IOSR Journal of Environmental Science, Toxicology and Food Technology (IOSR-JESTFT)
e-ISSN: 2319-2402,p- ISSN: 2319-2399.Volume 8, Issue 7 Ver. III (July. 2014), PP 44-48
www.iosrjournals.org

Assessment of Uric Acid Level of HIV Patients on Protease Inhibitors Attending Faith Alive Foundation, Jos.

Duru BN[1*].,Gambo PP[2].,Yakunat OE[2].,Dus CA[2].,Dalyop KA[2].,Adeyanju ON[2].,Duile PT[2].,Okafor NC[2].,Nimbut LB[3].,Timothy VB[3].,Ibrahim L[3].,Peter L[3].,Maxwell IK[3].,Okafor PA[3].,Plagnan AG[3].,Ukodei F[3].

[1](Dept of Chemical Pathology/Hematology, F C V M L T, Vom)
[2](Dept of ChemPath./Side Lab/Biochemistry,FCAH&PT/ CHT.Zawan/Pankshin)
[2](Dept of Virology/Haematology/Histology., F C V M L T, Vom)
[3](Div. Livestock Investigation/Viral/Bact.Vacc. Production, N V R I,Vom)
[3](Dept of ChemPath.ABU Zaria/University of Jos/Medical College FCE (T)Umunze)
Corresponding Author: Duru Boniface Nnamdi, email: aefuleforu@ymail.com Phone: +2348035873744.
Department of Chemical Pathology, F C V M L T, PMB 02, Vom. Postcode = 930010. Nigeria.

Abstract: *The effect of protease inhibitor used in treatment of HIV patients leading to abnormally increased Uric acid level was the focus of this research.100 HIV positive patient on Medication (protease inhibitor) and 100 HIV positive patients not on Medication (control) was investigated for Uric acid levels using Fortress Reagent Kit. The mean Uric acid level of HIV Patients on medication was 385.16mmol/l in males and 381.06mmol/l in females respectively, while mean Uric acid level of HIV Patients not on medication was 336.27mmol/l and 321.6mmol/l for male and female controls respectively. Comparism of mean Uric acid levels of HIV Patients on Medication with those not on Medication (control) was statistically significant ($p<0.05$). Comparism of mean Uric acid of male and female HIV Patients on Medication with corresponding male and female HIV Patients not on medication was statistically significant ($p<0.05$). However comparism between age groups of male and female on medication was not statistically significant ($p>0.05$). Comparism between age groups within male and female not on medication was not statistically significant ($p>0.05$).Conclusion was that uric acid level be monitored in HIV patients on medication (protease inhibitor) as treatment progresses since high uric acid level has been associated with gout as well as kidney stone formation.*

Keywords: *Protease Inhibitors, Uric acid, Monitoring, Gout, Kidney stone* **.**

I. Introduction

Human immunodeficiency virus (HIV) is a retrovirus figure1 that can lead to acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infection [1]. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate or breast milk. Within these body fluids, HIV is present as both free virus particles and virus within infected immune cells. The four major route of transmission are unprotected sexual intercourse, contaminated needle, breast milk, and transmission from an infected mother to baby at birth[1].

HIV primarily infects vital organs in the human immune system such as helper T-cells (specifically CD4+ T cells), macrophages and dendritic cells. HIV infection leads to low levels of CD4 cell through three main mechanisms: Firstly, direct viral killing of infected cells: secondly, increased rates of apoptosis in infected cells: and thirdly, killing of infected CD4 + T cell by CD8 cytotoxic lymphocytes that recognized infected cells. When CD4+ T cells numbers decline below a critical level, cell mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections [2]. If untreated, eventually most HIV-infected individual develop AIDS (Acquired Immunodeficiency Syndrome) and die; however, about one in ten remains healthy for many years with no noticeable symptoms.

A protease (also termed peptidase or proteinase) is any enzyme that performs proteolysis, that is, begins protein catabolism by hydrolysis of the peptide bonds that link amino acids together in the polypeptide chain forming the protein figure2. Proteases have evolved multiple times, and different classes of protease can perform the same reaction by completely different catalytic mechanisms. Proteases can be found in animals, plants, bacteria, archea and viruses [3].

Protease inhibitors (PIs) are a class of medications used to treat or prevent infection by viruses, including HIV and Hepatitis C. Protease inhibitor prevents viral replication by inhibiting the activity of HIV protease, an enzyme used by the viruses to cleave nascent proteins for final assembly of new virons. When the PIs bind to the enzyme, the new viruses still leave the cell, but they are unable to infect other cells. [4][5][6].

Most protease inhibitors are metabolised by the liver and can therefore interact with a number of other drug [7]. Protease inhibitors can cause a syndrome of Lypodystrophy, hyperlipideamia, diabetes mellitus type 2, and kidney stones figure3 [8].

Numerous drugs affect uric acid by competing with it for excretion by the kidneys, including many taken by people living with HIV. Kidney deficiency in people with HIV is commonly the result of toxicities associated with drugs such as Foscarnet (Foscavir) [9].

A high prevalence of hyper uricaemia was identified in a prospective analysis of urate levels in 2287 visits made by a cohort of 270 HIV-positive patients. In univariate and multivariate analysis, hyperuricaemia was associated with factors previously identified in HIV-uninfected individuals, but also with the use of some anti retroviral drugs, particularly with the use of stavudine [9].

1.1 Justification

Kidney deficiency in HIV patients may be caused by kidney stone formation due to abnormally high concentration of uric acid which remained uninvestigated and undiagnosed as a side effect of anti-retroviral drugs including protease inhibitors needs to be continually evaluated; hence this present study assesses the effect of protease inhibitors on uric acid profile of HIV patients.

1.2 Aims And Objectives.

1. To measure uric acid levels of HIV patients on antiretroviral medication (protease inhibitor) and those not on the medication (control).
3. To compare the levels of uric acid in HIVpatients on antiretroviral medications (protease inhibitor) and control.

II. Materials And Method

2.1 Subject selection/sample collection/ Analysis

The subjects for the research work are 100 HIV positive patients on medication (protease inhibitor) and 100 HIV positive patients without medication within the age group 20-60, all gotten from Faith Alive Foundation, Jos. The cubital foci of each of the patients were sterilized with cotton wool soaked in methylated spirit, 2 ml of venous blood was withdrawn by vene puncture without venous stasis using a new disposable syringe and needle for each patient. Each of the samples was transferred into appropriate labeled new, clean and dry disposable blood containers. This was allowed to stand for 30 minutes for it to clot and retract. It was then centrifuged at 3000 revolutions per minute (rpm) for 5 minutes and the sera were separated. The sera samples were estimated immediately. Estimation of serum uric acid using fortress reagent kit (colorimetric method by Rice et al., 1962).

2.2 Inclusion criteria

HIV patients only
HIV patients on protease inhibitor only
HIV patients who has not developed AIDS
HIV patients on protease inhibitor from two weeks and above.
HIV patients with CD4+ count of two hundred and fifty and above

2.3 Exclusion criteria

Non HIV positive patients
HIV patients on drugs other than protease inhibitor
HIV patients who has developed AIDS
HIV patients less than two weeks on protease inhibitor
HIV patients with CD4+ count of less than two hundred and fifty

III. Discussions And Conclusion

3.1 Discussion

This study investigated the serum uric acid levels of HIV patients on medication (protease inhibitor) and those without the medication attending Faith Alive Foundation, Jos.

The mean uric acid level in the HIV patients on medication (protease inhibitor) was found to be 381.06µmol/L in the female patients while that of male was found to be 385.16 µmol/L. Mean serum uric acid levels of the control female and male was 321.64 µmol/L and 336.27 µmol/L respectively (HIV patients without medication) as shown in table 1.

Comparism of the mean uric acid level of the HIV patients on medication and those without medication was found to be statistically significant using ANOVA statistical method with $p < 0.05$ also shown on table 1.

In other to ascertain where the significant difference lies between and within test and control, a Post Hoc's Test was carried out in which multiple comparism was made which showed a significant difference lying between control female and female test ($p<0.05$) as well as between control male and male test ($p<0.05$) table 2.

Further investigations were also made to check for any other statistical significant difference in the serum uric acid levels according to their age groups (20-60) tables 3 and 4. However, there was no statistical difference ($p>0.05$).

From this project work, the mean uric acid levels of HIV patients on medication (protease inhibitor) were higher than those without medication. These findings agree with the findings of [9] [10] both defined the prevalence of metabolic abnormalities in a population of HIV-infected patients treated with highly active antiretroviral therapy (HAART) including a protease inhibitor (PI). He collected-at three time points during a three months period and assayed for fasting glucose, uric acid levels and lipid profile in a series of 110 patients (94 on HAART and 16 on double-NRTI regimens). In the HAART group he also performed sub-analysis relative to each protease inhibitor. Hyperuricemia was found only in patients with HAART (about 8.5%). In two cases hyperuricemia was related to podagral crisis. His preliminary results point to protease inhibitors as a cause of elevated uric acid [9].

Also this study observed that the mean uric acid levels in test male(385.160) was higher than that of test female(381.06) and this was found to be in line with the findings of [9]. In his statistical analysis he observed that women had lower urate [0.64XULN (SD, 0.19)] than men [0.84XULN (SD, 0.21)] ($P < 0.001$). Urate was ≥ ULN at 37 of 895 visits (4.1%) for women and at 286 of 1392 visits (20.5%) in men ($P < 0.001$).

Furthermore, from tables 3 and 4 it was observed that as the age increases there was an increase in the mean uric acid levels and this findings agrees with the work of [11] who observed that serum uric acid level increases in men (male) from the age of twenty (20) and above while that of women (female) begins to rise as they reach their middle age. Also serum uric acid levels have been found to increase with age in Japanese men and women despite changes in drinking and in bmi [12].

3.2. Conclusion

Serum uric acid levels in HIV patients on medication (protease inhibitor) was found to be significantly higher than those of HIV patients not on medication.

3.3 Recommendation

We suggest the need to monitor serum uric acid levels in the HIV patients on protease inhibitor therapy so as to prevent them from developing uric acid associated diseases such as gout, Lesch-Nyhan syndrome, cardiovascular disease, kidney stone and other metabolic syndrome including diabetes.

Acknowledgement

We wish to thank Dr Chris Isichie and the entire staff and management of Faith Alive foundation for their unalloyed co-operation in granting us access to the patients and for allowing us to use their facilities without so much difficulty. It is also with great pleasure that we acknowledge Obinna, Edore and Tolu who helped in the typing and setting of the work.

Reference

[1]. Anonymous. (2006). "Protease Inhibitor; A Simple Fact Sheet from the AIDS Treatment Data Network".
[2]. Buchbinder, S.P., Katz, M.H., Hessol, N.A., O'Malley, P.M., Holmberg, S.D., (1994). "Long-term HIV-1 infection without immunologic progression." AIDS **Vol.8** No.8, pp. 1123-1128.
[3]. Dehghan, A. (2007). "High serum uric acid as a novel risk factor for type 2 diabetes mellitus".pp 61-76
[4]. FDA (Food and Drug Administration), (2006). Grants Fast Track "Hostile takeovers: viral appropriation of the NF-kappaB pathway". Designation To Oral HCV Protease Inhibitor SCH 503034.
[5]. Fantry, LE (2003). "Protease inhibitor-associated diabetes mellitus: A potential cause of morbidity and mortality". Journal of acquired immune deficiency syndromes (1999) **32** (3): 243–4. PMID 12626882.
[6]. Hézode C (2012) Boceprevir and telaprevir for the treatment of chronic hepatitis C: safety management in clinical practice. Liver International 32: 32-38.
[7]. James, D.S. (2005). Test Positive Aware Network. The Protease Inhibitor Drug. Curr. Opin. Infect. Dis Vol.**3** No.8, pp. 314-326.
[8]. Kuzuya M, Ando F, Iguchi A, Shimokata H(2002) Effect of aging on serum uric acid levels: longitudinal changes in a large Japanese population group. J Gerontol A Biol Sci Med Sci.Vol. 57 No.10, pp. 660-4.
[9]. Leonard, P. J. (1973).The effect of age and sex on biochemical parameter in blood of healthy human subjects. PP 134-140.
[10]. Manfredi, R., Mastroianni, A., Coronado, O.V., Chiodo, F. (1996). "Hyperuricemia and Progression of HIV disease. J Acquired Immune Deficiency Syndrome Human Retroviral." **12**:318-319.
[11]. Rawlings ND, Barrett AJ, Bateman A (January 2010). "MEROPS: the peptidase database". Nucleic AcidsRes. **38** (Database issue): D227–33. doi:10.1093/nar/gkp971. PMC 2808883. PMID 19892822
[12]. Rice, E.W. (1962). Tietz NW, "Clinical Guide to Laboratory Test.", 3rd Edition.8:181.
[13]. Rick Sowadsky. (1999). "What is HTLV-111."? Retrieved on 2006-08-24.

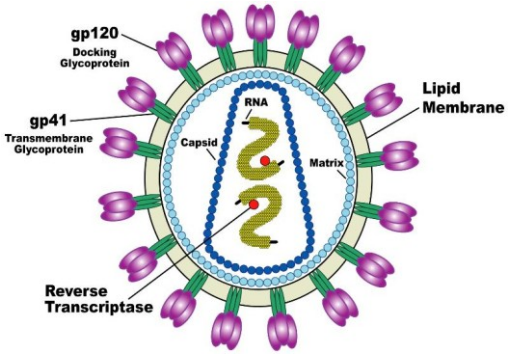

Figure 1 Diagram Of HIV **(**McGovern et al.,2002**)**

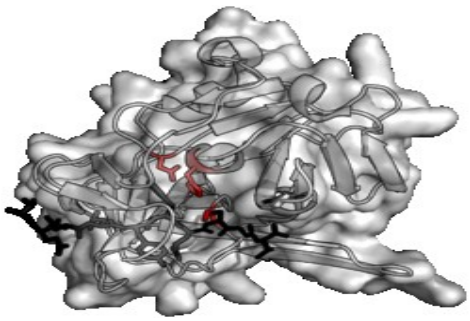

Figure 2 The structure of a protease (TEV protease) complexed with its peptide substrate in black with catalytic residues in red. PDB 1lvb

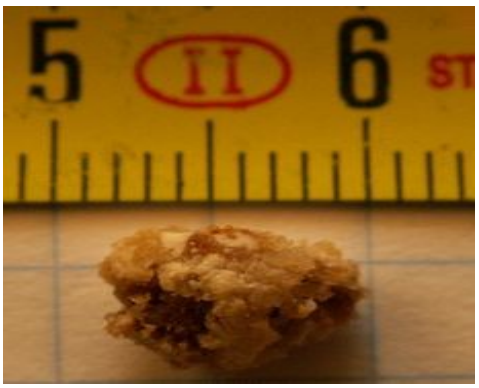

Figure 3 A formed kidney stone

IV. Results

Table 1

	N	MEAN	S/DEVIATION	P VALUE	REMARK
Control Female	78	321.64	155.751	0.037	Significant
Control Male	22	336.27	136.166		
Test Female	51	381.06	125.953		
Test Male	49	385.16	135.075		
Total	200	1424.13	552.945		

Table 1: Shows Comparison Of Uric acid Level within Sex for HIV Patients on Medication and without Medication

Table 2

		Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	Upper Bound
(I) Gender	(J) Gender					
Control Female	Control Male	-14.63	34.167	.669	-82.01	52.75
	Female (test)	-59.42	25.487	.021*	-109.68	-9.15
	Male (test)	-63.52	25.800	.015*	-114.40	12.64
Control Male	Control Female	14.63	34.167	.669	-52.75	82.01
	Female (test)	-44.79	36.102	.216	-115.98	26.41
	Male (test)	-48.89	36.323	.180	-120.52	22.74
Female (test)	Control Female	59.42	25.487	.021*	9.15	109.68
	Control male	44.79	36.102	.216	-26.41	115.98
	Male (test)	-4.10	28.312	.885	-59.94	51.73
Male test	Control female	63.52	25.800	.015*	12.64	114.40
	Control male	48.89	36.323	.180	-22.74	120.52
	Female (test)	4.10	28.312	.885	-51.73	59.94

Table 2: Shows Post Hoc's Test **(**Multiple Comparisons Dependent Variable: uric acid LSD)

Table 3

	N	MEAN	S/DEVIATION	P VALUE	REMARK
20-30	31	393.32	128.720	0.617	Not significant
31-40	35	359.46	138.260		
41-50	18	395.28	153.887		
51-60	16	401.13	77.089		
Total	100	1519.19	497.956		

Table 3: Shows Comparison of Uric acid Level of HIV Patients within Age group of Male and Female on Medication

Table 4

N	MEAN	S/DEVIATION	P VALUE	REMARK
20-30	56	310.59	141.669	0.755	Not significant
31-40	26	338.42	151.762		
41-50	15	347.27	174.242		
51-60	3	361.67	253.435		
Total	100	1357.95	721.108		

Table 4: Shows Comparison of Uric acid Level of HIV Patients within Age group of Male and Female not on Medication