

Clinical spectrum of renal disease in hospitalized HIV/AIDS patients: A teaching hospital experience

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ABSTRACT

Background: Renal involvement in HIV patients is relatively common and quite broad. However, despite an increasingly large number of HIV patients in Asia, systematic studies of renal involvement are lacking. **Objectives:** The study was carried out to delineate the clinical spectrum of renal disease in HIV/AIDS patients hospitalised in a tertiary care centre. **Patients and Methods:** A total of 510 consecutive hospitalised HIV/AIDS with age >18years were included in the study. Detailed demographic, clinical and laboratory data including urinalysis was obtained from all participants. **Results:** Electrolyte disorders were seen in 71% of patients, with the most frequent being hyponatremia (61%). Acute renal failure was seen in 15.8% and CKD was found in 13% of HIV patients. Dipstick proteinuria of grade $\geq 1+$ was seen in 147 patients (29% of total). CD4 count had a significant positive correlation with creatinine clearance, hyponatremia and total leukocyte count, and significant negative correlation with duration of disease and proteinuria. **Conclusion:** Electrolyte disorders and renal involvement are quite common in HIV/AIDS patients from India. Prompt diagnosis and management is required as their presence carry higher morbidity and mortality.

Keywords: Acute renal failure, CD4 count, chronic kidney disease, electrolyte disorders, proteinuria

Introduction

Human immunodeficiency virus (HIV) infection is a global pandemic with 36.9 million people infected worldwide.^[1] In India alone, 2.1 million people were estimated to be infected in 2017 with an adult prevalence of 0.2%, leading to 69,000 deaths.^[1] However, with wide availability and improvement of combination antiretroviral therapy regiments (cART), AIDS-related deaths and opportunistic infectious diseases have markedly decreased. This has resulted in prolonged survival of individuals leading to a change in clinical spectrum of HIV. Consequently, renal involvement has become relatively common and may be seen in up to one-third of the patients.^[2] The spectrum of kidney diseases in HIV patients is quite broad, ranging from proteinuria,^[3] electrolyte losses,^[4] and acute kidney injury (AKI)^[5] to various degrees of chronic kidney disease (CKD).^[6,7]

HIV patients are predisposed to a myriad of electrolyte imbalances owing to modified renal physiology, including reduced free water clearance. Moreover, they are exposed to various infections and inflammatory conditions which increase fever, vomiting, diarrhea, and polyuria which alter homeostasis. This is further exacerbated by a variety of medications including cARTs and antibiotics. As majority of electrolyte disorders are clinically silent, a high degree of clinical suspicion and awareness is required, because they contribute to both morbidity and mortality.^[8] AKI too is frequently encountered in HIV infections, affecting up to 20% of hospitalized patients and to a lesser degree in ambulatory patients.^[9] AKI requires prompt diagnosis and management as they greatly increase the risk of cardiovascular disease, end-stage renal disease (ESRD), and mortality in HIV-infected cases.^[10] Moreover, CKD has become epidemic in HIV-infected patients worldwide, particularly in Black population.^[11]

Despite large number of HIV-infected cases in Asian countries, systematic studies of renal involvement in such patients are

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lacking. With this perspective, this study was carried out to elucidate the clinical spectrum of renal disease in HIV patients from a tertiary care center from India. To our knowledge, this is the single largest study regarding comprehensive evaluation of renal disorders in HIV/AIDS patients from the Indian sub-continent.

Material and Methods

Study population and protocol

This was a single center observational study done at the Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi, India. All consecutive HIV-positive patients of ≥ 18 years of age, admitted in general medicine or nephrology departments, were included in the study. The participants were subjected to detailed history, physical examination, and laboratory investigation including complete blood picture, urine analysis, renal function test, liver function test, random blood glucose, HBsAg, Anti-HCV (hepatitis C virus), and CD4 count. The urine was tested using standard dipstick method for screening of proteinuria. The patients having a dipstick proteinuria of 1+ or more were subjected to quantitative 24-hour urinary protein estimation. The study was conducted according to the Helsinki Declaration and the Good Clinical Practice Guidelines. Written informed consent was obtained from all patients. Ethical approval for the study protocol was obtained from Ethics Committee of IMS, BHU.

Definitions

Diagnosis of HIV and AIDS were based on 1993 revised classification system by CDC (Centers for Disease Control and Prevention).^[12] Acute renal failure (ARF) was defined, according to Adult AIDS Clinical Trials Group, as an increase in serum creatinine level to values ≥ 1.5 mg/dL that returns to baseline values within 3 months.^[13] CKD was defined as kidney damage (structural or functional abnormalities of the kidney) or estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² for 3 months or more, irrespective of cause.^[14] Creatinine clearance (CrCl) was calculated by Cockcroft-Gault equation.^[14] Patients with serum creatinine ≥ 1.5 mg/dL and/or spot proteinuria $> 1+$ were classified as having renal involvement. Nephrotic range proteinuria was defined as a 24-hour urine protein ≥ 3.5 gm/day. Among electrolyte disorders, hyponatremia was defined as serum Na < 135 mmol/L, hypernatremia as serum Na > 145 mmol/L, hypokalemia as serum K < 3.5 mmol/L, and hyperkalemia as serum K > 5 mmol/L.

Statistical evaluation

The data were analyzed using GraphPad Prism 7, version 7.04 (GraphPad Software, Inc.). Continuous variables were presented as means and SDs and categorical variables were expressed as frequencies and percentages. The *P* value for comparing two independent continuous variables was from unpaired Student *t* test and for comparing two proportions was from the Chi-square test or Fisher exact test. Spearman and Pearson's correlation

coefficient was used to calculate the correlation between CD4 count and patient-related variables. All tests were two-sided, and statistical significance was at $P < 0.05$.

Results

Patient characteristics

A total of 510 consecutive hospitalized HIV/AIDS patients were included in the study. The mean age of the study population was 33.6 years, with a male predominance (71%). Most of the patients were between 20 and 40 years of age (67% of total), and only 2.6% belonged to > 60 years age group. Fever was the most common presenting complaint in the HIV positive patients, accounting for 59% of the patients. This was closely followed by vomiting (42%), weight loss (33%), and diarrhea (26%). Diabetes and hypertension were seen in 17.8% and 26.8% patients, respectively. Co-infection with hepatitis B was seen in 9% and hepatitis C in 13.3% cases. The mean hemoglobin was 11.1 gm/dL, with anemia being seen in 23% of the participants. The mean serum creatinine level was 1.2 mg/dL, with creatinine ≥ 1.5 mg/dL in 15.8% patients. The average duration of disease at the time of inclusion in study was 23 months and the mean CD4 count was 314 cells/mm³. In all, 61% of the patients were taking combination anti-retroviral treatment (ART) [Table 1].

Table 1: Patient characteristics and relation with proteinuria

Variable	Total	With proteinuria	Without proteinuria	P
Age (years)	33.6 \pm 11.6	32.8 \pm 11.2	34.1 \pm 12	NS
Male	362 (71)	173 (34)	189 (37)	NS
Diabetes	91 (17.8)	47 (9.2)	44 (8.6)	NS
Hypertension	137 (26.8)	76 (14.9)	61 (11.9)	NS
Hepatitis B	46 (9)	25 (4.9)	21 (4.1)	NS
Hepatitis C	67 (13.3)	36 (7)	31 (6)	NS
Duration of disease	23 \pm 21	29 \pm 26	19 \pm 17	< 0.001
Hemoglobin (gm/dL)	11 \pm 1.7	10.8 \pm 1.8	12.1 \pm 2.1	NS
Creatinine (mg/dL)	1.2 \pm 0.9	1.3 \pm 0.8	1.1 \pm 0.9	NS
CD 4 count (cell/mm ³)	314 \pm 175	190 \pm 152	370 \pm 186	< 0.001
Taking c-ART	311 (61)	117 (23)	194 (38)	< 0.001

Values shown represent numbers (percentages) and mean \pm SD. cART=Combination anti-retroviral therapy

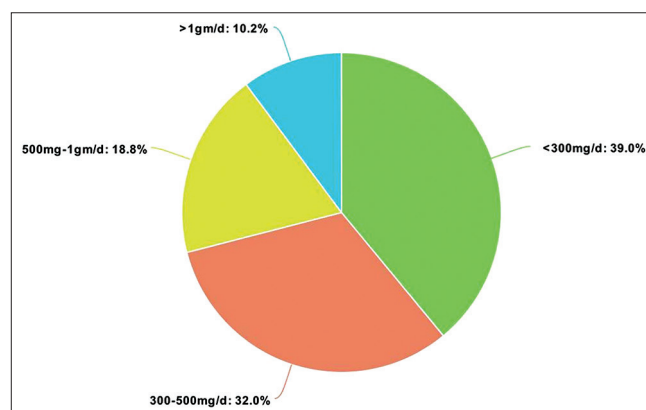


Figure 1: Spectrum of proteinuria in HIV/AIDS patients

Proteinuria quantification

Dipstick proteinuria of grade $\geq 1+$ was seen in 147 patients (29% of total) [Figure 1]. Moreover, 24-hour urinary protein estimation was done in all these patients. Out of these, proteinuria was in normal range (i.e., < 300 mg/day) in 39% patients ($n = 57/147$). About 50% patients had proteinuria between 300 mg and 1 gm/day. Only 15 patients (10.2%) had proteinuria > 1 gm/day, with three patients in the nephrotic range. There was no significant age and sex difference between patients with and without proteinuria [Table 1]. Similarly, the prevalence of diabetes, hypertension, hepatitis B, and hepatitis C were also similar. However, the duration of HIV/AIDS was significantly greater in patients with proteinuria (29 ± 26 vs. 19 ± 17 months, $P < 0.001$), and significantly lower number of patients were taking ART in the proteinuria group. The CD4 counts too were significantly lower in the proteinuric patients (190 ± 152 vs. 370 ± 186 cells/mm³, $P < 0.001$).

Correlation of CD4 Counts with Clinical Variables

Significant negative correlation was seen between CD4 counts and duration of disease ($r = -0.33$, $P = 0.04$) and also with proteinuria ($r = -0.45$, $P < 0.001$). However, there was no correlation with age and hemoglobin. A weak but significant positive correlation was seen with total leukocyte count (TLC). The CD4 counts were significantly correlated with serum creatinine ($r = -0.26$, $P = 0.02$) and CrCl ($r = 0.29$, $P = 0.01$). Among electrolyte disorders, CD4 count correlated well with hyponatremia ($P = 0.05$) but not with hypokalemia ($P = 0.09$) [Table 2].

Electrolyte disorders

Hyponatremia ($\text{Na} < 135$ mmol/L) was by far the most common disorder [Table 3]. It was present in 61.2% ($n = 311/510$) of the patients. Serum sodium < 130 mmol/L was present in 38%. However, severe hyponatremia ($\text{Na} < 120$ mmol/L) was present only in 7% of the patients. Hypernatremia comparatively was less common, present only in 4.1%, with serum sodium > 150 mmol/L seen in five patients only.

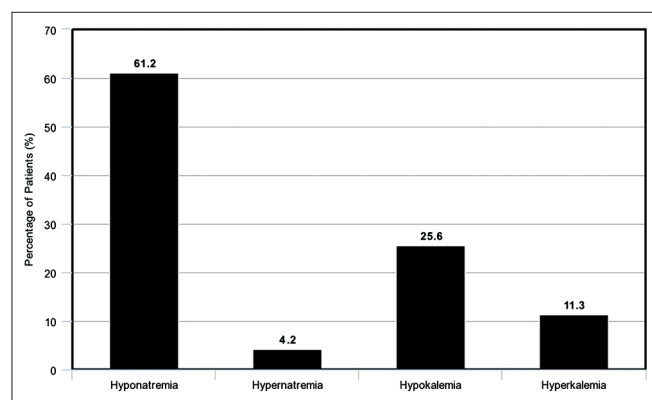


Figure 2: Spectrum of electrolyte disorders in HIV/AIDS patients

Hypokalemia ($K < 3.5$ mmol/L) was present in 25.4% patients, though significant hypokalemia ($K < 3$ mmol/L) was present only in 11.6% patients. Hyperkalemia ($K > 5$ mmol/L) was present in 11.2% cases, and potassium level > 6 mmol/L was found only in eight patients [Figure 2].

Spectrum of renal disease

Renal involvement in our study was seen in 214 patients (42%). This included 29% of patients with proteinuria and 15.8% with serum creatinine ≥ 1.5 mg/dL. Gross/microscopic hematuria was seen in 8.8% and electrolyte imbalances in 71% of the HIV/AIDS patients. Furthermore, CKD was found in 66 patients (13%) [Table 3].

Discussion

We have presented a single-center observational study describing spectrum of renal disease in HIV/AIDS patients, including proteinuria, electrolyte disorders, and renal dysfunction. The major strength of this study was a large sample size of HIV/AIDS patients from a tertiary care center.

The mean age in our study was 33.6 ± 11.6 years with male preponderance (2.4:1). This is similar to previous studies from India.^[15,16] However, the global sex distribution of HIV is quite heterogeneous, with male preponderance in North America and Europe, whereas in African studies, females constitute 60% to 70% of the patients.^[17] With prolonged survival and

Table 2: Correlation of CD4 count with various parameters

Parameter	Correlation coefficient (r)	P
Age	0.08	0.35
Hemoglobin	0.12	0.21
Total leukocyte count	0.21	0.05
Duration of disease	-0.33	0.04
Proteinuria	-0.45	<0.001
Hyponatremia	0.30	0.05
Hypokalemia	0.14	0.09
Creatinine	-0.26	0.02
CrCl	0.29	0.01

CrCl=Creatinine clearance

Table 3: Spectrum of renal disease and electrolyte disorders in HIV/AIDS patients

Renal abnormalities	Prevalence
$\geq 1+$ Dipstick proteinuria	147 (29)
Gross/microscopic hematuria	45 (8.8)
Dyselectrolytemia	362 (70.9)
Hyponatremia	312 (61.2)
Hypernatremia	21 (4.1)
Hypokalemia	130 (25.4)
Hyperkalemia	57 (11.2)
Creatinine ≥ 1.5 mg/dL	81 (15.8)
Chronic kidney disease	66 (13)
Renal involvement*	214 (42)

Values shown represent numbers (percentages). *Defined as dipstick proteinuria $\geq 1+$ and/or serum creatinine ≥ 1.5 mg/d

aging of the HIV-infected population, the comorbid diseases like hypertension and diabetes have begun to influence the spectrum of kidney disease in patients with HIV.^[18] The prevalence of diabetes and hypertension in this study was 17.8% and 26.8%, respectively. This is considerably higher than a recent meta-analysis reporting a worldwide median prevalence of diabetes as 6.1% and hypertension as 19%.^[17] Hepatitis B co-infection was seen in 9% patients and 13.3% were hepatitis C infected, which too is comparably higher than the global median of 5.6% and 11%, respectively.^[17] Worldwide, the risk factors for CKD such as hypertension, diabetes mellitus, and hepatitis C are more prevalent in North America and Europe than Africa.^[17] The high prevalence of this modifiable risk factors in HIV patients from India and abroad provides a window of opportunities to institute treatment and possibly retard CKD progression.

CD4 cell counts serve as surrogate marker of HIV viral load and activity.^[15] The mean CD4 count (cell/mm³) in our study was 314 ± 175. Accordingly, the significantly lower CD4 count (<350 cells/mm³) in our study indicates a poor control of the viral infection and presents a potential risk factor for development of CKD.^[13] Moreover, lower number of patients in our study were on cART (65.9%), compared to studies from the United States (77%) and Brazil (92%).^[19,20] We have also reported a comparatively higher prevalence of dipstick proteinuria in this study (29%). This is comparable to two large studies from the United States reporting proteinuria of 29.8% and 32%.^[19,21] Range of proteinuria was 17.6% to 36.5% in various Indian studies.^[16,22,23] This may be probably due to lack of awareness, low education level, delay in diagnosis and treatment, and poor availability and access to health care facilities in India.

Hyponatremia is the most frequent electrolyte abnormality in both hospitalized and ambulatory HIV and AIDS patients. Hyponatremia in our study was seen in 61.2% patients, which is comparable to previously reported prevalence of 23.5% to 75% in hospitalized HIV patients.^[8,24] Diarrhea and vomiting leading to volume depletion are the usual cause of hyponatremia in hospital admissions. Early recognition and treatment is warranted because hyponatremia in HIV/AIDS is a marker of disease severity and associated with higher morbidity and mortality.^[25,26] Hyponatremia is relatively uncommon, but has been reported in 31% of patients with very advanced disease.^[8] Potassium imbalances, hypokalemia, and hyperkalemia are common in HIV/AIDS patients. The major cause of hypokalemia in these patients is gastrointestinal potassium loss, arising from profuse diarrhea and vomiting secondary to intestinal infections. Recently, amphotericin B and tenofovir has been implicated in hypokalemia arising due to tubular dysfunction.^[27] We have relatively higher prevalence of hypokalemia (25.4%), compared to about 19% reported in previous studies.^[27] This may have been due to higher proportion of HIV patients presenting with vomiting (42%) and diarrhea (26%), in our study. Hyperkalemia was found in 11.2% patients, comparable to a reported prevalence of 5% to 53% of HIV/AIDS patients.^[27]

Severe hyponatremia, unlike other electrolyte disorder, is associated with a lower CD4 count.^[26,28] This may be the plausible reason behind association of hyponatremia with higher morbidity and mortality in HIV patients. There was a significant negative correlation of CD4 count with proteinuria in our study, similar to prior studies.^[15,29] However, unlike reported by Janakiraman *et al.*, we did not find any significant correlation with hemoglobin. Many recent studies too show no relation of CD4 count to hemoglobin levels.^[30,31] A positive, though weak, correlation was also seen with TLC. Of late, this novel association between CD4 count and TLC has been a target of many interesting speculations. Many recent studies suggest measurement of TLC as surrogate of CD4 count in resource poor settings.^[32,33] Moreover, TLC has also been suggested to be used as indicator to start cART, monitor treatment, and predict mortality in HIV/AIDS patients.^[34,35] Furthermore, significant correlation between CD4 count and renal function as reported in earlier studies was also confirmed in this study.^[29,36]

ARF as defined by serum creatinine ≥1.5 mg/dL was seen in 15.8% HIV patients in our study. Among hospitalized patients, AKI is two to five times more common in HIV infected persons than uninfected population. The incidence of AKI is variable across studies mainly due to retrospective nature and diverse diagnostic criteria. However, the incidence ranges from 6% to 18% in hospitalized patients^[37-39] and 3.9% in ambulatory patients with HIV.^[40] With the introduction and improvement of cART, the incidence of AKI has decreased but remains substantial, with an increase in more severe forms.^[41] The most frequent cause of AKI is volume depletion, sepsis, and nephrotoxicity, with 38% of the cases being pre-renal. A kidney biopsy series in HIV-infected patients with severe AKI, presumably not pre-renal, reported hemolytic uremic syndrome in 35% and acute tubular necrosis in 26% of the cases.^[42] Risk factors for AKI include hypertension, AIDS defining illness, cART toxicity especially tenofovir, HCV co-infection, and sepsis. AKI is associated with increased risk of adverse outcomes such as heart failure, cardiovascular disease, and ESRD.^[9] The diagnosis of AKI has been found to be associated with fivefold increase in mortality.^[10] Consequently, an early diagnosis and prompt management of AKI in both ambulatory and hospitalized patients is warranted.

CKD is now epidemic among HIV-infected populations in both Western and Eastern countries. The mechanism of renal involvement is diverse including intra-renal HIV gene expression, co-morbidities like hypertension and diabetes, immune dysfunction, drug toxicity, and opportunistic infections.^[43] Risk factors for CKD in HIV patients now include traditional risk factors like diabetes and hypertension in addition to HIV-related factors of low CD4 counts, high viral load, HCV co-infection, and cART use.^[44,45] The prevalence of CKD in studies varies from 3.5% to 32.6%^[44,46,47] depending on the characteristics of the study population and the criteria used to define CKD. In a recent meta-analysis, the overall CKD prevalence was 6.4% with Modification of Diet in Renal Disease (MDRD) equation,

4.8% with CKD-EPI, and 12.3% with Cockcroft-Gault.^[17] The prevalence of CKD in our study using Cockcroft-Gault equation was 13%. As discussed earlier, we encountered a high prevalence of diabetes (17.8%) and hypertension (26.8%), moreover with presence of diabetic nephropathy (10%) in kidney biopsy. In clinical practice, it is recommended to use measures of renal function like Cockcroft-Gault or estimated GFR (eGFR), rather than serum creatinine alone.^[13]

The findings of this study are especially relevant to primary care physicians involved in treatment of HIV/AIDS patients. A high degree of clinical suspicion is required because renal involvement is quite common. Renal abnormalities range from electrolyte disorders, proteinuria, AKI, and CKD. A timely diagnosis and treatment is required because such abnormalities are associated with increased morbidity and mortality. Urine analysis and renal function test should be done in all HIV/AIDS, particularly requiring hospitalization.

Conclusions

With improvement in survival due to availability of cART, renal involvement has become quite common in HIV/AIDS patients. In this study, electrolyte disorders were seen in 71% of hospitalized patients, with most frequent being hyponatremia (61%). ARF was seen in 15.8% and CKD was found in 13% of the patients. Early detection and possible correction of these disorders is mandatory as they are associated with significant morbidity and mortality in HIV-infected patients. CD4 count had significant positive correlation with CrCl, hyponatremia, and TLC, and significant negative correlation with duration of disease and proteinuria. Proteinuria as detected by dipstick was present in 29% patients, and of this proteinuria, ≥ 1 gm/day was seen in 10.2% of patients.

Authors' contribution

BV; concept, study design, experiments, data acquisition, analysis of information and draft of the manuscript. AS; data analysis, information analysis, design and approval of final manuscript.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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Conflicts of interest

There are no conflicts of interest.

References

- UNAIDS. AIDSinfo. Available from: <http://aidsinfo.unaids.org/>. [Last accessed on 2019 Feb 04].
- Rosenberg AZ, Naicker S, Winkler CA, Kopp JB. HIV-associated nephropathies: Epidemiology, pathology, mechanisms and treatment. *Nat Rev Nephrol* 2015;11:150-60.
- Szczzech LA, Menezes P, Byrd Quinlivan E, van der Horst C, Bartlett JA, Svetkey LP. Microalbuminuria predicts overt proteinuria among patients with HIV infection. *HIV Med* 2010;11:419-26.
- Musso CG, Belloso WH, Glassock RJ. Water, electrolytes, and acid-base alterations in human immunodeficiency virus infected patients. *World J Nephrol* 2016;5:33-42.
- Li Y, Shlipak MG, Grunfeld C, Choi AI. Incidence and risk factors for acute kidney injury in HIV infection. *Am J Nephrol* 2012;35:327-34.
- Gameiro J, Jorge S, Lopes JA. HIV and renal disease: A contemporary review. *Int J STD AIDS* 2018;29:714-9.
- Campos P, Ortiz A, Soto K. HIV and kidney diseases: 35 years of history and consequences. *Clin Kidney J* 2016;9:772-81.
- Perazella MA, Brown E. Electrolyte and acid-base disorders associated with AIDS: An etiologic review. *J Gen Intern Med* 1994;9:232-6.
- Li X, Zhuang S. Acute kidney injury in HIV infection. *J Trop Dis* 2013;1:101.
- Choi AI, Li Y, Parikh C, Volberding PA, Shlipak MG. Long-term clinical consequences of acute kidney injury in the HIV-infected. *Kidney Int* 2010;78:478-85.
- Fine DM, Perazella MA, Lucas GM, Atta MG. Kidney biopsy in HIV: Beyond HIV associated nephropathy. *Am J Kidney Dis* 2008;15:504-14.
- 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Recomm Rep* 1992;41:1-19.
- Gupta SK, Eustace JA, Winston JA, Boydston, Ahuja TS, Rodriguez RA, *et al*. 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* 2005;40:1559-85.
- KDIGO, CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation, prevention and management of chronic kidney disease-mineral and bone disorder. *Kidney Int* 2013;3:1-150.
- Janakiraman H, Abraham G, Matthew M, Kuruvilla S, Panikar V, Solomon S, *et al*. Correlation of CD4 counts with renal disease in HIV positive patients. *Saudi J Kidney Dis Transpl* 2008;19:603-7.
- Prakash J, Ganiger V, Prakash S, Sivasankar M, Sunder S, Singh U. Kidney disease in human immunodeficiency virus-seropositive patients: Absence of human immunodeficiency virus-associated nephropathy was a characteristic feature. *Indian J Nephrol* 2017;27:271-6.
- Ekrikpo UE, Kengne AP, Bello AK, Effa EE, Noubiap JJ, Salako BL, *et al*. Chronic kidney disease in the global adult HIV-infected population: A systematic review and meta-analysis. *PLoS One* 2018;13:e0195443.

18. Wyatt CM, Morgello S, Katz-Malamed R, Wei C, Klotman ME, Klotman PE, *et al.* The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. *Kidney Int* 2009;75:428-34.
19. Szczech LA, Gange SJ, van der Horst C, Bartlett JA, Young M, Cohen MH, *et al.* Predictors of proteinuria and renal failure among women with HIV infection. *Kidney Int* 2002;61:195-202.
20. Cavalcante MA, Coelho SN, Lacerda HR. Prevalence of persistent proteinuria in stable HIV/AIDS patients and its association with HIV nephropathy. *Braz J Infect Dis* 2007;11:456-61.
21. Kimmel PL, Umana WO, Bosch JP. Abnormal urinary protein in HIV-infected patients. *Clin Nephrol* 1993;39:17-21.
22. Gupta V, Gupta S, Sinha S, Sharma SK, Dinda AK, Agarwal SK, *et al.* HIV associated renal disease: A pilot study from north India. *Indian J Med Res* 2013;137:950-6.
23. Varma PP, Prasher PK, Deshpande GU, Mani NS, Nema SK, Sayal SK. Spectrum of renal lesions in HIV patients. *J Assoc Physicians India* 2000;48:1151-4.
24. Cusano AJ, Thies HL, Siegal FP, Dreisbach AW, Maesaka JK. Hyponatremia in patients with acquired immune deficiency syndrome. *J Acquir Immune Defic Syndr* 1990;3:949-53.
25. Tang WW, Kaptein EM, Feinstein EL, Massry SG. Hyponatremia in hospitalized patients with the acquired immunodeficiency syndrome (AIDS) and the AIDS-related complex. *Am J Med* 1993;94:169-74.
26. Xu L, Ye H, Huang F, Yang Z, Zhu B, Xu Y, *et al.* Moderate/Severe hyponatremia increases the risk of death among hospitalized Chinese human immunodeficiency virus/acquired immunodeficiency syndrome patients. *PLoS One* 2014;9:e111077.
27. Peter SA. Electrolyte disorders and renal dysfunction in acquired immunodeficiency syndrome patients. *J Natl Med Assoc* 1991;83:889-91.
28. Wen Y, Zhou Y, Wang W, Wang Y, Lu X, Sun CM, *et al.* Baseline factors associated with mortality within six months after admission among hospitalized HIV-1 patients in Shenyang, China. *Intern Med* 2014;53:2455-61.
29. Okafor U, Unuigbo E, Ojogwu L, Oviasu E, Wokoma F. Renal disease in HIV infected patients at University of Benin Teaching Hospital in Nigeria. *Afr Health Sci* 2011;11(Suppl 1):S28-33.
30. Alavi SM, Ahmadi F, Farhadi M. Correlation between total lymphocyte count, hemoglobin, hematocrit and CD4 count in HIV/AIDS patients. *Acta Medica Iranica* 2009;47:1-4.
31. Emuchay CI, Okeniyi SO, Okeniyi JO. Correlation between total lymphocyte count, hemoglobin, hematocrit and CD4 count in HIV patients in Nigeria. *Pak J Biol Sci* 2014;17:570-3.
32. Obirikorang C, Quaye L, Acheampong I. Total lymphocyte count as a surrogate marker for CD4 count in resource-limited settings. *BMC Infect Dis* 2012;12:128.
33. Sen S, Vyas A, Sanghi S, K Shanmuganandan, Gupta RM, Kapila K, *et al.* Correlation of CD4+ T cell count with total lymphocyte count, haemoglobin and erythrocyte sedimentation rate levels in human immunodeficiency virus Type-1 disease. *Med J Armed Forces India* 2011;67:15-20.
34. Mahajan AP, Hogan JW, Snyder B, Kumarasamy N, Mehta K, Solomon S, *et al.* Changes in total lymphocyte count as a surrogate for changes in CD4 count following initiation of HAART: Implications for monitoring in resource-limited settings. *J Acquir Immune Defic Syndr* 2004 May 1;36:567-75.
35. Oudenhoven HP, Meijerink H, Wisaksana R, Oetojo S, Indrati A, van der Ven AJ, *et al.* Total lymphocyte count is a good marker for HIV-related mortality and can be used as a tool for starting HIV treatment in a resource-limited setting. *Trop Med Int Health* 2011;16:1372-9.
36. Adedeji T, Adedeji NO, Adebisi SA, Idowu AA, Fawale MB, Jimoh KA. Prevalence and pattern of chronic kidney disease in antiretroviral-naïve patients with HIV/AIDS. *J Int Assoc Provid AIDS Care* 2015;14:434-40.
37. Wyatt CM, Arons RR, Klotman PE, Klotman ME. Acute renal failure in hospitalized patients with HIV: Risk factors and impact on in-hospital mortality. *AIDS* 2006;20:561-5.
38. Lopes JA, Melo MJ, Viegas A, Raimundo M, Câmara I, Antunes F, *et al.* Acute kidney injury in hospitalized HIV-infected patients: A cohort analysis. *Nephrol Dial Transplant* 2011;26:3888-94.
39. Valeri A, Neusy AJ. Acute and chronic renal disease in hospitalized AIDS patients. *Clin Nephrol* 1991;35:110-8.
40. Prakash J, Gupta T, Prakash S, Rathore SS, Usha, Sunder S. Acute kidney injury in patients with human immunodeficiency virus infection. *Indian J Nephrol* 2015;25:86-90.
41. Nadkarni GN, Patel AA, Yacoub R, Benjo AM, Konstantinidis I, Annapureddy N, *et al.* The burden of dialysis-requiring acute kidney injury among hospitalized adults with HIV infection: A nationwide inpatient sample analysis. *AIDS* 2015;29:1061-6.
42. Peraldi MN, Maslo C, Akposso K, Mougnot B, Rondeau E, Sraer JD. Acute renal failure in the course of HIV infection: A single-institution retrospective study of ninety-two patients and sixty renal biopsies. *Nephrol Dial Transplant* 1999;14:1578-85.
43. Swanepoel CR, Atta MG, D'Agati VD, Estrella MM, Fogo AB, Naicker S, *et al.* Kidney disease in the setting of HIV infection: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2018;93:545-59.
44. Cheung CY, Wong KM, Lee MP, Liu YL, Kwok H, Chung R, *et al.* Prevalence of chronic kidney disease in Chinese HIV-infected patients. *Nephrol Dial Transplant* 2007;22:3186-90.
45. Medapalli RK, Parikh CR, Gordon K, Brown ST, Butt AA, Gibert CL, *et al.* Comorbid diabetes and the risk of progressive chronic kidney disease in HIV-infected adults: Data from the veterans aging cohort study. *JAIDS* 2012;60:393-9.
46. Mocroft A, Kirk O, Gatell J, Reiss P, Gargalianos P, Zilmer K, *et al.* Chronic renal failure among HIV-1-infected patients. *AIDS* 2007;21:1119-27.
47. Han TM, Naicker S, Ramdial PK, Assounga AG. A cross-sectional study of HIV-seropositive patients with varying degrees of proteinuria in South Africa. *Kidney Int* 2006;69:2243-50.