OPEN ACCESS
Scholars International Journal of Biochemistry
Abbreviated Key Title: Sch Int J Biochem
ISSN 2616-8650 (Print) |ISSN 2617-3476 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

# Changes in the Metabolic Profile of HIV Infected Subjects on Highly Active Anti-Retroviral Therapy (HAART)

Johnson, J. T[1*], Ekpo, G. I[2], Obi, I. M[1]

[1]Department of Biochemistry, Faculty of Science, Federal Univesity Otuoke, Bayelsa State, Nigeria
[2]Department of Biochemistry, Faculty of Basic Medical Science, College of Medical Sciences University of Calabar, Calabar, Nigeria

**DOI:** 10.36348/sijb.2023.v06i01.002 | **Received:** 18.12.2021 | **Accepted:** 31.01.2022 | **Published:** 30.01.2023

***Corresponding author:** Johnson J. T
Department of Biochemistry, Faculty of Science, Federal Univesity Otuoke, Bayelsa State, Nigeria

## Abstract

The metabolic profile of HIV/AIDS patient on HAART was investigated in comparison with HIV/AIDS patient who are HAART naive and also with the zero negative controls. Sixty (60) HIV subjects were used for the study and were carefully divided into two groups of thirty (30) each; group one were those on HAART and the other HAART naive while thirty (30) zero negative subjects were used as the control. Patients used for these studies are those who have been on the treatment for at least a year and not more than three years. Metabolic parameters assessed included serum total protein, albumin, globulin, electrolytes, creatinine and lipid profile. Results obtained reveals no significant ($P > 0.05$) changes in the serum electrolyte and creatinine concentrations in all groups and similar trend was also observed for total protein and albumin levels but a significant ($P< 0.05$) reduction was observed in the level of serum globulin concentration of patients on HAART (2.86±0.67) compared with the HAART naive (3.41±0.62). More so, there was significant ($P<0.05$) elevation in the serum total cholesterol concentration for the HAART group (150.9±15.01) compared with HAART naive (114.5±17.04) and similar trend was also observed for LDL-cholesterol which may be a possibly indication of altered lipid metabolism. Thus, patients on HAART should carry out routine biochemical check most especially lipid panel assessment to avoid risk of altered metabolism; lipid dystrophy etc.

**Keywords:** Metabolic-profile, Changes, HIV-subjects, HAART.



## INTRODUCTION

Human Immunodeficiency Virus (HIV) belongs to a family of virus known as lentivirus (a subgroup family of retroviridae) that causes HIV infection and over time Acquired Immunodeficiency Syndrome (AIDS), (Douek *et al*., 2009). Many species of organism are infected by lentiviruses, which are characteristically responsible for long- duration illnesses with a long incubation period, (Levy, 1993) Lentiviruses are transmitted as single-stranded, positive-sense, enveloped RNA viruses and upon entry into the target cell, the viral RNA genome is converted(reverse transcribed) into double-stranded DNA by a virally encoded enzyme, reverse transcriptase that is transported along with the viral genome in the virus particle(HU and Hughes, 2012). The resulting viral DNA is then imported into the cell nucleus and integrated into the cellular DNA by a virally encoded enzyme integrase and host co-factors.(Smith and Daniel, 2006). Human Immunodeficiency Virus (HIV) can lead to Acquired Immunodeficiency Syndrome(AIDS), thus, it is a condition in humans in which the immune system begins to fail leading to life threatening occurrence of infections such as tuberculosis, pneumonia, diarrhoea, meningitis and tumours(Greener,2002). Once infected, individuals remain infected for life with fatal opportunistic infection as a result of HIV-induced deficiencies in the immune system and immune cells during HIV infection, release number of inflammatory mediators (cytokines) which hamper the T-cell proliferation, suppress the cell mediated function and deplete the cluster of differentiation -4(CD4) cells (Tilg and Moschen, 2006; Nguemaim *et al*., 2010) which is a characteristic feature of the disease.

Human Immunodeficiency Virus-associated nephropathy is an important cause of renal failure in HIV-1 seropositive patients (Brooks *et al*., 2010). Incidence of human immunodeciency virus-1-associated nephropathy is high among HIV-infected

individuals especially those on Anti-Retroviral drugs (Szczech *et al*., 2004) HIV-associated nephropathy can be the initial presentation of HIV-1 infection and can also develop late in the course of hiv-1 infection following the development of AIDS (Winston *et al*., 1999).

Serum proteins are proteins found in blood plasma. Serum total protein in blood is about 7g/dl with a reference range of 6-8g/dl. About 60% of the plasma proteins are made up mainly of the albumin, which is a major contributor of osmotic pressure of plasma and assist in the transport of lipids and steroid hormones. Globulins makes up 35% of plasma protein, 4% is fibrinogen and less than 1% of plasma proteins are in the form of enzymes, proenzymes and hormones (Anderson and Anderson, 1977); (Ekpo and Johnson, 2021).

Creatinine; a breakdown product of creatine phosphate which is an important part of muscle. Creatinine is removed from the body entirely by the kidneys, if the kidney function is abnormal, creatinine levels will increase in the blood.

Antiretroviral drugs are medications use in the treatment of infection by retroviruses, primarily HIV. The use of an approach involving a combination antiretroviral therapeutic agents is known as Highly Active Antiretroviral Therapy (HAART) (Dybul *et al*., 2002). The complexity of selecting and following a regimen, the severity of the side effects and the importance of compliance to prevent viral resistance led to the emphasis on the need to involve patients in therapy choices, timing, recommendation of the need to analyse the risks and the potential benefits to patients including those without symptoms (Dybul *et al*., 2002; Holkmann *et al*., 2007) The current standard of care for people with HIV indicated for treatment worldwide, is a combination of three or more antiretroviral drugs taken every day for life, known as Highly Active Antiretroviral Therapy (HAART). The introduction of Highly Active Antiretroviral Therapy (HAART) in 1996 led to a dramatic and sustained decrease in HIV-related morbidity and mortality (Fauci and lane, 2005).

The strength of the immune system is associated to the quality and quantity of nutrients intake and their bioavailability (Fernandes, 1991), and nutrients below optimal level according to report on the influence of nutrition on the function of the immune system leads to immunological deficiencies (Powell *et al*., 2000). Nevertheless, acute/chronic under nutrition and malnutrition such as evident in HIV infection maybe the major cause of the melt down in the defence walls and this may also lead to interference of the metabolic processes of the liver sequel to drug (HAART)-nutrient interaction, Ekpo and Johnson, 2021. However, there is scarce of scientific evidence to ascertain if there are metabolic changes in HIV infected subjects following the administration of HAART. Thus, this study investigated the metabolic profile of HIV infected subjects on HAART in comparison with HAART naïve subjects and HIV negative controls.

## MATERIALS AND METHODS

### Study Design

This analysis was carried out at Niger Delta University Teaching Hospital Okolobiri Bayelsa State. The study area is defined by longitude $8^{o}$ E and latitude $6^{o}$ N, elevated at 250ft above sea level with a The vegetation characteristic of tropical rain forest with an average annual rainfall of about 3,600mm and an average atmospheric temperature of $30^{o}$ C. Human Immunodeficiency Virus prevalence in the state is about 3.8% (Nigeria Federal Ministry of Health, 2016).

### Subjects Selection

Sixty (60) HIV infected subjects 30 males and 30 females aged 18-54 years drawn from patients attending Medical Out-patient Department of virology in Niger Delta University Teaching Hospital Okolobiri were recruited into the study. Patients included were those whose HIV status have been confirmed, whether symptomatic or asymptomatic but are receiving treatment (HAART). Excluded from the study were patients whose HIV/AIDS status are yet to be confirm or those who were also diabetic, hypertensive or have any chronic organ or systematic illness or on prolonged medication. The patients at the entry into the study were assigned into any of the two groups: HIV/AIDS patients not on HAART (n=30) and HIV/AIDS patients on HAART (n=30).

Thirty (30) apparently healthy volunteers, matched for age, sex and height comprising staff and medical student at the Niger Delta University Teaching Hospital (12 males and 18 female) who were non-obese, non-hypertensive and without any chronic organ or system illness and who tested negative to the virus(HIV) served as the controls.

The approval of this study by the ethical committee of Niger Delta University Teaching Hospital was on the agreement that patient anonymity must be maintained, good laboratory practice/quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only in compliance with the Helsinki declaration of 1975 (amended in 2000). Socio demographic data like age, sex, weight and height as well as duration of illness/infection and treatment details were obtained from case notes and folders of the patients while the controls were interviewed orally to obtain their age and sex, weight (in kg using a standard hospital balance) and height (in m using a metre rule) were measured (in light clothing, without shoes).

**Sample Collection**

Ten milliters (10) of venous blood was collected at 09.00hr in the morning after overnight fast. Five millilitres each (5ml) was dispense into EDTA bottles and plane dry grass test tubes. Serums in plane dry test tube were isolated by centrifuging in a laboratory centrifuge at 3000rpm. The serums were refrigerated $4^{o}$ C pending various laboratory assays.

**Biochemical Assay**

Standard laboratory procedures where adopted; the method of Siedel *et al.*, 1985 was use for the assessment of lipid profile, serum total protein, albumin, globulin and creatinine concentration were determined using the Biuret Method as described by Grant, *et al.*, (1987) while serum electrolytes was determined by method of Tiez 1994.

**Statistical Analyses**

Data obtained was expressed as Mean ± Standard Deviation and analyzed using the statistical package for social sciences (SPSS). Values at P< 0.05 were regarded as significant in comparison with appropriate controls.

## RESULTS

The level of total serum protein, albumin, creatinine and other metabolites were determined in 60 HIV- infected subjects aged 18-54 years and thirty HIV- seronegative individual, Age and gender matched individuals were monitored as controls. Thirty of the HIV/AIDS infected patients were on HAART while the other thirty were HAART naïve patients and were yet to commence HAART.

The result of serum total protein assessed reveals no significant (P > 0.05) changes in all the groups, HAART naive (7.20 ± 0.88), HAART treated (7.34 ± 0.65) and negative control (6.85 ± 0.87). Similar trend was observed for serum albumin. However, the serum globulin concentration assessed shows a significant (P < 0.05) reduction in HAART treated group (2.86 ± 0.67) compared with that of HAART naive (3.41 ± 0.62) and both groups were significant (P < 0.05) higher when compared with the negative control (1.69 ± 0.41). Serum electrolyte assessed were sodium ($Na^{+}$), Potassium ($K^{+}$), Chloride ($Cl^{-}$), Bicarbonate ($HCO^{-}_{3}$), Calcium ($Ca^{2+}$), Phosphorus ($PO_4^{-3}$) ion concentrations.

The result reveals no significant (P > 0.05) changes in the serum sodium ($Na^{+}$) levels of all the groups. HAART treated (139.31±7.51), HAART naive (135.53±8.12), and negative control (138.65±6.32). The potassium ($K^{+}$) shows no significant (P > 0.05) changes among all the groups. Similar trend was also observed for bicarbonate ($HCO^{-}_{3}$), chloride ($Cl^{-}$), calcium ($Ca^{+}$) and phosphorus ($PO_4^{-3}$) ions. The creatinine level in all three groups considered shows no significant (P > 0.05) variations. The serum lipid parameters investigated in all the groups were Total Cholesterol, LDL- cholesterol, HDL-cholesterol, LDL/HDL ratio and Triglyceride (TG).

The result of serum lipid profile obtained showed that the TC (Total cholesterol) concentration of HAART group (150.90±15.01) was significantly (P < 0.05) higher compared with that of the HAART naive (114±17.04) but shows no significant change (P > 0.05) when compared with that of the negative control (139.79±9.09), Similar trend was also observed for LDL. No significant (P > 0.05) change was noticed in HDL levels of all the groups.

More so, the TG level of the HAART naive (170.64±27.65) was significant (P >0.05) higher compared with the negative control (125.23±15.00).

**Table 1: Serum total protein albumin, globular, HIV/AIDS on HAART and HIV/AIDS HAART naïve and HIV/AIDS negative individual**

| Parameters/Group | Total Protein g/dl | Albumin g/dl | Globular g/dl |
|---|---|---|---|
| NAÏVE | 7.20±0.88 | 3.39±0.86 | 3.41±0.62 |
| HAART TREATED | 7.34±0.65 | 3.86±0.79 | 2.86±0.67* |
| NEGATIVE | 6.85±0.87 | 3.88±0.73 | 1.69±0.41*[a] |

Values expressed as mean ± SEM. * Significant at P < 0.05 compared with HAART naïve, [a] Significant at P < 0.05 compared with HAART treated

**Table 2: Serum electrolytes and creatinine levels in HIV/AIDS patient on HAART, HAART naive and negative controls**

| Parameters/Group | $Na^{+}$ mmol/L | K mmol/L | $HCO_3$ mmol/L | $Cl^{-}$ mmol/L | Ca mmol/L | $PO_4^{-3}$ mmol/L | Creatine mg/dl |
|---|---|---|---|---|---|---|---|
| NAÏVE | 135.53±8.12 | 3.54±0.61 | 26.52±3.10 | 88.50±5.03 | 2.54±0.23 | 1.3±0.4 | 0.81±0.21 |
| HAART TREATED | 139.31±7.51 | 3.91±0.90 | 29.0±3.42 | 98.01±5.98 | 2.30±0.11 | 1.3±0.4 | 0.99±0.09 |
| NEGATIVE | 138.65±6.32 | 3.70±0.74 | 26.81±2.89 | 104.01±8.10 | 2.18±0.13 | 1.52±0.1 | 0.96±0.22 |

Significant at (P > 0.05)

**Table 3: Lipid Profile in HIV/AIDS patient of HAART naïve, HAART treated and negative controls**

| Parameters/Group | TC mg/dl | HDL mg/dl | LDL mg/dl | TG mg/dl | LDL/HDL |
|---|---|---|---|---|---|
| NAÏVE | 114.58±17.04 | 36.00±3.8 | 65.40±22.80 | 170.64±27.65 | 1.82 |
| HAART TREATED | 150.90±15.01* | 40.9±1.90 | 99.89±25.80* | 150.11±30.21 | 2.44 |
| NEGATIVE | 139.79±9.09 | 42.01±1.70 | 75.4±8.30 | 125.23±15.00* | 1.79 |

* Significant at P < 0.05 compared with HAART naive

## DISCUSSION

The metabolic profile of HIV/AIDS patients on Highly Active Anti-Retroviral Therapy was evaluated in comparison with HAART naive and zero negative HIV controls subjects.

Significantly lower serum total protein in patients with HIV/AIDS and controls in a corroborative earlier finding (Scrimshaw and Sangiovanni 1997). Although serum total protein estimation has limited diagnostic importance when compared to albumin because of the compensatory increases in other serum proteins (the globulins) during infections, its relevance in the evaluation of patients with some clinical conditions such as malnutrition, malignancy, renal and liver diseases and immune disorders cannot be ignored (Gray *et al*., 1985). Decrease in serum total protein in HIV infection has been associated with either increased losses and/or catabolism or as a result of reduction in intake and/or absorption due to sores in the mouth, pharynx and/or oesophagus, fatigue, depression and side effects of medications (Macallan 1999). However, HAART users were found to have significantly higher serum total protein than non-users. It could therefore be conceived that HAART-use improves protein metabolism by improving the CD4 count), although it could not be established if the lower serum protein levels in HIV/AIDS patients in the present study were related to CD4 count since the count was not within the scope of this study. Reduced loss of protein in diarrhoea and catabolism in HAART users may also be a factor. However, with HIV progression protein loss may be more pronounced as it has been shown that about 0.6-1.2g of protein per kilogram body weight per day are lost in adults due to infection as a result of mobilisation of amino acids from skeletal muscles in response to the release of cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α) (Echevrria *et al*., 1999). These losses have been found to be highest in diarrhoea and dysentery, which are common in HIV infection.

Fluid and electrolytes in balance are common biochemical findings in HIV/AIDS (Hebden *et al.*, 1986) and have been attributed to increased losses, reduced intake or absorption or altered metabolism as a result of medications (Macallan, 1999; Babamento and Kotler 1997). More so, this study shows no significant level in the electrolyte level which may be occasioned by the fact that the kidney response to electrolyte concentration is at optimum facilitation.

Serum creatinine is an important indicator of renal health because it is an easily measured by-product of muscle metabolism that is excreted unchanged by the kidneys which is a factor why creatinine was not significant thus, found in minor levels. Creatinine itself is produced via a biological system involving creatine phosphate and adenosine triphosphate in a healthy body in motion but the insignificant level in our study shows that the function of the kidney is still intact.

In a study conducted in Ghana (Awah and Agughasi 2011) on serum lipid profiling in highly active retroviral therapy naive HIV positive patients, showed similar significant increase in TAG, decrease in TC, HDL-c and LDL when compared to control (Chow *et al*., 2006). Our study observed increase in TC, TAG, significant increase in LDL and decrease in HDL similar to the findings of a study on effect of highly active anti-retroviral therapy on lipid profile in a human immunodeficiency virus infected Nigerian population (Gallant *et al*., 2004). The possible explanation for low levels of TC, HDL and LDL in HIV infected HAART untreated subjects have been associated with β-2 microglobulin. Some studies attributed the increase in TAG to improper clearance of lipoproteins, increase in IFN-α and altered plasma HDL-C levels (NCEP 2002). A variation in LDL-c is due to the fact of degree of immunosuppression which has been observed in some studies stating that HIV infection affect the TC first, then HDL, followed by LDL and later TAG (Galli *et al*., 2002). On the contrary our findings show significant increase in TC, HDL, LDL and decrease in TG in HIV infected ART treated subjects when compared against HIV infected ART untreated subjects.

## CONCLUSION

Despite sparse body of information and literature on comparative study of serum electrolytes, creatinine, total protein, and lipid profile of HIV/AIDS patients on HAART, the results of this study show that minor electrolyte disturbances are experienced in persons living with HIV/AIDS, from our findings it is evident that HAART slightly or significantly affects certain metabolic indices, Total protein, globulin, total cholesterol, LDL and TG but has no effect on Albumin, electrolytes, creatinine and HDL. This evidence of altered lipid profile especially for TC and LDL in HAART patients compared to HAART naive group can lead to lipid dystrophy (which is characterized by degenerative lipid redistribution).

## REFERENCES


- Anderson, N. L., & Anderson, N. G. (1977). High Resolution Two Dimensional Electrophoresis of Human plasma proteins, *Proceeding of the National Academy of Sciences*, 74(12), 5421-5425.
- Awah, F. M., & Agughasi, O. (2011). Effect of highly active anti-retroviral therapy (HAART) on lipid profile in a human immunodeficiency virus (HIV) infected Nigerian population. *African Journal of Biochemistry Research*, 5(9), 282–286.
- Brooks, G. F., Carnoll, K. C., Janet. S., Butel, Morse, S. A., Mietne, T. A., Jawetz, Melnick, S., & Adelberg's. (2010). Medical Microbiology McGraw-Hill Companies North American, 25, 406-407.
- Babamento, G., & Kotler, D. P. (1997). Malnutrition in HIV infection. *Gastroenterol.Clin. North Am*, 26, 393-415.
- Chow, C., Day, L. J., Souza, S. A., & Shikuma, C. M. (2006). Metabolic Complications of HIV Therapy. *IAPAC*, 12(9), 303-311.
- Douek, D. C., Roederer, M., & Koup, R. A. (2009). Emerging Concepts in the Immunopathogenesis of AIDS. *Annual Review of Medicine*, 60, 471-484.
- Dybul, M., Fauci, A. S., Bartlett, J. G., Kaplan, J. E., & Pau, A. K. (2002). Panel on Clinical Practices for Treatment of HIV, *Ann Intern Med*, 137, 381–433.
- Echevrria, P. S., Jonnalagadda, S. S., Hopkins, B. L. & Rosenbloom, C. A. (1999). Perception of quality of life of persons with HIV/AIDS and maintenance of nutritional parameters while on protease inhibitors. *AIDS Patient Care and Stds*, 13(7), 427-33.
- Ekpo, G. I., & Johnson, J. T. (2021). Effect of *Ganoderma Lucidum*, Astaxanthin, Liv.52 Hb and Stc30 on C-Reactive Protein Concentrations of Animal Model with CCL4 Induced Hepatocellular Carcinoma. *Chemical and Pharmaceutical Research*, 3(1), 1-5.
- Ekpo, G. I., & Johnson, J. T. (2021). Effect of *Ganoderma Lucidum*, Astaxanthin, Liv.52 Hb and Stc30 on Renal Function Parameters of Animal Models with $CCl_4$ Induced Hepatocellular Carcinoma. *Journal of Advances in Medicine and Medical Research*, 33(21), 175-182.
- Fauci, A. S., & Lane H. C. (2005). Human immunodeficiency virus Disease; AIDS and related Disorders. In: Kasper, D. L, Fauci, A. S., editors. Harrison's Principle of Internal Medicine. 16th ed. New York: *McGraw-Hill Co*, 1076-1079.
- Gallant, J. E., Staszewski, S., & Pozniak, A. L. (2004). Efficacy and safety of tenofovir DF vs Stavudine in combination therapy in antiretroviral-naïve patients: a 3 year randomized trial. *JAMA*, 292, 191–201.
- Galli, M., Ridolfo, A. L. & Adorni, F. (2002). Body habituschanges and metabolic alterations in protease inhibitor-naïve HIV-1 infected patients treated with two nucleoside reverse transcriptase inhibitors. *J Acquir Immune Defic Syndr*, 29, 21–31.
- Gray, C. H., Howorth, P. N., & Rinsler, M. G. (1985). In plasma protein and immunoglobulins. Clinical Chemical Pathology 10th edition, Edward Arnold (Publishers) Ltd, Bedford, London, Pp 73-89.
- Greener, R. (2002). AIDS & Macroeconomics Impact" in Forsyth, S. (ed.) States of the Art: *AIDS and Economics IAEN*, 49-55.
- Hebden, R. A., Gardiner, S. M., Bennett, T., & MacDonald, I. A. (1986). The influence of streptozotocin-induced diabetes mellitus on fluid and electrolyte handling in rats. *Clin Sci (London)*, 70(1), 111-117.
- Holkmann, A., Olsen, C., Mocroft, A., Kirk, O., Vella, S., Blaxhult, A., Clumeck, N., Fisher, M., Katlama, C., Phillips, A. N., & Lundgren, J. D. (2007). Interruption of combination antiretroviral therapy and risk of clinical disease progression to AIDS or death. *HIV Med*, 8(2), 96-104.
- Hu, W., & Hughes, S. (2012). HIV-1 Reverse transcriptase. *Cold Spring Harb Pespect, Med 2*, 37, 378-380.
- Macallan, D. C. (1999). Wasting in HIV infection and AIDS. *J Nutr*, 129, 238S-242S.
- Powell, J., Andrea, T., Brochers, S., Yoshida, M., & Eric, G. (2000). "Evaluation of the Immune System in the Nutritionally 'At-Risk Host". *Nutrition and Immunology*, pp. 21-31.
- Nguemaïm, N. F., Mbuagbaw, J., Nkoa, T., Alemnji, G. & Této, G. (2010). Serum lipid profile in highly active antiretroviral therapy-naïve HIV infected patients in Cameroon: a case-control study. *HIV Med*, 11, 353-359
- Scrimshaw, S. N., & SanGiovanni, J. P. (1997). Synergism of nutrition, infection and immunity*: An overview*. *Am. J. Clin. Nutr*, 66, 464S-477S.
- Szczech, L. A., Gupta, S. K., Habash, R., Guasch, A., Kalayjian, R., Appel, R., Fields, T. A., Svetkey, L. P., Flanagan, K. H., & Klotman, P. E. (2004). The clinical epidemiology and course of the spectrumof renal diseases associated with HIV infection. *Kidney Int*, 66(3), 1145-1152.
- Winston, J. A., Klotman, M. E., & Klotman, P. E. (1999). HIV-associated nephropathy is a late, not early, manifestation of HIV-1 infection. *Kidney Int*, 55(3), 1036-1040.
- Tilg, H., & Moschen, A. R. (2006). Adipocytokines: mediators linking adipose tissue, inflammation and immunity. *National Revolution Immunology*, 6, 772-783.