Journal of Pharmaceutical Research International

Volume 36, Issue 7, Page 188-204, 2024; Article no.JPRI.119176
ISSN: 2456-9119, NLM ID: 101716968
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Assessment of Diabetic and Inflammatory Markers in HIV Infected Adults with and without Diabetes Mellitus in NAUTH, Nnewi, Nigeria

Chidera Vivienne Obilo [a*], Chukwuemeka Kingsley Obilo [b], Ofia Anya Kalu [c], Nkiru Chineye Nwoka [a], Chinenye Stellamaris Okeke [a], Ogalagu Romanus Ogai [d], Okezie Alozie Ogwuegbu [e], Chidinma Joy Iwuji [f], Chinonso Juliet Akaeme [g], Ezinne Gloria Ukibe [h], Blessing C Ukibe [h], Ezennia Victory Ukibe [i], Nancy Amarachukwu Mbachu [j] and Nkiriuka Rose Ukibe [k]

[a] Department of Chemical Pathology, Faculty of Medical Laboratory Science, Nnamdi Azikiwe University, Awka, Nigeria.
[b] Department of Radiology, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.
[c] Department of Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi Nigeria.
[d] Department of Biochemistry, Tansian University Umunya, Anambra State, Nigeria.
[e] Department of Chemical Pathology, Alex Ekwueme Federal University Teaching hospital Abakiliki, Nigeria.
[f] Department of Science Laboratory, Federal University of Technology, Owerri, Nigeria.
[g] Department of Chemical Pathology, Nnamdi Azikiwe University, Nigeria.
[h] Department of Medicine, College of Health Sciences, Nnamdi Azikiwe University,Nigeria.
[I] Department of Radiography and Radiological Sciences, College of Health Sciences, Nnamdi Azikiwe University, Awka, Nigeria.
[j] Department of Biochemistry, Faculty of Basic Medical Sciences Nnamdi Azikiwe University, Akwa, Nigeria.
[k] Department of Immunology, Faculty of Medical Laboratory Science, Nnamdi Azikwe University, Akwa, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/jpri/2024/v36i77550

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/119176

**Corresponding author: Email: deraobilo@gmail.com;*

Cite as: *Obilo, C. V., Obilo, C. K., Kalu, O. A., Nwoka, N. C., Okeke, C. S., Ogai, O. R., Ogwuegbu, O. A., Iwuji, C. J., Akaeme, C. J., Ukibe, E. G., Ukibe, B. C., Ukibe, E. V., Mbachu, N. A. and Ukibe, N. R. (2024) "Assessment of Diabetic and Inflammatory Markers in HIV Infected Adults with and without Diabetes Mellitus in NAUTH, Nnewi, Nigeria", Journal of Pharmaceutical Research International, 36(7), pp. 188–204. doi: 10.9734/jpri/2024/v36i77550.*

Original Research Article

Received: 21/04/2024
Accepted: 25/06/2024
Published: 28/06/2024

ABSTRACT

Background and Aim of Study: To assess the levels of fasting plasma glucose, insulin, insulin resistance, interleukin 10 (IL-10), high sensitive C - reactive protein (Hs-Crp) and tumour necrosis factor alpha (TNF-α) in HIV infected adult individuals with and without diabetes mellitus in NAUTH Nnewi, Nigeria.
Methodology: This was a cross-sectional study design carried out at HIV clinic, Nnamdi Azikiwe university teaching hospital, Nnewi Nigeria. A total of 150 participants were recruited using simple random sampling technique and comprised 50 HIV infected individuals with diabetes mellitus, 50 HIV infected individuals without DM and 50 apparently healthy participants without HIV nor DM (control). TNF-α, IL-10 and Hs-Crp was determined using ELISA technique. Anthropometric parameters and blood pressure were measured using standard laboratory methods.
Results: There was significantly higher mean level of TNF-alpha, fasting insulin, HOMA-IR, Hs-Crp and FPG in HIV infected individuals with and without DM when compared with control group ($p<0.05$) respectively. Significantly higher mean valueof BMI was observed in HIV infected individuals with DM compared with HIV infected individuals without DM ($p<0.05$).BP was significantly higher in HIV infected individuals with DM compared with their counterpart without DM and control ($P<0.05$) respectively. However, the mean IL-10 level did not differ significantly ($P>0.05$) between the groups studied.
Conclusion: This suggests some degree of inflammatory reaction in HIV infected individuals without DM and this may subsequently predispose the affected individuals to type 2 DM.

Keywords: HIV; type 2 diabetes mellitus; interleukin 10; high sensitive C - reactive protein; tumour necrosis factor alpha.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic condition caused by decreased or absent insulin production or possibly by decreased tissue sensitivity to insulin [1,2]. According to recent studies, the disease is currently on the rise in Nigeria with a prevalence of 5.77% among Nigerians [3].Type 2 diabetes mellitus (T2DM) is believed to be associated with low-grade chronic inflammation [4]. Both HIV and diabetes mellitus seems to be associated with inflammation which results from dsyregulation in cytokine release [5,6,7,8].

Changes in cytokine levels in HIV infected individuals can affect the function of the immune system and have the potential to directly impact the course of HIV disease by enhancing or suppressing HIV replication [9]. Most of these cytokines have been used as hallmarks of disease progression as well as assessment of patient's response to antiretroviral treatment [10]. It has been previously documented that HIV replication is the result of a balance between the effects of pro-inflammatory cytokines that increase viral replication and those of anti-inflammatory cytokines and chemokines that inhibit viral replication [11]. With the growing understanding of their roles during infections and disease progression, cytokines including IFN-γ, IL-10 and tumor necrosis factor alpha (TNF-α) have been assayed in plasma to assess the efficacy of antiretroviral therapy during HIV infection [12]. For example, HAART markedly increases plasma IFN-γ levels [13] and considerably lowers IL-10 systemic levels during HIV infection [14]. Hence, these actions co-operatively show that antiretroviral treatment markedly influences systemic cytokine levels. Chronic immune activation and inflammation are consistently found in PLWH and T2D is also characterized by similar findings [15]. Low grade systemic inflammation has been hypothesized as an underlying factor for the pathogenesis of T2D [16-18] when there is elevated plasma levels of C-reactive protein (CRP) and IL-6 [16]. CRP, an acute phase protein is synthesized by hepatocytes in response to pro-inflammatory cytokines, in particular IL-6 [19]. TNF- alpha is a cytokine that promotes inflammation [20], and has been linked to the development of insulin resistance, which aids in the development of type 2 diabetes [21]. Ingle and Patel reported that

hyperglycaemia stimulates the release of the inflammatory cytokines, tumour necrosis factor (TNF-α) and IL-6 from various cell types and can also result in the induction and secretion of acute phase reactants by adipocytes [22]. Additionally, research by Kumar et al. has demonstrated a significant correlation between HIV lipodystrophy and tumour necrosis factor-alpha [23]. This association may be due to the function of tumour necrosis factor-alpha in insulin resistance, impaired glucose tolerance, and possibly the development of diabetes mellitus [23]. The first proinflammatory cytokine implicated in the pathogenesis of insulin resistance and type 2 diabetes mellitus was tumour necrosis factor-alpha. The reason for this is because TNF-α inhibits the production of GLUT-4, an insulin-regulated glucose transporter that is mostly found in adipocytes as well as skeletal and cardiac muscles [24]. Furthermore, TNF-α can function as an inhibitor of peripheral insulin action, resulting in insulin resistance, by causing serine phosphorylation of insulin receptor substrate-1 can act as an inhibitor of peripheral insulin action which leads to insulin resistance[24].

C-reactive protein (CRP), a positive acute phase reactant (protein), was first detected in the bloodstream in response to hepatocyte inflammation [25]. It is a marker of inflammation which characterizes several chronic disorders. One biochemical test that is very sensitive in quantifying CRP is the high-sensitivity C-reactive protein test (Hs-CRP). The newly improved assay known as "high sensitivity" detects incredibly low plasma levels of CRP [25]. Giving us a general notion of the inflammatory status, it estimates the general amounts of inflammation in the human body [25].Prior studies have demonstrated elevated levels of both high-sensitive C-reactive protein and tumour necrosis factor-alpha in adult HIV-positive people, both with and without diabetics mellitus [26]. An increased CRP production could arise as a result many metabolic and inflammatory factors which are associated to the development of diabetes mellitus and they are: an increased blood pressure, adipokines and free fatty acids [27]. Also, asides from an increased CRP production leading to development of type 2 diabetes, an increased CRP could be a marker for detecting progression of cardiovascular complication in diabetic HIV people [28,29].

IL-10 on the hand has powerful anti-inflammatory properties and plays a significant role in limiting an excessive inflammatory response [30]. The immune system relies on IL-10 to maintain the proper balance in the immunological response required to defend the body and safeguard tissues from infection [31].

Plasma glucose is a metabolic fuel of the body, excess of which gives rise to hyperglycemia which characterizes diabetes mellitus [1]. Reports have shown High levels of fasting blood glucose levels in non diabetic HIV seropositive individuals and diabetic seropositive individuals [32], High levels of fasting plasma glucose in non-diabetic HIV seropositive individuals in combination with other glucose analytes could be an indicative that HIV is linked to development of type 2 diabetes mellitus [33]. The source of the higher plasma glucose levels may be due to the effects of antiretroviral medication, HIV infection, or both, which worsened the glucose metabolism in this individuals [34,35].

Insulin is a polypeptide hormone that controls blood glucose levels and is mostly secreted by beta cells in the pancreatic islets of Langerhans [36]. The onset and progression of certain chronic diseases are also influenced by insulin production and levels [36].

Insulin resistance (IR) is a common medical condition or state where normal responses require higher than usual insulin concentrations, which subsequently results in hyperinsulinemia and impaired insulin action in certain cases [37]. Insulin resistance affects several organs, including adipose tissue, muscle, and the liver, and impairs insulin signaling pathways [38]. A person with homeostatic model assessment index (HOMA-IR) ≥ 2.5 is considered to be insulin resistant [37]. It appears that HOMA-IR and FPG assessments in all models provide superiority in predicting the probability of developing diabetes mellitus; therefore, both parameters must be evaluated in order to diagnose diabetes [24]. Reports by Hu *et al*. have shown that those with diabetes mellitus had significant levels of HOMA-IR, or insulin resistance [24].

It is widely acknowledged that insulin resistance, which exacerbates dyslipidemia and dysregulated glucose metabolism, is correlated with activation of the innate immune system [39] Patients receiving continuous antiretroviral therapy (cART) and untreated HIV patients have both been shown to experience varying degrees of chronic inflammation as a result of immune

activation [40]. Nonetheless, untreated HIV patients exhibit a heightened inflammatory state that is linked to a procoagulant condition and is marked by elevated levels of proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukins (IL-6 and IL-1β) [41]. Insulin resistance is likely significant under these circumstances and may affect adipose, muscle, and liver tissue. According to reports, having high levels of C-reactive protein increases the risk of type 2 diabetes (T2DM). This is because most occurrences of T2DM are associated with a number of additional risk factors, such as obesity, a relatively high body mass index (BMI), and insulin resistance [42]. Research on the link between HIV duration, insulin resistance, and diabetes mellitus has also revealed insulin resistance in adult HIV-positive persons with diabetes mellitus [43].

There are evidences showing People living with HIV share common risk factors for non-communicable diseases (NCD) [44] and the underlying mechanism behind this is a complex interaction among HIV infection, antiretroval therapy and NCD risk factors [45] and these NCD's in HIV infected people occurs as a result of chronic immune activation, side effects of medications or co-infections and as the HIV infection gets old and these factors gets worse by the HIV infection and some antiretroviral drugs [46]. NCD's refer to a complex heterogenous group of diseases such as cardiovascular diseases(hypertension and stroke) ,diabetes mellitus, renal diseases, cancer [44] etc. These are cor-mobidities that could result in very complex disease patterns that could add and multiply hence causing some unfavourable health outcomes [47]

NCD's are the major cause of death in people living with HIV with cardiovascular disease having upto 46% of total deaths [48]. Insulin resistance plays a key role in the pathophysiology of type 2 diabetes mellitus and is linked to a number of cardiovascular and metabolic risk factors [49]. Obesity has been linked to type 2 diabetes mellitus as one of the modifiable risk factors, and this is due to its role in insulin resistance [49]. It is estimated that 300 million people worldwide will be obese by 2025 [49]. Another risk factor for type 2 diabetes mellitus is hypertension, which is linked to the development of complications in HIV-positive individuals [49]. The presence of hypertension is one of the cardiovascular diseases that is an NCD [44] and is defined as systolic blood pressure of ≥ 140 mmHg and or higher.

Anthropometric parameters are non-invasive bodily measurements, and anthropometry is used to evaluate an individual's and a child's nutritional status [50]. Both growth and body measurements are available [50]. While growth measurements are used to assess a child's overall well-being, body measurements are used to assess an adult's health, nutritional status, and diet in order to predict their risk of developing certain diseases in the future [51].Body measuring is utilised not just to assess nutritional status, food, and overall health, but also to assess body composition, which is crucial for diagnosing obesity [52] and identifying any underlying nutritional issues. The most significant modifiable risk factor for diabetes mellitus is obesity, and the diagnosis and definition of obesity are based on anthropometric measures [52].

Waist circumference, waist to hip ratio, waist-to-height ratio, weight, height, and BMI [52] are measurements obtained from anthropometry; however, due to the historical use of BMI [52], BMI is still primarily utilised among these anthropometric measurements in the classification of obesity [53]. Elevations in anthropometric measurements have also been linked to hyperglycemia and dyslipidemia, According to research [49]. Studies have indicated a correlation between hypertension and BMI [49]. Patients with type 2 diabetes mellitus who had a BMI of more than 27 kg/M2 were more likely to have hypertension, according to Ghulam et al[45].
Therefore, the current study is focused on determining the levels of fasting plasma glucose, insulin, insulin resistance, lL-10, Hs-Crp and TNF-α in HIV infected adult individuals with and without diabetes mellitus in NAUTH Nnewi, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Design

This research was a cross-sectional study designed to assess the levels of fasting plasma glucose, insulin, insulin resistance, lL-10, Hs-Crp and TNF-α in HIV infected adult individuals with and without diabetes mellitus in NAUTH Nnewi, Nigeria. A total number of 150 subjects categorized into 3 groups were recruited for the study using simple sampling technique. Group 1 comprised 50 HIV infected adult individual with diabetes mellitus, Group 2 comprised 50 HIV infected adult individuals without diabetes

mellitus while group 3 comprised 50 apparently healthy controls that are neither diabetic nor HIV positive.

The test subjects (Groups 1 and 2) were selected from the NAUTH HIV clinic. They were both male and female and ranged in age from 18 to 75. The control group comprised apparently healthy individuals between the ages of 28 to 53 years and was selected from the staff and students of the Nnamdi Azikiwe University Teaching Hospital Nnewi.Information on socio-demographic, medical history and life styles were obtained using standard questionnaire. Also, anthropometric parameters and blood pressure were determined using standard methods. All HIV infected individuals were on antiretroviral therapy.

2.2 Inclusion Criteria

According to CDC and WHO HIV disease staging,only HIV stage II subjects and subjects who had commenced anti-retroviral therapy were recruited. Additionally, test participants between the ages of 18 and 75 and control subjects (apparently healthy) between the ages of 28 and 53 were selected for this study.

2.3 Exclusion Criteria

This study excluded the following groups of people: pregnant women, HIV-positive people not receiving antiretroviral therapy (ART), people in Stage 3 of the infection, people with tuberculosis, people infected with malaria,people in the age range of 10 to 17 years, people with tumors or any inflammatory disease, and people with chronic illnesses other than HIV.

2.4 Blood Sample Collection and Processing

Six milliliters (6 ml) of venous fasting blood samples were collected aseptically after 10-12 hours of fast by venipuncture from each subject via the antecubital vein using a plastic syringe with minimum stasis into fluoride oxalate and plain containers. 2 ml of venous blood was dispensed into fluoride oxalate for determination of fasting plasma glucose (FPG) level which was assayed immediately without storage. The remaining 4 ml of the venous blood sample was dispensed into plain container and allowed to clot and retracted. It was then centrifuged at 4000 rpm for 5 minutes and serum separated and used for analysis of biochemical markers. Serum samples that were not analyzed immediately were stored frozen at -20°C.

2.5 Laboratory Methods

2.5.1 Determination of fasting plasma glucose concentration

Fasting Plasma glucose were determined by enzymatic method as described by Franket al [54].

2.5.2 Determination of fasting insulin using enzyme linked immunosorbent assay

Human insulin was assayed using the sandwich enzyme linked immunosorbent assay (ELISA) as described by Burgi et al [55].

2.5.3 Determination of insulin resistance index

The insulin resistance index of each subject was determined by Homeostatic model assessment (HOMA) according to the method described by Hashemipouret al [56]. The insulin resistance score was computed with the formula: Fasting plasma glucose (mmol/L) times fasting serum insulin (mU/L) divided by 22.5.

2.5.4 Determination of human Il-10 (interlukin10) by enzyme linked immunosorbent assay

Human IL-10 level was assayed using Sandwich Enzyme linked immunosorbent assay (ELISA) technique as described by Chiswick et al [57].

2.5.5 Determination of high sensitivity c-reactive protein enzyme immunoassay test

High sensitive C-reactive protein was assayed using the solid phase enzyme linkedimmunosorbent assay (ELISA) technique as described by Votruba and Rakosnik [58].

2.5.6 Determination of tumour necrosis factor-alpha

Tumour necrosis factor-alpha was assayed using the sandwich Enzyme immunosorbent linked method(ELISA) as described by Engelbertset al [59].

2.5.7 Anthropometric measurement

The weight and height of each participant were measured using a standard beam balance scale

and a stadiometer respectively.Body mass index (BMI) was calculated as weight (kg) divided by height squared in meters.

$BMI(Kg/m^2) = Weight(Kg)/Height^2 (m^2)$.

Also, systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured using sphygmomanometer and stethoscope.

2.6 Statistical Analysis

Statistical package for social sciences version 23.0 was used for data analysis. The data obtained were analyzed using ANOVA, Posthoc t-test and Pearson Correlation. Results were deemed significant at $p < 0.05$.

3. RESULTS

The result of analysis of variance (ANOVA) showed that the mean serum levels of TNF-α, fasting insulin, HOMA-IR, Hs-Crp and fasting plasma glucose were significantly different amongst the group (F=11.880, 16.222, 39.340, 7.624 and 8.312) (P<0.05) respectively, whereas, IL-10 did not differ significantly amongst the group (F=1.388; P>0.05) (See Table 1).

The mean (±SD) of serum TNF-α (pg/L) level in the HIV seropositive individuals with diabetes mellitus (15.82±2.59) was significantly higher compared with the corresponding values in the HIV seropositive individuals without diabetes mellitus (10.46±2.54) and control group (5.46±2.32) respectively (p=0.036; 0.024). Also, the mean serum TNF-α level was significantly higher in the HIV seropositive individuals without diabetes mellitus compared with control group (10.46±2.54 Vs 5.46±2.32; p=0.030). See Table 1.

Also the mean serum IL-10 (pg/L) level in the HIV seropositive individuals with diabetes mellitus did not differ significantly compared with the HIV seropositive individuals without diabetes mellitus and control group (p>0.05). There was no significant difference in the mean serum IL-10 level in the HIV seropositive individuals without diabetes mellitus compared with control group (p=0.352). See Table 1.

There was significantly higher mean serum fasting insulin (ng/ml) level in the HIV seropositive individuals with diabetes mellitus compared with HIV seropositive individuals without diabetes mellitus (24.79±7.69 Vs 13.10±3.35; p=0.000). Also, there was significantly higher mean serum level of fasting insulin observed in the HIV seropositive individuals with diabetes mellitus compared with control group (24.79±7.69 Vs 7.12±3.50; p=0.000). The mean serum insulin level wasalso significantly higher in the HIV seropositive individuals without diabetes mellitus compared with control group (13.10±3.35 Vs 7.12±3.50; p=higher0.028). See Table 1.

The mean (±SD) of HOMA-IR levels in the HIV seropositive participants with diabetes mellitus was significantly compared with the corresponding values in the HIV seropositive participants without diabetes mellitus and control group (p=0.000; 0.001) respectively. Also, the mean (±SD) of HOMA-IR level in the HIV seropositive participants without diabetes mellitus was significantly higher compared with the observed value in the control subjects (3.77±2.76 Vs 0.31±1.66; p=0.036). See Table 1.

There were significantly higher mean serum levels of Hs-Crp mg/dl) in the HIV seropositive participants with diabetes mellitus compared with those without diabetes mellitus and control subjects (p=0.023; 0.006) respectively. Also, the mean (±SD) of serum Hs-Crp level was significantly higher in the HIV seropositive participants without diabetes mellitus than in the control group (6.16±1.33Vs 2.28±1.35; p=0.041). See Table 1.

Furthermore, the mean plasma fasting glucose was significantly higher in the HIV seropositive participants with diabetes mellitus compared with those without diabetes mellitus (10.24±2.82 Vs 5.90±0.56; p=0.031). It was also significantly higher in the HIV seropositive participants with diabetes mellitus compared with control group (10.24±2.82 Vs 4.17±0.67; p=0.001). Furthermore, it was also significantly higher in the HIV seropositive participants without diabetes mellitus than in control group (5.90±0.56 Vs 4.17±0.67; p=0.047). See Table 1.

The result of analysis of variance (ANOVA) showed that the mean levels of body mass index (kg/m^2), systolic blood pressure (mmHg) and diastolic blood pressure (mmHg) were significantly different amongst the group (F=4.065, 15.832 and 9.501) (P<0.05) respectively, whereas, the mean age (years) did not differ significantly amongst the group (F=0.338; p=0.714) (See Table 1).

The mean body mass index (BMI) was significantly higher in the HIV seropositive participants with diabetes mellitus compared with those without diabetes mellitus (29.45±6.28 Vs 27.19±5.17; p=0.028), but it did not differ significantly when compared between the HIV seropositive participants with diabetes mellitus and control group (p=0.232) as well as between those without diabetes mellitus and control group (p=0.897). See Table 2.

There was significantly higher mean systolic blood pressure in the HIV seropositive participants with diabetes mellitus compared with those without diabetes mellitus (p=0.000) and control subjects (p=0.000) respectively but it did not differ significantly when compared between the HIV seropositive participants without diabetes mellitus and control group (p=0.462). See Table 2.

There was significantly higher mean diastolic blood pressure in the HIV seropositive participants with diabetes mellitus compared with those without diabetes mellitus (p=0.000). It was also significantly higher in the HIV seropositive participants with diabetes mellitus compared with control subjects (p=0.000) but it did not differ significantly when compared between the HIV seropositive participants without diabetes mellitus and control group (p=0.078). See Table 2.

Table 1. Levels of TNF-α, IL-10, fasting insulin, HOMA-IR, Hs-Crp and FPG in HIV infected adult individuals with diabetes mellitus, HIV infected adult individuals without diabetes mellitus and control (Mean ±SD)

Group	TNF-α (pg/L)	IL-10(pg/L)	Fasting insulin(ng/ml)	HOMA-IR	Hs-Crp (mg/dl)	FPG (mmol/L)
HIV WITH DM(A)	15.82±2.59	112.44±31.6	24.79±7.69	9.43±6.59	10.62±6.80	10.24±2.82
HIV W/O DM (B)	10.46±2.54	98.48±30.41	13.10±3.35	3.77±2.76	6.16±1.33	5.90±0.56
Control(C)	5.46±2.32	119.95±29.22	7.12±3.50	0.31±1.66	2.28±1.35	4.17±0.67
F-test	11.880	1.388	16.222	39.34	7.624	8.312
P- value	0.014*	0.255	0.001*	0.000*	0.000	0.020
A vs B	0.036*	1.000	0.000*	0.001*	0.023*	0.031
A vs C	0.024*	0.657	0.000*	0.000*	0.006*	0.001
B vs C	0.030	0.352	0.028*	0.036	0.041	0.047

Table 1showed that the mean serum levels of TNF-α, fasting insulin, HOMA-IR, Hs-Crp and fasting plasma glucose were significantly different amongst the group (F=11.880, 16.222, 39.340, 7.624 and 8.312) (P<0.05) respectively, whereas, IL-10 did not differ significantly amongst the group (F=1.388; P>0.05)

**Statistically significant at p<0.05*

TNF-α= Tumour necrosis factor-alpha, IL-10=Interlukin-10, Hs-Crp=High sensitive C-reactive protein, HOMA-IR= Homeostasis model assessment index, FPG= Fasting plasma glucose

Table 2. Age, BMI, Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in HIV infected adult individuals with diabetes mellitus, HIV infected adult individuals without diabetes mellitus and control (Mean ±SD)

Group	Age(Yrs)	Weight(Kg)	Height(m)	BMI(Kg/m^2)	SBP(mmHg)	DBP(mmHg)
HIV WITH DM (A)	37.89±4.36	88.04±14.21	1.74±0.10	29.45±6.28	125.96±11.95	72.16±10.00
HIV W/O DM(B)	39.03±7.14	76.86±13.83	1.68±0.05	27.19±5.17	108.07±8.98	65.86±6.52
Control (C)	39.84±12.81	82.48±11.25	1.69±0.08	27.15±5.16	112.65±15.02	71.55±6.35
F-test	0.338	5.096	3.850	4.065	15.832	9.501
P-value	0.714	0.008	0.025	0.024	0.000	0.000
A vs B	1.000	0.006	0.029	0.028	0.000	0.000
A vs C	1.000	0.333	0.117	0.232	0.000	0.000
B vs C	1.000	0.301	1.000	0.897	0.462	0.078

*Table 2 showed that the mean levels of body mass index (kg/m^2), systolic blood pressure (mmHg) and diastolic blood pressure (mmHg) were significantly different amongst the group (F=4.065, 15.832 and 9.501) (P<0.05) respectively, whereas, the mean age (years) did not differ significantly amongst the group (F=0.338; p=0.714) *Statistically significant at p<0.05*

Table 3. Correlation of TNF-α, IL-10, Hs-Crp, with Fasting insulin, HOMA-IR and FPG in HIV infected adult individuals with diabetes mellitus

Parameters	Fasting insulin(Ng/ml)	FPG(Mmol/L)	HOMA-IR
TNF-α			
(Pg/L) r-value	0.043	0.123	0.291
P value	0.830	0.542	0.141
IL-10 r-value	0.108	-0.482	0.090
(Pg/L) P value	0.591	0.011*	0.654
Hs-Crpr-value	0.473	0.401	0.113
P value	0.013*	0.038*	0.576

Table 3 showeda significant negative correlation between IL-10 and FPG levels (r=-0.482; p=0.011). Significant positive correlations was also observed between the levels of Hs-Crp and fasting insulin (r=0.473; p=0.013) and between Hs-Crp Vs FPG (r=0.401; p=0.038) although no significant correlation was observed between the levels of Hs-Crp and HOMA-IR in the HIV infected individuals with diabetes mellitus

**Statistically significant at p<0.05*

Key: TNF-α= Tumour necrosis factor-alpha, IL-10=Interlukin-10, Hs-Crp=High sensitive C-reactive protein, HOMA-IR= Homeostasis model assessment index, FPG= Fasting plasma glucose

Table 4. Correlation of TNF-α, IL-10, Hs-Crp with fasting insulin, HOMA-IR and FPG in HIV infected adult individuals without diabetes mellitus

Parameters	Fasting insulin	HOMA-IR	FPG
TNF-α r-value	0.173	0.289	0.209
P value	0.929	0.129	0.287
IL-10 r-value	0.018	0.154	0.148
P value	0.926	0.424	0.452
Hs-Crpr-value	0.027	0.072	0.303
P value	0.891	0.709	0.117

Table 4 showed no correlation between TNF-α, IL-10, Hs-Crp with fasting insulin, HOMA-IR and FPG in HIV infected adult individuals without diabetes mellitus

**Statistically significant at p<0.05*

Key: TNF-α= Tumour necrosis factor-alpha, IL-10=Interlukin-10, Hs-Crp=High sensitive C-reactive protein, HOMA-IR= Homeostasis model assessment index, FPG= Fasting plasma glucose

Table 5. Correlation between TNF-α, IL-10, Hs-Crp, with fasting insulin, HOMA-IR and FPG in control group

Parameters	Fasting insulin	HOMA-IR	FPG
TNF-α r-value	0.082	0.099	0.084
P-value	0.659	0.597	0.653
IL-10 r-value	-0.082	0.910	0.073
P value	0.659	0.654	0.659
Hs-Crpr-value	0.208	0.031	0.261
P value	0.262	0.867	0.156

Table 5 showed no correlation between TNF-alpha, IL-10 and Hs-Crp with fasting insulin,HOMA-IR and FPG in control group

**Statistically significant at p<0.05*

Key: TNF-α= Tumour necrosis factor-alpha, IL-10=Interlukin-10, Hs-Crp=High sensitive C-reactive protein, HOMA-IR= Homeostasis model assessment index, FPG= Fasting plasma glucose

There were no statistically significant correlation observed between the levels of TNF-α Vs fasting insulin, FPG and HOMA-IR in the HIV infected individuals with diabetes mellitus (p>0.05) respectively. See Table 3.

There were no statistically significant correlation observed between the levels of IL-10 Vs fasting insulin and HOMA-IR (p>0.05), but there was a significant negative correlation seen between IL-10 and FPG levels in the HIV infected individuals with diabetes mellitus (r=-0.482; p=0.011). See Table 3.

Also, significant positive correlations were observed between the levels of Hs-Crp and fasting insulin (r=0.473; p=0.013) and between Hs-Crp Vs FPG (r=0.401; p=0.038) although no significant correlation was observed between the levels of Hs-Crp and HOMA-IR in the HIV infected individuals with diabetes mellitus (p=0.576). See Table 3.

There was no significant correlation observed between the parameters studied in the infected individuals without diabetes mellitus ($p>0.05$). See Table 4.

Furthermore, no significant correlation was observed between the parameters studied in the control group ($p>0.05$). See Table 5.

4. DISCUSSION

The results of the current investigation demonstrated that, in comparison to HIV-positive individuals without diabetes mellitus, those with diabetes had a significantly higher mean level of FPG. Furthermore, compared to controls, adult HIV-positive persons with and without diabetes mellitus showed significantly higher mean levels of FPG. This is in keeping with previous similar research that shows increased blood glucose in diabetic people with and without HIV infection [32]. The source of the higher plasma glucose levels may be due to the effects of antiretroviral medication, HIV infection, or both, which worsened the glucose metabolism in this individuals [34,35]. According to Chukwuanukwu*et al.*, FPG levels were likewise considerably higher in the non-diabetic HIV seropositive group than in the non-diabetic HIV seronegative group [33], which is consistent with the findings of the current investigation.

The study findings showed that HIV-positive people with diabetes mellitus had a significantly higher mean serum level of fasting insulin than HIV-positive adults without diabetes mellitus or control subjects. This study also found a significantly higher mean serum insulin level in the HIV-positive individuals without diabetes mellitus as compared to the control group. The higher insulin levels observed in the HIV infected individuals without diabetes mellitus in this study may be an indication that these individuals are at risk of developing type diabetes mellitus as a result of insulin resistance orchestrated by HIV infection and due to the effect of antiretroviral drugs which promotes chronic inflammatory immune responses. Potential mechanisms associated with diabetes in HIV infected persons include HIV infection itself, use of antiretroviral drugs, insulin resistance and immune activation which induces inflammatory responses leading to the release of heightened levels of inflammatory cytokines [23]. In the event of prevailing hyperglycemia, insulin is secreted from the beta cells of the islets of Langerhans in the pancreas to enhance the uptake of the excess glucose into insulin-sensitive tissues, such as the liver, muscle, or adipose tissue. Insulin is a key hormone in the regulation of plasma glucose levels in the human body. Therefore, in cases of persistently high blood sugar, insulin-sensitive tissues may become resistant to the effects of insulin and lose their sensitivity. In response, the pancreas secretes more insulin than usual in an attempt to restore a normal metabolic response.

In this study, the mean insulin resistance as determined by homeostasis model assessment index (HOMA-IR) was significantly higher in the HIV seropositive individuals with and without diabetes mellitus than in control group respectively. This finding suggests that insulin resistance may be the main driver of diabetes mellitus among HIV-positive adults [60]. Insulin resistance in HIV infected patients could be due to immune activation whether the patient is on HAART or not [61].This immune activation has been observed in HIV infected patients undergoing therapy and those not undergoing therapy [40].Several studies have reported varying degree of prevailing insulin resistance in HIV infected with and without diabetes mellitus and this is in consonance with the present report [43,62].

In this study, there was no significant difference in the mean level of IL-10 in HIV infected adult individuals with diabetes mellitus, HIV infected adults individuals without diabetes mellitus and control group. This could be due to highly antiretroviral therapy which suppresses viral replication at different stages of HIV life cycle, improves immunological status of HIV infected individuals and delays drug resistance [63,64]. This is in keeping with the report of previous similar study that observed no significant difference in IL-10 level in HIV infected individuals compared to control participants after 12 months of antiretroviral therapy [10].

This study found significantly higher mean serum level of Hs-Crp in HIV infected individuals with diabetes mellitus compared with HIV infected individuals without diabetes mellitus and control group. This in line with reports of previous study which showed a significant increase in hs-CRP levels in people living with HIV (PLWH) on HAART when compared to negative control [65].Furthermore, in keeping with the current finding, Chukwuanukwu et al. in their study reported significantly higher mean serum C-reactive protein levels in Diabetic HIV seropositive subjects and non diabetic HIV

seropositive subjects compared to control subjects [33]. This may suggest that chronic inflammation in HIV seropositive individuals can predispose them to development of diabetes mellitus. An increased CRP level can be caused by both acute inflammation (which may then decrease) and unresolved persistent inflammation. Both resolved and unresolved inflammation can be identified and measured using high-sensitivity C-reactive protein [66].One of the main long-term problems for HIV patients is cardiovascular disease (CVD), and Hs-CRP is thought to be a possible biomarker for predicting CVD risk and long-term disease progression [66].

In this investigation, the mean serum level of TNF-α was shown to be significantly higher in HIV-positive adults with diabetes mellitus than in HIV-positive adults without diabetes mellitus or control subjects. Also, there was significantly higher mean serum TNF-α level in the HIV infected individuals without diabetes mellitus than in control group. This shows that both HIV infection as well as diabetes mellitus is characterized by inflammation which potentiates insulin resistance that may culminate in diabetes mellitus. Persistent cytokine activation leading to prolonged release of TNF-α and other inflammatory cytokines can lead to development of insulin resistance which can result in the development of diabetes mellitus [60].

This report agrees with the finding of Osuji *et al*. which showed significantly higher mean serum TNF-α level in HIV infected persons even after 12 months antiretroviral therapy [10].This phenomenon may be present even in the absence of exposure to antiretroviral therapy (ARV) medications typically associated with insulin resistance risk.

The present study showed the HIV-positive individuals with diabetes mellitus had a mean body mass index that was significantly higher than that of those without diabetes mellitus. Notably, when comparing HIV-positive people with and without diabetes mellitus to control subjects, no significant changes in their mean BMI were seen. Remarkably, according to the World Health Organization's classification of BMI, which is provided below, both the test individuals and the control group in this study were overweight: Below 18.5 kg/m^2, normal weight = 18.5 - 24.9 kg/m^2, overweight = 25.0 - 29.9 kg/m^2, obesity class I = 30.0 - 34.9 kg/m^2, obesity class II = 35.0 -39.9 kg/m^2, and obesity class III ≥ 40.0 kg/m^2 [67]. Being overweight raises insulin resistance, which can accelerate the development of a number of chronic diseases for which it is a significant risk factor. Ezeugwunne *et al*., in keeping with the present findings, found no statistically significant changes in the mean BMI between HIV-positive subjects on antiretroviral therapy (ART) and control subjects [68].

Also, a significantly higher mean value was observed in SBP in HIV infected adult individuals without diabetes mellitus and control. According to a prior cross-sectional study investigating the effect of HAART on hypertension in HIV-positive people residing in Cameroon's North West region (NWR), 29.84% of the participants had systemic hypertension [69]. This is consistent with current findings.

IL-10 and FPG levels were found to be significantly inversely correlated in HIV-positive persons with diabetes mellitus. Additionally, among HIV-positive persons with diabetes mellitus, there were noteworthy positive associations found between Hs-Crp levels and fasting insulin as well as between Hs-Crp and FPG. The nature of HAART, family history of diabetes mellitus or metabolic syndrome, lifestyle, cardiovascular risk status, and other confirmatory tests for glucose levels such as glucose tolerance test, 2-hour postprandial test, and CD 4 counts should all be closely observed in HIV-positive individuals without diabetes. If adjustments to HAART are necessary, it is because research has shown that HAART is the primary cause of insulin resistance (IR) in relation to diabetes mellitus. This is done primarily to manage the study groups and lower the likelihood of being burdened with additional co-morbidity. In addition to screening for metabolic syndrome or other co-morbidities, anthropometric measurements should be analysed for other aspects that can cause diabetes mellitus in HIV infected individuals be considered [70-72].

5. CONCLUSION

This study showed higher levels of TNF-alpha, fasting insulin, HOMA-IR, Hs-Crp and FPG in the HIV seropositive individuals with and without diabetes mellitus compared to the control group. This is suggestive of ongoing inflammatory reactions which could subsequently lead to development of insulin resistance (IR), thereby causing or predisposing the HIV infected individuals at risk of developing type 2 diabetes mellitus.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT

Before commencement, written consent of all the participants was obtained before enrolment into the study. The participants were assured of confidentiality of the information obtained from them during and after the study.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the board of ethics committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi (NAUTH/CS/66/VOL.13/VER.3/274/2021/057).

ACKNOWLEDGEMENTS

My immense gratitude goes to my supervisor Prof N.R Ukibe whose thorough mentoring and guidance helped give this research its feel. To every author: Chinenye Stellamaris, NwokaNkiru, Chidinma Joy Iwuji ,Dr Ofia Kalu ,Dr Kingsley Obilo all who have been mentioned above contributed their knowledge and their resources to the actualization of this study. Thank you for the efforts, time and energy.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ogbodo EC, Okafor CC, Ogah HGO, Ezeugwunne IP, Igwebuobi CF, Okezie AO et al. Thyroid hormone profiling and enzymatic antioxidant status in diagnosis and management of type-ii-diabetes mellitus: A review of literature. World J Pharmaceut Life Sci. 2019;5(12):6-21.
2. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020; 21(17):6275. DOI: 10.3390/ijms21176275.
3. Ademola SA, Bamikole OJ, Amodu OK. Is TNF alpha a mediator in the co-existence of malaria and type 2 diabetes in a malaria endemic population? Frontiers in Immunol. 2023;14. DOI: 10.3389/fimmu.2023.1028303
4. Alzamil H. Elevated serum TNF-*α* is related to obesity in type 2 diabetes mellitus and is associated with glycemic control and insulin resistance. J Obesity. 2020;5076858. DOI: 10.1155/2020/5076858
5. Alam MF, Ahmed JU, Jahan I, Roy SC. The Usefulness of Glycated Hemoglobin (HbA1c) in the Detection of Diabetes Mellitus. Asian J. Med. Health. [Internet]. 2021 Dec. 14 [cited 2024 Jun. 15];19(12):1-5. Available:https://journalajmah.com/index.php/AJMAH/article/view/620
6. Sakpa CL, Idemudia JO. Relationship between Glycated Haemoglobin, Fasting plasma glucose, packed cell volume and albumin creatinine ratio in diabetic patients in South-South Nigeria. J. Adv. Med. Med. Res. [Internet]. 2013 Oct. 19 [cited 2024 Jun. 15];4(2):766-75. Available:https://journaljammr.com/index.php/JAMMR/article/view/1888
7. Nichols GA, Hillier TA, Brown JB. Normal fasting plasma glucose and risk of type 2 diabetes diagnosis. The American Journal of Medicine. 2008 Jun 1;121(6):519-24.
8. Cosson E, Carbillon L, Valensi P. High fasting plasma glucose during early pregnancy: A review about early gestational diabetes mellitus. Journal of Diabetes Research. 2017;2017(1): 8921712.
9. French MA, Cozzi-Lepri A, Arduino RC, Johnson M, Achhra AC, Landay A; Insight Smart study group. Plasma levels of cytokines and chemokines and the risk of mortality in HIV-infected individuals: A case-control analysis nested in a large clinical trial. AIDS. 2015;29(7):847-51. DOI: 10.1097/QAD.0000000000000618
10. Osuji FN, Onyenekwe CC, Ahaneku JE, Ukibe NR. The effects of highly active antiretroviral therapy on the serum levels of pro-inflammatory and anti-inflammatory cytokines in HIV infected subjects. J Biomed Sci. 2018; 25(1):88-92. DOI: 10.1186/s12929-018-0490-9
11. Naif HM. Pathogenesis of HIV Infection. Infect Dis Rep. 2013; 5(Suppl 1):e6. DOI: 10.4081/idr.2013.s1.e6
12. Roff SR, Noon-Song EN, Yamamoto JK. The Significance of Interferon-γ in HIV-1

Pathogenesis, Therapy, and Prophylaxis. Front Immunol. 2014 Jan 13;4:498.
DOI: 10.3389/fimmu.2013.00498. PMID: 24454311; PMCID: PMC3888948.

13. Watanabe D, Uehira T, Yonemoto H, Bando H, Ogawa Y, Yajima K et al. Sustained high levels of serum interferon-γ during HIV-1 infection: A specific trend different from other cytokines. Viral Immunol. 2010; 23(6):619-25.
DOI: 10.1089/vim.2010.0065
14. Brockman MA, Kwon DS, Tighe DP, Pavlik DF, Rosato PC, Sela J et al. IL-10 is up-regulated in multiple cell types during viremic HIV infection and reversibly inhibits virus-specific T cells. Blood. 2009; 114(2):346-56.
DOI: 10.1182/blood-2008-12-191296.
15. Tingstedt JL, Hove-Skovsgaard M, Gaardbo J, Ullum H, Nielsen SD, Gelpi M, et al. Type II Diabetes on Immune Maturation, Immune Regulation and Immune Activation. APIMS. 2019; 127(7): 529–537.
DOI: 10.1111/apm.12956.
16. Dooko CBA, De Wit S, Neuhaus J, Palfreeman A, Pepe R, Pankow JS, et al. Interleukin-6, high sensitivity C-reactive protein, and the development of type 2 diabetes among HIV-positive patients taking Antiretroviral therapy. J AcqdImm Def Syndr. 2014; 67(5):538– 546.
17. Neuhaus J, Jacobs DR Jr, Baker JV, Calmy A, Duprez D, La Rosa A et al. Markers of inflammation, coagulation, and renal function are elevated in adults with HIV infection. J Infect Dis. 2010; 201(12):1788-95.
DOI: 10.1086/652749.
18. Okdahl T, Wegeberg AM, Pociot F, Brock B, Størling J, Brock C. Low-grade inflammation in type 2 diabetes: a cross-sectional study from a Danish diabetes outpatient clinic. BMJ Open. 2022; 12(12):e062188.
DOI: 10.1136/bmjopen-2022-062188.
19. Shrivastava AK, Singh HV, Raizada A, Singh SK. C-reactive protein, inflammation and coronary heart disease. The Egyptian Heart J. 2015;67(2):89-97.
DOI: 10.1016/j.ehj.2014.11.005.
20. Jang DI, Lee AH, Shin HY, Song HR, Park JH, Kang TB et al. The role of tumor necrosis factor alpha (TNF-α) in autoimmune disease and current TNF-α Inhibitors in Therapeutics. Int J Mol Sci. 2021; 22(5):2719.
DOI: 10.3390/ijms22052719.
21. Bashir H, Hayat Bhat M, Majid S. Molecular pathogenesis of inflammatory cytokines in insulin resistance diabetes mellitus. Intech Open; 2022.
DOI: 10.5772/intechopen.100971.
22. Ingle PV, Patel DM. C - reactive protein in various disease condition – an Overview. Asian J Pharm Clin Res. 2011;4(1):9–13.
23. Kumar M, Singh H, Chakole S. Exploring the relation between diabetes and HIV: A narrative review. Cureus. 2023;15(8):e43909.
DOI: 10.7759/cureus.43909.
24. Hu H, Nakagawa T, Yamamoto S, *et al*. Development and validation of risk models to predict the 7-year risk of type 2 diabetes: the Japan epidemiology collaboration on occupational health study. J Diabetes Investig. 2018;9:1052–1059.
DOI:10.1111/JDI.12809
25. Banait T, Wanjari A, Danade V, Banait S, Jain J. Role of high-sensitivity c-reactive protein (hs-crp) in non-communicable diseases: A review. Cureus. 2022; 14(10):e30225.
DOI: 10.7759/cureus.30225.
26. Brown TT, Tassiopoulos K, Bosch RJ, Shikuma C, McComsey GA. Association between systemic inflammation and incident diabetes in HIV-infected patients after initiation of antiretroviral therapy. Diabetes Care. 2010.33:2244-2249.
27. Julijana S,Jelena R,Katarina B,Milan O,Magbubah E,Sonja Z,Zoran G et al. Role of C-reactive protein in diabetic Inflammation. Mediators Inflamm. 2022;75:112.
DOI: 10.1155/2022/3706508
28. Mugabo Y, Li L, Renier G. The connection between C-reactive protein (CRP) and diabetic vasculopathy. Focus on preclinical findings. Curr Diabet Rev. 2010;6:(1):27–34.
DOI: 10.2174/157339910790442628.
29. Esser N, Paquot N, Scheen AJ. Inflammatory markers and cardiometabolic diseases. Acta Clinica Belgica. 2015;70(3):193-199.
DOI: 10.1179/2295333715Y.0000000004.
30. Ouyang W, O'Garra A. IL-10 Family Cytokines IL-10 and IL-22: from Basic Science to Clinical Translation. Immunity. 2019;50(4):871–891.
31. Obasanmi G, Lois N, Armstrong D, Hombrebueno JMR, Lynch A, Chen M et

al. Peripheral blood mononuclear cells from patients with type 1 diabetes and diabetic retinopathy produce higher levels of IL-17A, IL-10 and IL-6 and lower levels of IFN-γ-A Pilot Study. Cells. 2023; 12(3):467.
DOI: 10.3390/cells12030467.

32. Sydney C , Nandlal L, Haffejee F, Kathoon J, Naicker T. Lipid profiles of HIV-infected diabetic patients. J Endocrinol, Metabol Diabetes South Afr. 2023; 28(2):56–61.
DOI: 10.1080/16089677.2023.2178157

33. Chukwuanukwu RC, Nwosu NB, Ifeanyichukwu MO, Nsonwu-Anyanwu AC, Manafa PO. Evaluation of some immune and inflammatory responses in diabetes and HIV co-morbidity. Afr Health Sci. 2023; 23(1):120-128.
DOI: 10.4314/ahs.v23i1.14.

34. Rhee JY, Bahtila TD, Palmer D, Tih PM, Aberg JA, Le-Roith D, et al. Prevalence of and Factors Associated with Prediabetes and Diabetes among HIV-infected Adults in Cameroon. Diabetes Metab Res Rev. 2016;32(6):544–549.

35. Gebrie A, Tesfaye B, Gebru T, Adane F, Abie W, Sisay M. Diabetes mellitus and its associated risk factors in patients with human immunodeficiency virus on anti-retroviral therapy at referral hospitals of Northwest Ethiopia. DiabetolMetab Syndr. 2020; 12:20.
DOI: 10.1186/s13098-020-00527-1.

36. Rahman MS, Hossain KS, Das S, Kundu S, Adegoke EO, Rahman MA et al. Role of insulin in health and disease: An update. Int J Mol Sci. 2021; 22(12):6403.
DOI: 10.3390/ijms22126403.

37. Ogbu ISI, Ejike-Odeh EJ, Obeagu EI. Insulin Resistance: A review. Elite J Lab Med. 2024; 2(3):11-28.

38. Gu X, Al Dubayee M, Alshahrani A, Masood A, Benabdelkamel H, Zahra M et al. Distinctive metabolomics patterns associated with insulin resistance and type 2 diabetes mellitus. Front Mol Biosci. 2020;7:609806.
DOI: 10.3389/fmolb.2020.609806.

39. Pedro MN, Rocha GZ, Guadagnini D, Santos A, Magro DO, Assalin HB et al. Insulin Resistance in HIV-Patients: Causes and Consequences. Front Endocrinol (Lausanne). 2018;9:514.
DOI: 10.3389/fendo.2018.00514

40. Non LR, Escota GV, Powderly WG. HIV and its relationship to insulin resistance and lipid abnormalities. Transl Res. 2017;183:41-56.
DOI: 10.1016/j.trsl.2016.12.007.

41. Nasi M, De Biasi S, Gibellini L, Bianchini E, Pecorini S, Bacca V et al. Ageing and inflammation in patients with HIV infection. Clin Exp Immunol. 2017;187(1):44-52.
DOI: 10.1111/cei.12814.

42. Shahwan MJ, Khattab MH, Jairoun AA. Association of serum calcium level with waist circumference and other biochemical health-care predictors among patients with type 2 diabetes. J pharm Bioallied Science. 2019;11(3):292-298.

43. Tiozzo E, Rodriguez A, Konefal J, Farkas GJ, Maher JL, Lewis JE. The Relationship between HIV Duration, Insulin Resistance and Diabetes Risk. Int J Environ Res Public Health. 2021; 18(8):3926.
DOI: 10.3390/ijerph18083926.

44. Oni T, Youngblood E, Boulle A, et al. Patterns of HIV, TB, and non-communicable disease multi-morbidity in peri-urban South Africa – a cross sectional study. BMC Infect Dis. 2015; 15: 20-25.

45. Zenebework G, MulikenA, Taye A, Fantu A. Cormobidity of HIV, hypertension and diabetes associated factors among people living receiving antiretroviral therapy in Bahir Dar, City Ethopia. J Cormob. 2020;16:13-14.
DOI: 10.1177/2235042X19899319

46. Hemkens LG, Bucher HC. HIV infection and cardiovascular disease. Eur Heart J. 2014; 35(21): 1373–1381.

47. Kalyesubula R, Wearne N, Semitala FC, et al. HIV-associated renal and genitourinary comorbidities in Africa. J AcqImm Def Syndr. 2014;67: 68–78.

48. Bloomfield GS, Khazanie P, Morris A, et al. HIV and non-communicable cardiovascular and pulmonary diseases in low-and middle-income countries in the ART era: What we know and best directions for future research. J AcqImm Def Syndr. 2014;67:140-159.

49. Ghulam M D, Asim T U D ,Faroouq M D C, Azfar T, Khaleeq et al. Association of obesity indicator with hypertension in type 2 diabetes mellitus patients. Ceurus. 2019;11(7):12

50. Fryar CD, Gu Q, Ogden CL, Flegal KM. Anthropometric reference data for children and adults: United States, 2011-2014. Vital Health Stat 3 Anal Stud. 2016 Aug;(39):1-46.

51. Casadei K, Kiel J. Anthropometric measurement. Stat pearls. 2022;5:1-4.
52. Gavriilidou NN, Pihlsgård M, Elmståhl S. Anthropometric reference data for elderly Swedes and its disease-related pattern. Eur J Clin Nutr. 2015 Sep;69(9):1066-75.
53. Kidy FF, Dhalwani N, Harrington DM, Gray LJ, Bodicoat DH, Webb D, Davies MJ, Khunti K. Associations between Anthropometric measurements and cardiometabolic risk factors in white european and south asian adults in the United Kingdom. Mayo Clin Proc. 2017 Jun;92(6):925-933.
54. Frank EA, Shubha MC, D'Souza CJ. Blood glucose determination: plasma or serum? J Clin Lab Anal. 2012; 26(5):317-20.
DOI: 10.1002/jcla.21524.
55. Bürgi W, Briner M, Franken N, Kessler AC. One-step sandwich enzyme immunoassay for insulin using monoclonal antibodies. Clin Biochem. 1988; 21(5):311-4.
DOI: 10.1016/s0009-9120(88)80087-0.
56. Hashemipour S, Zohal M, Modarresnia L, Kolaji S, Panahi H, Badri M et al. The yield of early-pregnancy homeostasis of model assessment -insulin resistance (HOMA-IR) for predicting gestational diabetes mellitus in different body mass index and age groups. BMC Pregnancy Childbirth. 2023; 23(1):822.
DOI: 10.1186/s12884-023-06113-3.
57. Chiswick EL, Duffy E, Japp B, Remick D. Detection and quantification of cytokines and other biomarkers. Methods Mol Biol. 2012; 844:15-30.
DOI: 10.1007/978-1-61779-527-5_2.
58. Votruba T, Rákosník P. (ELISA) [Determination of C-reactive protein using the solid- surface immunoenzyme assay (ELISA)].Czech Epidemiol Microbiol Imunol. 1991;40(1):29-35.
59. Engelberts I, Möller A, Schoen GJ, van der Linden CJ, Buurman WA. Evaluation of measurement of human TNF in plasma by ELISA. Lymphokine Cytokine Res. 1991; 10(1-2):69-76.
60. Mulenga LB, Musonda P, Chirwa L, Siwingwa M, Mweemba A, Suwilanji S et al. Insulin resistance is associated with higher plasma viral load among hiv-positive adults receiving longer-term (1 Year) combination antiretroviral therapy (ART). J Infect Dis Ther. 2019; 7(4): 406.
61. Kiage JN, Heimburger DC, Nyirenda CK, Wellons MF, Bagchi S, Chi BH et al. Cardiometabolic risk factors among HIV patients on antiretroviral therapy. Lipids Health Dis. 2013; 12:50.
DOI: 10.1186/1476-511X-12-50.
62. Bratt G, Bra¨nnstro¨m J, Missalidis C, Nystro¨m T. Development of type 2 diabetes and insulin resistance in people with HIV infection: Prevalence, incidence and associated factors. PLoS One. 2021;16(6): e0254079.
DOI: 10.1371/journal.pone.0254079
63. Hileman CO, Funderburg NT. Inflammation, Immune Activation, and Antiretroviral Therapy in HIV. Curr HIV/AIDS Rep. 2017;14(3):93-100.
DOI: 10.1007/s11904-017-0356-x.
64. Ezeugwunne IP, Ogbodo EC, Analike RA, Okwara NA, Nnamdi JC, Iwuji JC et al. The pattern of alpha-fetoprotein, CD4+ count, albumin, AST, ALT and ALP in HIV subjects on long term antiretroviral therapy in Nauth Nnewi, Anambra State, Nigeria. Indian J Forensic Community Med. 2021; 8(1):45–51.
65. Mabhida SE, Mchiza ZJ, Mokgalaboni K, Hanser S, Choshi J, Mokoena H et al. High-sensitivity C-reactive protein among people living with HIV on highly active antiretroviral therapy: A systemic review and meta-analysis. BMC Infect Dis. 2024; 24(1):160.
DOI: 10.1186/s12879-024-09050-4.
66. Vishwanath A, Quaiser S, Khan R. Role of high-sensitivity C-reactive protein measurements in HIV patients. Indian J Sex Transm Dis AIDS. 2016; 37(2):123-128.
DOI: 10.4103/0253-7184.192127.
67. WHO. Physical Status: The Use and Interpretation of Anthropometry. Technical Report Series. World Health Organization, Geneva. 1995;854:1-1-9950.
68. Ezeugwunne IP, Ogbodo EC, Analike RA, Onuora IJ, Obi-Ezeani CN, Ugwu MC et al. Body Mass Index, Blood Pressure and Serum Cortisol Level As Stress Index in Symptomatic Hiv/Aids Male Subjects On Antiretroviral Therapy Negative to Malaria Parasite in Nnewi, Anambra State, Nigeria. Int J Clin Biomed Res. 2019;5(2):19-23.
69. Pangmekeh PJ, Awolu MM, Gustave S, Gladys T, Cumber SN. Association between highly active antiretroviral therapy (HAART) and hypertension in persons living with HIV/AIDS at the Bamenda

regional hospital, Cameroon. Pan Afr Med J. 2019;33:87.
DOI: 10.11604/pamj.2019.33.87.15574.

70. Akash MSH, Rehman K, Liaqat A. Tumor necrosis factor-alpha: role in development of insulin resistance and pathogenesis of type 2 diabetes mellitus. J Cell Bio. 2018;119(1):105–110.
DOI: 10.1002/jcb.26174.

71. Leitner DR, Frühbeck G, Yumuk V, Schindler K, Micic D, Woodward E, Toplak H. Obesity and type 2 diabetes: two diseases with a need for combined treatment strategies - EASO can lead the way. Obes Facts. 2017;10:483–492.

72. Munter P, Eihorn PT, William CC, Paul KW, Natalie AB , Paul ED, Beverly BG et al.Blood pressure assessment in adult in clinical praticeand clinical based research: JJAC Scientific expert panel. J Am Coll Cardiol. 2019;73(3):317-335.

APPENDIX

INFORMED CONSENT FORM

Affiliation Of research

I am OBILO CHIDERA VIVIENNE, a postgraduate student of the department of Medical Laboratory Science,Nnamdi Azikiwe University, Nnewi Campus.I am under supervision,carrying out a research on “Assessment Of Pancreatic Functions and Some Inflammatory Markers In Hiv infected Individual in NAUTH, Nnewi, Nigeria ”.

Purpose Of research

The research is a pre-requisite for an award of Master Of Science Degree in Medical Laboratory Science.

Aim of the study

This study aims to assess the pancreatic function and some inflammatory markers in Hiv infected individuals in NAUTH, Nnewi, Nigeria.

Confidentiality of information

The confidentiality of all participants in the study will be ensured.Information obtained from subjects will not be divulged to anyone unrelated to this study.No name will be recorded as information about participants will be stored with code numbers.

Requirement from each participant

Five (5) millilitres of blood will be taken via venepuncture using syringe and needle.

Voluntarism

Participation in this study is entirely voluntary participants can choose to withdraw from this research anytime

Risk/Benefits

This study will not expose a participant to any form of hazard.Thebenfits are that your results can be revealed to you and proper advice granted through the available facilities.

Cost

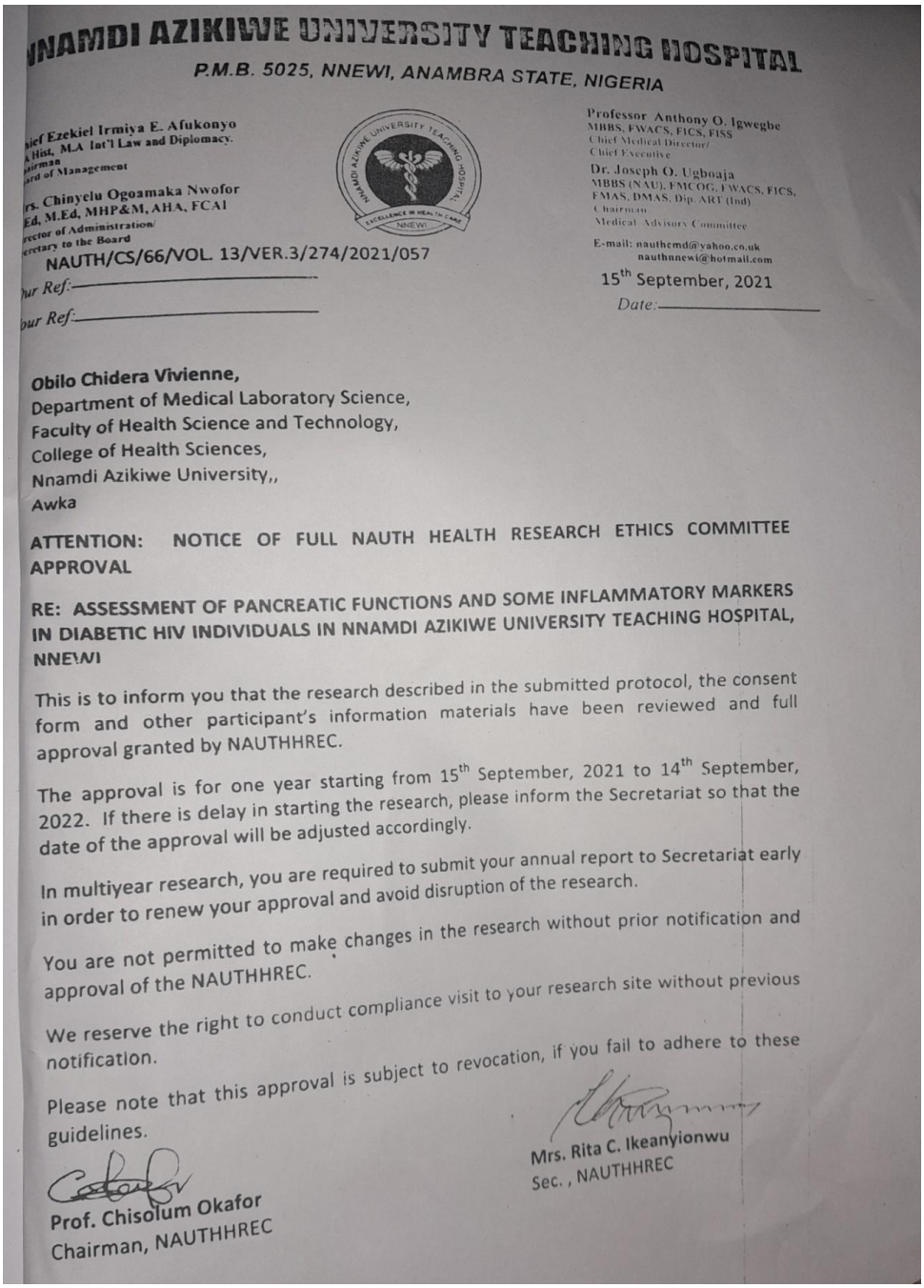
Participants will neither be paid nor charged.

Statement of person obtaining information consent: I have fully explained this research to volunteers.I have given sufficient information including risk and benefits to enable the participants make an informed decisions.

Date..... Signature.....
Name..... Phone No.....

Statement of person giving consent: I have read the description of the research and understood that any participation and withdrawal is voluntary.I have also been well informed of the risk benefits to judge that i want to participate in it.

Date..... Signature.....
Name..... Phone.....



NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL

P.M.B. 5025, NNEWI, ANAMBRA STATE, NIGERIA

hief Ezekiel Irmiya E. Afukonyo
A Hist, M.A Int'l Law and Diplomacy.
airman
ard of Management

rs. Chinyelu Ogoamaka Nwofor
Ed, M.Ed, MHP&M, AHA, FCAI
rector of Administration/
ecretary to the Board

Professor Anthony O. Igwegbe
MBBS, FWACS, FICS, FISS
Chief Medical Director/
Chief Executive

Dr. Joseph O. Ugboaja
MBBS (NAU), FMCOG, FWACS, FICS,
FMAS, DMAS, Dip. ART (Ind)
Chairman
Medical Advisory Committee

E-mail: nauthcmd@yahoo.co.uk
nauthnnewi@hotmail.com

NAUTH/CS/66/VOL. 13/VER.3/274/2021/057

Our Ref:

Your Ref:

15th September, 2021

Date:

Obilo Chidera Vivienne,
Department of Medical Laboratory Science,
Faculty of Health Science and Technology,
College of Health Sciences,
Nnamdi Azikiwe University,,
Awka

ATTENTION: NOTICE OF FULL NAUTH HEALTH RESEARCH ETHICS COMMITTEE APPROVAL

RE: ASSESSMENT OF PANCREATIC FUNCTIONS AND SOME INFLAMMATORY MARKERS IN DIABETIC HIV INDIVIDUALS IN NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL, NNEWI

This is to inform you that the research described in the submitted protocol, the consent form and other participant's information materials have been reviewed and full approval granted by NAUTHHREC.

The approval is for one year starting from 15th September, 2021 to 14th September, 2022. If there is delay in starting the research, please inform the Secretariat so that the date of the approval will be adjusted accordingly.

In multiyear research, you are required to submit your annual report to Secretariat early in order to renew your approval and avoid disruption of the research.

You are not permitted to make changes in the research without prior notification and approval of the NAUTHHREC.

We reserve the right to conduct compliance visit to your research site without previous notification.

Please note that this approval is subject to revocation, if you fail to adhere to these guidelines.

Prof. Chisolum Okafor
Chairman, NAUTHHREC

Mrs. Rita C. Ikeanyionwu
Sec., NAUTHHREC

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of the publisher and/or the editor(s). This publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© Copyright (2024): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/119176