International STD Research & Reviews

6(3): 1-8, 2017; Article no.ISRR.39118
ISSN: 2347-5196, NLM ID: 101666147

Nephroprotective Effect of Highly Active Antiretroviral Therapy among HIV Seropositive Individuals: A Case-Control Study in Ghana

Louis Boafo Kwantwi[1*], Christian Obirikorang[1] and Margaret Agyei Frempong[1]

[1]Department of Molecular Medicine, School of Medical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana.

Authors' contributions

Author LBK contributed to the conception of the research idea, research design, data collection, data analysis, interpretation of results, and first draft of the manuscript. Author CO contributed to the conception of the research idea, interpretation of results, and first draft of the manuscript. Author MAF contributed to data collection, design, and interpretation of results. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ISRR/2017/39118
Editor(s):
(1) Jose Eduardo Serrao, Professor, Department of General Biology, Federal University of Viçosa, Brazil.
Reviewers:
(1) K. J. Awosan, Usmanu Danfodiyo University, Sokoto, Nigeria.
(2) Helen Ifeoma Udujih, Imo State University, Nigeria.
Complete Peer review History: http://www.sciencedomain.org/review-history/22917

Original Research Article

Received 20th November 2017
Accepted 23rd January 2018
Published 30th January 2018

ABSTRACT

Background: Despite the widespread use of highly active antiretroviral therapy (HAART), renal insufficiency still exists among HIV infected individuals. This study aimed to use creatinine-based equations to determine the role of highly active antiretroviral therapy on renal function.
Methods: One hundred and ninety-two (192) HIV individuals consisting of one hundred and four (104) HIV patients on HAART and eighty-eight (88) HIV HAART naïve patients were recruited into the study. Serum creatinine, urea, CD4 count and weight were determined. Glomerular filtration rates were estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Kidney Disease (MDRD) equations.
Result: The calculated renal insufficiency (eGFR<60 ml/min /1.73 m^2) among the studied population was (7.8% for CKD-EPI and 10.9% for MDRD).The prevalence of renal insufficiency in HAART individuals was lower (1.9% for CKD-EPI and 2.9% for MDRD) than HAART naïve

**Corresponding author: Email: kwantwiboafo@yahoo.com;*

individuals (14.7% for CKD-EPI and 20.4% for MDRD).
Conclusion: The results of this study provide evidence of a significant improvement in renal function and a reduced prevalence of renal insufficiency among HIV individuals on HAART showing the importance and the effectiveness of HAART in improving renal function. Our result confirms the safety of tenofovir regimens given the fact that none of the patients on tenofovir-based regimen had renal insufficiency.

Keywords: Human immunodeficiency virus (HIV); highly active antiretroviral therapy (HAART); renal function.

1. INTRODUCTION

HIV infection is associated with numerous kidney diseases that may results from direct infection of the kidneys, from coinfections or malignancies which are commonly associated with HIV-disease, or from toxicities of medications that are used to treat HIV infection and its complications [1]. An abnormal renal function has been identified in about 30% of human immunodeficiency virus (HIV) infected patients [2], and a more recent analysis of a large urban United States (US), HIV clinic showed that approximately 15.5% of the patients had chronic or end-stage renal disease [3]. Individuals of African descent have been impacted mostly by renal disease as a complication of HIV infection with HIV-associated nephropathy (HIVAN) being the most commonly detected abnormality [4,5] but little is known about its prevalence.

In recent times there has been an increase to about 200-folds in the number of HIV patients receiving antiretroviral therapy (ART) from 197 in 2003 to over 45,000 in 2010 in Ghana [6]. Despite the increasing access to ART, renal dysfunction seems to exist in our population [7], hence there is the need to assess and monitor a plethora of kidney co-morbidities that are often present at the initiation or with the ageing of ART-treated patients. Although the highly active antiretroviral therapy has helped to curb renal dysfunction in the absence of other traditional risks factors for kidney damages, some studies have attributed renal insufficiency to be caused by medication [8] whereas others have found conflicting results [9,10] which have necessitated the assessment of the impact of highly active antiretroviral on kidney function.

Several guidelines including initial assessment to rule out kidney disease and to identify patients at risk for developing kidney disease [11] have been proposed for the management of HIV-infected patients. Glomerular filtration rate (GFR) compared to serum creatinine or 24- hour urine creatinine measurement is considered the best overall index of kidney function in health and disease because of the attendant problems associated with creatinine measurement and 24-hour urine creatinine clearance estimation [12,13]. This present study aimed to use creatinine-based equations to assess the role of HAART in resolving renal insufficiency among HIV patients on highly active antiretroviral therapy in Ghana.

2. MATERIALS AND METHODS

2.1 Study Design

This was a case control study carried out at the Antiretroviral Therapy (ART) Clinic of the Bomso Specialist hospital in the Ashanti region of Ghana from August 2015 to March 2016.

2.1.1 Study population

One hundred and ninety two (192) confirmed HIV seropositive individuals consisting of one hundred and four (104) HIV patients on highly active antiretroviral therapy (HAART) and eighty eight (88) HIV HAART naïve patients were recruited into the study. Patients who were confirmed HIV seropositive and were above 18 years were recruited into the study. Pregnant women, hypertensive, diabetic patients and patients with renal diseases were excluded from the study. All participants were placed into three groups according to the center for disease control classification which indicates the CD4 lymphocytes of patients. The groups were; CD4 counts less than 200 mm^{-3}, CD4 count between 200 and 499 mm^{-3} and the third group consisted of patients with CD4 above 500 mm^{-3}.

2.1. 2 Data collection and laboratory analysis

A well-structured questionnaire was used to obtain demographic and clinical characteristics from the patients. 4ml of venous blood was taken from each patient under sterile conditions after a tourniquet had been applied for less than a minute. 2 ml out of the blood taken were placed

in anticoagulated sequestrene tubes for CD4 and CD3 analysis using the Becton Dickenson and company haematological analyzer called the BD FACS Count from California in USA. The remaining blood was centrifuged and the serum obtained was used for the assay of creatinine, albumin and urea using an auto-analyzer known as ATAC® 8000 Random Chemistry System from USA by Elan Diagnostic System.

2.2 Data Analysis

The data were presented as median interquartile range (IQR) for all continuous variables whereas grouped variables were expressed as proportions. Comparison between HAART experienced and HAART naïve patients were carried out using Mann Whitney U test. Kruskal Wallis test was used where appropriate for comparison between more than two groups. Linear regression was also used to assess the predictive performance of creatinine, weight, CD4 count, age and albumin on GFR. A probability value less than 0.05 was considered to be statistically significant. All the analyses were done using the IBM Statistical package for social sciences (SPSS) version 20.

3. RESULT

Out of the 192 participants, there were more females than males for both the HAART experienced and the HAART naïve patients .The median age of the HAART experienced group (41 yrs) was not statistically different (p=0.203) from the HAART naïve group (40 yrs). Out of the total participants, a majority of them were junior high school graduates for both the HAART experienced (27.1%) and the HAART naive patients (19.8%) whereas trading (88.5%) was the major occupation of the studied participants [Table 1].

The median serum albumin of the HAART experienced group (40.05 g/L,) was significantly (p=0.0001) higher compared to the median albumin of the HAART naïve (34.75 g/L). The median CD4 count of the HAART experienced group (458 mm-3) was significantly (p=0.0001) higher than the HAART naïve group (229 mm-3). The HAART naïve group had a significantly (p=0.0001) higher creatinine levels (81.50 µmol/L) than the HAART experienced (62.00 µmol/L). Serum urea was also significantly (p=0.0001) higher in the HAART naïve group (3.2 mmol/L) than the HAART experienced (2.7 mmol/L). Majority of the HAART experienced patients were on Tenofovir, Lamivudine and Nevirapine (TDF+3TC+NVP) (57.7%), whereas only 5.8% were on Zidovudine, Lamivudine and Nevirapine (AZV+3TC+NVP) as shown in [Table 2].

Table 3 compares the prevalence of renal dysfunction between the HAART naïve and the HAART experienced using CKD-EPI and MDRD equations. Using the CDK-EPI equation, the

Table 1. Demographic characteristics of the study population

Parameter	HAART group(n=104)	HAART naïve(n=88)	P value
Age(yrs.)	41 (35-53)	40 (31.3-50)	0.203
Gender	N (%)		
Male	31(16.1)	27(14.1)	
Female	73(38.0)	61(31.8)	0.895
Marital status			
Married	78(40.6)	63(32.8)	
Single	21(10.9)	22(11.5)	
Widowed	1(0.5)	---------	
cohabiting	4(2.1)	3(1.6)	0.697
Educational level			
No education	17(8.9)	14(7.3)	
Primary	20(10.4)	14(7.3)	
JHS	52(27.1)	38(19.8)	
SHS	9(4.7)	17(8.9)	
Tertiary	6(3.1)	5(2.6)	0.311
Occupation			
Trading	94(49.0)	76(39.6)	
Formal	5(2.6)	4(2.1)	
Students	4(2.1)	8(4.6)	
No Job	1(0.5)	--------	0.386

JHS -junior high school, SHS-senior high school

Table 2. Biochemical parameters of the HAART group and HAART naïve group

Parameter	HIV-HAART	HIV Controls	P value
CD4 COUNT	458.00(307.50-633.75)	229.00(136.25-338.75)	0.0001
Albumin (g/L)	40.05(36.50-41.28)	34.75 (32.10-39.10)	0.0001
Urea (mmol/L)	2.70(2.30-3.20)	3.20 (2.70-4.60)	0.0001
Creatinine (μmol/L)	62.00(55.00-69.75)	81.50 (67.00-108.75)	0.0001
BMI(kg/m^2)	23.30(20.33-26.85)	22.55(19.13-26.98)	0.521
HAART regimens			
TDF+3TC+NVP	60(57.7)		
AZT+3TC+ NVP	6(5.8)		
CBV+NVP	18(17.3)		
TDF+3TC+EFV	20(19.2)		

CBV: Combivir, NVP: Nevirapine, EFV: Efavirenz, 3TC: Lamivudine, TDF: Tenofovir, AZV: Zidovudine

prevalence of renal insufficiency (eGFR<60 ml/min /1.73 m^2) was 7.8% in the studied participants. However, a high proportion (13, 14.7%) of the HAART naïve had renal insufficiency than the HAART experienced patients (2, 1.9%).There was a significantly high (p=<0.0001) number (96, 92.3%) of the HAART experienced having an increased renal function (Stage 1, eGFR≥90 ml/min /1.73 m2) than the HAART naïve (44, 50%).With the MDRD equation, the prevalence of renal insufficiency was 10.9 % in the studied participants. However, a high number (18, 20.4%) of the HAART naïve had renal insufficiency than the HAART experienced (3, 2.9%).There was a significantly high (p=<0.0001) number (92, 88.5%) of the HAART experienced patients having an increased renal function (Stage 1, eGFR≥90 ml/min /1.73 m2) than the HAART naïve (44, 50.0%).

None of the subjects on tenofivir based regimen had renal insufficiency (eGFR<60 ml/min /1.73 m^2) as compared to individuals on zidovudine based regimen which had subjects experiencing renal insufficiency as shown in [Table 4].

The median GFR values within the CD4 count categories are shown in [Table 5].With the CKD-EPI, GFR was significantly (p=<0.0001) increased with an increased in CD4 count for both the HAART experienced and the HAART naïve patients. Comparing the GFR between the HAART experienced and the HAART naïve subjects on the basis of the same CD4 category showed a significantly higher median GFR values in the HAART experienced than the HAART naïve except CD4 count category <200mm^{-3}. A similar trend was observed for the MDRD equation as shown in [Table 5].

Table 6 shows the beta and r^2 values from linear regression analysis .Creatinine showed an inverse relationship with the estimated GFR in both CKD-EPI and MDRD equations. Creatinine consistently showed a higher r^2 than the other

Table 3. Comparison of renal insufficiency among the study population

	Total(n=192)	HIV-HAART(n=104)	HIV Control (n=88)	P value
CKD-EPI				
Stage 1(eGFR>90)	147(76.6%)	96(92.3%)	51(58.0%)	<0.0001
Stage 2(eGFR 60-89)	30(5.6%)	6(5.8%)	24(27.3%)	<0.0001
Stage 3(eGFR 60-89)	14(7.3%)	2(1.9%)	12(13.6%)	<0.0001
Stage 4(eGFR 30-59)	1(0.5%)	0(0.0%)	1(1.1%)	>0.05
Stage 5(eGFR <15)	0(0.0%)	0(0.0%)	0(0.0%)	-------
Renal insufficiency	15(7.8%)	2(1.9%)	13(14.7%)	
MDRD				
Stage 1(eGFR >90)	136(70.8%)	92(88.5%)	44(50.0%)	<0.0001
Stage 2(eGFR 60-89)	35(18.2%)	9(8.7%)	26(29.5%)	<0.0001
Stage 3(eGFR 30-59)	20(10.4%)	3(2.9)	17(19.3%)	<0.0001
Stage 4(eGFR 15-29)	1(0.5%)	0(0.0%)	1(1.1%)	>0.05
Stage 5(eGFR <15)	0(0.0%)	0(0.0%)	0(0.0%)	---------
Renal insufficiency	21(10.9%)	3(2.9%)	18(20.4%)	

CKD-EPI- Chronic Kidney Disease Epidemiology Collaboration, MDRD- Modification of Diet in Kidney Disease, eGFR: estimated Glomerular Filtration Rate

Table 4. Renal function stratified by Type of HAART

	TDF+3TC+NVP	TDF+3TC+EFV	AZT+3TC+ NVP	CBV+NVP
CKD-EPI				
Stage 1 (eGFR>90)	58 (60.4%)	19(19.8%)	3(3.1%)	16(16.7%)
Stage 2(eGFR 60-89)	2(33.3%)	1(16.7%)	2(33.3%)	1(16.7%)
Stage 3(eGFR 30-59)	0(0.0%)	0(0.0%)	1(50.0%)	1(50.0%)
Stage 4(eGFR 15-29)	---	----	---	---
Stage 5(eGFR <15)	----	-----	----	---
Renal insufficiency	**-----**	**-----**	**1**	**1**
MDRD				
Stage 1(eGFR >90)	56(60.9%)	17(18.5%)	3 (3.3%)	16(17.4%)
Stage 2(eGFR 60-89)	4(44.4%)	3(33.3%)	2(22.2%)	0(0.0%)
Stage 3(eGFR 30-59)	0(0.0%)	0(0.0%)	1(33.3%)	2 (66.7%)
Stage 4(eGFR 15-29)	----	-----	-----	-----
Stage 5(eGFR <15)	----	-----	----	-----
Renal insufficiency	**-----**	**------**	**1**	**2**

CKD-EPI- Chronic Kidney Disease Epidemiology Collaboration, MDRD- Modification of Diet in Kidney Disease, eGFR: estimated Glomerular Filtration Rate. CBV: Combivir, NVP: Nevirapine, EFV: Efavirenz, 3TC: Lamivudine, TDF: Tenofovir, AZV: Zidovudine

Table 5. Median GFR levels stratified by CD4 categories using CKD-EPI and MDRD

		Median GFR		
	Total	**HIV-HAART**	**HIV Control**	**P value**
CD4 categories		**CKD-EPI**		
<200	90.50(61.75-104.00)	101.00(84.00-124.25)	80.50(57.25-102.25)	0.104
200-499	112.00(94.00-125.75)	117.00(100.50-130.50)	104.00(82.00-121.00)	0.003
<500	128.00(116.00-139.00)	132.00(118.50-139.50)	108.00(90.00-118.00)	0.002
P value	<0.0001	<0.0001	<0.0001	
CD4 categories		**MDRD**		
<200	85.00(58.00-97.00)	93.50(79.25-111.25)	74.50(54.00-96.00)	0.091
200-499	102.00(87.25-118.75)	108.00(95.00-130.50)	94.00(76.00-109.00)	0.003
<500	130.500(113.75-142.50)	133.00(121.00-144.50)	98.00(81.50-106.50)	0.001
P value	<0.0001	<0.0001	<0.0001	

CKD-EPI- Chronic Kidney Disease Epidemiology Collaboration, MDRD- Modification of Diet in Kidney Disease,

Table 6. Beta and r^2 values from linear regression of some studied variables

	Total subject		HIV HAART		HIV Control	
CKD-EPI	**BETA**	**r^2**	**BETA**	**r^2**	**BETA**	**r^2**
Age	**-0.27 ±0.17**	**0.07**	**-0.56±0.16**	**0.31**	**-0.19±0.25**	**0.03**
Weight	0.17±0.14	0.02	0.09±0.13	0.01	0.27±0.24	0.06
Creatinine	**-0.87±0.03**	**0.75**	**-0.79±0.08**	**0.61**	**-0.88±0.04**	**0.77**
Albumin	0.46±0.42	0.21	0.36±0.51	0.12	0.26±0.76	0.06
CD4	0.47±0.01	0.22	0.39±0.01	0.15	0.31±0.02	0.08
MDRD	**BETA**	**r^2**	**BETA**	**r^2**	**BETA**	**r^2**
Age	**-0.15±0.19**	**0.02**	**-0.34±0.23**	**0.11**	**-0.09±0.25**	**0.01**
Weight	0.13±0.16	0.01	0.06±0.18	0.00	0.22±.024	0.04
Creatinine	**-0.81±0.05**	**0.65**	**-0.75±0.12**	**0.55**	**-0.84±0.05**	**0.69**
Albumin	0.47±0.47	0.22	0.42±0.65	0.17	0.21±0.77	0.03
CD4	0.55±0.01	0.29	0.51±0.01	0.25	0.29±0.02	0.08

variables. Age also showed an inverse relationship with the estimated GRF in both equations. CD4, weight and albumin had a positive relationship with GFR in both equations.

4. DISCUSSION

In this study, we found that majority (76.6%) of the subjects to had normal renal function or

increased renal function using the CKD-EPI equation. This is similar to reports by [7] (75.7%) and (61.1%) by [14] .We also found a significant number of the HAART experienced individuals to had normal renal function and a minimal damage in renal function compared to HAART naïve patients. A study in Uganda by [15] reported improvement in renal function in HIV infected individuals after the initiation of HAART. An earlier retrospective study by [16] have also reported higher prevalence of renal insufficiency in HAART naïve individuals (44%) than individuals on HAART (15%). Although these studies did not include tenofivir based regimen, a study conducted by [17] in Zimbabwe and Uganda reported improvement in renal function regardless of HAART type including tenofivir based regimen [16-18] This highlights the effectiveness of HAART in maintaining the kidney in health like state thereby improving it function. Hence, in the face of conflicting reports on the utility of HAART in improving renal function, the findings of this study provide evidence of the safety of HAART in curbing renal insufficiency. A meta-analysis conducted by [18] found tenofovir to be associated with a significant, though clinically-modest, loss of renal function. Notably, none of the studies included in the meta-analysis was conducted in sub-Saharan Africa. Although other studies conducted to assess the safety of tenofovir in sub- Saharan Africa have yielded conflicting reports, leading to concerns about utilization of tenofovir in resource-limited settings [19-21], our result confirms the safety of tenofovir regimens, given the fact that none of the patients on tenofovir based regimen had renal insufficiency. The result of our study also supports the recommendation of the World Health Organization on the utility of tenofivir as first line ART regimen [22].

In this study, the prevalence of renal insufficiency stage 3 in the HAART experienced individuals was significantly lower (CKD-EPI 1.9% and MDRD 2.9%) than in the HAART naïve individuals (CKD-EPI 13.6% and MDRD 19.3%). Also the calculated renal insufficiency (eGFR<60 ml/min /1.73 m^2) in the HAART naïve was higher (CKD-EPI 14.7% and MDRD 20.4%) than those on HAART (CKD-EPI 1.9% and MDRD 2.9%). In a related study, renal insufficiency in an antiretroviral (ARV) naive Kenyan population, [23] was 11.5% and 4.8% (CrCl, 60 ml/min/1.73 m^2 and, 50 ml/min/ 1.73 m^2 respectively). A recent study among HAART naive individuals reported 14.7% renal insufficiency [24] which was similar to our study which reported 14.7%. This is an indication that chronic kidney diseases still exist in our population especially among patients who are HAART naïve.

In the quest to identify predictors of GFR among our study population, aging was associated with a decline in GFR in both equations. This is in line with earlier reports by [7,25]. This can be explained by the lower muscle mass in older persons which causes lower urine creatinine excretion because of the lower serum creatinine concentration. We found a significant increase in CD4 count to be associated with an increase in GFR in both the HAART experienced and the HAART naïve individuals. However, among individuals of the same CD4 category, the HAART experienced had a higher GFR values than the HAART naïve individuals. This can be attributed to the fact that, HAART in an attempts to bring down viral loads and increase CD4 counts, leads to a decrease in the rate of damage caused by HIV infection [26].Creatinine was found to be the best predictor of GFR among the studied variables.

5. CONCLUSION

The study has shown a significant improvement in renal function among HAART experienced individuals compared to HAART naïve individuals thus highlighting the effectiveness of HAART in reducing the prevalence of renal insufficiency among individuals placed on HAART. Our result confirms the safety of tenofovir regimens given the fact that none of the patients on tenofivir based regimen had renal insufficiency.

CONSENT

Participation was voluntary and written informed consent was obtained from each participant according to Helsinki declaration.

ETHICAL APPROVAL

Ethical approval was sought from the management of Bomso specialist Hospital and the committee on human research and publication of the School of Medical Science, Kwame Nkrumah University of Science and Technology (KNUST). Participation was voluntary and written informed consent was obtained from each participant according to Helsinki declaration. Respondents were assured that the information gathered was to be used strictly for research and academic purpose only. In addition, respondents were given the freedom

to opt out any time they thought they couldn't continue with the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Marras D, Bruggeman LA, Gao F, Tanji N, Mansukhani MM, Cara A, Ross MD, Gusella GL, Benson G, D'Agati VD. Replication and compartmentalization of HIV-1 in kidney epithelium of patients with HIV-associated nephropathy. Nature Medicine. 2002;8(5):522-526.
2. Szczech LA, Gange SJ, Van Der Horst C, Bartlett JA, Young M, Cohen MH, Anastos K, Klassen PS, Svetkey LP. Predictors of proteinuria and renal failure among women with HIV infection. Kidney International. 2002;61(1):195-202.
3. Wyatt CM, Winston JA, Malvestutto CD, Fishbein DA, Barash I, Cohen AJ, Klotman ME, Klotman PE. Chronic kidney disease in HIV infection: an urban epidemic. Aids. 2007;21(15):2101-2103.
4. Kimmel PL, Barisoni L, Kopp JB. Pathogenesis and treatment of HIV-associated renal diseases: lessons from clinical and animal studies, molecular pathologic correlations, and genetic investigations. Annals of Internal Medicine. 2003;139(3):214-226.
5. Laradi A, Mallet A, Beaufils H, Allouache M, Martinez F. HIV-associated nephropathy: outcome and prognosis factors. Groupe d'Etudes Néphrologiques d'Ile de France. Journal of the American Society of Nephrology. 1998;9(12):2327-2335.
6. Obirikorang C, Selleh PK, Abledu JK, Fofie CO. Predictors of adherence to antiretroviral therapy among HIV/AIDS patients in the upper west region of Ghana. Isrn Aids; 2013.
7. Owiredu W, Quaye L, Amidu N, Addai-Mensah O. Renal insufficiency in Ghanaian HIV infected patients: need for dose adjustment. African Health Sciences. 2013;13(1):101-111.
8. Crum-Cianflone N, Ganesan A, Teneza-Mora N, Riddle M, Medina S, Barahona I, Brodine S. Prevalence and factors associated with renal dysfunction among HIV-infected patients. AIDS patient care and STDs. 2010;24(6):353-360.
9. Gallant JE, Parish MA, Keruly JC, Moore RD. Changes in renal function associated with tenofovir disoproxil fumarate treatment, compared with nucleoside reverse-transcriptase inhibitor treatment. Clinical Infectious Diseases. 2005;40(8):1194-1198.
10. Jones R, Stebbing J, Nelson M, Moyle G, Bower M, Mandalia S, Gazzard B. Renal dysfunction with tenofovir disoproxil fumarate-containing highly active antiretroviral therapy regimens is not observed more frequently: a cohort and case-control study. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2004;37(4):1489-1495.
11. Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, Tashima KT, Roland M, Franceschini N, Palella FJ. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clinical Infectious Diseases. 2005;40(11):1559-1585.
12. Kopple JD. National kidney foundation K/DOQI clinical practice guidelines for nutrition in chronic renal failure. American Journal of Kidney Diseases. 2001;37(1):S66-S70.
13. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. *New England* Journal of Medicine. 2006;354(23):2473-2483.
14. 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):e99469.
15. Peters PJ, Moore DM, Mermin J, Brooks JT, Downing R, Were W, Kigozi A, Buchacz K, Weidle PJ. Antiretroviral therapy improves renal function among HIV-infected Ugandans. Kidney International. 2008;74(7):925-929.
16. Sarfo FS, Keegan R, Appiah L, Shakoor S, Phillips R, Norman B, Hardy Y, Bedu-Addo G, Longstaff L, Chadwick DR. High prevalence of renal dysfunction and association with risk of death amongst HIV-infected Ghanaians. Journal of Infection. 2013;67(1):43-50.

17. Reid A, Stohr W, Walker AS, Williams IG, Kityo C, Hughes P, Kambugu A, Gilks CF, Mugyenyi P, Munderi P et al. Severe renal dysfunction and risk factors associated with renal impairment in HIV-infected adults in Africa initiating antiretroviral therapy. Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America. 2008;46(8):1271-1281.
18. Cooper RD, Wiebe N, Smith N, Keiser P, Naicker S, Tonelli M. Systematic review and meta-analysis: renal safety of tenofovir disoproxil fumarate in HIV-infected patients. Clinical Infectious Diseases. 2010;51(5):496-505.
19. Chi BH, Mwango A, Giganti MJ, Sikazwe I, Moyo C, Schuttner L, Mulenga LB, Bolton-Moore C, Chintu NT, Sheneberger R. Comparative outcomes of tenofovir-and zidovudine-based antiretroviral therapy regimens in Lusaka, Zambia. Journal of Acquired Immune Deficiency Syndromes. 1999;2011:58(5):475.
20. Bygrave H, Kranzer K, Hilderbrand K, Jouquet G, Goemaere E, Vlahakis N, Trivino L, Makakole L, Ford N. Renal safety of a tenofovir-containing first line regimen: experience from an antiretroviral cohort in rural Lesotho. PLoS One. 2011;6(3):e17609.
21. De Beaudrap P, Diallo MB, Landman R, Gueye NF, Ndiaye I, Diouf A, Kane CT, Etard J-F, Girard PM, Sow PS. Changes in the renal function after tenofovir-containing antiretroviral therapy initiation in a Senegalese cohort (ANRS 1215). AIDS Research and Human Retroviruses. 2010;26(11):1221-1227.
22. WHO: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection; 2013.
23. Wools-Kaloustian K, Gupta SK, Muloma E, Owino-Ong'or W, Sidle J, Aubrey RW, Shen J, Kipruto K, Zwickl BE, Goldman M. Renal disease in an antiretroviral-naive HIV-infected outpatient population in Western Kenya. Nephrology Dialysis Transplantation. 2007;22(8):2208-2212.
24. Denue BA, Ndahi A, Alkali MB, Shehu DJ, Ekong E. Correlates of Impaired Renal Function in Highly Active Antiretroviral Therapy (HAART) Naive HIV Infected Patients in Maiduguri, Nigeria. Global Journal of Medical Research. 2012;12(8).
25. Heymsfield SB, Arteaga C, McManus C, Smith J, Moffitt S. Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. The American Journal of Clinical Nutrition. 1983;37(3): 478-494.
26. Okuonghae P, Olisekodiaka M, Onuegbu J, Amara A, Aberare L, Mukoro N, Dirisu J, Okwuokenye J, Ezenwa E, Nigeria C. Evaluation of renal function in HIV patients on antiretroviral therapy. Adv Lab Med Int. 2011;1:25-31.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/22917