EPIDEMIOLOGY OF HEPATITIS C VIRUS (HCV) IN HEALTHY ADULTS AND HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTED PATIENTS IN NORTH CENTRAL ZONE, NIGERIA.

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ABSTRACT
Human Immunodeficiency Virus (HIV) and Hepatitis C virus (HCV) infection has each emerged as huge global epidemics. Co-infection of HIV/HCV complicates an already complex set of issues related to diagnosis, clinical disease progression, monitoring disease activity, treatment options and basic immunology. This study was aimed to determine and evaluate the prevalence of HCV among healthy adults and HIV patients accessing healthcare in North Central Zone, Nigeria. A total of 612 apparently healthy adults and 2,322 sero-positive HIV patients participated in the study at the ART clinics from June, 2013 through February, 2015. Each blood sample collected from patients were screened for the presence of antibody to HCV using rapid enzyme linked immunosorbent assay (ELISA) HCV kit ACON (ACON laboratory INC) and ELISA positive samples were further subjected to third generation rapid ELISA HCV kit ORTHO HCV Version 3.0 ELISA (Ortho-Clinical Diagnostics, Raritan, NJ) according to the manufacturer’s instructions. Socio-demographic information’s of co-infected patients were collected by the use of questionnaire. The prevalence rates for HCV among the healthy adults and HIV patients were 11 (1.8%) and 109 (4.7%) respectively and it can be noticed that there is significant difference between the two population. Having acquired knowledge on the effect of HCV co-infection, therefore there is the need to fully integrate HCV screening as a routine test in our health facilities to reduce risk of HCV related advanced liver disease in the country.

KEYWORDS: HIV; HCV; HIV/HCV co-infection; ELISA; North Central Zone, Prevalence.

INTRODUCTION
Human Immunodeficiency Virus (HIV) infection, a worldwide phenomenon is a serious public health problem. HIV infection has globally claimed over 25 million lives, and recent studies have shown that over 40 million people carry the infection. The rate of infection is remarkably high in sub-saharan Africa, where the majority of HIV and AIDS cases are concentrated.

The hepatitis C virus (HCV) is a life threatening viral infection of the liver, transmitted primarily through infected blood and blood products. Fifteen years after the discovery of the HCV as a major cause of chronic liver disease, knowledge of the natural history of the HCV infection is still limited. Approximately 170 million people worldwide are chronically infected with the virus and the infection is often described as "silent" because people may be infected for 10 to 30 years and not exhibit symptoms.

Co-infection with human immunodeficiency virus (HIV) and the HCV is a growing public health concern. Both infections are spread in similar ways, notably through shared use of needles to inject drugs and sexual activity and most studies have shown that HIV infection leads to a more aggressive hepatitis C and a higher risk of liver damage. Natural history studies with HIV-HCV co-infection have also shown more rapid progression of liver disease and end stage liver disease due to hepatitis C is now a leading cause of death in HIV-infected patients.

Despite wide spread evidence that suggest increasing prevalence of HIV/HCV co-infection there has been limited published report about the frequency of infection among healthy adults and HIV –positive patients in this region, North Central zone Nigeria. Epidemiological survey showed that about 5% of the world populations are asymptomatic carriers. Chronic HCV infection is the major cause of mortality among children and adults who might be HIV sero-negative. Studies in Nigeria have
shown that HCV and HBV is the major etiological factor for liver cirrhosis and hepatocellular carcinoma.\textsuperscript{[27]}

Studies in Nigeria on the prevalence rate of HCV shows that 2.1% in the general population, 3.6-8.0% in blood donors, 5.1% in high risk population and 8.2% in HIV–infected population.\textsuperscript{[16],[20]}. In tune with this, different states in Nigeria, such as Lagos, Osun and plateau states have recorded anti HCV antibody prevalence rates of 8.4%, 9.2% \textsuperscript{[24]} and 5.7% \textsuperscript{[18]} respectively among blood donors, pregnant women and HIV patients. However, Imoru \textit{et al.},\textsuperscript{[17]} reported HCV virus antibody prevalence of as low as 0.4% (n= 2,288) among male blood donors in Kano state.

Co-infection of HIV/HCV complicates an already complex set of issues related to diagnosis, clinical disease progression, monitoring disease activity, treatment options and basic immunology.\textsuperscript{[23]} Studies show that HIV/HCV co-infected persons demonstrate a less effective T-cell response to highly active antiretroviral therapy (HAART) and their clinical progression to AIDS is faster than those infected with HIV alone.\textsuperscript{[28]} Globally, more attention is being given to HCV–HIV co-infection as a result of its higher frequency of chronic diseases and more so, HCV–HIV co-infection is capable of impairment of the immune system recovery after starting antiretroviral therapy, thereby complicating treatment.\textsuperscript{[25]} In view of the advantage of early detection and therapy, this study was designed to determine the sero-prevalence of HCV in healthy adults and apparently their co-infections among HIV patients.

**MATERIALS AND METHODS**

**Study area**
The study area for this research work was North Central Zone, Nigeria. The country is located in West Africa between latitudes 4\degree and 14\degree North and Longitude 3\degree and 15\degree East, with total land area of 923.8x10\textsuperscript{5}sqkm bordered with the Republic of Benin in the west, Chad and Cameroon in the east, and Niger in the north. Its coast lies on the Gulf of Guinea, a part of the Atlantic Ocean, in the south. The capital city is Abuja. The country Nigeria is generally comprises six geo-political zones, which includes South West, South South, South East, North West, North East and North Central or Central Nigeria known as the middle belt of Nigeria.\textsuperscript{[31]}

Three states from the North Central geo- political region and FCT of Nigeria Were chosen for the study. The states were Kogi, Nasarawa and Niger. The three states were selected using systematic random sampling technique. This method of selection guarantees that all possible States are equally likely to be drawn.

**Study population**
A total of two thousand three and twenty two (2,322) of HIV-positive ART-naive patients and six hundred and twelve (612) of healthy adults patients samples consisting of both males and females adult of various ages (18years and above) presenting at the various selected ART hospitals/clinics in North Central Zone, Nigeria were sampled.

**Ethical considerations**
Clearance from the Health Research and ethics Committee of health facilities used for the study in North Central Zone, Nigeria (Federal Capital Territory (FCT) Abuja, Federal Medical Center (FMC), Lokoja, Federal Medical Center (FMC), Keffi and General Hospital Suleja was obtained in accordance with the code of ethics for biomedical research involving human subjects.

The patients were enrolled after they were sufficiently counseled and their written informed consents obtained. To ascertain the prevalence of these viruses and socio-demographic information, a questionnaire were used in detailing the possible risk factor for transmission.

**Sample collection**
A total of two thousand nine hundred and thirty four (2,934) samples were collected over period of fifteen months from June, 2013 through February, 2015 at the various health facilities. Five milliliters (5ml) of blood were carefully drawn from the veins of the subjects into a well labeled EDTA blood sample container for plasma samples according to the standard protocol. Plasma was used for the study.

**Screening for HCV**
All the blood samples were screened for anti-HCV using rapid chromatographic immunoassay HCV kits ACON (Acon laboratories Inc, USA). The positive HCV antibodies samples were further confirmed using third generation enzyme-linked immunosorbent assay (ELISA) kit, commercially available (Hisen HCV card). Manufacturer's instructions were strictly followed to determine the plasma samples that were sero-positive for HCV antibody.

**STATISTICAL ANALYSIS**
The results obtained was analyzed using statistical Package for social sciences (SPSS) (version 16.0), descriptive statistics were presented in bar charts. Values obtained were statistically significant at p<0.05.

**RESULTS**
The Prevalence of Hepatitis C Virus (HCV) Infection Among the Healthy Adults in North Central Zone, Nigeria.

A total of 612 of healthy adults screened for HCV infection in the study, of which 260 (42.5\%) were males and 352 (57.5\%) were females. A total prevalence of 11 (1.8\%) were reported positive for HCV infection, 6 (1.0\%) were males and 5 (0.8\%) were females. It was observed that the highest prevalence (0.82\%) of HCV infection was at age brackets (28 – 37) and (38 – 47) years respectively. The least prevalence 1 (0.16\%) was observed at age bracket (18 – 27) years. There was no
case of HCV infection observed at other age brackets (48 - 57) and > 58 years (Figure 1).

The Prevalence of HCV Infection Among HIV Infected Patients in North Central Zone, Nigeria.
The results of two thousand three hundred and twenty two (2,322) HIV infected patients screened for HCV infection is shown in Figure 2. Nine hundred and four (38.9%) were males while 1418 (61.1%) were females. Of these patients, 109 (4.7%) were positive for HCV infection, of which 35 (1.5%) were males and 74 (3.2%) were females. HIV/HCV co-infection was highest at age bracket of (28 – 37) years with an occurrence of 52 which represent 2.24% of the total. This was followed by 35 or 1.51% at the age bracket of (38 – 47) years, and 13 or 0.56% at age bracket (18-27) years. The age bracket of 58 years and above showed the lowest occurrence of 1 representing 0.04%. The prevalence 109 (4.70%) of HIV/HCV co-infection was observed in North Central Zone, Nigeria.

Socio- Demographic Information of Patients Co-infected (HIV/HCV).
Analysis of the sex related sero-prevalence of HCV infection showed that the highest prevalence of co-infection 74 (67.9) was among the females HIV patients while the males had a lower value of 35 (32.1%). This infection however showed significant difference. This simply depicts that the viruses (HCV) has no host preference as both sexes are susceptible to it. As regards to the age bracket as social factor it was seen that the co-infection was at higher rate at the age bracket of (28 – 37) years with 52 (47.7%), followed by age bracket of (38 – 47) years with 35 (32.1%), than age bracket of (18 – 27) years 13 (11.9%) and lower at the age bracket of greater than 58 years as shown in Figure 3. There was no significant difference observed in relation to percentile difference. Therefore, it can be said that no age bracket that HIV patients can not be co-infected with HCV. It is however surprising that different in HCV prevalence was found across the different marital status. It would have been expected, arguably though, that divorcees and unmarried would be more exposed to transmission of HCV infection sexually, but reverse was the case in which co-infection among married patients were 81(74.3%), followed by 22 (20.2%) unmarried (single), 5 (4.6%) were widowed patients and 1 (0.9%) was a divorcee. The high prevalence of co-infection among the better educated individuals generally could be due to the level of awareness that may be associated with their attitude, behaviours and practices, which may increased the HCV transmission.
Fig. 3: Age bracket socio-demographic information of HIV infected patients co-infected with HCV in North Central Zone, Nigeria.

DISCUSSION
This study examined the sero-prevalence of HCV in healthy adults and HIV infected patients, and the observed positivity of HCV obtained was 11 (1.8%) and 109 (4.7%) respectively. The sero-prevalence of 1.8% for HCV antibody observed in this study for healthy adults was below the lower range of 5.8 - 12.3% prevalence reported by Halim and Ajayi. However, it was also lower than 3.0% (n=366) reported by Ejele et al., [21] in Niger Delta and 8.4% (n =167) sero-positivity reported by Chen et al., [2] among blood donors in Lagos, Nigeria.

In this study, patients at aged bracket (28 – 37) years had the highest HCV antibody prevalence. This was in agreement to observation of Ejele et al., [6] and Afolabi et al., [24] who reported highest prevalence of HCV antibodies in the age group (30 – 39) years, the supposedly sexually active group. The age bracket (18 – 27) years had lowest prevalence 1 (0.16%) of HCV antibody sero-positivity. The reason for this was not immediately apparent, but this was suggestive of the probability of transmission routes other than sexual as mode of acquisition of HCV among the sero-positive patients. This was, however, not statistically significant (p>0.05) between age of the patients and prevalence of HCV antibodies.

The percentage occurrence of the co-infection observed in this study with males 6 (54.5%) had higher HCV antibody prevalence than females 5 (45.5%) shares a concordant with the report of Inyama et al., [18] and Mutimer et al., [14] which observed that the prevalence of viral hepatitis is higher in male Nigerians than the females. This might be due to the higher frequency of exposure to infected blood and blood products by the male folks as a result of occupation and social behavior. But, this observation was not consistent with that of Ejele et al., [21] that Female had higher HCV antibody prevalence than Males in Niger Delta, Nigeria. There was no statistically significant difference (p>0.05) between the prevalence rates of the male and female individuals.

The observed prevalence of 4.70% co-infection in HIV infected patients in this study was somewhat in agreement with 4.8% reported by Inyama et al., [18] in Ibadan, but lower than 8.2% reported by Agwale et al., [16] in northern Nigeria, 11.1% reported by Forbi et al., [7] in Keffi and 5.7% reported by Inyama et al., [18] in Jos. The factor responsible for these regional variations are unclear, although the reported co-infection rates of HCV in HIV patients have been variable World wide depending on the geographic regions, risk groups and the types of exposure involved, [4, 25] and could also indicate a general decreased in the prevalence of HCV infection. Madhava et al., [22] also reported a co-infection rate of 5.1% among the high-risk populations in Nigeria. The HCV co-infection among HIV-infected patients have been reported infrequently from region to region which is in agreement with variations noticed in studies carried out in Nigeria. This co-infection prevalence is non-negligible, and patients co-infected with these two viruses should receive special care, as it is known that HCV infection causes increased morbidity and mortality in HIV-positive patients. [2, 25]

In an earlier study, HCV co-infection based on plasma HCV RNA quantification was detected in 8.2% of HIV – infected patients in Northern Nigeria. [16] But, in this study 4.7% was detected. However, cross-study comparisons may be misleading because of the difference in HCV detection techniques. Quantification plasma HCV RNA is present only in patients with active HCV replication. In contrast, anti- HCV can be detected in patients with previous HCV exposure, including those with ongoing HCV replication and those whose immune responses curtailed viral replication. There may be very rare case of falsely negative anti- HCV in clients with advanced immunosuppression. [1, 8]
The overall picture of co-infection endemicity in this study is that of co-infection cases among patients of age brackets (28 – 37) and (38 – 47) years respectively, which may probably be as a result of distant intragenetic transmission. Interestingly there were lower cases of HIV/HCV co-infection among 435 subjects screened within the age bracket (18 – 27) years. Therefore, the burden of chronic liver disease associated with HIV/HCV co-infection may not likely to increased in the coming decades.

CONCLUSION
The prevalence of HCV antibodies observed among the healthy adults population and HIV infected individuals was 1.8% and 4.7% respectively and these should be seen as high risk populations. It is an indication that HCV infection are on the increase among these population, which turns out to be a major contributor to the increase in morbidity and mortality rate among these individuals as a result of rapid progression to AIDS and hepatocellular carcinoma. This underscored need for preventive measures. There is therefore an urgent need for public enlightenment campaigns, collaboration with sexually transmitted diseases programs and the introduction of routine screening of prospective blood donors for both viruses in Nigeria.

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COMPETING INTERESTS
The authors declare that they have no competing interests.

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