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Original Research Article

Evaluation of microalbumin, cystatin c, creatinine and uric acid levels in HIV patients in Nnamdi Azikiwe University Teaching Hospital, Nnewi

Ifeoma Priscilla Ezeugwunne[1,*], Amaifeobu Clement[2], Samuel Chukwuemeka Meludu[1], Rosemary Adamma Analike[3], Johnjude Chinonso Nnamdi[3], Victor Nwabunwanne Oguaka[1], Emeka Callistus Onyeka Izuchukwu[3], D Eberechi Nwanguma[4], Nonso Samuel Nduka[5], Aikpitanyi-Iduitua GA[6]

[1]*Dept. of Human Biochemistry, Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Awka, Nigeria*
[2]*Dept. of Medical Laboratory Science, Faculty of Health Sciences Technology, Nnamdi Azikiwe University, Awka, Nigeria*
[3]*Dept. of Chemical Pathology, Faculty of Medicine, Nnamdi Azikiwe University, Awka, Nigeria*
[4]*Dept. of Medical Laboratory Science, Imo State University, Owerri, Nigeria*
[5]*Dept. of Chemical Pathology, University of Ibadan, Nigeria*
[6]*Medical Laboratory Science Council of Nigeria, Abuja, Nigeria*

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ABSTRACT

This study evaluated the microalbumin, cystatin C, creatinine and uric acid levels in HIV patients in Nnamdi Azikiwe University Teaching Hospital, Nnewi (NAUTH). A total of one hundred (100) male and female HIV positive and control participants who were aged between 18 and 60 years attending the voluntary counseling and testing unit (VCT) and antiretroviral therapy unit (ART) of NAUTH were randomly recruited for the study and grouped thus: Group A (HIV positive symptomatic participants on long term ART (HPSPLTART) (n= 25); Group B (HIV positive symptomatic participants on short term ART (HPSPSTART) (n= 25); Group C: Asymptomatic HIV positive participants NOT on ART (AHPPNART) (n=25) and Group D: control (n=25). 6mls of blood sample and 10mls of freshly voided urine samples were collected from each of the participants for the evaluation of biochemical parameters using standard laboratory methods. Results showed significantly higher BMI and SBP in HPSPSTART than in control (p=0.04; 0.02). SBP was significantly higher in HPSPLTART than in AHPPNART and Control (p=0.00). DBP was significantly higher in HPSPLTART than in HPSPSTART and control respectively (p=0.00). There were significantly higher plasma creatinine and Cys-C levels in both male HIV positives and male HIV positive participants on ART than in both females respectively (p0.00; 0.02). Also, BMI, creatinine, uric acid and Cystatin C levels were significantly higher in male HIV negative participants than in female HIV negative participants (p=0.00; 0.04; 0.02; 0.01). This study has revealed greater risk for renal disease among the HIV participants studied.

1. Introduction

Human immune deficiency virus (HIV) which causes Acquired Immunodeficiency Syndrome (AIDS), that affects the cells of the immune system, and destroys or impairs their function has continued to be an issue of public health

* *Corresponding author.*
E-mail address: goodnessifeoma007@yahoo.com (I. P. Ezeugwunne).

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discuss worldwide especially in the developing countries of Africa where it's ravaging effects seems to be on the increase despite the efforts been made on tackling the disease.[1] HIV targets the immune system and as the virus destroys and impairs the function of immune cells, infected individuals gradually become immunodeficient.[2–6] There is an emerging issue of kidney disease in HIV positive persons suspected to be linked with the use of ART drugs.[7–10] It follows therefore that long-term use of ART may cause kidney derangements that may become life-threatening.[11] Previously,[12] some authors have investigated several other biochemical parameters among HIV positive individuals[13,14], but in this study, the key interested shall be focused on evaluating microalbumin, cystatin C, creatinine and uric acid levels as renal diagnostic biomarkers of emerging relevance. The term microalbuminuria (MA) is used to describe albumin concentrations in the urine that are greater than normal, but not detectable with conventional urine dipstick analysis and it is useful as an early biomarker in the detection of kidney disease.[11] Elevated levels of microalbumin have been reported in HIV positive patients.[11,13–16] Cystatin C is a plasma protein (13 kDa) that is produced by all nucleated cells in the human body and functions as the cysteine protease inhibitor.[17] Some studies indicate that the changes in cystatin C levels may contribute in the detection of renal failure[18,19] andseveral studies have shown elevated levels of cystatin C in HIV positive patients in recent times.[20,21] Creatinine is freely excreted through kidneys which makes it useful to interpret kidney function and elevated levels of creatinine have been seen in HIV positive persons[11,13–23] although some others recorded no significant alterations.[24,25] Elevated serum uric acid levels are associated with endothelial dysfunction in HIV patients.[26,27] Thus, with the increasing prevalence and risk of renal disease among HIV patients, it is imperative to undertake this study.

2. Materials and Methods

2.1. Study design and participants recruitment

This is a case-controlled study designed to evaluate microalbumin, cystatin C, creatinine and uric acid levels in HIV positive patients in Nnamdi Azikiwe University Teaching Hospital, Nnewi. A total of hundred (100) Participants (HIV positive and control) who were aged between 18 and 60 years attending the voluntary counseling and testing unit (VCT) and antiretroviral therapy unit (ART) of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi were randomly recruited for the study. In line with World Health Organisation (WHO) criteria for staging HIV, the participants were grouped into:

1. Group A: HIV positive symptomatic participants on long term ART for a period of more than five (> 5) years (n= 25).
2. Group B: HIV positive symptomatic participants on short term ART for a period of 1-4 years (n= 25).
3. Group C: Asymptomatic HIV positive participants NOT on ART (n=25)
4. Group D: control participants (HIV seronegative) (n=25).

Lamivudine (150 mg twice daily), Stavudine (40mg twice daily) and Nevirapine (200 mg twice daily) were administered to the symptomatic HIV stage 11 participants on ART. Six millilitres (6mls) of blood sample and 10mls of freshly voided urine were collected from each of the participants and dispensed into plain and universal containers respectively for the determination of biochemical parameters.

2.2. Inclusion and exclusion criteria

HIV positive Participants on triple combination of Stavudine, Lamivudine and Nevirapine based on WHO first line of ART and those not on ART was included in this study. Only participants aged between 18 and 60 years and fulfilled WHO criteria for HIV staging were included in the study.

Pregnant women, and subjects who has history of smoking, hypertension, tuberculosis, diabetes, heart and renal diseases and any other clinical condition apart from HIV infection were excluded from the study.

2.3. Methods

2.3.1. HIV determination

The participants were screened for HIV-1 and HIV-2 infection using Immunoassay and Immunochromatographic method using the kits from Abbott Japan Co.Ltd.Tokyo, Japan and CHEMBIO Diagnostic system, Inc, New York, USA.

2.3.2. Determination of biochemical parameters

Microalbumin level was determined using turbidimetric method[28] using Biobase Microalbuminuria (MALB) Test Kit (Biobase Biodustry, Shandong Co., Ltd, Jinan, China), *Human Cystatin C (cys- C)* was assayed using Immnoturbidimetric method[29], creatinine levels was determined by using Jaffe slot alkaline picric acid method as described by Laron[30] and Serum uric acid estimation was assayed using Uricase method described by Ochei and Kolhatkar.[31]

2.3.3. Anthropometrics measurements

Body mass index (BMI) of participants was determined according to WHO protocol.[31]

2.3.4. Blood pressure reading

Systemic blood pressure was obtained using an OMRON automatic digital blood pressure monitor on the left arm

Table 1: Comparison of mean±SD of age, anthropometric indices and blood pressure in participants studied**.**

Variables	Age (years)	Height (meter)	Weight (Kg)	BMI (Kg/m^2)	SBP (mmHg)	DBP (mmHg)
Symptomatic HIV Participants on Long term ART(A)(n=25)	43.20±6.65	1.66±0.89	64.45±5.93	23.65±2.72	127.35±7.08	81.15±3.42
Symptomatic HIV Participants on Short term ART(B)(n=25)	42.40±9.97	1.68±0.11	63.40±8.62	22.40±2.68	124.55±27	75.65±6.31
Asymptomatic HIV Participants Not on ART(C)(n=25)	30.70±10.03	1.70±0.94	69.95±7.90	23.30±1.81	121.40±6.68	78.80±6.50
HIV Seronegative Participants (D)(n=25)	37.68±8.06	1.69±0.69	69.52±8.04	24.32±3.52	119.60±6.22	75.92±7.16
f-value	8.62	8.70	2.82	1.79	5.54	3.82
p-value	0.00	0.46	0.04	0.16	0.00	0.01
A Vs B	0.77	0.44	0.66	0.15	0.23	0.00
A Vs C	0.00	0.18	0.27	0.49	0.00	0.16
A Vs D	0.02	0.11	0.02	0.22	0.00	0.00
B Vs C	0.00	0.63	0.18	0.64	0.16	0.13
B Vs D	0.09	0.60	0.02	0.04	0.02	0.90
C Vs D	0.01	0.95	0.29	0.25	0.36	0.17

*Statistically significant at p<0.05.

Table 2: Comparison of mean±SD of creatinine, microalbumin, cystatin C and uric acid levels in participants studied.

Variables	Creatinine (μmol/L)	Microalbumin (mg/L)	Cystatin C (mg/L)	Uric acid (μmol/L)
Symptomatic HIV Participants on Long term ART(A)(n=25)	75.25±22.07	44.55±34.16	1.30±6.65	430.20±6.65
Symptomatic HIV Participants on Short term ART(B)(n=25)	79.50±16.19	61.45±50.83	1.19±0.44	399.25±123.93
Asymptomatic HIV Participants Not on ART(C)(n=25)	75.60±23.67	31.78±7.11	1.07±0.32	300.70±10.03
HIV Seronegative Participants ART(D)(n=25)	73.52±19.63	31.60±6.32	0.95±0.32	370.68±8.06
F-value	0.32	1.15	3.64	8.62
P-value	0.81	0.34	0.02	0.00
A Vs B	0.60	0.23	0.44	0.50
A Vs C	0.93	0.67	0.06	0.04
A Vs D	0.66	0.77	0.00	0.02
B Vs C	0.54	0.36	0.32	0.03
B Vs D	0.28	0.12	0.04	0.66
C Vs D	0.75	0.44	0.21	0.01

*Statistically significant at p<0.05.

Table 3: Comparison of mean±SD of parameters studiedin male and female HIV positive participants.

Parameters	Males (n=23)	Females (n=57)	T-value	P-value
Age (years)	42.61±11.09	38.75±9.80	0.62	0.13
Height (meters)	1.75±5.05	1.65±9.19	13.02	0.00*
Weight (Kg)	70.04±7.1	62.05±6.29	0.92	0.00*
BMI (Kg/m^2)	22.96±2.33	22.93±2.66	0.78	0.97
SBP (mmHg)	126.48±7.88	125.40±7.91	0.25	0.58
DBP (mmHg)	79.70±5.64	78.81±6.03	0.01	0.55
Creatinine (μmol/L)	84.83±19.39	71.23±18.08	0.02	0.00*
Microalb (mg/L)	50.83±33.74	44.93±38.23	0.44	0.52
Cys- C (mg/L)	1.34±0.37	1.04±0.43	0.31	0.00*
Uric Acid (μmol/L)	398.83±87.85	360.02±121.17	2.58	0.17

*Statistically significant at p<0.05.

Table 4: Comparison of mean±SD of parameters studied in male and female HIV positive participants on ART

Variables	Age (yrs)	HT (m)	WT (Kg)	BMI (Kg/m^2)	SBP (mmHg)	DBP (mmHg)	Creat (μmol/L)	μAlb (mg/L)	Cys- C (mg/L)	Uric acid (μmol/L)
Male (n=23)	46.58± 7.88	1.75± 4.70	68.25± 7.11	22.31± 2.47	126.69± 8.78	78.63± 5.94	82.06± 14.75	49.50± 32.27	1.38± 0.41	390.94± 85.44
Female (n=27)	41.59± 8.29	1.64± 9.04	61.75± 6.41	23.00± 2.87	127.32± 7.44	79.34± 5.75	72.41± 18.42	44.48± 40.98	1.06± 0.46	392.52± 107.70
T-value	0.10	1.46	0.25	0.37	2.24	0.25	0.59	0.79	0.21	1.68
P-value	0.04*	0.00*	0.00*	0.40	0.78	0.67	0.07	0.66	0.02*	0.96

*Statistically significant at p<0.05.

Table 5: Comparison of mean±SD of parameters studied in male and female HIV seronegative participants

Variables	Age (years)	HT (meter)	WT (Kg)	BMI (Kg/m^2)	SBP (mmHg)	DBP (mmHg)	Creat (μmol/L)	μAlb (mg/L)	Cys- C (mg/L)	Uric acid (μmol/L)
Male (n=11)	41.92± 7.91	1.69± 0.82	75.92± 5.96	26.58± 3.34	120.75± 6.54	76.58± 6.56	81.83± 10.89	43.50± 24.06	1.10± 0.35	463.92± 73.06
Female (n=14)	33.77± 6.17	1.70± 0.58	63.62± 4.25	22.23± 2.17	118.54± 5.98	75.31± 7.89	65.85± 23.01	39.85± 38.20	0.81± 0.23	367.73± 83.07
t-value	1.63	0.22	1.55	2.27	0.05	1.05	1.94	1.29	2.91	0.14
p-value	0.01	0.09	0.00	0.00	0.39	0.67	0.04	0.78	0.02	0.01

*Statistically significant at p<0.05.

Table 6: Levels of association observed between parameters studied in the participants

Parameters	Subjects	Correlation pearson r	P-value	P-value
HT Vs WT	100	0.42	0.00	<0.05
HT Vs BMI	100	-0.49	0.00	<0.05
WT Vs Uric acid	100	0.40	0.00	<0.05
WT Vs BMI	100	0.58	0.00	<0.05
SBP Vs DBP	100	0.49	0.00	<0.05
SBP Vs Creatinine	100	0.26	0.02	<0.05
SBP Vs Age	100	0.41	0.00	<0.05
DBP Vs Age	100	0.22	0.04	<0.05
Creatinine Vs Cys- C	100	0.39	0.00	<0.05
Creatinine Vs Uric acid	100	0.25	0.00	<0.05
Creatinine Vs Age	100	0.24	0.03	<0.05
Uric acid Vs Age	100	0.27	0.01	<0.05

*Statistically significant at p<0.05.

Table 7: Levels of association observed between parameters studied in HIV participants on long term ART.

Parameters	Subjects	Correlation pearson r	F-value	P-value
HT Vs Uric acid	25	0.55	0.01	<0.05
HT vs BMI	25	-0.62	0.00	<0.05
WT Vs BMI	25	0.45	0.046	<0.05
SBP Vs μAlbumin	25	0.47	0.04	<0.05
Creatinine Vs Cys-C	25	0.50	0.03	<0.05
Creatinine Vs Age	25	0.47	0.04	<0.05

*Statistically significant at p<0.05.

Table 8: Levels of association observed between parameters studied in HIV participants on short term ART.

Parameters	Participants	Correlation pearson r	F-value	P-value
HT Vs Uric acid	25	0.55	0.01	<0.05
HT vs BMI	25	-0.62	0.00	<0.05
WT Vs BMI	25	0.45	0.046	<0.05
SBP Vs μAlbumin	25	0.47	0.04	<0.05
Creatinine Vs Cys-C	25	0.50	0.03	<0.05
Creatinine Vs Age	25	0.47	0.04	<0.05

*Statistically significant at p<0.05.

Table 9: Levels of association observed between parameters studied in control group.

Parameters	Participants	Correlation pearson r	F-value	P-value
HT vs SBP	25	-0.41	0.04	<0.05
HT Vs μAlbumin	25	0.44	0.03	<0.05
HT Vs BMI	25	-0.63	0.00	<0.05
WT Vs BMI	25	0.77	0.00	<0.05
WT Vs Uric acid	25	0.67	0.00	<0.05
SBP Vs DBP	25	0.74	0.00	<0.05
SBP Vs BMI	25	0.42	0.04	<0.05
BMI Vs Uric acid	25	0.44	0.03	<0.05

*Statistically significant at p<0.05.

Table 10: Levels of association observed between parameters studied in asymptomatic HIV participants.

Parameters	Participants	Correlation pearson r	F-value	P-value
HT Vs WT	25	0.77	0.00	<0.05
WT Vs Age	25	0.52	0.02	<0.05
WT Vs BMI	25	0.47	0.04	<0.05
SBP Vs Uric acid	25	0.52	0.02	<0.05
SBP Vs Age	25	0.52	0.02	<0.05
SBP Vs BMI	25	0.51	0.02	<0.05
Creatinine Vs Uric acid	25	0.59	0.01	<0.05
μAlbumin Vs Cys-C	25	0.54	0.01	<0.05
Cys-C Vs Uric acid	25	0.46	0.04	<0.05
Age Vs BMI	25	0.47	0.04	<0.05

*Statistically significant at p<0.05.

after 10-minute rest using a cuff of appropriate size with the participants in the sitting position. Blood pressure was expressed as Systolic and Diastolic rate. Hypertension was defined as systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥90mmHg

2.4. Ethical approval

The ethical approval for this research was obtained from Nnamdi Azikiwe University Teaching Hospital Ethical Committee (Reference no: NAUTH/CS/66/VOL.14/VER 3/29/2021/015).

2.5. Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 23.0 was used for the analysis of the results. Data obtained was presented as mean ± standard deviation (SD) and analyzed statistically using one way analysis of variance (ANOVA), posthoc t-test and Pearson correlation. The level of significance was set at P< 0.05.

3. Results

The result of analysis of variance showed that the mean age, weight, systolic blood pressure (SBP) and diastolic blood pressure were significantly different amongst the groups (f-value: 8.62, 2.82, 5.54 and 3.82) (p<0.05) respectively. However, the mean height and body mass index (BMI) did not differ significantly when compared amongst the groups (p=0.46 and 0.16) respectively. The mean age of the participants were significantly higher in symptomatic HIV participants on long term antiretroviral therapy (ART) (43.20±6.65) when compared with the value observed in the asymptomatic HIV participants NOT on ART (30.70±10.03) and HIV seronegative participants (37.68±8.06) respectively (p<0.05).Also, the mean age of the symptomatic HIV participants on short term ART was

significantly higher than in asymptomatic HIV participants NOT on ART (42.40±9.97 Vs 30.70±10.03; p=0.00). The mean age of asymptomatic HIV participants NOT on ART was significantly higher than the values observed in the seronegative HIV participants (30.70±10.03 Vs 37.68±8.06; p=0.01). The mean weight of the symptomatic HIV subjects on long term ART was significantly lower than in the HIV seronegative participants (64.45±5.93 Vs 69.52±8.04; p=0.02). Also, the mean weight of the symptomatic HIV participants on short term ART was significantly lower than in the HIV seronegative participants (63.40±8.62 Vs 69.52±8.04; p=0.02). Again, the mean SBP were significantly higher in symptomatic HIV participants on long term ART (127.35±7.08) when compared to the values obtained in the asymptomatic HIV participants NOT on ART (121.40±6.68) and HIV seronegative participants (119.60±6.22) respectively (p=0.00) in each case. Meanwhile, the mean SBP was significantly higher in symptomatic HIV participants on short term ART than in the HIV seronegative participants (124.55±27 Vs 119.60±6.22; p=0.02). See table 1. The mean diastolic blood pressure (DBP) were significantly higher in symptomatic HIV participants on long term ART (81.15±3.42) than in symptomatic HIV participants on short term ART (75.65±6.31) and HIV seronegative participants (75.92±7.16) (p=0.00)respectively. See Table 1.

The result of analysis of variance showed that the mean urine microalbumin and plasma creatinine levels were not significantly different amongst the groups (p<0.05) respectively. However, the mean plasma cystatin C (Cys-C) and uric acid levels differed significantly when compared amongst the groups (p=0.02 and 0.00) respectively. Paired wise comparison showed no significant differences in the mean plasma creatinine and microalbumin levels when compared between the groups studied (p>0.05) respectively. However, the mean plasma Cys-C level was significantly higher in symptomatic HIV participants on long term ART than in HIV seronegative participants (1.30±6.65 Vs 0.95±0.32; p=0.00). Also, the mean plasma Cys-C level was significantly higher in symptomatic HIV participants on short term ART than in HIV seronegative participants (1.19±0.44 Vs 0.95±0.32; p=0.04). The mean plasma uric acid level observed in the symptomatic HIV participants on long term ART was significantly higher than in both asymptomatic HIV participants NOT on ART and HIV seronegative participants (p<0.05) respectively. Also, the mean plasma uric acid level was significantly higher in the symptomatic HIV participants on short term ART than in asymptomatic HIV participants NOT on ART (p<0.05). Meanwhile, the mean plasma uric acid level was significantly lower in the asymptomatic HIV participants NOT on ART when compared with the control group (p>0.05). See Table 2.

Furthermore, the mean plasma creatinine level was significantly higher in the male HIV positive participants than in the female HIV positive participants (84.83±19.39 Vs 71.23±18.08; p=0.00). Also, the mean plasma Cystatin C level was significantly higher in the male HIV positive participants than in the female HIV positive participants (1.34±0.37 Vs 1.04±0.43; p=0.00). Meanwhile, there were no significant differences observed in the mean urine microalbumin and plasma uric acid levels when compared between the HIV positive male and female participants respectively (p>0.05). See Table 3.

The mean BMI, SBP, DBP, plasma creatinine and uric acid levels as well as the microalbumin level were not significantly different when compared between the male and female HIV positive participants on ART (p>0.05) respectively. However, the mean plasma Cystatin C level was significantly higher in the male HIV positive participants on ART than in the female HIV positive participants on ART (1.38±0.41Vs 1.06±0.46; p=0.02). See Table 4.

The mean age, weight and BMI of the subjects were significantly higher in the male HIV seronegative participants than in the female HIV seronegative participants (p=0.01; 0.00; 0.00) respectively. However, the mean plasma creatinine level was significantly higher in the male HIV seronegative participants than in the female HIV seronegative participants (81.83±10.89 Vs 65.85±23.01; p=0.04). Also, the mean serum Cystatin C and uric acid level was significantly higher in the male HIV seronegative participants than in the female HIV seronegative participants (p=0.02; 0.01). See Table 5.

There were significant positive correlations observed between the mean height (HT) and weight (WT); between WT and Uric acid, between WT and BMI, between SBP and DBP, between SBP and Creatinine, between SBP and Age, between DBP and Age, between Creatinine and Cys- C, between Creatinine and Uric acid, between Creatinine and Age and between Uric acid and Age respectively (p<0.05) in the participants studied. On the other, HT Vs BMI showed a significant negative correlation (r=-0.49; p=0.00) in the participants studied. See Table 6.

There were significant positive correlations observed between HT Vs Uric acid, WT Vs BMI, SBP Vs μAlbumin, Creatinine Vs Cys-C and Creatinine Vs Age in HIV participants on long term ART (p<0.05) respectively. While HT vs BMI showed a significant negative correlation in HIV participants on long term ART (r= -0.62; p=0.00). See Table 7.

There were significant positive correlations observed between HT Vs Uric acid, WT Vs BMI, SBP Vs μAlbumin, Creatinine Vs Cys-C and Creatinine Vs Age in HIV participants on short term ART (p<0.05) respectively. While HT vs BMI showed a significant negative correlation in HIV participants on short term ART (r= -0.62; p=0.00). See

Table 8.

There were significant positive correlations observed between HT Vs μAlbumin, WT Vs BMI, WT Vs Uric acid, SBP Vs DBP, SBP Vs BMI and BMI Vs Uric acid in HIV seronegative participants ($p<0.05$) respectively. While HT Vs SBP and HT Vs BMI showed a significant negative correlation in HIV seronegative participants ($p=0.00$) respectively. See Table 9.

HT Vs WT, WT Vs Age, WT Vs BMI, SBP Vs Uric acid, SBP Vs Age , SBP Vs BMI, Creatinine Vs Uric acid, μAlbumin Vs Cys-C, Cys-C Vs Uric acid and Age Vs BMI were significantly correlated in asymptomatic HIV participants studied ($p<0.05$) respectively. See Table 10.

4. Discussion

HIV infection is a major public health concern that has claimed many live worldwide [32,33] and especially in Nigeria in which over nine percent of the people living with HIV globally reside. [33] The advert of antiretroviral therapy (ART) came with so much hope and so far has improved the life expectance rate among HIV positive individuals, although not without its own nightmares. Apart from the deleterious effects arising from the activity of the human immunodeficiency virus on its host, antiretroviral therapy have been linked to renal toxicity and this is an emerging issue of grave health concern.

In this study, the mean age of the participants studied ranged between 30.70±10.03 and 42.40±9.97 years. This point to the fact that these subjects are young and vibrant individuals within the active work force age bracket of between eighteen (18) years to sixty five (65) years and therefore has a grave implication for the work force and economic productivity of the country by extension. This is line with several studies which reported that HIV and AIDS affect more of the young people. UNIAIDS reported that young people (between the ages of 15-49 years) are more infected with HIV, which may lead to serious economic implications. [33]

The present study showed that there was no significant difference observed in the mean body mass index (BMI) in the participants studied when compared between the groups except that the mean BMI was significantly lower in symptomatic HIV participants on short term ART than in the seronegatives. This may be due to the impact of HIV which is associated with muscle wasting and for the fact that the participants have been on antiretroviral therapy for only a short period. The body mass index (BMI=weight (kg)/height (m^2)) continues to be the most commonly used index of weight status [33] and is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults where normal weight is a BMI 18.5−25.9 kg m^{-2}; overweight is a BMI 25.0−29.9 kg m^{-2}; obese a BMI >30.0 kg m^{-2}. [31] Most of the current subjects fall within the normal BMI (18.5−25.9 kg m^{-2}). This result does not agree with the previous report of similar studies which recorded no significant differences in mean body mass index of HIV participants on ART compared with control but noted significant differences in BMI in HIV subjects on ART than in those not on ART [22] which was attributed to the lipodystrophic (fat accumulation and fat atrophy) effects of some antiretroviral drugs.

In this study, the mean SBP was significantly higher in symptomatic HIV participants on both short and long term ART (127.35±7.08) when compared to the values obtained in the asymptomatic HIV participants NOT on ART and HIV seronegatives. Also, the mean diastolic blood pressure (DBP) were significantly higher in symptomatic HIV participants on long term ART than in symptomatic HIV participants on short term ART and HIV seronegatives respectively. However, of key interest is the fact that despite these alterations in blood pressure between the studied subjects, the subjects were still within the normotensive region (systolic blood pressure ≤140mmHg and/or diastolic blood pressure ≤90mmHg). According to World Health Organization (WHO), hypertension is diagnosed if, when it is measured on two different days, the systolic blood pressure readings on both days is ≥140 mmHg and/or the diastolic blood pressure readings on both days is ≥90 mmHg. [31] This is in contrast with the findings of Ezeugwunne et al. which reported no significant alterations in SBP and DBP in HIV participants on antiretroviral therapy compared with control. [22]

Interestingly, no statistically significant differences were observed in the mean plasma creatinine levels in the participants studied. This is in keeping with the work of Yilma et al. that found no significant difference in serum creatinine level between HIV positive and negative adults. [24] However, the present result is in contrast with the results of some other similar studies documenting significantly elevated creatinine levels in HIV participants and HIV participants on ART compared to control group. [11,13–25] Creatinine is a non-protein nitrogenous compound that is produced by the breakdown of creatine in muscle. Creatinine is found in serum, plasma, and urine and is excreted glomerular filtration at a constant rate and in the same concentration as in plasma. [34] Plasma creatinine levels are used as an index for renal function although it is affected by some factors including age, gender, diet, and muscle mass and liver disease. [34]

Furthermore, this study showed no significant differences in the mean urine microalbumin levels in the HIV participants on long term and short ART, asymptomatic HIV participants NOT on ART and HIV seronegative individuals when compared respectively. This may imply that these persons do have renal damage either as a result of the impact of HIV on the kidney or due to the effect of ART on the kidneys. Elevated levels of microalbumin have been reported in HIV positive patients in previous times

which are in contrast with the present finding.[11,13–15,22] Expectedly, Cystatin C level was found to be significantly higher in HIV participants than in control. This implies that the HIV population may be at a higher risk of renal disease in the near future compared with HIV negative individuals. Several studies have shown elevated levels of cystatin C in HIV positive patients in recent times which confirm the current result.[19,20]

In this study, there was no significant difference in the mean plasma uric acid level observed in the symptomatic HIV participants on long term ART when compared to symptomatic HIV participants on short term ART ($p>0.05$). This may mean that duration of ART does not affect uric acid level in HIV participants. However, the mean plasma uric acid level observed in the symptomatic HIV participants on long term ART was significantly higher than in both asymptomatic HIV participants NOT on ART and HIV seronegatives ($p<0.05$) respectively. Also, the mean plasma uric acid level was significantly higher in the symptomatic HIV participants on short term ART than in asymptomatic HIV participants NOT on ART but remained similar in the HIV seronegatives. Meanwhile, the mean plasma uric acid level was significantly lower in the asymptomatic HIV participants NOT on ART when compared with the control group. Hyperuricemia a predisposing condition for gout[34–37] is defined as elevated blood uric acid. Hyperuricemia is established as serum uric acid level >450 μmol/L for males and >390 μmol/L for females.[38] Excessive production and accumulation of monosodium urate with a reduction in the urinary excretion lead to high level of uric acid in body fluids. This results in the formation and continual deposition of the crystals in and around the joints and tissues thereby causing severe pains and inflammation in the joints and subsequently leads to impaired health.[39] Elevation of uric acid is associated with a variety of metabolic diseases including inflammatory gout, hypertension and cardiovascular death, renal disease, atherosclerosis, and ischemic heart disease.[40–42] Notably, the mean BMI was not significantly different when compared between the male and female HIV positive participants. This may suggest that HIV status does not have a gender based influence on the BMI in HIV positive participants. Previously, Ogunmola et al. showed a significant difference in BMI between HIV-negative and HIV-positive drug-naïve participants (P=0.001), and between HIV-negative and HIV-positive ART subjects (P=0.002), but not between HIV-positive drug-naïve and HIV-positive ART participants (P=1.000) and this is similar to our present result.[43]

Also, the mean SBP and DBP were not significantly different when compared between the male and female HIV positive participants respectively. Ogunmola et al. had earlier reported no significant differences in SBP and DBP in HIV subjects which is in consonance with the present report.[43] Also, Ezeugwunne et al. recorded similar result in their study that evaluated the body mass index, blood pressure and serum cortisol level as stress index in symptomatic HIV/AIDS male participants on antiretroviral therapy negative to malaria parasite in Nnewi, Anambra State, Nigeria.[22] Furthermore, the mean plasma creatinine level was significantly higher in the male HIV positive participants than in the female HIV positive participants. This is expected following the fact that the plasma creatinine level is affected by gender and tends to be higher in male individuals than in females as a result of the higher muscle mass found in male individuals in preference to females.[44] In this study, we also recorded a significantly higher mean plasma cystatin C level in the male HIV positive participants than in the female HIV positives. This may be due to the impact of the virus on the kidneys. In contrast to creatinine, Cystatin C is not affected by gender, body mass or diet, and hence is a more reliable marker of kidney function than creatinine.[45] Surprisingly, no significant alterations were observed in the mean urine microalbumin and plasma uric acid levels when compared between the HIV positive male and female participants in this study. Contrary to the popularly held opinion that uric acid levels are affected by gender, this study shares no such view with respect to the value of uric acid recorded in the HIV positive male and female population.

In the present study, the mean BMI, SBP, DBP, plasma creatinine and uric acid levels as well as urine microalbumin level were not significantly different when compared between the male and female HIV positive participants on ART respectively. However, the mean plasma Cystatin C level was significantly higher in the male HIV positive participants on ART than in the female HIV positive participants on ART. This is similar to the results documented in the HIV positive male and female participants in this study. Antiretroviral therapy had no effect on the BMI, SBP, DBP, plasma creatinine, uric acid and urine microalbumin level in both gender although there was a gender based influence of ART on cystatin C level in the males on ART than in the females on ART. Besides, in this study, the BMI of the subjects were significantly higher in the male HIV seronegatives than in the female HIV seronegatives. The HIV negative males in this study were overweight (mean BMI=26.58±3.34) based on the WHO classification of BMI (25.0−29.9 kg m^{-2}).[31] According to WHO[31], the fundamental cause of overweight is an energy imbalance between calories consumed and calories expended. Globally, there has been an increased intake of energy-dense foods that are high in fat and sugars and an increase in physical inactivity due to the increasingly sedentary nature of many forms of work, changing modes of transportation, and increasing urbanization. Overweight is a known risk factor for non communicable diseases (NCDs) and is an important issue to

address in NCD prevention [46–51] especially in Nigeria where the prevalence rate of overweight individuals ranged from 20.3%-35.1%. [47–49]

Furthermore, the mean SBP, DBP and microalbumin (μalb) levels were not significantly different when compared between the male and female HIV seronegative participants respectively, although plasma creatinine level was significantly higher in the male HIV seronegative participants than in the female HIV seronegatives. it is a known factor that there is a gender based disparity in plasma creatinine level as a result of differences in muscle mass which is usually higher in men than in women. Also, the mean plasma Cystatin C levels were significantly higher in the male HIV seronegatives than in the female HIV seronegatives. This may suggest that there is a possibility of a greater risk in men towards development of renal disorder than in women over time. However, there is need to thread with cushion in interpreting the result of these results in male and females as it may be gender related.

The mean plasma uric acid levels were significantly higher in the male HIV seronegative participants than in the female HIV seronegatives. This is in keeping with the previous report of Onwubuya et al. in which they observed significantly higher serum uric acid level in obese and overweight males than female and control counterpart respectively. [50] Also Ewenighi et al. further documented significantly higher mean uric acid concentration in the obese and overweight male groups compared to the normal weight group which corroborate well with the present study. [51] Elevation of uric acid is associated with a variety of metabolic diseases including inflammatory gout, hypertension and cardiovascular death, renal disease, atherosclerosis, and ischemic heart disease. [40–42] Serum uric acid may be grossly elevated in starvation due to accelerated tissue turnover and reduced renal excretion of uric acid.

In this study, there were significant positive correlations observed between the mean height (HT) and weight (WT); between WT and Uric acid, between WT and BMI, between SBP and DBP, between SBP and Creatinine, between SBP and Age, between DBP and Age, between Creatinine and Cys- C, between Creatinine and Uric acid, between Creatinine and Age and between Uric acid and Age respectively in the participants studied. This implies that an increase in one of the variables results in a corresponding increase in the other. Both uric acid and creatinine levels tend to increase with advancing age. On the other, HT Vs BMI showed a significant negative correlation (r=-0.49; p=0.00) in the participants studied. There were significant positive correlations observed between HT Vs Uric acid, WT Vs BMI, SBP Vs μAlbumin, Creatinine Vs Cys-C and Creatinine Vs Age in HIV and seronegative participants. In conclusion, this study has revealed greater risk for renal disease among the HIV participants studied and also implicated hyperuricemia and overweight as important risk factors for development of renal dysfunction in male HIV seronegative persons. Therefore, it is recommended that regular and proper monitoring of renal indices in HIV positive individuals using novel markers are incorporated into the routine ones to ensure early detection of renal issues in order to facilitate and enhance better management of HIV patients.

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6. Conflict of Interest

None.

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Author biography

Ifeoma Priscilla Ezeugwunne, Senior Lecturer

Amaifeobu Clement, Medical Laboratory Scientist

Samuel Chukwuemeka Meludu, Professor

Rosemary Adamma Analike, Chief Medical Laboratory Scientist

Johnjude Chinonso Nnamdi, Lecturer

Victor Nwabunwanne Oguaka, Lecturer

Emeka Callistus Onyeka Izuchukwu, Lecturer and Consultant Chemical Pathologist

D Eberechi Nwanguma, Assistant Lecturer

Nonso Samuel Nduka, Medical Laboratory Scientist

Aikpitanyi-Iduitua GA, Director of Education

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