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Review Article

Evaluation of Metabolic and Some Renal Function Indices in Human Immunodeficiency Virus Seropositive Subjects on Antiretroviral Therapy in ABA Metropolis

Dunga Kingsley Excel[1], Emmanuel Testimony Chiziterem[1], Ofoegbu Nnamdi Jude[1], Okoro Chinyere Ihuarulam[2] and Nnodim Johnkennedy[3]

[1]*Department of Medical Laboratory Science, College of Medicine and Health Sciences Rhema University, Nigeria*

[2]*Department of Microbiology/Parasitology, Federal Teaching Hospital, Nigeria*

[3]*Department of Medical Laboratory Science, Imo State University, Nigeria*

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[*]**Corresponding author:** Dunga Kingsley. Excel, Department of Medical Laboratory Science, College of Medicine and Health Sciences Rhema University, Nigeria.

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Abstract

A group of illnesses collectively referred to as Acquired Immunodeficiency Syndrome (AIDS) are defined by a progressive loss of immune function. Comparatively speaking to other parts of the world, Sub-Saharan Africa is more affected by HIV and AIDS. Renal problems are a major feature of advanced HIV disease and a major cause of morbidity and mortality among HIV/AIDS patients. This study's objective was to evaluate the HIV participants' metabolic and renal function indices at the Rhema University Teaching Hospital in Aba Metropolis. Biochemical data and samples were collected from patients attending the ART clinic at Rhema University Teaching Hospital, Aba, Nigeria, as part of a cross-sectional study using a comparative design. Ninety volunteers had their renal functions evaluated, and the data was collected and analyzed using SPSS version 29.0 through the use of ANOVA and the student's t-test. 90 people in all were divided into three groups for the study: 30 HIV-seronegative controls, 30 HIV-seropositive treatment-naive patients, and 30 HIV-seropositive patients receiving antiretroviral therapy. Subjects on ART groups had mean blood total protein levels higher than those of treatment-naive individuals. Both HIV-positive groups showed a significant ($p < 0.05$) decrease in serum total protein when compared to the control group. There was no significant difference in the mean serum creatinine level between the three groups. Individuals without treatment had a poorer creatinine clearance than both the control group and the ART individuals. When comparing the creatinine clearance levels of HIV-positive people (both naive and treated) to negative controls, no statistically significant changes were observed.

Compared to those on ART and the HIV-seronegative control, treatment-naive patients had a greater prevalence of renal impairment, defined as CrCl< 60 mL/min.

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Keywords: **M**etabolic, Renal function indices, Human immunodeficiency virus seropositive subjects, Antiretroviral therapy

Introduction

Since Highly Active Antiretroviral Therapy (HAART) became available in areas where people can afford it, the landscape of HIV infection has undergone dramatic changes. The normal course of HIV infection has undergone a significant alteration since the advent of HAART [1]. Extensive research over the years has demonstrated the existence of a unique disease called HIVAN, or human immunodeficiency virus associated nephropathy. Furthermore, between 1995 and 1999, the use of combination antiretroviral medication was linked to a significant decrease in the prevalence of HIV-related opportunistic infections and illnesses. Nonetheless, research on the precise impact of HAART on the incidence of HIVAN and end-stage renal disease in HIV-positive people is still underway, and some findings point to a possible decrease in the risk of chronic kidney disease [2].

According to data from the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases in 2001, a noteworthy study found that, as of May 2000, 6,179 HIV-positive patients in the United States had undergone renal replacement treatment. This demonstrates the substantial burden of renal disease among people living with HIV/AIDS and emphasises how crucial it is to comprehend how HAART and the prevalence of renal problems in this community are related [3].

Apart from antiretroviral treatment-induced side effects, HIV-positive persons might also have a variety of underreported biochemical abnormalities that fall into three categories: specific HIV-related abnormalities, coincidental renal diseases, and HIV-related abnormalities. The higher risk of drug-induced kidney damage in HIV-positive patients is especially concerning. Renal toxicity has been frequently linked to medications including pentamidine, acyclovir, and Trimethoprim-Sulfamethoxazole (TMP-SMZ) in this population. Additionally, there have occasionally been reports of a connection between acute renal failure with the use of specific antiretrovirals, such as Idinavir, Ritonavir, Adefovir, Cidofovir, and Tenofovir [4,5].

Although there hasn't been any prior research on metabolic and renal function indices among HIV seropositive patients in Aba, Abia State, it's possible that a protracted HIV/AIDS infection is hinting at a potential kidney impact.

Materials and Methods Study Area

The study was conducted at the ART/HIV Clinic, which is part of Rhema University Teaching Hospital (RUTH, Aba). RUTH is a well- equipped hospital which is popular in South-eastern Nigeria. The research focused on individuals infected with HIV who regularly attended clinical appointments.

Subjects

Inclusion Criteria

HIV infected patients' naive to combination Antiretroviral Therapy (cART); HIV infected patients on cART for at least 3 months; HIV-negative participants seen at the clinic of Rhema University Teaching Hospital were included in the study.

Exclusion Criteria

Patients known to have acute or chronic kidney disease; taking nephrotoxic drugs; or pregnant; or known to have diabetes mellitus, known to be hypertensive; HBsAg +ve; HCV Ab +ve; were excluded from the study.

Ethical Approval

Ethical approval was granted by the Research and Ethical Committee of Rhema University Teaching Hospital (R.U.T.H) Aba to collect blood samples from the patients.

Informed Consent

Appropriate advocacy was carried out and patient consent gotten after due explanation of the study with assurance of the patients' identity confidentiality.

Study Design

During the 2022/23 period, the ART/HIV Clinic had a significant number of adult patients. First line regimens that patients were taking included 4a = d4T/3Tc/NVP (Stavudine, Lamivudine, Nevirapine), 4b = d4T/3Tc/EFV (Stavudine, Lamivudine, Efavirenz), 4c = AZT/3Tc/NVP (Zidovudine, Lamivudine, Nevirapine), and 4d = AZT/ 3Tc/EFV (Zidovudine, Lamivudine, Efavirenz). Some patients were also on the following second line regimens: ABC/ddi/LPv/r (Abacavir, Didanosine, ritonavir, enhanced Lopinavir), AZT/3Tc/LPv/r (Zidovudine, Lamivudine, Ritonavir, enhanced Lopinavir) and D4T/3TC/LPv/r (Stavudine, Lamivudine, retonavir enhanced Lopinavir).

Eligible participants for the study were identified by reviewing records from the ART clinic, based on established clinical and laboratory criteria. These eligible patients were sequentially approached, both those who were not on ART and those currently receiving ART treatment, for inclusion in the study. In addition to this, a control group was enrolled consisting of individuals who tested negative for HIV.

Sample Size Determination

Assuming an average of 6% prevalence rate of renal insufficiency among ART naive patients, at 5% precision and 95% level of confidence interval, the sample size calculated using the formula shown below is 87.

Using the formula

$$\mathbf{N = Z^2 P (1\text{-}p) / \alpha^2}$$

Where N = sample size

Z = 1.96 Critical value at 95% level of confidence

p = Proportion of renal insufficiency

α = type-I error (0.05)

Among the three arms of the study, these numbers were equally split; hence 30 patients were recruited at each arm. Quota sampling were employed i.e. all patients who fulfil the inclusion criteria and consenting for the study were recruited consecutively.

Clinical and Anthropometric Assessments

Clinical and anthropometric data were gathered for each participant, including information on their gender, age, height, pulse rate, blood pressure, and specific parameters of interest. These specific parameters included the duration of known HIV infection (time since HIV diagnosis), medical history related to kidney health and factors associated with kidney disease, systemic complications, and details of their treatment regimen. We used a standardized questionnaire or data sheet format to record this information.

Participants with pre-existing diagnoses of diabetes mellitus, hypertension, acute or chronic kidney disease, individuals taking nephrotoxic medications, pregnant women, and patients with hepatitis B or C were not included in the study.

Measurement of Weight, Height and Body Mass Index

Analog scale with kg reading was used to measure the weight of study subjects. Height was also measured while they were standing erect there by lowering the horizontal scale bar snugly to the crown of the head.

Body Mass Index (BMI): BMI = weight (kg)/height squared (m^2).

Sample Collection and Handling

Blood samples were collected with minimal stasis during the timeframe of 8:00 AM to 10:00 AM. These samples were acquired through venepuncture from the antecubital vein after sterilization with methylated spirit. Subsequently, the samples were placed into dry plain bottles following the removal of the needle, and each bottle was carefully labeled to prevent any mixing or confusion. The blood was allowed to clot and retract, after which it was centrifuged at 1000rpm for 5 minutes, resulting in the separation of serum into appropriately pre-labeled clean small bottles. These samples were then stored at freezing temperatures until they were ready for analysis.

Laboratory Analysis

Sodium and potassium ions were measured by standard flame photometric method.

Bicarbonate was estimated by back titration method using modified Vanslyke method.

Chloride was measured by using the modified mercuric nitrate Hg (NO^{3-}) titrimetric method of Schales and schales.

Urea was measured by Diacetylmonoxime Method, (DAM method) using thiosemicarbozide [6].

Determination of Total Protein

This was done by Refractometry.

The serum creatinine was estimated using the Rehbery-Follin modification of Jaffes Method [7].

CD4+ and CD8+ T cell count tests were determined by BD Fluorescence-activated Cell Sorting (FACS) count version 1.0 01/08 machine.

Creatinine clearance was calculated from the patient's sex, age and serum creatinine using Cockcroft and Gault formula (Cockroft and Gault, 1976) as follows:

$$\text{Male CrCl} = (140 - \text{age}) \text{ x } \frac{(\text{weight})}{(\text{SCr} \times 72)}$$

$$\text{Female CrCl} = (140 - \text{age}) \text{ x } \frac{(\text{weight})}{(\text{SCr} \times 72)} \text{x } 0.85$$

Where CrCl = Creatinine clearance in mL/min

Age is in years, weight is in kilograms, and SCr is serum creatinine in mg/dL

Statistical Analysis

The IBM Statistical package for Social Sciences (IBM SPSS) version 29.0.1.0(171) Window 7 was used in statistical analysis. The data were expressed as mean ±SD and compared for statistical significant difference. Student's t-test was used to compare two treatments while Analysis of Variance (ANOVA) was used for three treatments.

Result

The tables below show the results that were obtained from this study. There were 90 subjects in total. 30 were HIV seropositive on ART, 30 were HIV seropositive but not on ART while 30 were control subjects who were HIV seronegative with no history of renal complications.

The data were expressed as mean ±SD and compared for statistical significant difference. Student's t-test was used to compare two treatments while Analysis of Variance (ANOVA) was used for three treatments.

Tables 4.1, 4.2 and 4.3 show a comparison of one of the three groups against the other, in order to determine if a significant difference exists between the means using student's t-test.

Table 4.1: Immunological, Metabolic and Renal Function Parameters of HIV Subjects on ART *vs* HIV Subjects not on ART Using two tailed t-test

Parameters	HIV-Infected and on ART±SD	HIV-Infected and not on ART± SD	Tcalc	Tcritical	Conclusion
CD8+ (cell/uL)	815.7 ± 412.3	1173.6 ± 486.8	-3.19	1.672	Significant
CD4+ (cell/uL)	379 ± 249	351.7 ± 233	0.38	1.672	Insignificant
K^+ (mmol/L)	4.28 ± 0.55	4.32 ± 0.76	-0.23	1.672	Insignificant
Cl^- (mmol/L)	102.00 ± 4.0	102.98±4.12	-0.91	1.672	Insignificant
HCO_3^- (mmol/L)	25.24 ± 2.75	25.58 ± 3.12	-0.45	1.672	Insignificant
Urea (mmol/L)	3.31 ± 1.17	4.80 ± 1.45	-4.38	1.672	Significant
Creatinine (mmol/L)	64.06 ± 15.50	73.78 ± 19.2	-2.17	1.672	Significant
Total protein	5.78 ± 1.39	4.76 ± 2.19	2.163	1.672	Significant
Creatinine Clearance (ml/min)	114.76 ± 28.54	111.05±11.33	0.661	1.672	Insignificant

Table 4.2: Immunological, Metabolic and Renal Function Parameters of HIV Subjects on ART *vs* Control using two tailed t- test

Parameters	HIV-Infected and on ART±SD	Control ± SD	Tcalc	Tcritical	Conclusion
CD8+ (cell/uL)	815.7± 412.3	508.2 ± 196.5	3.687	1.672	Significant

CD4+ (cell/uL)	379 ± 249	722,43 ± 339	-4.472	1.672	Significant
K^+ (mmol/L)	4.28 ± 0.55	4.02 ± 0.52	1.882	1.672	Significant
Cl^- (mmol/L)	102.00 ± 4.0	103.32 ± 4.03	-1.273	1.672	Insignificant
HCO_3^- (mmol/L)	25.24 ± 2.75	24.60 ± 2.91	0.876	1.672	Insignificant
Urea(mmol/L)	3.31 ± 1.17	4.00 ± 1.15	-2.303	1.672	Significant
Creatinine (mmol/L)	64.06± 15.50	99.22 ± 17.88	-5.15	1.672	Significant
Total protein	5.78 ± 1.39	7.56 ± 0.68	-6.301	1.672	Significant
Creatinine Clearance (ml/min)	114.76± 28.54	115.05 ± 44.41	-0.031	1.672	Insignificant

Table 4.3: Immunological, Metabolic and Renal Function Parameters of HIV Subjects not on ART *vs* Control using two tailed t-test

Parameters	**HIV-Infected and not on ART±SD**	**Control ± SD**	**Tcalc**	**Tcritical**	**Conclusion**
CD8+(cell/uL)	1173.6 ± 486.8	508.2 ± 196.5	6.942	1.672	Significant
CD4+ (cell/uL)	351.7± 233	722.43 ± 339	-4.936	1.672	Significant
K^+ (mmol/L)	4.32 ± 0.76	4.02 ± 0.52	1.784	1.672	Significant
Cl^- (mmol/L)	102.98 ± 4.12	103.32 ± 4.03	-0.327	1.672	Insignificant
HCO_3^- (mmol/L)	25.58 ± 3.12	24.60 ± 2.91	1.258	1.672	Insignificant
Urea(mmol/L)	4.80 ± 1.45	4.00 ± 1.15	2.367	1.672	Significant
Creatinine (mmol/L)	73.78 ± 19.2	99.22 ± 17.88	-5.311	1.672	Significant
Total protein	4.76 ± 2.19	7.56 ± 0.68	-6.69	1.672	Significant
Creatinine Clearance (ml/min)	111.05±11.33	115.05 ± 44.41	-0.408	1.672	Insignificant

Note: Values are expressed as mean ± SD; the 0.05 level of significance was used

Table 4.4 shows a comparison of the Immunological, Metabolic and Renal Function of the study participants using ANOVA.

Table 4.4: Comparison of the Immunological, Metabolic and Renal Function of the study participants using ANOVA

Parameters	**HIV-Infected and on ART±SD**	**HIV-Infected and not on ART± SD**	**Control ± SD**	**P value**
CD8+(cell/uL)	815.7 ± 412.3	1173.6 ± 486.8	508.2 ± 196.5	0.003
CD4+ (cell/uL)	379 ± 249	351.7 ± 233	722.43 ± 339	0.001
K^+ (mmol/L)	4.28 ± 0.55	4.32 ± 0.76	4.02 ± 0.52	0.456
Cl^- (mmol/L)	102.00 ± 4.0	102.98 ± 4.12	103.32 ± 4.03	0.654
HCO_3^- (mmol/L)	25.24 ± 2.75	25.58 ± 3.12	24.60 ± 2.91	0.327
Urea(mmol/L)	3.31 ± 1.17	4.80 ± 1.45	4.00 ± 1.15	0.136
Creatinine (mmol/L)	64.06 ± 15.50	73.78 ± 19.2	99.22 ± 17.88	0.061
Total protein	5.78 ± 1.39	4.76 ± 2.19	7.56 ± 0.68	0.001
Creatinine Clearance (ml/min)	114.76 ± 28.54	111.05 ± 11.33	115.05 ± 44.41	0.879

Note: Values are expressed as mean ± SD; $p < 0.05$ is significant when control group is compared with HIV positive groups

Table 4.5 shows a comparison of proportion in Creatinine clearance of controls with HIV patients.

Table 4.5: Comparison of proportion in Creatinine clearance of controls with HIV seropositive subjects (percentage in parenthesis)

Variable	Cut off	Controls	HIV infected and not on ART	HIV infected and on ART
CrCl (ml/min)	≤60	0 (0.00)	2 (6.7)	0
	60.00 – 90	7 (23.33)	5 (16.67)	6 (20.00)
	≥90.01	23 (76.67)	23 (76.67)	24 (80.00)

Discussion

The study's findings demonstrated that no HIV+ person receiving ART had a creatinine clearance of less than 60 millilitres per minute, and the same was true for the control group. Nevertheless, renal impairment was evident in 2 HIV+ participants (6.7%) who were not on ART, as evidenced by a creatinine clearance of less than 60 millilitres per minute. The proportion of HIV+ on ART [6 (20%)] with a creatinine clearance between 60 and 90 is higher than that of HIV+ off ART [5 (16.67%)]. The percentage of controls who have a creatinine clearance of more than 90 millilitres per minute is virtually the same as the percentage of HIV+ on ART and HIV+ on HAART [23, 76.67% and 24, 80%], respectively. This is consistent with other research [8,9]. The increased proportion of patients in this study who had lower creatinine clearance when compared to controls may have resulted from dietary changes or disease-related weight loss.

Compared to HIV-positive individuals receiving ART, controls had a mean CD4+ count that was noticeably higher. In comparison to people with HIV who were not using ART, it was also noticeably higher in controls. Additionally, it was demonstrated that HIV seropositive individuals using ART had a mean CD4 count that was considerably greater than that of HIV seropositive individuals not receiving ART. This is in line with other research that found low CD4+ counts and severe immune suppression in HIV-positive individuals with compromised renal function [10,11]. It is well recognised that immunological AIDS (CD4+ count <200 cell/μL) is linked to the emergence of opportunistic infections, cancers, and other organ disorders that impair kidney function [12].

In the study, the control group's CD8+ cell counts was significantly lower than those of HIV-positive persons not receiving Antiretroviral Therapy (ART), suggesting a response to continuous viral replication. This seems sense in light of [13,14]. Nevertheless, the outcomes demonstrate that the viral control of antiretroviral medication (ART) resulted in decreased CD8+ numbers. The CD4/CD8 ratio is a more important measure of immunological function since elevated CD8+ levels in untreated HIV may indicate the development of the disease. The results show how Antiretroviral Therapy (ART) affects immunological responses to HIV, indicating the need for more studies on immune markers to have a more complete understanding. Interestingly, relative to the control group, total protein dropped by 23.54% in people receiving Antiretroviral Therapy (ART) and by 37.03% in HIV-positive persons without treatment. The study's finding that HIV-positive participants' serum total protein levels were considerably lower is consistent with earlier findings [15]. In the study, the control group's CD8+ cell counts was significantly lower than those of HIV-positive persons not receiving Antiretroviral Therapy (ART), suggesting a response to continuous viral replication. This seems sense in light of [13,14]. Nevertheless, the outcomes demonstrate that the viral control of Antiretroviral Medication (ART) resulted in decreased CD8+ numbers. The CD4/CD8 ratio is a more important measure of immunological function since elevated CD8+ levels in untreated HIV may indicate the development of the disease. The results show how Antiretroviral Therapy (ART) affects immunological responses to HIV, indicating the need for more studies on immune markers to have a more complete understanding. Interestingly, relative to the control group, total protein dropped by 23.54% in people receiving Antiretroviral Therapy (ART) and by 37.03% in

HIV-positive persons without treatment. The study's finding that HIV-positive participants' serum total protein levels were considerably lower is consistent with earlier findings.

.. When compared to the control group, it was shown that K+ levels were likewise significantly different among HIV seropositive persons who were not on ART.

The study's findings demonstrated that the levels of urea and creatinine varied significantly throughout all groups. This may be because, as suggested by [17], ART nephrotoxicity causes urea and creatinine imbalances and variations. There was no discernible difference between the bicarbonate and creatinine clearance.

Conclusion

Our study's findings highlight the critical role Antiretroviral Therapy (ART) plays in preserving immunological health, as demonstrated by the much higher CD4+ and lower CD8+ levels in treated HIV-positive patients. Overall protein levels are declining in HIV-positive groups, which may indicate problems; nonetheless, stable electrolyte data point to general homeostasis. Significant variations in the student's t-test Na+ and K+ levels highlight the effect of ART on electrolyte balance. Considerable fluctuations in urea and creatinine levels highlight the necessity of continuous renal function monitoring by suggesting a possible connection to ART nephrotoxicity. This work provides important new understandings of immunological and renal dynamics in HIV patients, and it calls for more research to achieve a more thorough understanding and better therapy outcomes.

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