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THE INCIDENCE OF JAUNDICE AND ACUTE PANCREATITIS IN HIV POSITIVE PATIENTS ON ANTI-RETROVIRAL THERAPY IN NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL, NNEWI

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ABSTRACT

A prospective study to find out the prevalence of jaundice and acute pancreatitis was carried out in Nnamdi Azikiwe University Teaching Hospital Nnewi. The study period was from March 2009 to May 2009.Prior to the study, baseline determinations of serum alpha amylase and bilirubin levels were obtained. A total of 75 HIV seropositive patients were studied. 50 (66.7%) of these subjects had been on the first-line HAART drugs (such as Nevirapine, Didanosine and Tenofovir) for more than two years. None were on second line drugs. 25 out of the 75 HIV positive patients (33.3%) were not on anti-retroviral therapy at all (pre HAART). 25 HIV-seronegative individuals were used as controls in this study. 50 (66.7%) of the75 were females while 25 (33.3%) were males. Only 5(6.7%) were aged above 50. HIV screening was carried out for all the subjects studied using Determine Stat Pak and Unigold in accordance with the current national serial algorithm. Serum alpha-amylase assay was carried out for the 75 HIV patients using fully automated VITROS 350 analyser.3 subjects (4%) had acute pancreatitis. Also, serum total and conjugated bilirubin assay were performed manually using Van den Bergh diazo reaction and only 1 patient (1.33%) had elevated plasma bilirubin level (jaundice). The CD4 counts of these subjects were evaluated using cyflow SL-3 Flowcytometer and 39 patients (52%) had their CD4 count greater than 200 while 36 patients (48%) had their CD4 count less than 200.

INTRODUCTION

It has been reported that acute pancreatitis occurs more frequently in HIV infected patients than in the general population[1].Combination antiretroviral therapy (ART) was introduced over a decade ago and has led to great reduction in morbidity and mortality amongst people living with HIV/AIDS[2].With the HIV burden in sub-Saharan Africa and the observed benefits of antiretrovirals[3], it is obvious that HAART has come to stay in this region. As with most drugs, side-effects are to be expected. Finzi *et al*[4] reported that HIV positive subjects on antiretroviral therapy usually develop acute pancreatitis and jaundice more often than positive subjects not on ARTs. The incidence of jaundice and acute pancreatitis in these subjects in our environment is the subject of this study.

MATERIALS AND METHODS

Subjects

A total of 75 HIV Positive Subjects within the age bracket of 18-65 years were recruited for the study. Of these, 50 were receiving highly active antiretroviral drugs (HAART) such as tenofovir, didanosine, nevirapine, indinavir, atazanavir and ritonavir during the study period. All recruited subjects had been on antiretroviral treatment for two years and above. 25 of the HIV positive subjects were not on antiretroviral drugs while 25 apparently healthy HIV negative individuals , drawn from staff and students of Nnamdi Azikiwe University Nnewi campus, were used as

controls in this study. 36% of the study population were male while 64% were female. Ethical approval was obtained from the Ethical Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi before commencement of the study. Informed consent was also obtained from the subjects. Direct personal interview was used to obtain information from the study population.

METHODS

5ml of blood sample was collected into plain vacutainer tubes from the antecubital vein of the subjects. The samples were first tested to determine their HIV status using Determine, Stat Pak and Unigold test Kits in line with the national serial algorithm. Procedure was according to the manufacturers' instruction.

The alpha amylase assay was performed using fully automated Vitros analyser (VITROS 350) based on the principle of reflectance photometry while the total bilirubin assays were performed manually using the Van den Bergh reaction. CD4 counts were evaluated using CYFLOW SL-3 flowcytometer.

STATISTICAL METHOD

Statistical analysis was performed using Chi-square method of statistical analysis.

RESULTS

A total of 75 HIV positive subjects were studied. 50 of these (66.7%) were in the HAART era while the remaining 25 patients (33.9%) were in the pre HAART era. 25 HIV negative individuals were used as controls. 50 HIV positive subjects in the HAART era were tested for acute pancreatitis, 3 (6%) presented with acute pancreatitis while none of the subjects in the pre HAART era presented with acute pancreatitis. None in the control group had pancreatitis as well. This is shown in Fig. 1

	No of subjects with acute pancreatitis	No of subjects without pancreatitis	Total
HAART era	3	47	50
Pre HAART era	0	25	25
Total	3	72	75

Fig 1: Incidence of Pancreatitis in Antiretroviral Medication

The table shows that more people in the HAART era had acute pancreatitis, though statistical analysis using Chi-square method of data analysis revealed that the antiretroviral agents were not responsible for the pancreatitis observed.($P<0.05$).

Of the 50 HIV-infected patients in the HAART era tested for jaundice, none had elevated plasma bilirubin level. Only 1 patient (4%) had elevated plasma bilirubin level out of the 25 HIV patients in the pre HAART era. No subject in the control group had elevated plasma bilirubin level. This is shown in fig 2.

	No of jaundiced subjects	Non-jaundiced subjects	Total
HAART era	0	50	50
Pre HAART	1	24	25
Total	1	74	75

Fig 2: Incidence of jaundice in Anti-retroviral therapy

DISCUSSION

A prospective study in which 75 HIV positive subjects were studied, evaluated the incidence of jaundice and acute pancreatitis in HIV positive subjects on anti-retroviral therapy. An incidence of 1.33% had elevated plasma bilirubin while 4% had acute pancreatitis. Increased incidence of jaundice in antiretroviral therapy has been reported. Krammer and Horl[5] reported 10.40% elevation in plasma bilirubin in the HIV positive subjects they studied, though they

reported that 7.69% of these were jaundiced due to anti-retroviral therapy. In some studies where the specific anti-retroviral drugs causing elevated plasma bilirubin were evaluated, approximately 14% of the HIV patients had elevated plasma bilirubin level due to indinavir therapy [6,7], while 33-41% had elevated bilirubin due to atazanir [8,9]. On the other hand, quite a number of studies have observed higher rates of pancreatitis than those observed in the general population[10,11,12,1]. A study by Dutta et al[13], found an incidence of 14%. Gan *et al*[1] attributed 46% of the cases to medication-induced while 26% was idiopathic. Reisler[14] reported a 0.85 per 100 person years in the period of 1996-2006.

The prevalence of one or more risk factors or co-morbidities in the study area may have accounted for the differences in the results obtained. For instance alcohol consumption is linked to pancreatitis[15,16] and prevalence of alcohol ingestion is more in urban HIV clinics. Also, pancreatitis linked to gallstones is common in older HIV positive populations[17]. In the same vein, the prevalence of alcoholic liver disease, opportunistic infections, neoplsias in certain areas of study may account for the differences in the incidence of jaundice observed. Our findings may be linked to the dose-dependent effects of didanosine, tenofovir and nevirapine. This is however unlikely presently, because there is better dosage effect management unlike before, when these drugs were administered without effective recourse to dosage effect relationship especially in developing countries. This may have accounted for the side effects of acute pancreatitis observed in earlier studies[18,13].

The incidence of jaundice and acute pancreatitis in HIV infected subjects, was the focus of this study and we conclude that the anti-retroviral agents were not responsible for the jaundice and acute pancreatitis observed in this tertiary institution. However, more work needs to be done to assess the effect of the risk factors mentioned above.

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