International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(RESEARCH ARTICLE)

Check for updates

The effect of highly active antiretroviral therapy on the urea and creatinine of HIV/AIDS patients in Enugu Southeast of Nigeria

Ifeoma Chinwe Ikegwuonu [1, *], Nkechinyere Mercy Nwegbo [1], Promise Ezinne Chukwu [1], Adanna Perpetua Ikebudu [2], Patrick Tobenna Ikegwuonu [3], Joel Ifesinachi Agbo [1], Ifeanyi Emmanuel Arinze [1], Nzube Samuel Nwosu [1], Samuel Onuzulike Ebede [4] and Chika Betina Mba [5]

[1] *Department of Medical Laboratory Sciences, Faculty of Health Sciences and Technology, College of Medicine, University of Nigeria Enugu Campus. Enugu State, Nigeria.*
[2] *Department of Pharmaceutical Chemistry and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University Awka. Anambra State, Nigeria.*
[3] *Department of Orthopedics and Traumatology, College of Medicine, University of Nigeria Teaching Hospital, Enugu. Enugu State, Nigeria.*
[4] *Department of Medical Microbiology, University of Nigeria Enugu Campus. Enugu state, Nigeria.*
[5] *Department of Haematology/Immunology, University of Nigeria Teaching Hospital, Enugu. Enugu State, Nigeria.*

International Journal of Science and Research Archive, 2023, 09(02), 979–985

Publication history: Received on 11 July 2023; revised on 22 August 2023; accepted on 25 August 2023

Article DOI: https://doi.org/10.30574/ijsra.2023.9.2.0681

Abstract

Objective*:* The human immunodeficiency virus (HIV) affects the immune system of human and can lead to Acquire Immunodeficiency Syndrome if not managed, this in turn affect the functionality of the body system especially the kidney. Highly Active Antiretroviral Therapy (HAART) is frequently prescribed as frontline drug in reducing viral load on a carrier. Creatinine and urea are makers for kidney function test. This study investigated the effects of HAART on the urea and creatinine of HIV positive individuals in Enugu, Nigeria.

Methods*:* We recruited about seventy subjects' age (18-50years) for this cross-sectional study. Twenty-five HIV positive individuals on HAART as test subjects while twenty HIV positive HAART naive subjects and twenty-five HIV negative individuals as controls. 5mls of blood were collected from each participant and used in the analysis of creatinine and urea using colorimetric methods. All data obtained were analysed using Statistical Package for Social Science (SPSS) version 25 computer software and results were expressed as mean ± Standard Deviation.

Results*:* The result obtained shows a significant increase ($p<0.05$) in both creatinine and urea levels among HIV positive HAART Naive subjects to compare with HIV positive subjects on HAART and HIV negative individuals. When individuals with HIV positive on HAART were compared with HIV negative subjects, there exist no significant different ($P> 0.05$) in both creatinine and urea levels.

Conclusion*:* This study concludes that HAART significantly increases kidney functionality on HIV positive individuals and ameliorate the effect of the virus on the nephrons of the kidney.

Keywords: HAART; HIV-positive; Urea; Creatinine; Enugu

* Corresponding author: Ifeoma Chinwe Ikegwuonu

1. Introduction

The human immunodeficiency virus (HIV) targets the immune system and weakens people's defense against many infections and some types of cancer that people with healthy immune systems can fight off [1, 2]. As the virus destroys and impairs the functions of immune cells, infected individuals gradually become immunodeficient, immune function is typically measured by CD4 cell count [3]. HIV damages the immune system, untreated HIV affects and kills CD4 cells, which are a type of immune cell called T-cell [4]. HIV virus leads to Acquired Immunodeficiency Syndrome (AIDS) if not properly managed [5]. HIV strains are of two types; HIV-1 and HIV-2, HIV-1 is the most common type of HIV amounting to about 95% of the virus whereas HIV-2 is less common, it is 55% genetically different from the HIV-1, it is mostly seen in West Africa, it is less infectious and progresses slowly compared to its counterpart thereby leading to fewer death but if not properly treated or managed can lead to AIDS or even death [6].

Acquired Immunodeficiency syndrome (AIDS) is a life threatening disease which causes a shift in the immune function of the body, AIDS can be diagnosed in HIV patient when the CD4 cells count falls below 200 per milliliter [4]. If AIDS is left untreated, life expectancy is about 3 years; the shortened life span of AIDS patients is due to diseases and complications of the weakened immune system [7]. The introduction and use of antiretroviral therapies (ART) have revolutionized the management and the treatment of HIV/AIDS globally resulting in increased life expectancy [8].

Highly Active Antiretroviral Therapy (HAART) also called Combination Antiretroviral Therapy (cART), this drug has been in use since 1996 and it is a combination of three or more antiretroviral drugs depending on an individual viral load [9]. It is a drug use in the treatment of HIV usually HIV type 1(HIV-1) and in the management of AIDS, this drug functions to inhibit the replication of virus by several mechanism [10]. HAART is frequently prescribed as a frontline drug in reducing viral load, in order to keep the immune system strong to fight opportunistic infection [11]. HAART functions to improve the quality of life of an infected person, to reduce viral load, to prevent transmission to others, especially preventing mother to child transmission during childbirth and breastfeeding and to also improve immune function [12-13]. HAART naive can easily transmit the virus to others due to increase viral load, they have decreased life expectancies because of CD4 count< 200 cells/µl [14]. HIV/AIDS can cause inflammation in different parts of the body which increases the risk of cardiovascular disease, kidney disease, liver disease and some cancers [4]. The kidney is one of the major organs of the body; it removes wastes, extra fluid and acid that is produced by the cells of the body to maintain a healthy balance of salts, water and minerals [15]. When there is impairment in the kidney, it leads to kidney malfunctioning and disorders. This could be assessed by evaluating some of the kidney biomarkers like urea and creatinine [16].

Creatinine is the end product of creatine metabolism which is formed during muscle breakdown and dietary meat, it is released into the circulation at a relatively constant level, it is present in all body fluid and secretion and is freely filtered by the glomeruli but neither metabolized nor actively reabsorbed within the tubules rather it is secreted and these makes it a major maker for kidney function test. [17,18]. Creatinine values vary within individual depending on race, age, gender, body mass index, dietary intake and physical activities [19].

Urea is the byproduct of protein metabolism, it is been synthesized from ammonia by liver enzyme of the urea cycle and then excreted by the kidney, it is not actively reabsorbed nor secreted by the tubules but it is freely filtered by the glomeruli, some factors affecting urea level includes; malnutrition, increased protein intake, pregnancy, cirrhosis, use of steroid [20]. Kidney disease prevalence in subjects with HIV infection is reported between 3.5% and 48.5% [15, 17], this affects their ability to filter waste and toxins as it ought to and has cause a remarkable change in the creatinine and urea level of HIV patient [21]. Antiretroviral therapy is used to improve life expectancy in HIV-infected subjects therefore; this study investigated the effects of highly active antiretroviral therapy on the creatinine and urea levels of HIV/AIDS subjects in Enugu, Nigeria.

2. Material and methods

2.1. Study Design/Selection

This was a cross sectional study carried out at the University of Nigeria Teaching Hospital (UNTH) Ituku-Ozalla, Enugu. The study involved seventy adult human volunteers aged (18-50 years) from Enugu metropolis. Twenty-five HIV/AIDS positive subjects on HAART were used as test group, while control groups were 20 HIV/AIDS positive subjects HAART naïve and 25 HIV/AIDS negative subjects. Informed consent was obtained from each participant. Questionnaires were distributed and duly filled by the participants.

2.2. Inclusion and Exclusion criteria

2.2.1. Inclusion criteria

- Subjects: 18-50years of age
- Gender: Both male and female
- Apparently healthy individuals that tested negative to HIV/AIDS as control subjects 1
- HIV/AIDS positive patients on HAART as test subjects
- HIV/AIDS patients not on HAART (naïve patients) as control subjects 2

*2.2.2. **E**xclusion criteria*

- Patients suffering from other known cause of renal disorder
- Individuals on any other therapy that can induce renal disorder
- Chain smokers and alcoholic individuals.

2.3. Ethical Considerations and Informed Consents

Ethical approval was duly obtained from the College of Medicine Research Ethics Committee of University of Nigeria Enugu Campus, Enugu State (Protocol No: 0136/11/2021). Written consent of willingness to participate in the study as subject was obtained from all the participants.

2.4. Sampling Techniques

Venous blood was collected into appropriately labelled five millilitres (5ml) plain tube. Sample was allowed to clot and retract, centrifuged at 5,000 rpm and the supernatant (serum) was separated into another labelled vial and stored at -20 °C until analysed, and the analyses were carried out within 48 hours of collection. All analysis of the samples was done by the researchers at the laboratory of University of Nigeria Teaching Hospital Ituku-Ozalla Enugu.

2.5. Biochemical Analysis

Serum urea and creatinine were estimated on each collected sample.

2.5.1. Serum urea estimation

Estimation was done using urease –Berthelot method [22] with the manufacturer's instructions duly followed.

2.5.2. Serum creatinine estimation

Estimation was done using Jaffe method [23] with the manufacturer's instructions duly followed.

2.6. Data Analysis

Data obtained from this study were analysed using the statistical package for social sciences (SPSS) for Windows Inc. Chicago, IL, USA. Significant differences between means were determined using Anova. Student's T- test was used to calculate differences between the means. Results were recorded as mean ± standard deviation. P-value <0.05 was considered statistically significant.

3. Results

Table 1: shows the urea and creatinine levels in HIV positive individuals on HAART, HAART NAÏVE and HIV negative individuals. The result shows a significant difference ($p<0.05$) in the mean ± standard deviation (SD) of urea (3.11 ± 1.52, 4.96 ± 5.03, 2.78 ± 0.61) (mmol/l) and creatinine (117.28 ± 28.18, 171.21 ± 86.47, 117.68 ± 30.28) (mmol/l) in HIV-positive individual on HAART, HAART NAÏVE and HIV negative individual respectively.

Table 1 The urea and creatinine levels of HIV positive individuals on HAART, HAART NAÏVE and HIV negative individuals

Groups	Urea(mmol/l)	Creatinine (mmol/l)
HIV positive individuals on HAART N=25	3.11±1.52	117.28±28.18
HIV positive individuals not on HAART (HAART NAÏVE) N=20	4.96±5.03	171.21±86.47
HIV negative individuals N=25	2.78±0.61	117.68±30.28
P-value	0.033*	0.001*
F-ratio	3.591	7.383

Values are given as mean ± standard deviation (SD). (* Significant value, p<0.05)

Table 2 shows the creatinine and urea levels of HIV positive individuals on HAART and HIV negative individuals. The result shows no significant difference (p> 0.05) in urea (3.11±1.52, 2.78 ± 0.61) and creatinine (117.28 ± 28.18, 117.68 ± 30.28) of HIV positive individuals on HAART and HIV negative individual respectively.

Table 2 The urea and creatinine levels of HIV positive on HAART and HIV negative individuals

Groups	Urea(mmol/l)	Creatinine (mmol/l)
HIV positive individuals on HAART N=25	3.11 ± 1.52	117.28 ± 28.18
HIV negative individuals N=25	2.78 ± 0.61	117.68 ± 30.28
P-value	0.911	1.000

Table 3 shows comparison of creatinine and urea levels between HIV positive individuals on HAART and HAART naïve. The result shows a significant decrease in creatinine (117.28 ± 28.18, 171.21 ± 86.47) and urea (3.11±1.52, 4.96 ± 5.03) of HIV individuals on HAART and HAART naïve respectively.

Table 3 The urea and creatinine levels of HIV positive individuals on HAART and HAART Naive

Groups	Urea(mmol/l)	Creatinine(mmol/l)
HIV positive individuals on HAART N=25	3.11 ± 1.52	117.28 ± 28.18
HIV positive individuals HAART Naive N=20	4.96 ± 5.03	171.21 ± 86.47
P-value	0.085	0.003

Table 4 shows a significant increase in urea and creatinine level of HIV positive individuals not on HAART (4.96 ± 5.03, 171.21 ± 86.47) when compared to HIV negative individual (2.78 ± 0.61, 117.68 ± 30.28). P-value of urea and creatinine (0.038, 0.003) respectively.

Table 4 Urea and creatinine levels of individuals HIV positive HAART NAÏVE and HIV negative

Groups	Urea(mmol/l)	Creatinine (mmol/l)
HIV positive HAART NAÏVE individuals N=20	4.96±5.03	171.21±86.47
HIV negative individuals N=25	2.78±0.61	117.68±30.28
P-value	0.035*	0.003*

*= Significant value

4. Discussion

Human immunodeficiency Virus (HIV) affect the human immune system and can result to Acquired immunodeficiency syndrome (AIDS) if not properly managed making the patients immunocompromised thereby inhibiting or lowering the ability of the immune system to defend the body from other infections, diseases and may even cause death [1-2]. Highly active antiretroviral therapy (HAART) is a drug or therapy which inhibits the actions of virus on its carriers and is used to improve life expectancy in HIV-infected subjects [10, 12]. Renal disease is a common complication of HIV infection; creatinine and urea are markers for kidney function tests; analysis of these analytes gives the information about the kidney to know the extent at which the virus or the drug has affected the patient's kidney [24]. The result in this study(table 1) shows that the Urea level of HIV positive HAART Naive individuals was significantly increase to compare with HIV positive individuals on HAART as well as HIV negative individuals. This was attributed to the action of the viral cell on the kidney showing that HAART protect the effect of the virus on Urea level. Also the creatinine level of HIV positive HAART Naïve individuals was highly increase to compare with HIV negative and HIV positive individuals on HAART which was almost the same value. This could also be attributed to the ameliorative effect of HAART on those individuals. These findings were in line with the work by Scialla *et al* [25] who correlated viral load, decreasing CD4 cells count and occurrence of renal failure and stated that administration of HAART suppresses viral load and returns renal function to normal at a close proximity. Again a previous study in Zambia [26] reported that individuals living with HIV on HAART had better kidney function when compared to HIV positive HAART naïve subjects.

Table 2 of this study shows a non-significant difference ($p > 0.05$) in the creatinine and urea level of HIV positive individual on HAART and HIV negative individuals. This was attributed to the action of the antiretroviral drugs which the patients were placed on that halted the viral actions on the kidney. This work agrees with a previous study [27] which stated that renal failure associated with HAART is rare; also the values gotten from this study were within normal biochemical range.

Furthermore this study compared the creatinine and urea levels between HIV positive HAART naïve subjects and HIV positive individuals on HAART. The result presented in table 3 shows a significant increase ($P = 0.003$) in creatinine level and also increase in urea level though not statistical significant ($P = 0.085$). This finding in table 3 is in line with previous studies by [2, 26] showing the ameliorative effect of HAART on the kidney of those subjects placed on HAART.

Again table 4 of this study compared the levels of creatinine and urea between HIV positive HAART naïve individuals and HIV negative individuals. There was a significant increase in urea ($P = 0.035$) and creatinine ($P = 0.003$) in the two groups. The increase in urea and creatinine found in the HIV positive HAART naïve individuals could be as a result of the actions of the virus inhibiting the biological functions of the kidney since the subjects were not on any drug or therapy to protect the kidney. This finding is in agreement with the previous studies by [15, 17, 28] that reported increases in kidney diseases among subjects with HIV infections.

5. Conclusion

This study observed that there is significant increase in creatinine and urea levels of HIV positive HAART Naïve subjects when compared to those on HAART and HIV negative subjects.

The study also shows that there is no significant different in the creatinine and urea levels of HIV positive subjects on HAART and HIV negative individuals.

The study concludes that HAART significantly improves kidney functionality on HIV positive subjects and ameliorate the effects of the virus on the nephron of the kidney.

Compliance with ethical standards

Acknowledgments

The authors wish to appreciate all the participants and everyone who contributed in any way to the success of this research work.

Disclosure of conflict of interest

The authors declare no conflict of interest, financial or otherwise.

Statement of ethical approval

Ethical approval was duly obtained from the college of medicine research ethics committee of University of Nigeria Enugu Campus, Enugu State (Protocol No: 0136/11/2021).

Statement of informed consent

Informed consent was obtained from all participants in this study before commencement.

References

[1] Kasembeli A. N., Duarte R., Ramsay M and Naicker S. African origins and Chronic kidney Disease susceptibility in the Human Immunodeficiency virus Era. *World Journal of Nephrology*. 2015; 4: 295-306

[2] Daniel Yilma., Alemseged Abdissa., Pernille Kaestel., Markos Tesfaye., Mette F. Olsen., Tsinuel Girma., Christian Ritz., Henrik Friis., Ase B. Andersen., Ole Kirk. Serum creatinine and estimated glomerular filtration rates in HIV positive and negative adults in Ethiopia. PLOS One. 2019; 14(2): e0211630 doi: 10.1371/journal.pone 0211630 PMCID: PMC 6372225/PMID: 30753190

[3] World Health Organization. HIV/AIDS Factsheet". Home/Newsroom/Fact sheets/Detail/HIV. 2021.

[4] Ann P. A Comprehensive Guide to HIV and AIDS. *American Journal of Medical Sciences*. 2021; 4(1): 13-17

[5] Kapila, A., Chaudhary, S., Sharma, R. B., Vashist, H., Sisodia, S. S., & Gupta, A. A review on: Hiv aids. *Indian Journal of Pharmaceutical and Biological Research.* 2016; 4(3), 69-73.

[6] Ariën, K. K., Abraha, A., Quinones-Mateu, M. E., Kestens, L., Vanham, G., & Arts, E. J. The replicative fitness of primary human immunodeficiency virus type 1 (HIV-1) group M, HIV-1 group O, and HIV-2 isolates. *Journal of virology*. 2005; 79(14), 8979-8990.

[7] Adam F. Explaining HIV and AIDS. *American Journal of Medical Sciences*. 2020; 1(1):11- 14

[8] Kester D. A., Ray O. G., Samson E. S. and Harrison E. O. Effects of Highly Active Antiretroviral Therapy (HAART) on some Serum Micronutrients and Electrolytes Levels in HIV Infected Patients in Southern Nigeria. *Biomedical Journal.* 2018; 3(1):1, 9.

[9] National AIDS Control Organization . Antiretroviral therapy guideline for HIV-Infected adult and adolescence. Ministry of health and family welfare, government of India. *Biomedical Journal*. 2013; 1(2): 3- 6

[10] Mark C. "How HAART (Highly Active Antiretroviral Therapy) Works". The Triple Therapy That Turned the HIV Epidemic Around*. Journal of medical science*. 2022; 3 (1): 6-8

[11] Abdulazeez A.. Frequency of human immunodeficiency virus infection among students of tertiary and secondary institutions in an endemic state. *American Journal of Medical Sciences*. 2012; 4(4): 170-173.

[12] Thompson M. A., Aberg J. A., Hoy J. F., Telenti A., Benson C., Cahn P., & Volberding P. A. Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society–USA panel. *Jama*. 2012; 308(4): 387-402.

[13] Tseng A., Seet J. and Phillips E. J.. The evolution of three decades of antiretroviral therapy: challenges, triumphs and the promise of the future. *British Journal Clinical Pharmacology*. 2015; 79(2):182-94.

[14] Walensky R. P., Wolf L. L., Wood R., Fofana M. O., Freedberg K. A., Martinson N. A., Paltiel A. D., Anglaret X., Weinstein M. C. and Losina E. When to Start Antiretroviral Therapy in Resource-Limited Settings. Annual Internal Medicine. 2009; 151: 157-166.

[15] Naicker S., Rahmanian S., Kopp J B. HIV and chronic kidney disease. Clinical Nephrology. 2015; 83: S32-38 [PMC free article] [PubMed] [Google Scholar]

[16] Ifeoma Chinwe Ikegwuonu., Chibueze Joseph Obi-george., Adanna Perpetua Ikebudu., Patrick Tobenna Ikegwuonu., Sylvester Ogbonna Ogbodo., Chika Betina Mba and Ifeanyi Emmanuel Arinze. Correlative study on the effect of toxic paint chemicals on the hepatorenal of paint factory workers in Enugu, Nigeria. *World Journal of Advanced Research and Reviews.* 2022;15(02): 432-439

[17] Cristelli MP., Cofan F., Rico N., *et al.* Estimation of renal function by CKD-EPI versus MDRD in a cohort of HIV-infected patients: a cross-sectional analysis. BMC Nephrol 2017; 18: 01-7. [PMC free article] [PubMed] [Google Scholar]

[18] Perrone R.D., Madias N.E. and Levey A.S. Serum creatinine as an index of renal function: New insights into old concepts. Clinical chemistry. 1912; 38: 1933-1953 [PubMed] [Google Scholar]

[19] Khan, K. U., Khan, A. H., Sulaiman, S. A., Soo, C. T., & Aftab, R. A. Adverse Effect of Highly Active Anti-Retroviral Therapy (HAART) in HIV/AIDS Patients. *Indian Journal of Pharmacy Practice.* 2014; 7(3).

[20] Oscar Antonio Garza Tovar., Alberto Alejandro Miranda Perez., Maria Elena Gutienez Perez., Ivonne Urraza Robledo., Faviel F., Gonzalez Galarza and Francisco Carlos Lopez Marquez. Serum electrolytes and renal alterations in HIV-seropositive Mexican subjects. Medicine (Baltimore) 2021 May 21; 100(20): e 26016. doi: 10.1097/MD.0000000000026016 PMCID: PMC8137016/PMID: 34011103

[21] Salifu M. O. and Misra N.. HIV-Associated Nephropathy. *Medical Scape.* 2015; 3(2):23- 44

[22] Narsh N.H., Fringerhunt B., Millar A. Automated and manual direct method for determination of urea. Clin Chem. 1965, 11, 624-627.

[23] Mitchell R.J. Improved method for specific Determination of creatinine in serum and urine. Clin Chem. 1973, 19(4), 408-410.

[24] Obirikorang C., Osakunor DNM., Ntaadu B., Adarkwa OK. Renal function in Ghanaian HIV-infected patients on Highly Active Antiretroviral Therapy: A case-control study. PLoS ONE. 2014; 9(6): e 99469. doi: 10.1371/journal.prone.0099469

[25] Scialla, J. J., Atta, M. G., & Fine, D. M. Relapse of HIV-associated nephropathy after discontinuing highly active antiretroviral therapy. *Aids.* 2007; 21(2): 263-264.

[26] Pry JM., Vinikoor MJ., Bolton Moore C., Roy M., Mody A., Sikazwe I et al. Evaluation of kidney function among people living with HIV initiating antiretroviral therapy in Zambia. *PLoS Glob Public Health*. 2022;2(4): e0000124. doi: 10.1371/journal.pgph.0000124

[27] Celestine, U. A., Christopher, G. B., & Innocent, O. O. Phytochemical profile of stem bark extracts of Khaya senegalensis by Gas Chromatography-Mass Spectrometry (GC-MS) analysis. *Journal of Pharmacognosy and Phytotherapy.* 2017; 9(3): 35-43.

[28] Cohen SD., Kopp JB., Kimmel PL. Kidney diseases associated with human immunodeficiency virus infection. *Northern England Journal of Medicine*. 2017; 377: 2363-2374 [PubMed] [Google Scholar]