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METABOLIC DYSFUNCTIONS IN NON-ANTIRETROVIRAL TREATED HIV/AIDS PATIENTS

SA Isezuo, MA Makusidi
Department of Medicine, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

ABSTRACT

Background: AIDS related metabolic and morphologic disorders have been attributed to protease inhibitor based antiretroviral therapy. HIV/AIDS is however a multi-systemic disease with potential for alteration of metabolic and endocrine functions.

Objective: To determine if metabolic disorders occur in non-antiretroviral treated HIV/AIDS patients.

Methods: Case control study of prospectively recruited 48 HIV seropositive patients, and randomly selected age and sex-matched controls. Main outcome measures included plasma lipid concentrations and intravenous glucose tolerance measured using glucose assimilation coefficient, K. A K-value less than 1.2 constituted an impaired glucose tolerance.

Results: Compared to the controls, HIV/AIDS patients had significantly lower glucose assimilation coefficient (1.5 ± 0.5 versus 2.7 ± 0.9; $p < 0.001$); higher proportion of individuals with impaired glucose tolerance (35.4% versus 7.5%; $P = 0.01$); and higher plasma triglyceride concentration (166.5 ± 20.7 mg/dL versus 148.9 ± 13.5 mg/dL; $p = 0.04$). The proportion of patients with hypertriglyceridaemia was also significantly higher among patients than controls (56.3% versus 17.5%; $p = 0.04$).

Conclusions: Metabolic dysfunctions occur in HIV/AIDS independent of antiretroviral therapy. Routine monitor of plasma lipids and glucose is therefore advocated in HIV/AIDS patients.

Key Words: HIV/AIDS, metabolic dysfunctions. *(Accepted 28 October 2008)*

INTRODUCTION

Metabolic and morphologic disorders have been described in human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) patients treated with protease inhibitor based highly active antiretroviral therapy (HAART) [1-3]. Morphologic abnormalities including central obesity and dorsocervical fat accumulation occur in 30-50% of such patients, while metabolic derangements include impaired glucose tolerance (46%), diabetes mellitus (1-7%) and dyslipidaemia (15-30%)[1-4]. HIV/AIDS is however a multisystemic disease with potential for alteration of endocrine and metabolic functions via virus-induced cytopathy, and opportunistic infections and diseases. In Nigeria, about 5% of the population is afflicted with HIV/AIDS[5]. This study aimed at determining the metabolic derangements in anti-retroviral treatment naïve HIV/AIDS patients.

METHODOLOGY

Patients

Forty-eight indigenous Nigerians (males, 82%; females, 18% aged 34.8 ± 9.1 years (range: 22-52 years) with HIV/AIDS were consecutively recruited between January 2002 and June 2003 in the out and in-patient units of the medical department of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Inclusion criteria were as follows:

1.Two positive enzyme linked immunosorbent assay (ELISA) test for HIV-1 and HIV-2 done using two different kits.
2.Satisfying the case definition of AIDS [6].
3.Informed consent for HIV screening and participation in the study.

Patients with lipid altering conditions including systemic hypertension, diabetes mellitus, hypothyroidism, renal and hepatobiliary diseases were excluded using clinical and basic biochemical parameters. Other exclusion criteria included use of lipid lowering and antiretroviral drugs, cigarette smoking and alcohol ingestion.

Demographic data including age, marital status and occupation were obtained. Anthropometric indices including height and weight, and waist, hip and mid upper arm circumferences were measured with subjects lightly clothed and without shoes. Body mass index was calculated. Blood pressure was measured using standard procedures [7]. Forty age, sex and exclusion criteria-matched HIV seronegative individuals were randomly selected from blood donors and volunteers as controls.

Correspondence: Dr S A Isezuo
E-Mail:sisezuo@ skannet.com

Intravenous glucose tolerance test (IGTT)

After about 10 hours of overnight fasting, subjects were rested for 15 minutes in supine position. Intravenous glucose tolerance test was carried out [8]. A cannula, size I6G was inserted into a vein in the aiitecubital fossa and left in-situ at about 7.30 am on each day of the IGTT. About 10mls of fasting blood was withdrawn into fluoride oxalate bottle for fasting blood sugar, plasma lipid concentrations, electrolytes, urea, creatinine and uric acid. Subsequently, 0.5 gm/kg body weight of 50% glucose was given intravenously over 2-4 minutes. About 3mls of blood was withdrawn immediately (within 2 minutes of glucose injection) and at 10, 20, 30, 40, 50 and 60 minutes after the end of glucose injection. The blood samples were put into separate fluoride oxalate bottles, appropriately labelled with exact time of blood sampling indicated and sent immediately to the laboratory for blood glucose determination using glucose oxidase test[8]. Intravenous glucose tolerance test was reported as glucose assimilation coefficient (K) calculated from a standard formula: $K = 0.693 \times 100 \times t_{1/2}$; where $t_{1/2}$ is the time taken in minutes for the blood glucose concentration immediately after glucose injection to be reduced to half of its value. K values were interpreted as follows (impaired glucose tolerance: $K < 1.2$) (borderline: $K = 1.2$-1.29) (normal: $K = 1.3$) [8]. Glucose tolerance curve was obtained by plotting the mean blood glucose concentration (y-axis) against time in minutes (x-axis).

Total plasma cholesterol, high-density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglyceride were determined. Total plasma cholesterol > 200 mg/dl, triglyceride > 150 mg/dl, LDL-C > 135 mg/dl and HDL-C < 40 mg/dl constituted dyslipidaemia.

Statistical Analysis

Data entry and analysis were done using Statistical Package for Social Sciences (SPSS) software. Means were presented as mean ± standard deviation. Independent t-test (2- tailed) was utilised in comparing continuous biochemical variables between patients and controls. The categorical variables among the two groups were compared using chi-square test with Yates's correction. A P-value < 0.05 was considered statistically significant.

RESULTS

The baseline characteristics of patients are shown in Tables 1. Majority of them were young married male civil servants with weight loss, and chronic fever, cough and diarrhoea. The biochemical characteristics of patients and controls are compared in Table 2. Compared to the controls, patients had significantly lower mean glucose assimilation coefficient (1.5 ± 0.5 versus 2.7 ± 0.9; t = 5.3; p < 0.001), and higher proportion of individuals with impaired glucose tolerance (35.4% versus 7.5%; $X^2 = 8.16$; p = 0.01). The glucose tolerance curve of patients and controls are shown in Figure 1.

Table 1:**Demographic and clinical characteristics of HIV/AIDS patients.**

Characterises	Frequency. N= 48 N (%)
Occupation:	
Civil service	20 (41.7)
Housewives	9 (18.8)
Farming	4 (8.3)
Driving	4 (8.3)
Petty trading	4 (8.3)
Military	3 (6.3)
Others	4(8.3)
Marital status:	
Married	37 (77.1)
Single	7 (14.6)
Divorced	2 (4.2)
Widow	1 (2.1)
Separated	1 (2.1)
Clinical features	
Weight loss	48(100)
Fever	41(85.4)
Cough	41 (85.4)
Diarrhoea	33 (68.8)
Oral thrush	15 (31.3)
Generalised lymhadenopathy	13 (27.1)
Dermatological lesions	10 (20.8)
Herpes zoster	7 (14.6)
Recurrent lobar pneumonia	7 (14.6)
Pyomyositis	3 (6.3)
Encephalopathy	3 (6.3

Figure 1: **Glucose Tolerance Curve of Patients and Controls.**

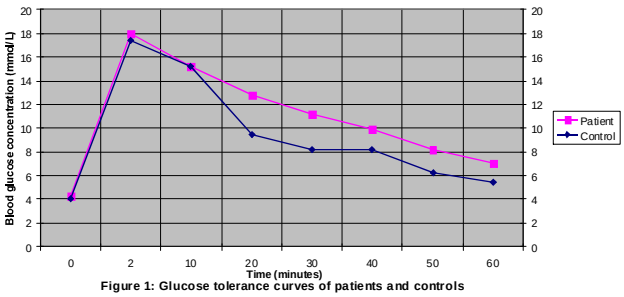

Figure 1: Glucose tolerance curves of patients and controls

Table 2:**Comparison of the biochemical parameters of HIV/AID patients and controls.**

Parameters	Patients N = 48	Controls N = 40	P value
Clinical			
Age (years)	34.8 ± 9.1	37.8 ± 8.5	0.5
Male (N%)	39 (81.3)	32 (80)	0.9
Mid upper arm circumference (cm)	18.9 ± 3.3	25.9 ± 4.8	0.001
Body mass index (kg/m^2)	19.5 ± 5.3	27.8 ± 3.7	0.001
Plasma lipid profiles.			
Total cholesterol (mg/dL)	185.0 ± 13.5	179.3 ± 11.2	0.07
Triglyceride (mg/dL)	166.5 ± 18.1	148.9 ± 20.7	0.04
LDL- C (mg/dL)	100.2 ± 16.1	106.0 ± 34.3	0.09
HDL – C (mg/dL)	47.3 ± 6.1	47.3 ± 3.6	0.09
Glucose assimilation coefficient	1.5 ± 0.5	2.7 ± 0.9	0.001< 0.001
Hypertriglyceridaemia (%)	27 (56.3)	7 (17.5)	0.002
Impaired glucose tolerance (%)	17 (35.4)	3 (7.5)	
Electrolytes, urea and uric acid			0.08
Sodium (mmol/L)	137.0 ± 5.1	139.3 ± 4.5	0.1
Potassium (mmol/L)	4.7 ± 1.5	4.2 ± 0.6	0.1
Calcium (mg/dl)	8.9 ± 0.4	9.1 ± 0.2	0.09
Magnesium (mg/dl)	1.6 ± 0 .5	1.7 ± 0.3	0.06
Bicarbonate (mmol/L)	24.2 ± 2.4	25.4 ± 2.1	0.1
Urea (mmol/L	6.4 ± 1.5	5.7 ± 1.9	0.2
Uric acid (mmo1/l)	6.0 ± 1.3	5.8 ± 1.3	

DISCUSSION

The general characteristics of IHV/AIDS patients are similar to the previous data from our centre [9]. The current report shows that metabolic derangements occur in non-antiretroviral treated HIV/AIDS patients, though their frequencies are lower than that reported among those on HAART[1-4]. In a comparative analysis of insulin sensitivity in HIV seropositive patients receiving protease inhibitors, HIV scropositive patients who were not on protease inhibitors and HIV scronegative controls, previous workers[10] noted that insulin sensitivity was lower in protease inhibitor treated HIV scropositive patients compared to controls. Further, compared to the controls, insulin sensitivity was also lower in HIV scropositive patients who were not on protease inhibitors.

This suggests that factors other than antiretroviral drugs may be contributory to the pathogenesis of AIDS related insulin insensitivity, and metabolic and morphologic disorders[10]. Tendencies to proatherogenicity and lipid disorders have been previously reported in other chronic infections such as Chlamydia pneumonia [11]. The mechanisms underlying metabolic disorders in HIV/AIDS have not been clearly defined. An inverse relationship was previously thought to exist between HIV/AIDS and diabetes mellitus [12]. This hypothesis was based on the progressive depletion of CD4 helper lymphocytes in HIV/AIDS. CD4 lymphocytes mediate pancreatic beta cell destruction in diabetes mellitus [12]. However, CD4 lymphocyte depletion in HIV infection is variable and may still be sufficient to mediate beta cell destruction. HIV itself has a virally encoded molecule (Vpr) that may activate glucocorticoid receptor [13]. .HIV/AIDS induced immune reconstitution has also been associated with inflammatory responses including increased tumour necrosis factor alpha, interferon alpha, interleukins and cortisol [14]. These changes may lead to decreased lipoprotein lipase activity, increase triglyceride synthesis and decrease triglyceride catabolism [14]. The major significance of metabolic alterations in HIV/AIDS is the potential for accelerated atheroselerosis [15].

Further, other cardiovascular abnormalities such as myocarditis, pericarditis, pericardial effusion and dilated cardiomyopathy have been described in HIV/AIDS patients[16,17]. HIV/AIDS is therefore a potential risk factor for increased cardiovascular morbidity and mortality.

In conclusion, metabolic cardiovascular risk factors occur in HIV/AIDS patients independent of antiretroviral therapy. Blood sugar and lipid concentrations should therefore be monitored in these patients irrespective of antiretroviral treatment.

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