Factors of Low CD4 Cells Count in Treatment-naïve HIV Subjects in Southeast Nigeria

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Abstract

Background and objectives: Human immunodeficiency virus (HIV) infection is a global healthcare problem. Low CD4 cells count, an index of immunosuppression, is associated with escalating activity and progression of HIV infection. The factors which influence low CD4 cells count have not been completely identified nor are they evaluated in routine clinical practice. The aim of this study was to determine the prevalence of low CD4 cells count and to evaluate the factors which might influence immunosuppression in treatment-naïve HIV subjects in Southeast Nigeria.

Methodology: This was a cross-sectional study involving treatment-naïve HIV subjects. Anthropometric and demographic data were obtained and CD4 cells count and other relevant investigations performed. The data were compared between those who have low CD4 cells count, defined, here, as CD4 <200 cells/ml, and those with CD4 ≥200 cells/ml. Potential risk factors of low CD4 cells count were determined.

Results: The mean age of the subjects was 39±11 years. Females were made up 283 (72.0%) and males 110 (28.0%). The median value of the CD4 cells count was 391. Low CD4 cells count was prevalent in 49 (12.5%) of the subjects. There was significant association between CD4 cells count and body mass index (df=2, p=0.017), as well as serum low density lipoprotein cholesterol (df=1, p=0.027) and anemia (df=3, p=0.025). Significant, but poor, correlation was observed between CD4 cells count and 24 hour urine protein (r=-0.117, p=0.023), creatinine clearance (r=-0.122, p=0.018), as well as hemoglobin (r=0.224, p<0.001). Creatinine clearance was a predictor of low CD4 cells count, p=0.001

Conclusion: The prevalence of low CD4 cells count was high in this study. Abnormal weight, dyslipidemia and proteinuric renal damage were common among treatment-naïve subjects who have low CD4 cells count.

Keywords: HIV; Low CD4 cells count; Abnormal weight; Dyslipidemia; Proteinuric renal damage

Introduction

Human immunodeficiency virus (HIV) infection is a global healthcare problem. The enormity of the burden of HIV infection is overwhelming, especially in Sub-Saharan African countries which account for about 70.0% of world HIV-infected individuals [1]. Mass media campaigns for HIV awareness from local authorities, World Health Organization and International Agencies have tremendously increased voluntary testing and counselling [2,3]. As a result, HIV subjects tend to report at the early stage of the infection [4].

However, despite these efforts and the relative availability of, and accessibility to, HIV centers, many HIV subjects still report late and, as a result, the diagnosis of HIV infection is often made in the course of these subjects presenting to hospital for other illnesses, mainly opportunistic infections that signal a state of immunosuppression [5,6].

Reduced immunosuppression is known to occur in many disease states, including HIV infection [7,8]. In HIV infection, disease activity and progression highly correlate with low CD4 cells count [9-12]. Low CD4 cells count has been used as a marker for the initiation of antiretroviral therapy (ART): CD4 <350 cells/ml for subjects in clinical stage iii and CD4 <200 cells/ml for any subject irrespective of clinical stage [13]. Low CD4 (CD4 <200 cells/ml), alongside HIV viral load, is therefore of immense clinical significance as it has been shown to be associated with batteries of opportunistic infections and opportunistic malignancies [7,10].

Some factors associated with low CD4 cells count have been identified. These include demographic and genetic factors, low body mass index (BMI), commercial sex workers, and behavioral factors, all in HIV-negative individuals [8,14-17]. In HIV-infected individuals, it has been demonstrated that low CD4 cells count is a predictor of AIDS syndrome and disease progression. In addition, low CD4 cells count is associated with the advent of opportunistic infections and opportunistic malignancies [9-12].

There is a paucity of studies on CD4 cells count and the factors which influence low CD4 cells count in both the general population and HIV subjects in Nigeria. This has prompted us to embark on this study to evaluate CD4 cells count and to identify the factors which might influence low CD4 cells count in treatment-naïve HIV subjects with a view to instituting measures to stem down immuno compromise and poor clinical outcomes in the early stage of HIV infection.

Materials and Methods

This was a cross-sectional study of 393 patients recruited consecutively from the HIV Unit in Federal Medical Centre (FMC), Owerri, Southeast Nigeria. This study was conducted between April and August 2011. The hospital sub-serves the state and also receives

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referrals from the neighboring states. Owerri, where the hospital situates, has a local municipal population of about 125,337, whereas the state population is conservatively put at 3,927,563 [18].

The criteria for inclusion in this study were age range of 16-65 years and treatment-naive HIV-positive status. Pregnancy, adrenal disease, renal or terminal illness and malignancy were the exclusion criteria. From each of the study subjects, informed written consent was obtained. The Ethics Committee of the hospital gave approval for the study.

From each of the subjects anthropometric and demographic data were obtained with the aid of a questionnaire administered by our laboratory technicians who explained to them the aim of the study. The place of domicile and origin, gender and age of the subjects were obtained. Weight and height were taken and BMI rendered as weight/height² (kg/m²). Blood pressure was measured [19].

Clear instructions were given to all the subjects on how to collect 24 h urine sample. For each subject, a day-time random spot urine sample and blood samples were collected at the end of the 24 h urine sample collection [19-21].

From the random spot urine samples collected, spot urine protein (SUP), spot urine creatinine (SUCr) and spot urine osmolality (SUOsm) were performed. Also from the 24 h urine samples collected, 24 h urine protein (24HUP), 24-hour urine creatinine (24HUCr) and 24 urine osmolality (24HUOsm) were performed. Hemoglobin (Hb), CD4 cells count and serum creatinine were performed on the blood samples collected. Other tests done from the blood samples were HIV screening and confirmatory tests, fasting blood sugar and fasting serum lipid profile (FSLP) [total cholesterol, triglyceride, HDL, LDL]. Osmolality was determined by freezing point depression method using Precision Osmette 5002 osmometer, creatinine by modified Jef’s method and protein by photometric method. Creatinine clearance (CICr) was determined [19-21].

Statistical Analyses

The data were analyzed using SPSS version 17.0 (SPSS Int. Chicago, IL, USA). The distribution and characterization of the clinical and laboratory features among the subjects with different levels of CD4 cells count were analyzed using cross-tabulation. For continuous variables, mean values and standard deviations were calculated and the means compared using ANOVA or two sample t-test. Categorical variables were compared using the nonparametric tests - Chi-squares. Multivariate linear regression analyses were used to determine the strength of variables to predict low CD4 cells count (CD4 <200 cells/ml). All tests were two-tailed. P ≤ 0.05 was taken as statistically significant [19-23].

The potential risk factors of low CD4 cells count evaluated were SUCr, SUOsm, BMI, serum triglyceride, serum HDL, SCr, SUP, 24HUCr, 24HUOsm, CICr, 24-hour urine volume (24HUV) and Hb.

Definition of Terms

WHO classification was used to define BMI levels as follows [19,24]; Underweight =BMI<18.5 kg/m²; Normal weight =BMI 18.5 - 24.9 kg/m²; Overweight =BMI 25.0 - 29.9 kg/m²; Obesity class I= BMI 30.0-34.9 kg/m²; Obesity class II = BMI 35.0 - 39.9kg/m²; Obesity class III = BMI ≥ 40.0kg/m². However, in this study, obesity was defined as class I, class II and class III obesity added together.

Normal urine osmolality: 24HUOsm 300-750 mOsm/kg H₂O [19,25,26]

Dilute urine: 24HUOsm <300 mOsm/kgH₂O. Concentrated urine: 24HUOsm >750 mOsm/kgH₂O.

Anemia was defined according to the WHO criteria: [19,27,28] No anemia: Hb >13.0 g/dl in males and Hb >12.0 g/dl in females. Mild anemia: Hb 11.0 - 13.0 g/dl in males and Hb 11.0 - 12.0 g/dl in females. Moderate anemia: Hb 8.0-10.9 g/dl in males and Hb 8.0 - 10.9 g/dl in females. Severe anemia: Hb <8.0 g/dl in males and Hb <8.0 g/dl in females. However, in this study, anemia was defined as Hb <13.0 g/dl in males and Hb <12.0 g/dl in females. Overall, in this study, anemia was defined as Hb ≤ 12.0 g/dl.

Desirable serum LDL: serum LDL <2.6 mmol/l. Borderline serum LDL: serum LDL 2.6 - 4.1mmol/l. High serum LDL: serum LDL >4.1mmol/l. Desirable serum cholesterol: serum cholesterol ≤5.2mmol/l. Borderline serum cholesterol: serum cholesterol 5.2 – 6.2mmol/l. High serum cholesterol: serum cholesterol >6.2mmol/l. Desirable serum triglyceride: serum triglyceride <1.7mmol/l. Borderline serum triglyceride: serum triglyceride 1.7 – 2.2mmol/l. High serum triglyceride: serum triglyceride >2.2mmol/l. Low serum HDL: serum HDL <1.0mmol/l. Desirable serum HDL: serum HDL ≥ 1.0mmol/l [19,29].

Results

This study evaluated CD4 cells counts in 393 treatment-naive HIV subjects. Females constituted 72.0% while males made up 28.0%. The mean age of the subjects was 39 ± 11 years. Majority (97.0%) of them were Igbos. The median value of the CD4 cells count was 391. The mean values of other variables are shown in Table 1. Low CD4 cells count (CD4 <200 cells/ml) was observed in 49 (12.5%) of the subjects, whereas 343 (87.5%) have CD4 cells count ≥ 200 cells/ml.

No significant association was observed between CD4 cells count and CICr (df=1, p=0.296) as well as 24HUP (df=3, p=0.863) (Table 2). There was significant association between CD4 cells count and BMI (df=2, p=0.017). Out of 48 subjects who have CD4<200 cells/ml count, 1(2.0%) has BMI<18.5 kg/m², 15 (30.6%) have BMI 18.5-24.9 kg/m², 28 (57.1%) have BMI 24.9-29.9kg/m², whereas 5 (10.2%) have BMI ≥ 30.0 kg/m². This showed that the prevalence of low CD4 cells count <200 cells/ml declined with underweight as well as with obesity (Table 2 and Figure 1).

| Variables (mean ± SD) | HIV Subjects |
|-----------------------|--------------|
| Body Mass Index (kg/m²) | 26.2 ± 5.4 |
| CD4 count cells/ml (Median) | 391 |
| Hemoglobin (g/dl) | 11.2 ± 1.8 |
| SUOsm (mOsm/kgH₂O) | 464 ± 271 |
| Spot Urine Protein(mg/dl) | 11.89 ± 19.13 |
| Spot Urine Creatinine (mg/dl) | 137.21 ± 98.47 |
| 24-Hour Urine Protein (g) | 0.187 ± 0.290 |
| Serum Cholesterol (mmol/l) | 3.8 ± 1.2 |
| Serum Triglyceride (mmol/l) | 1.2 ± 0.4 |
| Serum HDL (mmol/l) | 1.2 ± 0.3 |
| Serum LDL (mmol/l) | 2.3 ± 1.0 |
| 24-Hour Urine Creatinine (mg) | 1507 ± 781 |
| 24HUOsmkgH₂O | 564 ± 501 |
| Creatinine Clearance (mls/min) | 91.42 ± 22.98 |

Table 1: Characteristics of variables in treatment-naive HIV subjects.

SD: Standard Deviation; SUOsm: Spot Urine Osmolality; 24HUOsm: 24-Hour Urine Osmolality.
The prevalence of low CD4 cells count (<200 cells/ml) of 28.6% observed in those subjects who have borderline serum LDL (2.6-4.1 mmol/l) was significantly lower than 71.4% in those whose serum LDL was normal, df=1, p=0.027 (Table 2).

No significant association was observed between CD4 cells count and serum HDL (df=1, p=0.495) as well as serum triglyceride (df=3, p=0.720) (Table 2).

The prevalence of low CD4 cells count (<200 cells/ml) in subjects who have anemia was significantly higher than 18.4% in those who have no anemia, df=3, p=0.025 (Table 2 and Figure 2).

There was no significant association observed between CD4 cells count and 24HUP, df=2, p=0.134 (Table 2). Significant but poor correlation was observed between CD4 cells count and 24HUP (r=-0.117, p=0.023), BMI (r=0.137, p=0.006), ClCr (r = -0.122, p=0.018), as well as Hb (r = 0.224, p<0.001) (Table 3). Conversely, there was no significant correlation between CD4 cells count and Scr, Sur, Sucr, SUOsm, 24HUH, 24HUOsm, serum triglyceride, as well as serum HDL (Table 3).

Multivariate linear regression analysis showed that both ClCr and Hb predicted CD4 cells count whereas only ClCr predicted isolated low CD4 cells count (<200 cells/ml) in the study subjects (Table 4 and Table 5).

**Discussion**

The median CD4 cells count value of 391 found in this study is slightly higher than the 241 reported in a study in India [30] despite the background racial differences, but very much lower than the values found in normal healthy states [17]. This, together with the high prevalence of low CD4 cells count (CD4<200 cells/ml) of 12.5% tend to suggest that...
The prevalence of low CD4 cells count (<200 cells/ml) of 28.6% observed in those subjects who have borderline serum LDL (2.6-4.1 mmol/l) was significantly lower than 71.4% in those whose serum LDL was normal. This showed that dyslipidemia was associated with CD4 cells count abnormality. Dyslipidemia is commonly observed in subjects with higher socioeconomic status as well as in urban dwellers, and less in rural dwellers, majority of whom might have a sense of wellbeing, but paradoxically reduced immunity, as it has been shown that obesity impairs immunity [33].

This study did not observe any significant association between CD4 cells count and serum HDL as well as serum triglyceride. Nonetheless, dyslipidemia, which includes isolated low serum HDL, isolated serum triglyceride, or in combination with other abnormal serum lipids, is usually observed in conditions of over-nutrition, liver diseases and other chronic illnesses with depressed immunity [33].

The prevalence of low CD4 cells count (<200 cells/ml) 81.6% observed in the subjects who have anemia was significantly higher than 18.4% in those who have no anemia, as shown in this study. This observation is similar to that documented in another study [28]. Anemia is a catabolic state that might be associated with stressors that deplete CD4 cells [34,35]. In addition, anemia is associated with a lot of infection, especially in the developing countries, which might diminish the CD4 cells [36]. These, perhaps, might account for the high prevalence of low CD4 cells observed in our study, indicating also that these subjects might have a substantial level of anemia.

In this study, there was no significant association between CD4 cells count and 24HUP. There was a dearth of studies, from literature search, that evaluated the relationship between CD4 cells count and 24HUP. Stress may cause alterations in water intake, and the state of hydration. In addition, the kidney may be involved in the cause of HIV disease progression. Renal interstitial involvement may result in a salt-losing nephropathy. These may alter urine osmolality in a setting of low CD4 cells count [37]. These, however, were not observed in our study subjects.

Renal filtration function, determined by CI Cr has been shown to decline with the progression of HIV infection [20]. A study has also documented a high prevalence of chronic kidney disease in treatment-naive HIV subjects. This study by Anyabolu et al. demonstrated that renal damage in this group of subjects involved both proteinuric renal disease defined by significant urine protein excretion, and renal damage defined only by impaired renal filtration function (CI Cr) [22]. The prevalence of low CD4 cells count noted in this study probably suggests that these subjects might have a measure of renal disease that might explain the association between the low CD4 cells count and CI Cr as well as 24HUP.

![Figure 2: Association between CD4 cells count and anemia.](image)

### Table 3: Correlation of CD4 cells count with selected variables in treatment-naive HIV-positive subjects (n=393).

| Variables                        | Correlation coefficient(r) | P value | 95% CI |
|----------------------------------|----------------------------|---------|--------|
| Body mass index                  | 0.137                      | 0.006   |        |
| Hemoglobin                       | 0.224                      | <0.001  |        |
| Spot urine protein               | -0.069                     | 0.171   |        |
| Spot urine creatinine            | 0.015                      | 0.763   |        |
| Spot urine osmolality            | 0.037                      | 0.467   |        |
| 24-hour urine protein            | -0.117                     | 0.023   |        |
| 24-hour urine creatinine         | -0.019                     | 0.707   |        |
| 24-hour urine volume             | 0.033                      | 0.052   |        |
| 24-hour urine osmolality         | 0.073                      | 0.160   |        |
| Serum creatinine                 | <0.001                     | 0.999   |        |
| Creatinine clearance             | -0.122                     | 0.018   |        |
| Serum triglyceride               | 0.035                      | 0.488   |        |
| Serum HDL                        | 0.076                      | 0.134   |        |

CI: Confidence Interval, R=0.026, df=3, p=0.002.

### Table 4: Multivariate linear regression of variables with CD4 cells count in treatment-naive HIV-positive subjects (n=393).

| Variables                        | Beta     | T   | P value | 95% CI          |
|----------------------------------|----------|-----|---------|-----------------|
| Body mass index                  | -0.051   | 0.959| 0.338   | -2.35 - 0.303   |
| Hemoglobin                       | 0.225    | 4.453| <0.001  | 13.925-35.949   |
| 24-hour urine protein            | -0.076   | -1.511| 0.132   | -123.747-16.218 |
| Creatinine clearance             | -0.131   | -2.620| 0.009   | -2.046- -0.292  |

CI: Confidence Interval, R=0.517, df=4, p=0.001

### Table 5: Multivariate linear regression of variables with low CD4 cells count (<200 cells/ml) in treatment-naive HIV-positive Subjects (n=49).

| Variables                        | Beta     | T   | P value | 95% CI          |
|----------------------------------|----------|-----|---------|-----------------|
| Body mass index                  | -0.183   | -1.240| 0.222   | -0.039 - 0.007  |
| Hemoglobin                       | 0.058    | 0.400| 0.692   | -0.025 - 0.037  |
| 24-hour urine protein            | -0.006   | -0.044| 0.965   | 1.230 - 0.257   |
| Creatinine clearance             | -0.547   | -3.667| 0.001   | -0.008 - -0.002 |

CI: Confidence Interval, R=0.517, df=4, p=0.001

CD4: Cluster of Differentiation; HIV: Human Immunodeficiency Virus; HDL: High Density Lipoprotein Cholesterol
It was observed in this study that CD4 cells count has no significant correlation with 24HUV. There was a paucity of studies, from literature search, on the relationship between CD4 cells count and 24HUV. Some environmental conditions, some disease state and some physiologic state might influence urine volume [25]. These influencing factors of urine volume were not, however, evaluated in this study.

The myriads of the clinical implications of high prevalence of low CD4 cells count in treatment-naïve HIV subjects are daunting and need to be addressed. Perhaps, the Leonardo Project as assessed and demonstrated by Ciccone et al. has shown that such an integrative and collaborative system, a multi-disciplinary, multi-level framework involving all the stake holders in the management of a chronic disease would also help in no small measure if applied to HIV subjects. Central to good outcomes in this system is a resource care manager, an anchoring coordinator, whose inputs would include empowerment of HIV patients through health education and implementation of all the recommendations of the different strata of clinicians involved in the management of HIV infection and its complications [40]. Those among HIV subjects who have dwindling, or overtly, low CD4 cells count, as in our study subjects, would be timely identified for evaluation that should include, among others, assessment for proteinuric renal damage, dyslipidemia, anemia, and abnormal weight, in the early stage of the infection. This care manager should coordinate the harmonious flow of patient care between primary care centers, HIV clinics, general practitioners and specialist clinicians for target patients’ management outcomes.

Conclusion

The prevalence of low CD4 cells count was high in this study. Abnormal weight, dyslipidemia, anemia and proteinuric renal damage were common among treatment-naïve subjects who have low CD4 cells count. There is a need for clinicians to routinely evaluate CD4 cells count and to further search for abnormal weight, dyslipidemia, proteinuric renal damage and anemia in subjects who have low CD4 cells count <200 cells/ml at the early stage of HIV infection.

Limitations

This study did not assess the different levels of CD4 cells. This would have helped in also determining other factors that influence CD4 cells at different levels of immunosuppression.

References

1. UNAIDS (2013) Global Report: UNAIDS Report on the Global AIDS Epidemic.
2. Obermeyer CM, Osborn M (2007) The utilization of testing and counseling for HIV: A review of the social and behavioral evidence. Am J Public Health 97: 1762-1774.
3. Sanga Z, Kapanda G, Musya S, Mwangi R (2015) Factors influencing the uptake of voluntary HIV counseling and testing among secondary school students in Arusha city, Tanzania: A cross sectional study. BMC Public Health 15: 452.
4. Medu KPO, Welch V, Dahal GP, Tyndall M, Rader T, et al. (2014) Effect of rapid HIV testing on HIV incidence and services in populations at high risk for HIV exposure: An equity-focused systematic review. BMJ Open 4: e008859.
5. Crabtree-Ramirez B, Caro-Vega Y, Shepherd BE, Grinsztejn B, Wolff M, et al. (2016) Time to HAART Initiation after Diagnosis and Treatment of Opportunistic Infections in Patients with AIDS in Latin America. PLOS One 11: e0153921.
6. Mhozya H, Bintabara D, Kibusi S, Neilson E, Mpendo BC (2015) Late-stage disease at presentation to an HIV clinic in eastern Tanzania: A retrospective cross-sectional study. Malawi Med J 27: 125-127.
7. Fantin B, Joly V, Elbim C, Golmard JL, Gougerot-Pocidalo MA, et al. (1996) Lymphocyte subset counts during the course of community-acquired pneumonia: Evolution according to age, human immunodeficiency virus status, and etiologic microorganisms. Clin Infect Dis 22: 1095-1098.
8. Aldrich J, Gross R, Adler M, King K, MacGregor RR, et al. (2000) The effect of acute severe illness on CD4+ lymphocyte counts in nonimmunosuppressed patients. Arch Intern Med 160: 715-716.
9. Okoye AA, Picker LJ (2013) CD4+ T-cell depletion in HIV infection: Mechanisms of immunological failure. Immunol Rev 254: 54-64.
10. Mellors JW, Muñoz A, Giorgi JV, Margolick JB, Tassoni CJ, et al. (1997) Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Ann Intern Med 126: 946-954.
11. Benito JM, López M, Lozano S, Ballesteros C, Martínez P, et al. (2005) Differential upregulation of CD38 on different T-cell subsets may influence the ability to reconstitute CD4+ T cells under successful highly active antiretroviral therapy. J Acquir Immune Defic Syndr 38: 373-381.
12. Gottlieb GS, Sow PS, Hawes SE, Ndoye I, Redman M, et al. (2002) Equal plasma viral loads predict a similar rate of CD4+ T cell decline in human immunodeficiency virus (HIV) type 1- and HIV-2-infected individuals from Senegal, West Africa. J Infect Dis 185: 905-914.
13. UNAIDS/WHO (2007) Epidemiological fact sheets on HIV/AIDS and sexually transmitted infections, 2006 update. World Health Organization, Geneva.
14. Clerici M, Butto S, Lukwiya M, Saresella M, Declercq S, et al. (2000) Immune activation in Africa is environmentally-driven and is associated with upregulation of CCR5. Italian-Ugandan AIDS Project. AIDS 14: 2083-2092.
15. Messele T, Rinke de Wit TF, Brouwer M, Akliltu M, Birru T, et al. (2001) No difference in vitro susceptibility to HIV type 1 between high-risk HIV-negative Ethiopian commercial sex workers and low-risk control subjects. AIDS Res Hum Retroviruses 17: 433-441.
16. Tollerud DJ, Clark JW, Brown LM, Neulander CY, Pankiw-Trost LK, et al. (1989) The influence of age, race, and gender on peripheral blood mononuclear-cell subsets in healthy nonsmokers. J Clin Immunol 9: 214-222.
17. Maier C, Hawes SE, Agne HD, Sow PS, Ndoye I, et al. (2008) Factors associated with CD4 lymphocyte counts in HIV-negative Senegalese individuals. Clin Exp Immunol 151: 432-440.
18. Federal Republic of Nigeria Global AIDS Response and Progress Report (2012) UNAIDS.
19. Anyabolu EN (2017) Low density lipoprotein cholesterol in a general out-patient population in a tertiary hospital in Southeast Nigeria: Associations and implications. Clin Med Diagn 7: 8-17.
20. Anyabolu EN, Chukwuonye II, Arodiwe E, Ijoma CK, Ulasi I (2016) Prevalence and predictors of chronic kidney disease in newly diagnosed human immunodeficiency virus patients in Owerri, Nigeria. Indian J Nephrol 26: 10-15.
21. Anyabolu EN, Chukwuonye II, Mabayoje M, Ejike A, Ijoma CK, et al. (2015) Comparison of Spot Urine Protein/Creatinine Ratio, Spot Urine Protein/ Osmolality Ratio with Measured 24-Hour Urine Protein in HIV Subjects in Nigeria. J AIDS Clin Res 6: 445.
22. Anyabolu EN (2016) BMI and Risk Factors of Underweight and Obesity in HIV Subjects in Eastern Nigeria. World J AIDS 6: 8-15.
23. Anyabolu EN (2016) Body mass index and associated factors of obesity and underweight in a general out-patient population in a tertiary hospital in Nigeria. Am J Int Med 4: 58-92.
24. WHO (1995) Physical Status: The use and interpretation of anthropometry. World Health Organization, Geneva 854.
25. Yeh HC, Lin YS, Kuo CC, Weidemann D, Weaver V, et al. (2015) Urine osmolality in the US population: implications for environmental biomonitoring. Environ Res 136: 482-490.
26. Anyabolu EN, Chukwuonye II (2016) Urine osmolality in adults attending a general out-patient clinic: Clinical implications. Am J Med Sci 6: 145-151.
27. Hemoglobin concentrations for the diagnosis of anemia and assessment of severity (2011) Vitamin and Mineral Nutrition Information System.

28. Anyabolu E (2016) Prevalence and associated factors of anemia in treatment-naïve HIV-positive subjects in Southeast Nigeria. Am J Med Sci Med 4: 41–46.

29. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2001) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 285: 2486-2497.

30. Antwai M, Gurjar R, Childrawar S, Pawar J, Gaikwad S, et al. (2014) Clinical profile of HIV infected patients attending a HIV referral clinic in Pune, India. Indian J Med Res 140: 271-277.

31. Crum-Cianflone NF, Roediger M, Eberly LE, Ganesan A (2011 Jun) Impact of Weight on Immune Cell Counts among HIV-Infected Persons. Clin Vaccine Immunol 18: 940-946.

32. Asfaw M, Wondaferash M, Taha M, Dube L (2015) Prevalence of undernutrition and associated factors among children aged between six to fifty nine months in Bule Hora district, South Ethiopia. BMC Public Health 15: 41.

33. Andersen CJ, Murphy KE, Fernandez ML (2016) Impact of Obesity and Metabolic Syndrome on Immunity. Adv Nutr 7: 66-75.

34. Fibach E, Rachmilewitz E (2008) The role of oxidative stress in hemolytic anemia. Curr Mol Med 8: 609-619.

35. Irwin M (2001) LOW CD4+ T LYMPHOCYTE COUNTS. A variety of causes and their implications to a multifactorial model of AIDS.

36. Volberding PA, Alexandra ML, Dieterich D, Mildvan D, Mitsuyasu R, et al. (2004) Anemia in HIV infection: Clinical impact and evidence-based management strategies. Clin Infect Dis 38: 1454-1463.

37. Madariaga H, Kumar A, Khanna A (2015) A rare mechanism of hyponatremia in HIV disease. Am J Case Rep 16: 707-710.

38. Bellasi A, Mandreoli M, Baldrati L, Corradini M, Nicolò P, et al. (2011) Chronic kidney disease progression and outcome according to serum phosphorus in mild-to-moderate kidney dysfunction. Clin J Am Soc Nephrol 6: 883-891.

39. Tynkevich E, Flamant M, Haymann JP, Metzger M, Thervet E, et al. (2014) Decrease in Urinary Creatinine Excretion in Early Stage Chronic Kidney Disease. PLOS ONE.

40. Ciccone MM, Aquilino A, Cortese F, Scicchitano P, Sassara M, et al. (2010) Feasibility and effectiveness of a disease and care management model in the primary health care system for patients with heart failure and diabetes (Project Leonardo). Vasc Health Risk Manag 6: 297-305.