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Research Article

Liver function tests of HIV/AIDS patients at the nylon district hospital, Douala, Cameroon

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ABSTRACT

Background: Antiretroviral therapy (ART) which substantially reduces morbidity and mortality in human immunodeficiency virus (HIV) seropositive patients has been associated with hepatotoxicity. This study was aimed at investigating the effects of HIV infection and ART on liver function amongst HIV seropositive patients in Douala, Cameroon.
Methods: A cross- sectional study was conducted from March to August, 2012 at the Nylon District Hospital, Douala. Demographic data were collected using a structured questionnaire. Serum alanine and aspartate aminotransferases (ALT and AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) activities were determined using colorimetric techniques.
Results: The mean age of the study participants was 37.9 ± 6.02 years. A majority of the study participants (68.0%) were females. The mean CD4+ T lymphocyte cell count of HIV/AIDS patients on ART was significantly higher than the ART- naïve patients ($p<0.05$). The mean serum AST and ALT activities of ART-naïve patients were significantly higher than the control subjects ($p<0.05$). Similarly, the mean serum transaminases and GGT activities of HIV/AIDS patients on ART were significantly higher than the control subjects ($p<0.05$). The mean serum ALP and GGT activities of HIV/AIDS patients receiving ART were significantly higher than the ART- naïve patients ($p<0.05$).
Conclusions: The present study provides evidence to suggest that both infection with HIV and treatment with ART are associated with liver injury.

Keywords: Human immunodeficiency virus, Antiretroviral therapy, Liver function enzymes, Hepatotoxicity

INTRODUCTION

In 2013, an estimated 35 million people were reported to have lived with the human immunodeficiency virus (HIV).[1] The first AIDS case in Cameroon was reported in 1985.[2] At the end of 2013, the prevalence of HIV/AIDS in Cameroon was estimated to be 5.4% with people aged between 15 and 49 years the most commonly infected.[3] Although antiretroviral therapy (ART) has led to dramatic improvements in the survival of HIV infected patients on treatment in resource-limited settings, it has been associated with both short- and long-term toxicities including hepatotoxicity, which may be life threatening.[4-6] Liver enzymes elevations of varying degree are common among HIV seropositive patients receiving all classes of highly active antiretroviral therapy (HAART)

and the extent of injury varies substantially with the type of agent used.[7,8,9-11] HIV directly damages hepatic cells leading to apoptosis and mitochondrial dysfunction.[12] Elevated baseline transaminase levels, hepatitis B virus (HBV), hepatitis C virus (HCV) coinfection and the simultaneous use of antituberculosis or other hepatotoxic drugs are other risk factors.[13-15] In Cameroon, patients infected with HIV often ingest a cocktail of drugs in association with the ART regimen with the aim of controlling the infection. Some of these alternative and complementary medications have the potential of damaging the liver and therefore pose a high risk for developing drug induced hepatotoxicity.[16,17] The current Cameroon antiretroviral therapy guidelines recommend monitoring of liver function every 6-12 months.[18] Liver disease aetiology in HIV-1 infected persons in sub-Saharan Africa may differ from what has been described in the West and may change with the recent expansion of access to HAART. This study examines the effect of HIV infection and ART on liver function using serum alanine and aspartate aminotransferases (ALT and AST), gamma glutamyl transferase (GGT) and alkaline phosphatase (ALP) activities as biochemical markers.

METHODS

Between March and August 2012, one hundred HIV seropositive patients on one of the three first line ART regimen for at least six months were randomly selected from the Voluntary Counselling and Treatment Centre of the Nylon District Hospital, Douala, Littoral Region, Cameroon and designated 'ART treated'. One hundred newly diagnosed HIV seropositive patients who were not qualified to initiate ART, according to the Cameroon National guidelines for initiating ART were designated as "ART- naive".[18] One hundred apparently healthy HIV seronegative participants were recruited over the same period and served as control subjects. Patients were admitted in the study if they had confirmed HIV-1 infection and agreed to sign a written informed consent form. Pretested questionnaires were used to gather information on life style, anthropometric and demographic characteristics of participants. About five millilitres of venous blood was collected from each participant into plain tubes which were centrifuged at 4,000 rpm for 10 minutes to obtain sera. The rapid antibody technique and the enzyme-linked immunosorbent assay (ELISA) kits were used to screen for hepatitis B surface antigen and antibody to hepatitis C virus. Serum was used to confirm HIV status by ELISA technique. Whole blood CD4+ T lymphocyte cell count was determined using a flow cytometer (Partec Gmbh, Germany, 2006) according to the procedure described by the manufacturer. Serum ALT and AST; ALP and GGT activities were determined by enzymatic colorimetric techniques using commercial kits produced by San Diagnostics Ltd, India and Hospitex Diagnostics Ltd, Italy respectively on an automated clinical chemistry autoanalyzer (Erba Diagnostics). Data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 20 for windows (IBM Statistics, USA). Group means ± SEM and percentages were calculated. The student's t test or analysis of variance (ANOVA) was used to compare group means. Statistical significance was designated as $P < 0.05$.

RESULTS

Table 1: Baseline characteristics of study participants.

Characteristic	n = 300
Females n (%)	204(68.0%)
Mean age in years ± SEM	37.9 ± 6.02
Weight(kg), mean ± SEM	68.53± 7.76
Mean BMI(kg/m^2) ± SEM	27.73 ± 3.71
Cotrimoxazole use, n (%)	47(16.0%)
Herbal medicine use, n (%)	75(25.0%)
TB treatment, n (%)	8(3.0%)

n = Number of participants; SEM = Standard error of mean; TB = Tuberculosis; BMI = Body mass index.

A majority of the study participants were females (68%). The main source of exposure to HIV in all the infected patients was heterosexual transmission. The ratio of male to female participants was 30:70 in HIV-infected patients and 65:35 in controls. The mean ages were 38.18 ± 4.65 years, 38.81 ± 6.76 years and 36.7 ± 4.2 years for the ART-treated patients, ART-naive patients and control subjects respectively. Christianity was the predominant religion in the study population (87%). A majority of the participants were married (57.8%). 3.0% of the study participants had TB-HIV co-infection during the study period (Table 1). About 18% and 37.5% of HIV seropositive patients confirmed taking herbal medicines and alcohol respectively. The mean duration of treatment with ART was 14.37 ± 1.5 months. The mean CD4+ T lymphocyte cell count of 435.5 ± 45.2 cells/ l in HIV seropositive patients on ART was significantly higher ($p<0.05$) than 352.1 ± 28.7 cells / l observed in ART-naïve patients. The mean serum ALT and AST activities of ART- naïve patients were significantly higher ($p<0.05$) than the control subjects (Table 2). Similarly, the mean serum transaminases and GGT activities of HIV/AIDS patients on ART were significantly higher ($p<0.05$) than the control subjects (Table 2). The mean serum ALP and GGT activities of HIV/AIDS patients on ART were significantly higher ($p<0.05$) than the ART-naive patients (Table 2).

Table 2: A comparison of serum AST, ALT, ALP and GGT activities (IU/L) amongst control subjects, ART-naïve patients and HIV/AIDS patients on ART.

	Mean ± SEM			Level of significance		
	Control[a]	ART naive[b]	ART treated[c]	$p^{a,b}$	$p^{b,c}$	$p^{a,c}$
AST	23.98 ± 1.31	34.98 ± 1.89	38.74 ± 2.39	0.001*	1.000	0.001*
ALT	24.10 ± 1.18	32.37 ± 1.81	37.43 ± 2.30	0.001*	0.223	0.001*
ALP	113.38 ± 5.67	116.47 ± 10.04	153.21 ± 11.05	0.787	0.010*	0.180
GGT	39.73 ± 4.55	29.41 ± 3.66	64.28 ± 9.48	0.108	0.001*	0.026*

ART = Antiretroviral therapy; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; ALP = Alkaline phosphatase; GGT = Gamma glutamyl transferase; IU/L = International unit per liter; SEM = Standard error of mean; [a]control subjects; [b]ART-naïve patients; [c]HIV/AIDS patients on ART; *the mean difference is significant at $p < 0.05$.

DISCUSSION

The finding of a higher prevalence of HIV infection in women in Cameroon is in agreement with similar findings in previous studies.[19-21] This study reports an elevation in the serum transaminases activities in ART - naïve patients. HIV infection or the presence of opportunistic infections is known to stimulate an immunological response by hepatic phagocytes against the infection.[22] Apart from ART-derived hepatotoxicity, some liver diseases are often linked with HIV infection leading to increased transaminases.[23] Due to religious and cultural beliefs, some HIV seropositive patients in this study admitted they used herbal medicines in an effort to improve on their health. Some of these locally manufactured concoctions are potentially hepatotoxic.[24] A study on drug interactions in HIV patients reported a significant association between the administration of sulfonamides, antituberculosis agents and grade 1 hepatotoxicity in children.[25] The finding of increased serum ALT and AST activities in HIV seropositive patients on ART is in agreement with previous studies which reported a characteristic increase in liver transaminases as a result of administration of ART on patients.[26-28] Liver enzymes elevation due to other causes such as acute viral hepatitis, reconstitution of chronic hepatitis B or C, alcohol ingestion as well as complementary drugs or medicines associated with ART have been reported.[29] Patients recruited in the present study did not have risk factors for liver disease such as hepatitis B and C. In addition, most patients recruited into the present study were receiving co-trimoxazole prophylaxis and prompt treatment for opportunistic infection and very few of them had baseline liver enzyme elevations, a risk factor for severe hepatotoxicity in patients on HAART.[30] Results of the present study also showed that both serum ALP and GGT activities were higher in patients receiving ART than the ART-naive group. This corroborates findings of elevated serum ALP and GGT activities in AIDS patients and mild elevations of serum ALP activity in patients infected with Mycobacterium avium intercellulare, Cytomegalovirus and Kaposi's sarcoma.[31-34] Nearly two third of AIDS patients have raised serum AST, ALT and ALP activities at some stage of their disease.[35]

An elevation in serum ALP and GGT activities as observed in the ART treated patients in this study is suggestive of a near cholestatic condition and may identify patients requiring further investigations. The present study provides evidence to suggest that both infection with HIV and treatment with ART are associated with liver injury. Investigation of serum ALP and GGT activities may help in the management of HIV patients on ART.

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