and HCV infections, studies have shown that where prevalence of HIV is high, you also have high prevalence of HBV and HCV co-existing with HIV. This study was to derive a baseline data and to ascertain the magnitude of co-infections of HIV with HBV and or HCV infections within the region of authors practice. Co-infection with HBV and or HCV makes the clinical course, management and treatment of HIV more difficult,

hence the need to be aware of the burden and therefore seek to diagnose early for prompt and proper treatment of the affected individuals which ultimately result in better quality of health and treatment outcome.

The prevalence of HIV and HBV co-infection in this study was found to be 297 out of 2,224 (13.4%) persons found with HIV and on HAART, while the prevalence of HCV among the same group of people was found to be 97 of 2,224 (4.3%). Globally the results obtained in this study is comparable with WHO estimate of the disease burden which is 5-20%

for HBV co-infection with HIV and 2-15% for HCV co-infection with HIV.<sup>6</sup>

Our result was higher than the prevalence of HIV – HBV, HIV – HCV co-infection found in India in two separate studies where HIV – HBV co-infection prevalence was 9% and HIV – HCV co-infection was 2.2% in one study and 12% and 2% in the second study respectively.<sup>13,14</sup> The result obtained in this study was however similar to a sub-Saharan African study in which a systematic and meta-analysis was carried out to show the association between highly prevalent infections. In that review it was found that Nigerian had prevalence of HIV and Hepatitis B viral co-infection rate of 13.1% and HIV and Hepatitis C viral co-infection rate of 3.8% respectively.<sup>15</sup> Other studies in Nigeria showing higher prevalence rates include a Lagos study (28.4%) for HIV – HBV co-infection, 14.7% for HIV – HCV co-infection and 3.9% for HIV – HBV-HCV co-infection. The Lagos study was however carried out amongst very high risk groups for HIV infections.

Other studies in Nigeria that showed high prevalence rates for hepatitis C co-infection include that of Keffi (11.1%), Abuja (8.2%) while from other countries like South Africa its (13.4%) and France (17%).<sup>4,17</sup>

The reason for this high prevalence rates has been attributed to shared routes of transmission for both hepatitis B and C with the HIV virus.<sup>4,17</sup>

The HIV co-infection with HBV and HCV was however found to be 7 of 2,224 (0.31%) in this study. Again the number of females affected was more than that of males 5 out of 7 as was the case in HIV – HBV and HIV – HCV co-infections. The explanation for this may be because it has been acknowledged globally that the number of females with HIV infection at any time is usually more than the males with HIV infection and this study was not an exception where 68.7% of the study subjects were females. Results from other centres where triple viral co-infections were reported varied with this study report as follows: from Lagos 3.9%, Keffi 7.2% and Ibadan 1% all in Nigeria.<sup>4</sup>

However it must be noted that some of the studies quoted above had small sample sizes for instance that of Lagos was amongst 102 study subjects while that of this study was 2,224 and hence may have contributed to the variance in the prevalence reports. The population dynamics even though not mentioned in some of the reports could have also played a role.

The prevalence rates from other countries like Kenya was however comparable to our own report for the triple viral co-infection, since Kenya reported the same prevalence rate with our study report of 0.3% while for France it was 1.6%

The female preponderance found in this study was similar to what was found in India, but was the opposite of what was found in a study carried out in Benin City and Lagos both in Nigeria where male preponderance in the Hepatitis B and C co-infections with HIV were observed. The explanation given for this was that men were more likely to have multiple sex partners and be involved with other high risk behaviours.<sup>4,16</sup> The female preponderance observed in this study could also be explained by the fact that more females (1,527 of 2,224) 68.7% participated in this study compared with the study in Iran, Lagos, Nigeria and Benin city in Nigeria.<sup>4,13-19</sup>

In another study on HIV, Hepatitis B and C viral co-infection carried out in Iran, male preponderance was also observed but then this study was among Injecting drug users (IDU) and again the population study subjects was grossly skewed towards the male gender; thus explaining the male gender preponderance in the study (861 male and 38 female).<sup>18</sup> Another study that showed male preponderance in the reportage of HIV – HBV and HIV – HCV co-infection was the Brazilian national survey where it was reported that hepatitis B viral co-infection was more likely, the older one becomes and less likely when one is 24 years and below.<sup>19</sup> They also observed that white immigrants were more affected in the co-infection than the natural inhabitants of Brazil.<sup>20</sup>

The age group mostly affected in our study were those between the age group 31 to 40 years of age, 865 of 2,224 (38.9%) followed by age group 41 – 50 years of age, 775 of 2,224 (34.8%). This shows that greater numbers of people living with these co-infections are within the young and energetic members of our populace and thus may have an economic impact on our nation, thus making it imperative for the government of Nigeria to pay particular attention to prompt diagnosis and treatment of the affected individuals in our society.

Similar age range mostly affected, was found in a tertiary centre study in Lagos where HIV – HBV, and HIV – HCV co-infections were compared with HBV and HCV infections in HIV negative individuals.<sup>4</sup>

The ages of persons studied in our work ranged between 10 and 80 years while a study in Iran among injecting drug users showed age range of between 16

and 65.<sup>18</sup> Although the age range for the two studies were different but the age group mostly affected were the same and this may mean that a greater population of those co-infected in Nigeria may also be injecting drug user, hence underscoring the need for a study of this nature amongst injecting drug users in Nigeria.

### CONCLUSION:

We conclude that the burden of HIV, Hepatitis B and C co-infection in a tertiary institution in North Central Nigeria is significant and therefore recommend as follows:

That there is need for a standardized national strategies that will ensure prompt and uninterrupted health segment interventions and services necessary to reduce or eradicate the spread of these infections, including interventions that will reduce vulnerability and risk as well as prevention, transmission and enable early and accurate diagnosis thereby linking individuals to care and treatment.

The national strategies should also ensure standardized simple protocols and guidance, decentralization of service delivery, equitable community participation, meaningful and intentional involvement of private sector health facilities, making sure that the interventions and services offered are affordable/free and is accessible to the affected communities.

This means that, there will be promotion of public health approach that moves from focusing on individual clinical focus to population – centred nationwide protocols.

We also note that in patient management decision making, it is important to screen clients living with HIV for hepatitis B and C as important co-morbidities that could alter the course of management.

Finally the findings from this study has raised the important need for a nationwide description of the epidemiological profile of HIV – HBV and HIV – HCV co-infections in Nigeria which will be important for planning events in the Nigerian epidemiological survey works at the Federal Ministry of Health.

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