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PREVALENCE OF HEPATITIS C VIRUS IN HIV INFECTED PERSONS IN A TERTIARY HOSPITAL IN NIGERIA.

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ABSTRACT

Objectives: To assess the prevalence of hepatitis C virus (HCV) infection among HIV/AIDS patients in a tertiary hospital in Nigeria.

Methods: All infected persons confirmed by Elisa and aged 15 years and above seen at the University of Benin Teaching Hospital were included in the study. The subjects were recruited over a period of one year. All patients with sickle cell anemia and other immuno compromising diseases were excluded from the study. Age and sex matched controls were pooled from patients attending the out patient clinics of the hospital who were HIV negatives. A medical history and complete physical examination under bright light was carried out on all the subjects. Assays done for each of the patients were HIV screening by Elisa techniques and confirmed by double Elisa and hepatitis C virus screening.

Results: A total of 370 subjects were involved in the study of which 204 were cases (HIV positive patients) while 166 were HIV negative controls. Comparing the patients who were widowed with other marital groups, more of the widows were HIV positive than other marital groups. This difference was found to be statistically significant (X^2 =12.807, df = 1: P = 0.000). Nine (4.4%) HIV positive patients were found to be Hepatitis C seropositive while 4 (2.4%) HIV negative controls were hepatitis C seropositive. There was no statistical difference between the prevalence of Hepatitis C virus infection among HIV positive patients and the controls (HIV negative patients)

Conclusion: This study has shown that there is no statistical significant difference between the prevalence of hepatitis C virus infection in HIV positive and HIV negative patients. This is in agreement with findings in other developing countries, in the South/South (Niger Delta) of Nigeria and other regions of Nigeria.

Key Words: Prevalence, hepatitis C, HIV patients. *(Accepted 23 December 2008)*

INTRODUCTION

Human immunodeficiency virus (HIV) infection is caused by HIV-1 and HIV-2 which are members of the Lentivirus subfamily of retroviruses. They are slow acting in comparism with other acute virus infections. It is the cause of the acquired immune deficiency syndrome(AIDS).This infection has reached pandemic proportion with sub Saharan Africa being the worst hit.[1] In Eastern and Southern Africa the prevalence ranges from 9% in males to 34% in females,[1] while in Nigeria, West Africa, the prevalence is 3.9% in adults aged 15-49 and 4.4% in the population.[2]

The HIV/AIDS pandemic has affected the prevalence of several diseases notable amongst which are tuberculosis[3], toxoplasmosis[4], superficial and deep mycosis[5]etc. Hepatitis C (HCV)formerly designated Non-A, Non-B hepatitis is a linear, single stranded RNA virus belonging to the Flaviviridae with at least six genotypes identified.[6,7] It is transmitted sexually and parenterally and leads to acute and chronic hepatitis, liver failure ,cirrhosis and hepatocellular carcinoma in those infected. It is also a very important potentially lethal and presently treatable infection, which may affect the course and worsen the outcome of HIV disease, even when these patients are on adequate treatment with antiretroviral drugs (ARVs), and may be affected by the presence of HIV disease.[8,9]

The prevalence of HCV in the developed world appears to be lower than in the developing world. A prevalence of 0.3% has been reported in Canada and Northern Europe 0.6% in United States of America and Central Europe 1.2 1.5% in Japan and southern Europe, as compared with 3.5% to 6.4% in certain regions in Africa.[10] South African reports put the prevalence at between 0-1.5%.[11]In Nigeria, the prevalence rate of HCV varies between 5.8-12.3%[12-15]. In Benin City it was 12.3%, in Lagos ,6%, in Ilorin, 5.8%.Literature available shows that HIV disease affects the prevalence and prognosis of HCV infection. The prevalence of HCV in the developed world is 0.3%- 0.6% but it is 38-43% in HIV infected

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persons.[16] Among drug users it may be as high as 80%.[16] A study in Malawi amongst pregnant women showed that there was no statistical evidence to suggest that HIV positively was associated with an increased prevalence of HBV or HCV markers.[17] Daar and his colleagues reported that in a large cohort of hemophilliacs, hepatitis C may accelerate HIV disease progression[9] and this finding was corroborated with a Swiss Cohort study.[18]

Sulkowski and co-workers suggested that HCV/HIV co-infection was not associated with increased risk of death or development of opportunistic diseases,[19] while Mao and colleagues did not find evidence for increased HCV genetic substitution in early HIV infection.[20]

The prevalence rate of HCV is shown to be higher in HIV infected patients than in the general population worldwide.[16,21] The prevalence of HCV in HIV infected persons in Nigeria ranges between 0.9% in the Niger delta[22] to 18.3% in North central Nigeria[23,24]. This study will provide data that can be used for further studies and useful recommendations and policies on this subject can be formed.

MATERIALS AND METHODS

Subjects for the study were recruited from the University of Benin Teaching Hospital (UBTH). UBTH is a tertiary healthcare facility set up in 1973. It caters for the tertiary health care needs of patients referred from Edo, Delta, Ekiti, Bayelsa, Kogi and Ondo States. Its coverage serves a population of over 5million people. The Dermatology/Venerology unit in UBTH handles cases of sexually transmitted diseases including HIV/AIDS referred from these areas and even beyond. It has facilities for diagnostic and confirmation tests for HIV/AIDS.

All HIV infected persons, confirmed by ELISA and aged 15years and above of either gender seen in the University of Benin Teaching Hospital were included in the study. The subjects were recruited over a period of one year (Ist January to 31st December 2002). Exclusion criteria included HIV negative patients or HIV positive patients with sickle cell anemia and other immune compromising diseases such as diabetes mellitus and lymphoma. Age and sex matched controls were pooled from patients attending the out patient clinics of the hospitals who were HIV negative.

All HIV infected patients on presentation were interviewed, examined, tested and included in the study until the sample size was achieved. Pre-test and post-test HIV counselling was administered to all the subjects. The tests were carried out with the informed consent of all patients. Using a prevalence of 4%[8], sample size for comparative study[16] per group was 48. However a sample size of 204 patients (HIV positive patients) and 166 controls (HIV negative patients) was used. A medical history and a complete physical examination under bright light were also carried out. The data acquisition sheet was researcher administered after a written consent.

LABORATORY TESTS

Assays done for each of the patients were

1. HIV screening by ELISA techniques and confirmed by double ELISA
2. Hepatitis C virus screening

Fasting blood sugar and Hemoglobin electrophoretic pattern were used to rule out diabetes and sickle cell anemia. Full blood counts, electrolytes and urea and liver function tests were also done.

HIV Testing

Determine test™ kit by Abbot was used. It is an immunochromatographic test for the qualitative immunoassay for the detection of antibodies to HIV- 1 and HIV 2 in human serum, plasma or whole blood. It was used in parallel with STAT-PAK® by CHEMBIO diagnostics inc. Where results were indeterminate, GENIE II by BIO-RAD was used to break the tie. The principles and procedures of these tests are similar. GENIE II is a dual recognition immunochromatography and immunoconcentration test.

Sample is added to the sample pad. As it migrates through the conjugate pad, it reconstitutes and mixes with the selenium colloid antigen conjugate.This mixture continues to migrate through the solid phase to the immobilized recombinant antigens and synthetic peptides at the patients' window site. If antibodies to HIV -1 and or HIV- 2 are present in the sample, they bind to the antigen selinium colloid and to the antigen at the patient window, forming a red or pink/purple line at the patient window site. If not present no red line is formed.

Procedure

Human serum plasma or whole blood was collected by venupuncture in an aseptic manner in such a way to prevent hemolysis. For serum and plasma samples, 50ul of samples using a precision pipette for Determine, 5ul for STAT-PAK was dropped on the sample pad. Fifteen to sixty minutes (15-60minutes) after, the result was read for Determine test, STAT-PAK results were read in 10 minutes.

Interpretation

In a positive Determine test, 2 red bars appear in the control window and in the patent window of the strip. When only one bar appears in the control window, it is negative. It is invalid if no bar appears. STAT-PAK is positive when two pink/purple lines appear one in the test area one in the control area and invalid when none appears.

Hepatitis C testing

The test was done using Clininotech (Clini-Tech Diagnostic pharmaceuticals Canada) anti HCV cassette which is a rapid direct binding procedure, which usually determines antibodies to Hepatitis C

infection. This test is primarily based on the principle of double antigen sandwich immunoassay in which purified recombinant antigens are employed sufficiently to identify anti-HCV with high sensitivity and specificity.

Specimen collection and preparation

Anticoagulant is not required in serum collection. The blood was allowed to clot and the serum separated from the clot, which was then used for testing. The serum was stored in fridge or freezer if not used that day and brought to room temp prior to testing.

Test procedure

The test device was removed from its pouch, it was then dipped into fresh serum specimen for 2-3 seconds with the arrow end pointing down. It was then laid flat on a clean dry non-absorbent surface (test bench)

Results were read within 10 20 minutes depending on the concentration of Anti HCV in serum. After 30minutes results were considered invalid. A positive result shows 2 distinct red bands on the positions indicated T (test) and C (control). A single band at ' C' indicated a negative result. All tests were carried out at room temp and at least 2 people visualized the test bands in a well-lit laboratory.

The data were analysed using the EPI-INFO 2000 statistical program version 6.0 and PEPI version 3. Continuous variables were described with means while discontinuous variables were described with proportions. When comparing groups of subjects, the X^2 (Chi square) test was applied to determine the significance of the difference observed.

RESULTS

A total of 370 subjects were involved in the study. Two hundred and four (204) were HIV positive patients while another 166 were HIV negative controls. The two groups of patients in the study were comparable as regards age and sex. (Table1). Amongst the HIV positive patients, 81 (39.7%) were males and 123 (60.3%) were females with a mean age of 37.14± 10.94 and an age range of 15- 70 years. For the controls, 66 (39.8%) of them were males, while 100 (60.2%) were females with a mean age of 37.21± 11.4 and range of 15-70. There is no significant age and sex difference between HIV positive patients and controls (P>0.05) (Table 1). All patients were recruited into the study prior to the commencement of anti retroviral therapy. (Table 1)

Table 2 shows the clinical staging of HIV patients used in the study. A total of 145 (71.1%) were asymptomatic. 56 (69.1%) of them were males while 89 (72.4 %) were females. 2 (1.0%) had persistent generalized lymphadenopathy, and were both males. 57 (27.9 %) patients had full blown AIDS, 23 (28.4%) of whom were males while 34 (27.6 %) were females.

Table 3 shows the distribution of the HIV positive patients and the HIV negative controls according to marital status. (Table 3) Among the HIV positive patients, 5 (2.5%) were divorced, 116 (56.9%) married, 5 (2.5%) separated, 58 (28.4%) single and 20 (9.8%) were widowed. Among the HIV negative patients (control group), none was divorced or separated, 110 (66.3%) were married, 55 (33.1%) were single, while 1 (0.6%) was widowed.

Comparing the widowed group with the other marital groups, more of the widows were HIV positive then other marital groups. This difference was found to be statistically significant. (X^2= 12.807, df = 1: P = 0.000 [3.45E-04] Table 4.

Comparing the divorced patients with other marital groups, all 5(100.0%) were HIV positive, while none was HIV negative. For the other marital groups, 199 (54.5%) were HIV positive, while 166 (45.5%) were HIV negative. This difference was found to be statistically significant using Likelihood ratio Chi-square (X^2= 2.943, df = 1; P=0.086). (Table 4)

Comparing married group with unmarried (single, divorced, separated and widowed) group, 116 (51.3%) were found to HIV positive, while 110 (48.7%) were found to be HIV negative. Among the unmarried group 88 (61.1%) were found to be HIV negative, while 56 (38.9%) were found to be HIV negative. This difference was not found to be statistically significant (X^2= 3.421, df = 1: P = 0.064). (Table 4)

Table 5 shows the prevalence of Hepatitis C virus infection amongst HIV seropositive patients compared to HIV seronegative patients. 9 (4.4%) HIV positive patients were found to be Hepatitis C seropositive, while 4 (2.4%) HIV negative controls were hepatitis C seropositive. This difference was not found to be statistically significant (Likelihood ratio Chi- square with Yates's correction = 0.584, df = 1: P = 0.45)

Table 1: **Age and Sex Data of Patients and Controls.**

Demographic Data	HIV Positive Patients	HIV Negative Patients (Controls)
Sex		
Male	81 (39.7%)	66 (39.8%)
Female	123 (60.3%)	100 (60.2%)
Total	**204 (100.0%)**	**166 (100.0%)**
Age (years)		
Mean age	37.14	37.21
Standard deviation	10.94	11.30
Range	15-70	15-70

Table 2: **Clinical Staging of HIV Positive Patients.**

Clinical stage	Male	Female	Total (%)
Asymptomatic, generalized Iympadenopathy (Stage I)	0	0 (0%)	0 (%)
Weight loss<10%, prurigo, fungal Nail infection, H.zoster*, recurrent URTI (stage II)	56 (69.1%)	89 (72.4%)	145(71.1%)
Weight loss >10%, chronic diarrhea, Fever, oral candidiasis/HL*, PTB*, Severe bacterial infections (stage III)	2 (2.5%)	0 (0.0%)	2 (1.0%)
AIDS- defining illnesses (stageIV)	23 (28.4%)	34 (27.6%)	57 (27.9%)
Total	**81 (100%)**	**123 (100%)**	**204 (100%)**

- Herpes zoster
- Oral hairy Ieukoplakia
- Pulmonary Tuberculosis

Table 3: **Marital Status of HIV Positive Patients (HIV+) and Controls (HIV-).**

Marital status	HIV+ (%)	HIV – (%)
Divorced	5(2.5)	0(0.0)
Married	116(56.9)	110(66.3)
Separated	5(2.5)	0(0.0)
Single	58(28.4)	55(33.1)
Widowed	20(9.8)	1(0.6)
Total	**204(100.0)**	**166(100.0)**

Table 4: **Marital Status of HIV Positive Patients (HIV+) and Controls (HIV-).**

HIV status	Marital status (N = 370)		X^2	df	P
	Divorced	Other Marital groups			
HIV+	5 (100.0%)	199(54.5%)			
HIV-	0 (0.0%)	166(45.5%)			
Total	5 (100%)	365(100%)	2.943	1	0.086
	Widowed	Other Marital groups			
HIV+	20(95.2%)	184(52.7%)			
HIV-	1(4.8%)	165(47.3%)	12.807	1	0.000
Total	21(100%)	349(100%)			
	Married	Unmarried groups			
HIV^+	116(57.3%)	88(61.1%)			
HIV^-	110(48.7%)	56(38.9%)	3.421	1	0.064
Total	**226(100%)**	**144(100%)**			

Table 5: **Hepatitis C Status of HIV+ Patients and Controls.**

Hepatitis C Sero-status	HIV+ (%)	HIV-(%)	Total
Hepatitis C+	9(4.4)	4(2.4)	13(3.5)
Hepatitis C-	195(95.6)	162(97.6)	357(96.5)
Total	**204(100.)**	**66(100.)**	**370(100.)**

Likelihood ratio Chi- square with Yates's correction = 0.584, df = 1: P = 0.45)

DISCUSSION

The prevalence of hepatitis C infection among HIV positive patients in this study was found to be 4.4%, while among HIV negative (controls) patients was 2.4%. Though there was a higher prevalence among the HIV positive patients, this difference was not found to be statistically significant. ($X^2 = 0.584$, df = 1: P=0.445)

The prevalence rates of hepatitis C infection in both the controls and patient were higher than the findings in the developed world Canada and Northern Europe (0.3%)[8], United States of America and Central Europe (0.6%)[8], Southern Europe and Japan (1.2 -1.5%)[8] but similar to that in certain regions in Africa (3.5 6.4%)[10]. In Nigeria, the prevalence ranges from 5.8-12.3%[12-15] it is 0,9-18.3% amongst HIV infected persons[22-24] This study corroborates the fact that the prevalence of Hepatitis C infection is higher among the developing then the developed countries. Among HIV infected patients, the prevalence of HCV seem to be higher in the developed countries (38-43%) than the findings of this study (4.4%). This is the case among drug users in the developed countries (80%). This may be explained by the fact that in sub-Saharan Africa, the major route of HIV transmission is Heterosexual contact. This route is not a major route for Hepatitis C transmission.[19] HCV is most frequently transmitted via blood transfusion (83%), organ transplanted (78%), vertical transmission (6.2%) and needle stick injury (6.1%)[26-27] However in the developed world, HIV is co-transmitted with HCV during intravenous drug abuse, and homosexual intercourse which are major routes of HIV transmission.

Imarengiaye and his collegues in their study on the risk of transfusion transmitted hepatitis C virus in a tertiary hospital found at the University of Benin Teaching Hospital, Edo State, Nigeria, a 3% frequency of HCV among transfused units of Whole blood[28]. This is similar to the findings of this study. This also compares with other studies done in Nigeria where the prevalence ranges from 5.8-12.3% and 0.9-18.3% in HIV infected patients.[12-15,22-24]The finding of 4.4% in this study is within this range.

An interesting finding of this study was that all the divorced patients were HIV positive. This difference was found to be statistically significant when the divorced patients were compared with other marital groups using, Likelihood ratio Chi- square (X^2= 2.943, df = 1; P=0.086). This could be as a result of the fact the being divorced exposed them to irregular sexual partners or their (former) spouses being HIV positive. The prevalence of HCV in Nigeria is not known but data from other countries indicate that the virus increases morbidity and mortality. HCV infection runs a chronic course. It may be asymptomatic but may present as chronic liver

disease. HCV infection is an important cause of chronic liver disease, transplants and liver carcinoma in developed countries where screening is routinely done.[29] This underscores the need for institution of routine screening in centres in Nigeria especially blood transfusion units and maternities. The advent of HIV/AIDS which worsens HCV disease progression[19] is also a very important reason for routine screening of HCV in institutions. This will serve as an effective preventive strategy.

This study investigated the prevalence of HCV in HIV/AIDS patients. The results indicate that HCV infection is 4.4% amongst HIV/AIDS patients. This underscores the need for more aggressive screening of HCV both in this group of patients and in the general population as the sequalae of this disease are very severe.

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