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Assessment of the Effects of Antiretroviral Medications on Kidney Status in Rwanda

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Abstract

According to the previous research, ART over different durations of time has an effect on the nephron as well as on liver hepatoxicity by inducing toxicity. Renal dysfunction by ART has been associated primarily with tenofovir disoproxil, which is actively accumulated in the proximal renal tubule. CKD is the major problem in ART patients and can lead to loss of kidney function, leading to complications and kidney failure, and development of cardiovascular disease.

The main objectives of this study was to assess the effect of antiretroviral drugs on kidney function among the patients attended Nyanza DH during the period of two years. The research is retrospective study done to identify the effect of antiretroviral drugs on kidney Status in Nyanza DH. In total, 755 patients received the antiretroviral medications in Nyanza DH during a period of two years from the 1st of January 2015 to the 31st of December 2017. However 98 patients had data complying with the objective of this study. Those patients with kidney tests conducted every 6months, with elevated CD4 count, and eliminated viral charge. Furthermore nephrotoxicity incidence was considered for both higher concentration of Serum creatinine and lower creatinine Clearance.

The results showed that among 98 patients, 24.4% had kidney dysfunction characterized by elevated serum creatinine level at the beginning of treatment. After 6, 12 and 18 months of treatment the percentages of patients with elevated serum creatinine increased to 41.8%, 48.9 % and 50% respectively. It was found that the severity of the problem depends on: combinations the patient is taking, duration of exposure, and other medications the patient is using in combination. In this context it was found that 96.7% of patients that developed nephrotoxicity after 18months were using TDF .The results showed a higher frequency of nephrotoxicity in the population of the study. Therefore, a systematic kidney function monitoring from the beginning of the treatment should be of a great importance, those test could help to take appropriate measures.

Keywords: Antiretroviral Medications; Kidney; Nephrotoxicity

Abbreviations: AIDS: Acquired Immunodeficiency Syndrome; AKI: Acute Kidney Injury; ART: Antiretroviral Treatment; Arvs: Antiretroviral; CD4: Cluster of Differentiation 4; CKD: Chronic Kidney Disease; DH: District Hospital; GFR: Glomerular Filtration Ratio; HAART: Highly-Active Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; HIVAN: HIV-Associated with Nephropathy; IHDPC: Institute of HIV/AIDS Disease Prevention and Control; MOH:

Ministries of Health; NASCOP: National AIDS and STI Control Programme; Nnrtis: Non-Nucleoside Reverse Tranacriptase Inhibitors; STI: Sexually Transmitted Infections; UNAIDS: The Joint United Nations Programme on HIV and AIDS; WHO: World Health Organization.

Introduction

HIV infection is globally a public health issue. According to estimates, in 2012, 35.3 million people were living with HIV worldwide, including 25 million in sub-Saharan Africa. An overall increase is recorded compared to previous years due to the increase in the number of people on antiretroviral therapy [1]. HIV spares no organ: the digestive tract, brain, lungs, and kidneys. HIV infection is the third leading cause of kidney failure among Blacks American from 20 to 64 years [2]. In the United States, in 2007, the annual incidence of chronic kidney disease in the population infected with HIV was estimated at 9.7/100 patient-years; six times higher than. that observed in the non-infected with HIV population [3]. In France, the prevalence of kidney failure in a cohort study of 7378 patients with HIV was 4.7%, [4]. In a London-based retrospective analysis of HIV patients, nearly 6% of patients developed acute renal failure (ARF). CD4 nadir and AIDS diagnosis were associated with ARF in the first three months of antiretroviral therapy and there were over 19 episodes per 100 person-years. After three months of therapy, just one episode of ARF was found per 100 person-years and this was associated with CD4 nadir, injection drug use, and hepatitis C co-infection. In this population, ARF was associated with advanced immunodeficiency and incidence decreased remarkably after receiving antiretroviral therapy [5].

In Africa, on the contrary, this prevalence is four times higher than in developed countries [3]. Particular genetic susceptibility to the development of HIV-Associated with Nephropathy (HIVAN) is now clearly established in the black race [3]. The HIVAN is the leading cause of kidney failure in African HIV [2]. Benin is a country in West Africa which has 9. 983 884 million inhabitants according to the results of the last census in 2013. The prevalence of HIV infection in 2013 in the general population was estimated at 1.1% [1]. It is a low prevalence country. According to national standards and procedures for the management of HIV infection in Benin, the detection of kidney disease in people with HIV is necessary at the initiation of antiretroviral treatment followed by regular biannual control [6]. This directive is not always respected for various reasons, as is probably the case in many developing countries, In Zambia, nearly 33% of the 26,000 persons initiating antiretroviral therapy between 2004 and 2007 in Zambia had renal disease at baseline. Rwanda has had a sustained general adult HIV prevalence of 3.0% countrywide and 7.0% in the capital city Kigali over the last 10 years [7]. However, the HIV prevalence is much higher in vulnerable populations. The 2007/2008 Kigali HIV Incidence Study (KHIS) found an HIV prevalence of 24% in female sex workers and 13% in female clients of HIV counseling and testing (HCT) sites [8]. The adjusted hazard ratio for mortality (adjusted by baseline CD4 count, WHO HIV stage, hemoglobin, and adherence) in those with mild and moderate disease was twice that of those individuals without renal disease at baseline. Patients with severe renal disease at baseline had a fivefold increased risk of mortality as compared to those without renal disease. This points to the need to include simple screening and treatment algorithms for renal disease in antiretroviral treatment programmes, particularly in settings where tenofovir use is widespread [9].

15.8 million people had access to highly active antiretroviral therapy (HAART) based on a 2015 report [10].The primary goal of HAART is maximal and durable suppression of viral load, preservation and restoration of immunologic function, improvement of quality of life, and reduction of HIV-related morbidity and mortality [11]. HAART over different durations of time has an effect on the nephron by inducing toxicity [12]. Renal dysfunction by HAART has been associated primarily with tenofovir disoproxil fumarate, which is actively accumulated in the proximal renal tubule [13].

CKD is the major problem in HAART patients and can lead to loss of kidney function, leading to complications and kidney failure, and development of cardiovascular disease [14]. In studies conducted in Nigeria and Burundi with CKD prevalence of 47.6% and 45.7% among HIV patients, respectively [15]. HIV prevalence in adult population aged from 15- 49 years is 3% estimated at 206,000 people living with HIV, about 125,000 people who are HIV positive are effectively taking antiretroviral medications [16]. During my internship at Nyanza DH the results of serum creatinine show that among their patient under ARVs some of them show kidney disfunction especially those who were using TDF, Although those patients face those challenges there is no research done to monitor the frequency of nephrotoxicity among patients under ARVs in Rwanda.

Methodology

The main focus of this study was assessment of the effect of ARVs medications on kidney status amongst patients attended Nyanza District hospital from January 2015 to December 2017. To achieve specific objectives, patient demographical data(ages and sex of the patients) were required, Medical information (antiretroviral medication the patient is using and other medications the patient is taking in combination with ARVs medications), patients renal clearances before and after 6 months, 12 months and 18months of medications and their serum creatinine

respectively were collected. Those data were recorded from patient's medical files available in the records department using a simple data collection sheet provided in annex at page A,B,C and D.

Study Area

The study was conducted at Nyanza DH, it is a district hospital located in Busasamana sector in Nyanza District.

Study Design

This is a retrospective study done to investigate among patients attended Nyanza DH on ARVs medication, Medical records of patients of all ages attended Nyanza DH under ARVs medications between 1st January 2015 and 31st December 2017 was useful.

Target Population and Study Population

The target population of this study involved HIV positive patients attended Nyanza DH between 1st January 2015 and 31st December 2017.

Limit of the Study

The study was composed by all patients with ARVs medications in Nyanza DH, and whose medical files are available during the period of two years starting from 1st January 2016 to 31st December 2017 with kidney status test was done every 6 months.

Inclusion Criteria

The study used medical records of patients under ARVs medications, with kidney status test records every 6 months for a period of 2 years. To differentiate with HIV-associated nephropathy only patients with eliminated viral charge, attended Nyanza DH between specific periods (1st January 2016 to 31st December 2017) were considered.

Exclusion Criteria

Medical records and files of HIV patients having medications other than ARVs medications and those having ARVs but who were referred to Nyanza DH out of the study period and during the study period, those with ARVs medications but without successive kidney status test and the ones with high viral charge was excluded from the study to differentiate it with HIV associated nephrotoxicity.

Ethical Consideration

Before starting to collect data, the permission from Nyanza DH administration, research and ethical committee was given. The study protocol was examined and approved by college of Medicine and Health Sciences, School of Medicine and Pharmacy of the University of Rwanda. The research was organized and implemented in a way that respects honesty in scientific communications, respects promises and agreement. A written authorization was requested from the hospital's authority prior to data collection process, protects confidential information for patients, In this regards no patient's names and addresses appeared on the data collection sheet.

Results and Discussion

Among seven hundred fifty five (755), patients, received during the period of two years starting on January 1st, 2016 to December 31st, 2017, kidney status test at the beginning of treatments was done for 356patients considered for further results. Among them, only 98patients had tests done before starting and after 6months of ARVs therapy. This difference in number of patients for the initial and tests after 18months is due to various factors including death during treatment and the fact that for patients who didn't show kidney dysfunction symptoms during treatment and kidney status exam was not requested.

Sociodemographic Information

The table below shows the demographic data for 98study participants. In this table, information on age and sex are recorded. According to the results obtained in the study, females occupy 61.2% while males make 38.8%. According to the results, during ARVs therapy, patients with age between 35 to 100 years old make 62.2% of total participants, while patient with age between 16 to 35years old represent 30.6% of total participants lastly 1 to 16years 7.1% of the total number of participants.

age of patients	frequency	percent	Valid percent	Cumulative percent
1-16years	7	7.1	7.1	7.1
16-35years	30	30.6	30.6	37.8
35-100years	61	62.2	62.2	100
Total	98	100	100	

Table 1: Age of patients.

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Male	38	38.8	38.8	38.8
Female	60	61.2	61.2	100
Total	98	100	100	

Table 2: Gender of Total Participants.

Results for Serum Creatinine during Antiretroviral Therapy

The table3 shows the results of serum creatinine for the participants in our study during the whole period of their treatment with antiretroviral drugs.

Reference values of serum creatinine are [0.5-1.2] mg/dl for men, [0.4-1.1] mg/dl for women [17]. In fact serum creatinine has been found to be a fairly reliable indicator of kidney function. According to Vadde, et al. [18]. Elevated serum creatinine level signifies impaired kidney function. While low levels of the waste product creatinine in the body could be a sign that the liver or muscles are not working as they should [19].

The results of the initial test of serum creatinine, showed that the number of males with serum creatinine above normal range was 12 out of 38 male participants. Among females, it was found that 12 out of 60 female participants corresponding to 24.4% of all participants had serum Creatinine above normal range.

Serum Creatinine	Frequency	Percent	Valid Percent	Cumulative Frequency
Male patient's serum creatinine bellow 0.5mg/dl	5	5.1	5.1	5.1
Male patient's serum creatinine between 0.5-1.2mg/dl	21	21.4	21.4	26.5
Male patient's serum creatinine above 1.2mg/dl	12	12.2	12.2	38.8
Female patient's serum creatinine bellow 0.4mg/dl	9	9.2	9.2	48
Female patient's serum creatinine between0.4-1.1mg/dl	39	39.8	39.8	87.8
Female patient's serum creatinine above 1.1mg/dl	12	12.2	12.2	100
Total	98	100	100	

Table 3: Patient's Serum Creatinine in mg/dl of Male or Female Initially.

As shown in Table 4, after 6months of treatment with antiretroviral drugs serum creatinine test results show that the number of males with serum creatinine level above normal range was 17out of 38 male participants. Among females, results show that 24 out of 60 female participants had serum creatinine above normal range. Therefore in total, 41out of 98participants corresponding to 41.8% of all participant had serum creatinine that was above normal range.

Serum Creatinine	Frequency	Percent	Valid Percent	Cumulative Frequecy
Male patient's serum creatinine bellow 0.5mg/dl	8	8.2	8.2	8.2
Male patient's serum creatinine between 0.5-1.2mg/dl	12	12.2	12.2	20.4
Male patient's serum creatinine above 1.2mg/dl	17	17.3	17.3	37.8
Female patient's serum creatinine bellow 0.4mg/dl	9	9.2	9.2	46.9
Female patient's serum creatinine between0.4-1.1mg/dl	28	28.6	28.6	75.5
Female patient's serum creatinine above 1.1mg/dl	24	24.5	24.5	100
Total	98	100	100	

Table 4: Patient's Serum creatinine in mg/dl of Male or Female after 6 Months.

After 12 months of treatment with antiretroviral medications, serum creatinine test result show that the number of males with serum creatinine level above normal range is 19 out of 38 male participants. Among females

the results show that the number of females with serum Creatinine level above normal range was 29 out of 60 female participants. In total 48 out of 98 participants corresponding to 48.9 %of all participant present serum creatinine above normal range.

Serum Creatinine	Frequency	Percent	Valid Percent	Cumulative Frequecy
Male patient's serum creatinine below 0.5mg/dl	9	9.2	9.2	9.2
Male patient's serum creatinine between 0.5-1.2mg/dl	9	9.2	9.2	18.4
Male patient's serum creatinine above 1.2mg/dl	19	19.4	19.4	37.8
Female patient's serum creatinine bellow 0.4mg/dl	10	10.2	10.2	48
Female patient's serum creatinine between0.4-1.1mg/dl	22	22.4	22.4	70.4
Female patient's serum creatinine above 1.1mg/dl	29	29.6	29.6	100
Total	98	100	100	

Table 5: Patient's Serum Creatinine in mg/dl of Male or Female after 12 Months.

As shown in Table 6, after 18months of treatment with antiretroviral drugs, serum creatinine test results show that the number of males with serum creatinine level above normal range was 20 out of 38 male participants. Among females, results show that 29 out of 60 female participants above normal range. 49 out of 98participants corresponding to 50.0% of all participant, had serum creatinine above normal range after 18 months.

Serum creatinine	frequency	percent	Valid percent	Cumulative frequency
Male patient's serum creatinine bellow 0.5mg/dl	8	8.2	8.2	8.2
Male patient's serum creatinine between 0.5-1.2mg/dl	9	9.2	9.2	17.3
Male patient's serum creatinine above 1.2mg/dl	20	20.4	20.4	37.8
Female patient's serum creatinine bellow 0.4mg/dl	17	17.3	17.3	55.1
Female patient's serum creatinine between0.4-1.1mg/dl	15	15.3	15.3	70.4
Female patient's serum creatinine above 1.1mg/dl	29	29.6	29.6	100
Total	98	100	100	

Table 6: Patient's serum creatinine in mg/dl of male or female after 18 months.

Antiretroviral Medications and Kidney Function Relationship

After 18 months of antiretroviral Therapy, 20male patients (100%) of total male with elevated serum creatinine, were using TDF containing regimen. While 27 out of 29 females (93.1%) of total female participants with elevated serum creatinine were using TDF containing regimen. In total, 47 out of 49 participants corresponding to 95.9% of total participants with elevated serum creatinine were using TDF containing regimen. While only 2 out of 29 female corresponding to 6.9% of total female participant with elevated serum creatinine were using non TDF containing regimen. This means that 2 out 49 participants corresponding to 4.08% of total participants with elevated serum creatinine, were using non tenofovir containing regimen.

Antiretroviral the patient is using	Patient's serum creatinine in mg/dl of male after 18months					
	Male patient's serum creatinine bellow 0.5mg/dl	Male patient's serum creatinine between 0.5-1.2mg/dl	Male patient's serum creatinine above 1.2mg/dl	Female patient's serum creatinine bellow 0.4mg/dl	Female patient's serum creatinine between 0.4-1.1mg/dl	Female patient's serum creatinine above1.1mg/dl
Efavirenz-lamivudine-Tenofovir	0	3	7	7	6	9
Stavudine-lamivudine-Efavirenz	2	3	0	3	0	2
Tenofovir-Lamivudine-Nevirapine	6	3	10	6	8	15
Tenofovir-lamivudine-kaletra	0	0	3	1	1	3
Total	8	9	20	17	15	29

Table 7: Antiretroviral Medications and Kidney Function Relationship.

Discussions

In the study, the patients developed antiretroviral-induced nephrotoxicity indicated by increase and decease of all of the two indicators, Serum creatinine and creatinine clearance respectively. According to Vadde, et al. [18] long-term exposure to HAART may be associated with significant toxicity. The previous researches reviewed the potential nephrotoxicity of specific antiretroviral agents and the impact of antiretroviral therapy on related metabolic disorders. The antiretroviral agents most strongly associated with direct nephrotoxicity include the nucleotide reverse transcriptase inhibitor, tenofovir, and the protease inhibitor indinavir, although other agents have been implicated less frequently. Tenofovir and related nucleotide analogs have primarily been associated with proximal tubular dysfunction and acute kidney injury, whereas indinavir is known to cause nephrolithiasis, obstructive nephropathy, and interstitial nephritis Jao, et al. [19]. The results of this research show that 95.9% of total participants with abnormal kidney function were using Tenofovir containing regimen. Similar study conducted in southern Malawi noted that 4.0% of patients had renal impairment at the initiation of therapy and 4.8% developed nephrotoxicity during the first 18 months of treatment. In Tanzania research showed that 64.3% of patients under ART develop nephrotoxicity. 58.8% of patients with acute kidney injury (AKI) and 43.1% of all patients with AKI were taking tenofovir disoproxil fumarate (TDF)-based ARTs, in Kenya 11% of patients under ART developed a decline in kidney function after 12months of antiretroviral medications [20-42]. In this case the frequency seems to be higher as 24.4% of patients had renal impairement at the initial test, 41.8% developed nephrotoxicity after 6 months, 48.9 % of patients developed nephrotoxicity after 12 months and 50% of patients develop kidney toxicity after 18months considering serum creatinine results (Appendix). This is simply due to the fact that our study population is composed by patients with Serum creatinine and creatinine clearance test results that were recorded every 6 months and in most of cases this was done in case of TDF containing regimen and nephrotoxicity suspicion [43-47].

Conclusion and Recommendation

Conclusion

The present study was conducted in Nyanza DH using the medical records of patients on antiretroviral medication from the 1st of January 2016 to the 31st of December 2017. Only patients with creatinine clearance and serum creatinine tests results at the beginning of antiretroviral therapy have been part of this study [48-52]. The main objective of this study was to assess the effects of antiretroviral medications on kidney function. Creatinine clearance, serum creatinine have been considered as indicators for kidney function and any results above the references ranges for this indicators was considered as a kidney dysfunction [18]. Knowing that Serum creatinine is the most specific indicator for kidney

function, the results of this study showed a high frequency (50%) of kidney dysfunction in the population of the study. This during this study, it was found the severity of problem depends on: combinations the patients is taking, duration of exposure, and other medications the patient is using in combination in this context it was found that 96.7% of patients that developed nephrotoxicity after 18months were using TDF. This lead to conclude that patients on antiretroviral medications are exposed to nephrotoxicity and kidney dysfunction.

Recommendation

At the end of this study, to systematically realize kidney function test before and during antiretroviral treatment is the main recommendation to hospitals and health policy makers in Rwanda. In fact, for the moment this test is done only for patient under Tenofovir and Stavudine containing regimen and in case of nephrotoxicity suspicion. The regimen should be changed in case of nephrotoxicity to avoid increase of kidney damages.

References

1. Karina S, Campos P, Ortiz A (2016) HIV and kidney diseases: 35 years of history and Consequences. Clin Kidney J 9(6): 772-781.

2. Wyatt C (2008) Kidney Disease in Patients with HIV Infection and AIDS. Clin Infect Dis 47: 1449-1457.

3. Ahuja ST, Gupta KS, Eustace AJ, Winston AJ, Bodystun I, et al. (2005) 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. Clin Infect Dis 40(11): 1559-1585.

4. Cuzin L, Flandre P, Pugliese P, Bagnis IC, Tack I, et al. (2011) Risk factors of chronic kidney disease in HIV-infected patients. Clin J Am Soc Nephrol 6(7): 1700-1707.

5. Roe J, Campbell JL, Ibrahim F, Ibrahim MB, Post AF (2008) HIV care and the incidence of acute renal failure. Clinical Infectious Diseases 47(2): 242-249.

6. Cotonou (2012) National Program of Fight against AIDS/ STI) Policy, standards and procedures for the care of people living with HIV in Benin.

7. UNAIDS (2013) Global Report: UNAIDS Report on the Global AIDS Epidemic 2013, UNAIDS Geneva, USA.

8. Geubbels E, Braunstein LS, Ingabire MC, Vyankandondera J, Nash D, et al. (2011) High burden of prevalent and recently acquired HIV among female sex workers and female HIV voluntary testing center clients in Kigali, Rwanda. PLoS One 6(9): e24321.

9. Mulenga LB, Kruse G, Lakhi S, Cantrell AR, Reid ES, et al. (2008) Baseline Renal insufficiency and risk of death among HIV-infected adults on antiretroviral therapy in Lusaka, Zambia AIDS 12(14): 1821-1827.

10. UNAIDS (2016) Global AIDS Response Progress Reporting (GARPR) estimates.

11. Hawkins (2010) Understanding and managing adverse effects of antiretroviral therapy. Antiviral Res 85(1): 201-209.

12. Peters JP, Moore MD, Mermin J, Brooks TJ, Downing R, et al. (2008) Antiretroviral therapy improves renal function among HIV-infected Ugandans. Kidney Int 74(7): 925-929.

13. Cihlar T, Ho ES, Lin CD, Mulato SA (2001) Human renal organic anion transporter 1 (hOAT1) and its role in the nephrotoxicity of antiviral nucleotide analogs. Nucleosides Nucleotides Nucleic Acids 4-7(20): 641-648.

14. National Kidney Foundation (2002) K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 39(2S1): 261-266.

15. Olusegun T, Dada AS, Aderibigbe A, Chijioke A, Rafiu OM, et al. (2015) Prevalence of chronic kidney disease in newly diagnosed patients with human immunodeficiency virus in Ilorin, Nigeria. J Bras Nefrol 37(2).

16. MOH (2011) Report.

17. Horowitz G (2014) Serum creatinine

18. Vadde (2013) Serum creatinine.

19. Jao (2010) Antiretroviral Medications: Adverse Effects on the Kidney. Adv Chronic Kidney Dis pp: 72-82.

20. Chris NK (2013) Effects of highly active antiretroviral therapy on the liver and kidney functions in HIV patients at Coast Province General Hospital, Kenya.

21. Cihlar T, Ho ES, Lin DC, Mulato AS (2001) Human renal organic anion transporter 1 (hOAT1) and its role in the nephrotoxicity of antiviral nucleotide analogs. Nucleosides Nucleotides Nucleic Acids (20): 641-648.

22. Daugas E, Rougier PJ, Hill G (2005) HAART-related nephropathies in HIV-infected patients. Kidney Int 67(2): 393-403.

23. Mermin J, Peters PJ, Moore MD, Brroks TJ, Downing R (2008) Antiretroviral therapy improves renal function among HIV-infected Ugandans. Kidney International 74(7): 925-929.

24. (2011) National Guidelines on Management of HIV in Rwanda.

25. Richards DC, Pocock G (2006) Human physiology: the basis of medicine 656.

26. Wyatt CM, Jao J (2010) Antiretroviral medications: adverse effects on the kidney. Advanced Chronic Kidney Diseases 17(1): 72-82.

27. Moore RD, Chaisson RE (1999) Natural history of HIV infection in the era of combination antiretroviral therapy. AIDS 13(14): 1933-1942.

28. Lundgren JD, Neaton JD, Gordin F, Abrams D, Arduino RC, et al. (2006) CD4 count-guided interruption of antiretroviral treatment. N Engl J Med 355(22): 2283-2296.

29. Dybul M (2002) Clinical practices for treatment of HIV.

30. Eaton ME (2005) Selected rare, noninfectious syndromes associated with HIV infection. Top HIV Med 13(2): 75-78.

31. Foundation NK (2002) Clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med pp: 261-266.

32. Greener R (2002) AIDS & Macroeconomics Impact. In: Forsyth S (Ed.), State of the Art: AIDS and Economics. IAEN, pp: 49-55.

33. Izzedine H (2005) Renal tubular transporters and antiviral drugs. AIDS 19: 455-462.

34. Jao J, Wyatt CM (2009) Antiretroviral medications: adverse effects on the kidney. Adv Chronic Kidney Dis 17(1): 72-82.

35. Kalim S, Szczech L, Wyatt CM (2008) Acute kidney injury in HIVinfected patients. Semin Nephrol 28(6): 556-562.

36. Leport C (2009) Long-term evolution and determinants of renal function in HIV-infected patients who began receiving combination antiretroviral therapy in 1997-99, ANRS CO8 APROCO-COPILOTE. Clin Infect Dis 49: 1950-1954.

37. Lucas GM (2004) Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. AIDS 18(3): 541-546.

38. Maggi P (2012) Renal complications in HIV disease: Between present and future. AIDS 14(1): 37-53.

39. Meynard JL (2002) Fanconi syndrome and renal failure induced by tenofovir: A first case report Am J Kidney Dis 40(6): 1331-1333.

40. Moore RD, Chaisson RE (1999) Natural history of HIV infection in the era of combination antiretroviral therapy. AIDS 13(14): 1933-1942.

41. NASCOP (2002) Clinical Guidelines on antiretroviral Therapy.

42. (2011) National guidelines for comprehensive care of people living with HIV in Rwanda.

43. (2011) National guidelines on management of HIV in Rwanda. 4th (Edn.).

44. National Kidney Foundation (2002) clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification, pp: 261-266.

45. Nelson (2005) Pathologic basis of disease. Elsevier, St. Louis MO.

46. Obirikorang (2014) Renal function in Ghanaian HIV-infected patients on highly active antiretroviral therapy: a case control study. Plos One.

47. Ogundahunsi (2008) The prevalence of renal disorder in HIV/AIDS patients on HAART. International Journal of Biomedical and Health Sciences, pp: 1-4.

48. Pataki (2006) Managing side effects of HIV medication. Department of Health, Rev.11. State of New York, USA.

49. Rao TKS (2001) Human Immunodeficiency Virus infection and renal failure. Infectious Disease Clinics of North America 15(3): 833-850.

50. Richards (2006) Human physiology: the basis of medicine. 3rd (Edn.), Oxford University Press, Oxford, pp: 349.

51. Thompson M (2011) Phosphate (Thompson Liver, Kidney, Bone: Emerging Issues of Long Term Antiretroviral Therapy. 20th Annual HIV Conference of the Florida/ Caribbean AIDS Education and Training Centre, pp: 13-14.

52. Wyatt CM (2009) The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. Kidney International 75(4): 428-434.