Original article

Prevalence of hepatitis B, C and D among patients on highly active antiretroviral drug therapy (HAART) in Calabar metropolis, Nigeria

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Abstract

Co-infection of Human Immunodeficiency Virus/Acquired Immune Disease Syndrome (HIV/AIDS) with hepatitis is linked with amplified morbidity and mortality. This study was to investigate the prevalence of hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) among patients on highly active antiretroviral drug therapy (HAART). A total of 200 subjects currently on HAART and 50 non-HIV positive individuals (control subjects) aged 10-75 years were recruited for the study. Hepatitis B surface antigen and hepatitis C viral antibodies were screened with ACON test strip while HDV was screened with human hepatitis D virus ELISA kit. Demographic data of subjects were obtained with questionnaires. Determination of the CD4 counts was done using the Cytoflow counter. Among the test subjects, prevalence of HBV infection was 16(8%), HCV was 6(3%), mixed infection with HBV and HCV was 2(1%), and HDV was 0(0%). Among the control subjects, infection with HBV was 6(12%), 4(8%) for HCV and none for HDV or mixed infection. There was no statistically significant difference (p=0.491). Males had a higher occurrence of HBV infection 9(11.4%) and HCV infection 4(5.1%) than the females who had 7(5.8%) for HBV and 2(1.6%) for HCV, but this was not statistically significant (p=0.0879). Subjects with CD4 count range of 1401-1600 had the highest occurrence 1(20%) for HBV and 1201-1400 range for HCV 1(8.3%) but the difference was not statistically significant (p=0.504). In conclusion, infection with HBV and HCV is widespread among patients on HAART and routine screening is advocated for efficient management of the disease.

Key words: Calabar, HAART, HBV, HCV, HDV, Prevalence

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In developing countries like Nigeria, one of the significant public health problems is HIV/AIDS. But with the advent of effective antiretroviral therapy, the disease has now become a controllable chronic infection. Human immunodeficiency virus (HIV) and hepatitis co-infection has been reported to amplified morbidity and mortality of the disease. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are associated with serious liver complications like chronic hepatitis, cirrhosis...
and hepatocellular carcinoma\textsuperscript{3,4}. In Nigeria, there have been reports of a serious burden of HIV/AIDS co-infections with HBV and HCV\textsuperscript{5,6}. This is probably due to their shared route of transmission. Hepatitis D virus has been shown to rely on HBV for transmission since it uses the hepatitis B surface antigen (HBsAg) as its own viron coat\textsuperscript{6}. Rapid reduction in the CD4 count has been reported to occur in HDV and HIV co-infections, which results in rapid progression and fatality of HIV infection\textsuperscript{10}. Disease progression in HIV/Hepatitis co-infection is faster and associated with antiretroviral drug hepatotoxicity\textsuperscript{11}. This research was to investigate the prevalence / co-infection of HBV, HCV and HDV with HIV among patients on HAART and to offer suggestions that will enhance the effective management of the disease.

Materials and Methods

\textit{Study area:} This study was carried out in Calabar metropolis in Cross River State, Nigeria. Calabar metropolis is comprised of two local government areas (Calabar Municipality and Calabar South). The geographical coordinates of Calabar are 4° 57’ 0” North, 8° 19’ 0” East. It has an area of 406 square kilometers and a population of 371,022 at the 2006 census.

\textit{Ethical clearance}

Ethical clearance was obtained from the Cross River State Ministry of Health, Calabar. Informed consents were obtained from the subjects. Structured questionnaires were used to obtain demographic data of subjects.

\textit{Collection of samples}

Blood samples were collected from subjects on HAART and the sera separated. The sera were stored at a temperature of \textdegree{}C prior to testing, samples were brought to room temperature before being analyzed according to the different manufacturer’s instructions as listed below.

Serial algorithm of screening for HIV was followed using Determine test strip and UniGold\textsuperscript{12}. Pantee Cyflow counter machine was used for determination of CD4 count.

The sera were analyzed for HBsAg and HCV antibodies using ACON hepatitis test strip manufactured by ACON laboratory Inc\textsuperscript{13-15}. Diagnosis of HDV was done with human HDV antibody kit (IgG ELISA Kit) with Catalog Number MBS702477 manufactured by Mybiosource, Inc. San Diego, California.

\textit{Data analysis:} Data was analyzed using Statistical Package for Social Sciences (Version 20). Chi-square test was used to compare differences among groups. Probability value of less than or equal to 0.05 was considered significant.

\textbf{Results}

Two hundred (200) HIV positive subjects on highly active antiretroviral therapy (HAART) were enrolled as the test group while 50 HIV negative subjects were used as control. Table 1 demonstrates the prevalence of HBV, HCV and HDV among subjects by age. Among the test subjects, prevalence of infection was 16(8%) for HBV infection, 6(3%) for HCV, 2(1%) for mixed infection with HBV and HCV and 0(0%) for HDV infection. In the control group, a prevalence of 6(12%) was recorded for HBV, 4(8%) for HCV and none for HDV or mixed infection. The difference was not statistically significant ($\chi^2 = 1.422$ df(2) $p=0.491$). In the test group, those between the ages of 51-60 years had the highest infection rate 2(25%) for HBV while subjects aged 0-10, 11-20 and >71 years had no infection 0(0%). The age group of 21-30 years also showed the highest prevalence rate with HCV infection with 3(4.8%) while subjects aged 0-10, 11-20, 51-60, 61-70, and ≥71 years had no infection 0(0%). There was no infection among any age group for HDV infection. Among those with both infection (HBV and HCV), subjects in age group 31-40 years had the highest prevalence rate 1(1.9%). Among control subjects with age group 21-30 years had the highest rate of infection for HBV 3(15.8%) while subjects aged 31-40 years had the highest infection rate for HCV 2(12.5%). There was no mixed infection in the control group. The prevalence of HBV, HCV and HDV according to gender is shown in table 2. Males had a higher occurrence of HBV infection 9(11.4%) and HCV infection 4(5.1%) than the females who had 7(5.8%) for HBV and 2(1.6%) for HCV. But this was not statistically significant ($\chi^2 = 0.257$ df(2) $p=0.0879$). In the control subjects, the females 4(14.3%) were more infected than the males 2(9.1%) for HBV infection while males 3(13.6%) were more infected than the females 1(3.6%) for HCV infection.

The distribution of infection according to CD4 count is as shown in table 3. Subjects with CD4 count 1401-1600 had the highest infection rate for HBV 1(20%) and CD4 count 1201-1400 for HCV 1(8.3%). But the difference was not statistically significant ($\chi^2 = 11.292$ df(12) $p=0.504$). No group was infected with HDV infection. Among those with mixed infection for HBV and HCV, subjects with CD4 count 201-400 had a prevalence rate of
In the control group, subjects with CD4 count 401-600 had the higher infection rate for HBV (320%) while those with CD4 count 0-200, 201-400, 1001-1200, 1201-1400, 1401-1600 and 1601-1800 had no infection 0(0%). Subjects with CD4 count of 801-1000 had a higher prevalence rate of 2(28.6%) for HCV. There were no infections for HDV and no mixed infection.

Table 1: Prevalence of HBV, HCV, and HDV amongst subject examined according to age

| Age group | Test subjects | Control subjects |
|-----------|---------------|------------------|
|           | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection |
| 0-10      | 5 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 11-20     | 6 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 21-30     | 63 (5.7)      | 3 (4.8)          | 0 (0.0)                  | 0 (0.0)                           | 19 (15.9)     | 2 (10.5)         | 0 (0.0)                  | 0 (0.0)                           |
| 31-40     | 53 (4.7)      | 2 (3.8)          | 0 (0.0)                  | 1 (1.9)                           | 16 (21.2)     | 2 (12.5)         | 0 (0.0)                  | 0 (0.0)                           |
| 41-50     | 56 (4.7)      | 1 (1.8)          | 0 (0.0)                  | 1 (1.8)                           | 8 (12.5)      | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 51-60     | 8 (0.0)       | 2 (25)           | 0 (0.0)                  | 0 (0.0)                           | 4 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 61-70     | 7 (1.4)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| ≥71       | 2 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| Total     | 200 (8.0)     | 6 (3)            | 2 (1)                    | 50 (12.5)                         | 4 (8)         | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |

Table 2: Prevalence of infection amongst subject examined according to gender

| Gender | Test subjects | Control subjects |
|--------|---------------|------------------|
|        | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection |
| Female | 121 (7.5)     | 2 (1.6)          | 0 (0.0)                  | 1 (0.8)                           | 28 (14.3)     | 1 (3.6)          | 0 (0.0)                  | 0 (0.0)                           |
| Male   | 79 (11.4)     | 4 (5.1)          | 0 (0.0)                  | 1 (1.3)                           | 22 (3.1)      | 3 (13.6)         | 0 (0.0)                  | 0 (0.0)                           |
| Total  | 200 (16.8)    | 6 (3)            | 2 (1)                    | 50 (12.5)                         | 6 (12)        | 4 (8)            | 0 (0.0)                  | 0 (0.0)                           |

Table 3: Distribution of infection according to CD4 count of subjects examined

| CD4 count | Test subjects | Control subjects |
|-----------|---------------|------------------|
|           | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection | n (%) with HBV infection | n (%) with HCV infection | n (%) with HDV infection | n (%) with both HBV & HCV infection |
| 0-200     | 18 (16.7)     | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 201-400   | 42 (7.1)      | 1 (2.4)          | 0 (0.0)                  | 2 (4.8)                           | 0 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 401-600   | 47 (8.5)      | 2 (4.3)          | 0 (0.0)                  | 0 (0.0)                           | 15 (23)       | 2 (13.3)         | 0 (0.0)                  | 0 (0.0)                           |
| 601-800   | 35 (8.6)      | 1 (2.9)          | 0 (0.0)                  | 0 (0.0)                           | 13 (21.4)     | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 801-1000  | 18 (11.1)     | 1 (5.6)          | 0 (0.0)                  | 0 (0.0)                           | 7 (14.3)      | 2 (28.6)         | 0 (0.0)                  | 0 (0.0)                           |
| 1001-1200 | 10 (0.0)      | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 4 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 1201-1400 | 12 (0.0)      | 1 (8.3)          | 0 (0.0)                  | 0 (0.0)                           | 5 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 1401-1600 | 5 (20)        | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 2 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| 1601-1800 | 13 (0.0)      | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           | 4 (0.0)       | 0 (0.0)          | 0 (0.0)                  | 0 (0.0)                           |
| Total     | 200 (16.8)    | 6 (3)            | 2 (1)                    | 50 (12.5)                         | 6 (12)        | 4 (8)            | 0 (0.0)                  | 0 (0.0)                           |
Discussion

This study observed a prevalence of 8% and 6% for HBV and HCV respectively among patients on highly active antiretroviral drug therapy (HAART) in Calabar. There was mixed infection of both HBV and HCV. No HDV was detected. This is similar to report by Collenberg et al. in Burkina Faso who observed 4.8% for HBV. This prevalence of 8% for HBV and 6% for HCV are lower than that reported by Balogun et al. who had HBsAg and HCV positive cases in 28.4% and 14.7%. These results are also lower than that reported by Forbi et al. in North Central Nigeria, Parboosingh et al. in South Africa, Diop-Ndiaye et al. in Senegal and Larsen et al. in France. The results in this work are also lower than that of Vincent et al. who had a prevalence of 23% for HBV, 16% for HCV and 10% mixed infection on hepatitis B and C in HIV/AIDS subjects and Soriano et al. who had 23% for HBV, 16% for HCV and 10% mixed infections in Hong Kong.

Similarly, this result is lower when compared to 11.5% prevalence rate for HBV by Adewole et al. in Ile Ife and Denue et al. with 12.3% prevalence of HBV in Maiduguri, Nigeria. The high prevalence of infection in 25% with HBV obtained among subjects in the age group 51-60 years is similar to that of Inyang-Etoh et al. who observed 25% in the age group 51-60 years among patients on antiretroviral drug therapy in Calabar. But this prevalence is lower than 12.3% for HBV which Denue et al. observed in Maiduguri, Nigeria among HIV patients. Those in the age group 21-30 years had the highest prevalence with HCV infection (4.7%). This is higher than that reported by Denue et al. of 1.4% for HCV. Among those with mixed infection, subjects within the age group 31-50 years had a prevalence of 1.7% but there was no statistical significant difference in mixed infection (p>0.05). In this study males were more infected with HBV and mixed infection than females but the difference was not statistically significant (p>0.05). This might be due to the tendency of men to have multiple sexual partners.

Conclusion

This work has shown that HBV and HCV are common among patients on HAART probably due the routes of HIV transmission being similar to those of HBV, HCV and HDV. We therefore recommend that this category of patients be screened for HBV and HCV before baseline treatment is given for effective management.

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