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Renal disease in human immunodeficiency virus infection; a divergent array

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ABSTRACT

Background: Renal disease is an important cause of morbidity and mortality in populations with HIV infection. Widespread use of combination antiretroviral therapy has altered the spectrum of renal disease. Studies among the HIV affected population in India are few.
Objectives: The study was carried out to determine the various histopathological lesions in HIV patients with renal dysfunction, undergoing a renal biopsy, and to establish the clinico-pathological correlation.
Patients and Methods: Thirty HIV-positive patients, diagnosed by enzyme-linked immunosorbent assay (ELISA) method according to the National AIDS Control Organization (NACO) guidelines, undergoing a renal biopsy for renal dysfunction were studied. Descriptive statistics were applied.
Results: Rather than the classic human immunodeficiency virus associated nephropathy (HIVAN) or a few prototypical lesions, the cases were spread across the entire spectrum of glomerular and tubulointerstitial pathologies described in the HIV population. A higher proportion of diabetic nephropathy, IgA nephropathy and chronic interstitial nephritis were encountered in the present study.
Conclusions: In the present scenario of increasing incidence of HIV infection, studying its various manifestations are relevant. As none of the clinical or laboratory variables are found to predict glomerular versus non-glomerular lesions on biopsy, a renal biopsy is indicated in renal dysfunction associated with HIV, to make an accurate diagnosis and for therapy.

Implication for health policy/practice/research/medical education:
HIV-related kidney disease has become a relatively common cause of ESRD requiring dialysis, and kidney disease may be associated with progression to AIDS and death. For patients with declining renal function, knowledge of their renal histology obtained by renal biopsy, would provide powerful prognostic information that would alter the therapy in appropriate clinical circumstances.

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1. Background

Human immunodeficiency virus (HIV) infection and the acquired immune deficiency syndrome (AIDS) has appeared as a multi-system disease which involves almost all organs of the body (1). In spite of advances in the treatment protocols of HIV infection, patients infected with HIV are still susceptible to a variety of complications that are either due to immunodeficiency or from the side effects of highly active anti-retroviral therapy (HAART) regimens. The kidneys are increasingly affected by a variety of disease processes. Opportunistic infections including those caused by atypical organisms, malignancies such as lymphoma and Kaposi sarcoma, and disease processes specific to HIV infection such as

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human immunodeficiency virus associated nephropathy (HIVAN) have all been shown to affect the kidneys (2). With the prevalence of HIV infection and the survival rate of HIV-infected patients increasing, early recognition and diagnosis of the cause of renal impairment in these patients cannot be overstated. Radiological findings in HIVAN are nonspecific, and the histological diagnosis plays a decisive role in this situation. It is paramount that the pathologist be familiar with the histological features that can be encountered in these patients for better patient management (2).

HIV affects the glomerular, tubulointerstitial and vascular compartments of the kidney (3). Renal biopsy in an HIV infected patient in the setting of clinical renal dysfunction is justified not only to determine whether the patient has HIVAN, as this worsens the prognosis of these patients, but also to identify or exclude other renal lesions that may be treatable or potentially reversible (1). India faces the threat of an AIDS epidemic; nevertheless risk factors and the racial background of our HIV positive population are different from those in the western countries (1). As studies pertaining to renal diseases in HIV and data on their histopathological lesions from India are limited, (4,5) this study was conducted to document the clinicopathological features of various renal diseases in an HIV-positive patient population in a south Indian tertiary care center.

2. Objectives

The study was carried out to determine the various histopathological lesions in HIV patients with renal dysfunction, undergoing a renal biopsy, and to establish the clinico-pathological correlation.

3. Patients and Methods

3.1. Study population

A total of thirty patients were studied. It included patients seropositive for HIV by ELISA and who underwent a renal biopsy during the course of their clinical care as determined by their treating nephrologists. Demographic and clinical information, preliminary investigations including routine hematological profile, urinalysis, blood urea, creatinine, serum electrolytes, and ultrasound imaging of the kidney were done prior to the biopsy procedure. Renal biopsy was performed under local anaesthesia, two cores were taken and the tissue was placed in 10% formalin for light microscopic (LM) examination and in saline or Michele's medium for immunofluorescence (IF) studies.

For LM, multiple step serials (32) from the renal core were stained and studied using hematoxylin and eosin,

periodic acid Schiff, Masson trichrome and Jones silver methenamine stains. For IF, the biopsy specimens were washed in phosphate-buffered saline (PBS) thrice followed by embedding the tissue for frozen section in optimum cutting temperature (OCT) medium. Once the tissue was frozen, 2-3 micron thin sections were cut. One to two sections were layered on each slide and were labeled as IgG, IgA, IgM, C3, C1q, kappa and lambda. The slides were then stained with fluorescein isothiocyanate (FITC) labeled anti-human antibodies of IgG, IgA, IgM, C3, C1q, kappa and lambda light chains respectively (DACO). The slides were then incubated for an hour at 37 degrees Celsius. After incubation the slides were again washed thrice with PBS, mounted with glycerin and viewed under immunofluorescent microscope-Olympus BX 41.

The demographic and laboratory parameters were described for the study group overall and for groups of patients defined by their histological diagnosis.

3.2. Ethical issues

The study protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of JSS medical college and hospital, JSS University (India). An informed consent was taken from all the patients prior to the biopsy procedure.

3.3. Statistical evaluation

Descriptive statistics were expressed as mean ± standard deviation and results on categorical measurements as numbers (%). Statistical analysis was performed by utilizing the software IBM SPSS© Statistics version 21. Microsoft Word and Excel were used to generate graphs and tables.

4. Results

The age of the patients ranged from 24 to 71 years (mean ± SD; 45.9 ± 12.27 years). Of the 30 patients studied, 23 (76.7 %) were males and seven (23.3%) were females, and the male: female ratio was 3.29: 1.

The predominant presenting features were decreased urine output and edema. The commonest indication for renal biopsy was rapidly progressive renal failure in ten (33.3 %) followed by nephrotic syndrome and chronic renal failure in nine patients each (30%).

All the patients were HIV positive. In five cases, serology test for HIV was incidentally found to be positive during pre-biopsy work up. In others, the duration of sero-positivity ranged from 2 months to 12 years. Eleven patients (33 %) with renal dysfunction were on HAART, with seven on first and four on second line of therapy.

Two of the patients were also positive for hepatitis B surface antigen (HBsAg), and one for hepatitis C virus (HCV) antigen.

Twelve patients had diabetes and ten were hypertensives. Of these, seven patients had both diabetes and hypertension. Three patients had tuberculosis and were on treatment.

The serum creatinine at the time of presentation ranged between 0.9 and 16.2 mg/dL (mean 4.24 ± 3.62 mg/dL). The blood urea ranged between 44.0 to 64.0 mg/dL (mean 52.4 ± 7.3 mg/dL). By dipstick analysis, proteinuria was seen in 15 cases. Five patients had 4+ proteinuria. A maximum 24-hour urine protein of 18.2 mg/dL was observed. The urine protein creatinine ratio (PCR) ranged between 2.0 and 6.5 mg/dL (mean 3.83 ± 2.09 mg/dL). Red blood cells (RBCs) in urine was seen in seven cases, pus cells in two and urine casts (hyaline, granular, RBC and pus cells) were noted in six cases. CD4 counts were available in eight patients, and ranged from 10–404 cells/mm^3 (Mean = 237.12 ± 138.88 cells/mm^3)

The various lesions encountered are described in Table 1. In the 30 cases, a total of 36 discrete defined lesions were studied. This was because some of the patients had combined lesions.

4.1. Glomerular lesions

The proportion of glomeruli in the biopsies varied from 1 to 31, with a mean of 13.66 ± 7.47. The proportion of obsolescent glomeruli ranged from 0-20 (mean 3.10 ± 4.44).

Glomerular size was normal, except in one case. Segmental sclerosis was observed in five cases, including a case of IgA nephropathy. Glomerular tuft collapse was seen in five cases. Podocyte hyperplasia and hyalinosis were noted in one case each. Increased mesangial matrix deposition was seen in one case and 12 cases showed mesangial hypercellularity. Formation of Kimmelstiel-Wilson nodule of diabetic glomerulosclerosis was recognized in six cases. Capillary lumina were patent in all the cases except in one where it was obliterated. Variably thickened basement membrane (BM) was noted in eight cases and double contoured basement membrane and BM spikes (Figure 1) were seen in one case each. Crescents were noted in three cases, of which two were partial fibro-cellular and one was circumferential cellular. No necrotizing or fibrinoid lesions were seen.

4.2. Tubulointerstitial lesions

Varying degrees of tubular injury was noted in eight (26.6%) cases. Apart from the five cases diagnosed as acute tubular injury (toxic/ischemic), changes of tubular injury were noted in cases of IgA nephropathy, diffuse proliferative glomerulonephritis (DPGN) and membranous nephropathy (Table 2).

Tubulointerstitium was normal in 13 cases. In the rest 17 cases, tubular atrophy ranged from 10-50 %(Mean = 15.34%). Urinary casts (hyaline, granular RBC and pus cell casts) were noted in six cases. An interesting finding in a case was the presence of needle shaped urate crystals

Table 1. Histopathology of HIV associated renal diseases

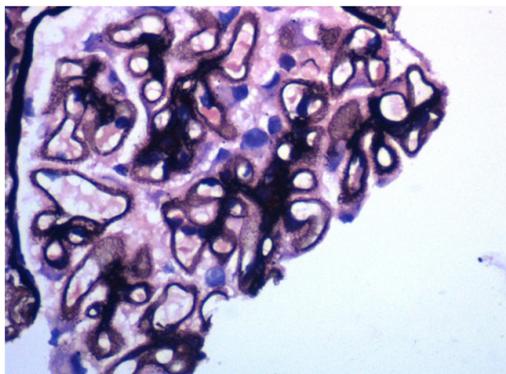| Histopathological diagnosis	Number of cases	Percent
Acute interstitial nephritis (AIN)	1	3.3
Acute on chronic pyelonephritis (APN)	1	3.3
Acute tubular injury (ATI)	3	10.0
Acute tubular injury with acute interstitial nephritis (ATI, AIN)	2	6.6
IgA nephropathy with acute tubular injury (ATI, IgA)	1	3.3
Chronic interstitial nephritis (CIN)	4	13.3
Diabetic nephropathy (DN)	4	13.3
Diabetic nephropathy with membranous nephropathy (DN, MN)	1	3.3
Diabetic nephropathy with thrombotic microangiopathy (DN, TMA)	1	3.3
Diabetic nephropathy with diffuse proliferative glomerulonephritis (DPGN, DN)	1	3.3
Diffuse proliferative glomerulonephritis (DPGN) with acute interstitial nephritis and acute tubular injury	1	3.3
Focal segmental glomerulosclerosis (FSGS)	4	13.3
IgA nephropathy (IgA)	2	6.7
Immune complex mediated glomerulonephritis (ICGN)	1	3.3
Mesangial proliferative glomerulonephritis (MesPGN)	1	3.3
Membranous nephropathy (MN) with acute tubular injury	1	3.3
Urate induced chronic interstitial nephritis (UCIN)	1	3.3
Total	30	100.0

Figure 1. Basement membrane thickening with spikes in membranous glomerulonephritis. (JMS, X200)
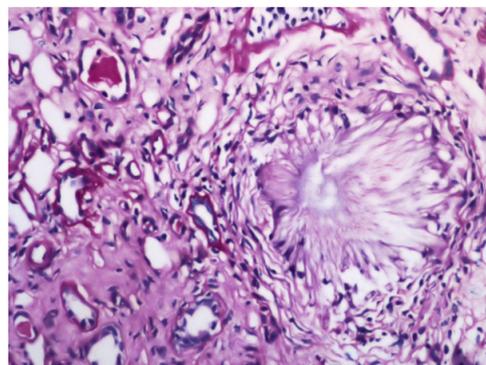

Figure 2. Needle shaped urate crystals forming urate granuloma. (PAS, X200).

Table 2. Histopathology of tubulointerstitial lesions in HIV

Tubulointerstitial lesions	No. of cases	Percent
Acute tubular injury	8	26.6
Acute tubulointerstitial nephritis	4	13.3
Chronic interstitial nephritis	4	13.3
Acute on chronic pyelonephritis	1	3.3
Urate induced nephropathy	1	3.3

and forming a urate granuloma (Figure 2).

4.3. Vascular lesions

One patient had thrombotic microangiopathy. Hyaline arteriosclerotic changes were seen in ten cases. Most cases (24 of 30) showed hyperplasia of the tunica media. Intimal fibroplasia was noted in ten cases. Intraluminal thrombi were seen in two cases.

4.4. IF findings

The immunofluorescence was negative in all the tubulointerstitial diseases and in a few glomerular diseases (focal segmental glomerulosclerosis and diabetic nephropathy). It was positive in diffuse proliferative glomerulonephritis (DPGN), IgA nephropathy, immune mediated glomerulonephritis (GN), and membranous GN. No light chain restriction was observed. However in all the three cases of IgA nephropathy, the intensity of lambda chain staining was more than kappa.

5. Discussion

The course and prognosis of patients infected with the HIV virus is changing dramatically following the introduction of HAART, with increased patient survival and decreased morbidity (6). Current therapy offers patients increased survival but, is in turn making them more susceptible to certain co-morbidities. The spectrum of kidney disease in patients with HIV also reflects the growing burden of co-morbid diabetes, hypertension and development of chronic renal disease (7,8).

Patients with HIV infection may develop different types of glomerular diseases, vascular lesions, and tubulointerstitial nephritis related in some cases with the virus itself and in others due to co-infections or nephrotoxic drugs.

Renal disease in patients infected with HIV was first described (9) in 1984, as a focal and segmental glomerulonephritis, subsequently termed as 'HIVAN'. The available studies have shown that HIVAN is more common in USA and UK, whereas mesangioproliferative glomerulonephritis, membranous nephropathy and membranoproliferative glomerulonephritis (MPGN) are more common in Italy, Thailand, and in northern India (10). While the exact cause of the discrepancy is not entirely clear, racial predisposition, viral genotype and other immunomodulatory host susceptibility factors may play a role or simply because of dearth of data in the said-population (3).

As the prevalence of HIV is increasing, the spectrum of renal disorders in HIV patients is also changing (5). In this study, we have reviewed different types of renal diseases found in patients with HIV infection, highlighting its possible etiology, clinical presentation and more importantly pathological diagnosis.

The patient age ranged from 24 to 71 years (mean ± SD; 45.9 ± 12.24 years) in the present study. The male to female ratio was 3.29: 1. The mean age was higher in this study when compared to other study groups, but the age range was similar (Table 3) (5,7,11-14). This can be explained by the presence of a few cases in the higher age group, increasing the mean age. In addition, it might

Table 3. Comparison of age and gender distribution

Studies	Age		Gender		
	Range	Mean	Males	Females	M:F ratio
Gupta et al (India)	25-45	36.5	21	5	4.5
Vali et al (India)	20-60	38.2	23	4	5.75
Janakiraman et al (India)	-	34.4	6	4	1.5
Szczech et al (USA)	-	42.35	73	16	4.56
Gutiérrez et al (Spain)	24-51	38.3	23	4	5.75
Gerntholtz et al (South Africa)	-	33.75	64	40	1.6
Present Study	24-71	45.9	23	7	3.29

also indicate the increased survival and later presentation of renal disease in the affected patients.

The mode of clinical presentation was categorised into five groups in the present study into; acute kidney injury (AKI), chronic kidney disease (CKD) - defined as evidence of kidney damage that persists for ≥3 months (15), nephritic/nephrotic syndrome, nephrotic syndrome and rapidly progressive renal failure (RPRF). Similar to other studies, the proportion of patients presenting with acute kidney injury and RPRF was the predominant reason for performing a kidney biopsy. However, an increased number of chronic kidney diseases were also encountered in the present study (Table 4) (5,7-14).

HIV infection appears to be a risk factor for developing CKD. Other known risk factors include hepatitis C virus (HCV) co-infection, family history, increased viral load levels (>4000 copies/mL), reduced CD4 cell count (<350 cells/mm³), and older age (16).

The data regarding the time, duration since diagnosis of retroviral positivity and initiation of ART was obtained along with CD4 cell counts at biopsy.

The Infectious Disease Society of America (IDSA) indicates viral load levels of >4000 copies/mL and CD4 counts of less than 350 cells/mm³ as risk factors for kidney disease (17). Viral load assay was not done in the present study. Absolute CD4 counts are accepted as the best indicator of immunologic competence of patients with HIV infection and as an indirect reflection of HIV viral load and activity (12). The mean CD4 count in the present study was lower than 350 cells/mm³ (227.6 cells/mm³).

A few patients were diagnosed to be retroviral positive only at the time of biopsy. Others in whom it was previously diagnosed, the mean duration of infection was 22.5 months compared to the study by Janakiraman et al (12), but higher than Gupta et al (12) and Vali et al (5).

The association of diabetes mellitus and hypertension with HIV-related renal disease is complex. While they add to the disease burden, therapy associated diabetes mellitus and hypertension is also known (18). Hypertension and diabetes are also important causes of CKD in HIV. In one cross-sectional analysis, 55% of patients with HIV and CKD had hypertension and 20% had diabetes (19). With prolonged survival and aging of the HIV-infected population in the United States and Western Europe, the spectrum of kidney disease in patients with HIV also reflects the growing burden of comorbid diabetes and hypertension (7,20). In the present study, 12 patients had diabetes and ten were hypertensives. Of these, seven patients had both diabetes and hypertension, which could be the cause of increased number of patients presenting with CKD in the present study.

In a study by AIIMS New Delhi, a higher percentage of

Table 4. Comparison of clinical syndromes at the time of biopsy

Clinical syndromes	AKI	RPRF	AKI + RPRF	CKD	Nephritic/ nephrotic syndrome	Nephrotic syndrome	Acc HTN
Gupta et al (India)	-	-	-	-	-	50	-
Vali et al (India)	37.04	14.85	51.89	7.4	3.7	33.84	3.7
Janakiraman et al (India)	4.7	-	-	-	-	-	-
Szczech et al (USA)	-	-	-	-	-	-	-
Gutiérrez et al (Spain)	59.3		59.3		3.7	51.9	33.3
Gerntholtz et al (S Africa)	-	-	-	-	-	-	-
Present Study	3.3	33.3	36.6	30	3.3	30	-

Abbreviations: AKI, acute kidney injury; RPRF, rapidly progressing renal failure; CKD, chronic kidney disease; Acc HTN, accelerated hypertension.

patients (80.21%) were found to have proteinuria (11). In the present study, proteinuria was found in 63.3% of cases. Nephrotic range proteinuria was observed in nine (30%) cases. The clinical evaluation of patients at increased risk for CKD includes assessment of markers of kidney damage, such as proteinuria, kidney function, and blood pressure. Even in patients with normal kidney function, the presence of proteinuria may indicate early kidney disease which reiterates the importance of screening of patients with HIV for proteinuria (16).

A strong correlation with serum creatinine levels and progression to end-stage renal disease (ESRD) in HIV patients has been linked to an index of chronic damage on renal histology (21). The mean serum creatinine (5.85) in the present study was higher and comparable with other studies (5,11,14).

The earlier studies on HIV associated renal disease involving native Africans showed a significant number of cases of HIVAN indicating it to be the hallmark of renal HIV infection (22). However, subsequent studies involving other racial groups around the world have shown a myriad of glomerular and tubulointerstitial lesions, which was also observed in the present study (Table 5) (1,5,7,11-14,23,24).

Diseases such as MPGN, membranous nephropathy, and postinfectious glomerulonephritis are often seen in the setting of hepatitis B and/or hepatitis C viral infection, are also common in HIV-infected patients with renal disease (25). Nochy et al (26) described four types of glomerulonephritis in patients with HIV infection in a population of French patients, which also included immune complex mediated glomerulonephritis. In HIV-infected patients, the deposition of circulating immune complexes, leading to localized inflammation, or as a consequence of polyclonal B-cell activation against an antigen in renal tissue, such as an HIV protein, can cause an immune complex disease (27,28).

There are three distinct HIV-associated immune complex glomerulonephritis: (1) a proliferative glomerulonephritis, (2) a mixed sclerotic-immune complex nephropathy, and (3) IgA nephropathy (26,29). IgA nephropathy has been seen in several patients with HIV infection (30). Study by Beaufils et al, demonstrated a 7.75% prevalence of diffuse mesangial deposits of IgA in patients who died of AIDS (30). Idiotypic IgA antibody was found in eluates of renal biopsy tissue (31). An immunoregulatory dysfunction associated with HIV infection, evokes an idiotypic immune reaction, formation of immune complexes and their deposition in the kidneys resulting in IgA glomerulonephritis. Nine cases of immune complex mediated glomerulonephritis (30%) were encountered in the present study, which included three cases of IgA nephropathy, two cases of DPGN and membranous GN and one case each of immune complex mediated GN and mesangioproliferative GN, the probable pathogenesis of which have been discussed.

Table 5. Frequency of glomerular and tubulo-interstitial lesions in various studies

Predominant histopathological lesions	No of cases	Glomerular lesions	Tubulointerstitial lesions
Gupta et al (India)	26	MesPGN 38%, MPGN 7.6%, Collapsing FSGS 7.6%	AIN 15%
Vali et al (India)	27	Collapsing FSGS 11.1%, FSGS 7.4% Amyloidosis 1.1%, DPGN 7.4%	AIN/ATIN 22.2%, APN 7.4%, Acute on CIN 7.4%
Janakiraman et al (India)	10	HIVAN 70%, DPGN 10%, MN 10%	CIN 10%
Szczech et al (USA)	89	HIVAN 47.2%, ICGN 14.6%, MN 8.9%	A/CIN 3.3% APN 1.1%
Gutiérrez et al (Spain)	27	MPGN 29.6%, FSGS 25.9%, MESPGN 22.2%, HIVAN 14.8%	
Gerntholtz et al (S Africa)	99	HIVAN 27%, ICGN 21%, MN 13%, PIGN 8%, MESPGN 6%, IgA 5%	
D'agati et al	136	FSGS 64.7%,MPGN 9.5%, MCD 4.4%, amyloidosis 2.9% 6.6%	
Madiwale et al		85%	
Peraldi et al		60%	
Present Study	30	DiabeticN 23.3%, FSGS 13.3%, IgAN 10%, DPGN 6.6%	ATI 26.6%, AIN 13.3%, CIN 13.3%

Abbreviations: Mes PGN, mesangioprolferative glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; FSGS, focal segmental glomerulosclerosis; AIN, acute interstitial nephritis; DPGN, Diffuse proliferative glomerulonephritis; MN, membranous nephropathy; ATIN, acute tubulointerstitial nephritis; APN, acute pyelonephritis; CIN, chronic interstitial nephritis; HIVAN, human immunodeficiency virus associated nephropathy; ICGN, immune complex mediated glomerulonephritis; PIGN, post infectious glomerulonephritis; MCD, minimal change disease; DiabeticN , diabetic nephropathy; IgAN, IgA nephropathy

The prevalence of tubular and interstitial lesions in various studies have ranged from 10%–16.7% and 11-20% (8,17,24,26,32,33,34), compared to 26.6% and 33.3% in the present study. The increased prevalence of these diseases in the study population can be explained by the fact that the tubulointerstitial lesions secondary to glomerular diseases were also included in the study. Considering the therapeutic implications of diagnoses of drug toxicity, infections, and dysimmune syndromes, it is important to monitor the renal parameters in HIV-infected patients and to perform a kidney biopsy when indicated, to allow an accurate diagnosis (34).

To summarise, the lesions encountered, did not point towards any specific group of diseases in the study population. Though the study sample was small, all of them had renal dysfunction, in turn representing the patients at risk. As seen in the general population, all the common renal pathological lesions were observed in the study. This may be due to a change in the pattern of HIV related renal diseases. With early institution of HAART therapy, the epidemiology of the renal diseases may be approaching the general population.

6. Conclusions

HIV-related kidney disease has become a relatively common cause of ESRD requiring dialysis, and kidney disease may be associated with progression to AIDS and death. For patients with declining renal function, knowledge of their renal histology obtained by renal biopsy would provide powerful prognostic information that would alter the therapy in appropriate clinical circumstances.

HIVAN is associated with rapid decline in GFR and nephrotic proteinuria and shows good response to anti-retroviral therapy. The non-HIVAN renal diseases, with significant heterogeneity are associated with inconsistencies in the response to antiretroviral therapy. Also recognized causes of kidney diseases such as diabetes mellitus and hypertension are increasingly being reported in the HIV-infected population. As patients with HIV live longer and experience chronic co-morbidities in addition to HIV, these may contribute more to morbidity and mortality than HIV itself. Screening these patients for diabetes and hypertension must be an integral part of follow up, especially among patients who are on ART. Several large studies have been reported from all around the world. Studies involving the Indian population are sparse. The racial background and risk factors of our HIV population differ from those of western countries. This study which focuses on renal pathology will be an important addition to the knowledge base and also provide information to increase the clinical utility of renal biopsy among HIV-infected patients with renal dysfunction.

Limitations of the study

The study population was small. More longitudinal studies with outcome based study design and large sample size are necessary to develop clinically useful prognostic information.

Authors' contribution

SS and DN; study design, data acquisition, analysis and interpretation. SS and MV; revising critically for important intellectual content. MS; consultant of the study. All authors read and approved the final manuscript.

Conflicts of interest

There were no points of conflicts to declare.

Ethical considerations

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

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References

1. Madiwale C, Venkataseshan VS. Renal lesions in AIDS: A biopsy and autopsy study. Indian J. Pathol. Microbiol. 1999;42(1):45-54.
2. Symeonidou C, Standish R, Sahdev A, Katz RD, Morlese J, Malhotra A. Imaging and Histopathologic Features of HIV-related Renal Disease. Radiographics. 2008;28(5):1339-54. doi: 10.1148/rg.285075126.
3. Naaz I, Wani R, Najar MS, Banday K, Baba KM, Jeelani H. Collapsing glomerulopathy in an HIV-positive patient in a low-incidence belt. Indian J Nephrol. 2010;20(4):211-3. doi: 10.4103/0971-4065.73451.
4. Das U, Dakshinamurty KV, Prayaga A. Pattern of biopsy-proven renal disease in a single center of south India: 19 years' experience. Indian J Nephrol. 2011;21(4):250-7. doi: 10.4103/0971-4065.85482.
5. Vali PS, Ismal K, Gowrishankar S, Sahay M. Renal disease in human immunodeficiency virus - Not just HIV-associated nephropathy. Indian J Nephrol. 2012;22(2):98-102. doi: 10.4103/0971-4065.97117.
6. Mocroft A KO, Gatell J, Reiss P, Gargalianos P, Zilmer K, Beniowski M, et al. Chronic renal failure among HIV-1-infected patients. AIDS. 2007;21(9):1119-27.doi: 10.1097/QAD.0b013e3280f774ee.
7. Szczech LA GS, Habash R, Guasch A, Kalayjian R, Appel R, Fields TA, et al. Association between renal disease and outcomes among HIV-infected women receiving or not

receiving antiretroviral therapy. Clin Infect Dis. 2004; 39(8):1199-206. doi: 10.1086/42401.

8. 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(4):428-34. doi: 10.1038/ki.2008.604.

9. Rao TK, Filippone EJ, Nicastri AD, Landesman SH, Frank E, Chen CK, et al. Associated focal and segmental glomerulosclerosis in the acquired immunodeficiency syndrome. N Engl J Med. 1984;310(11):669-73. doi: 10.1056/NEJM198403153101101.

10. Praditpornsilpa K, Napathorn S, Yenrudi S, Wankrairot P, Tungsaga K, Sitprija V. Renal pathology and HIV infection in Thailand. Am J Kidney Dis. 1999;33(2):282-6.

11. 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(5):950-6.

12. 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(4):603-7.

13. Gutiérrez E, Morales E, Gutiérrez Martínez E, Manzanares MJ, Rosello G, Mérida E, et al. Glomerulopathies associated to HIV infection: a Spanish perspective. Nefrologia. 2007;27(4):439-47.

14. Gerntholtz TE, Goetsch SJ, Katz I. HIV-related nephropathy: a South African perspective. Kidney Int. 2006;69(10):1885-91. doi: 10.1038/sj.ki.5000351.

15. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39(2 Suppl 1):S1-266.

16. Gupta SK, Eustace JA, Winston JA, Boydstun II, 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(11):1559-85.doi: 10.1086/430257.

17. Szczech LA, Gange SJ, van der Horst C, Bartlett JA, Young M, et al. Predictors of proteinuria and renal failure among women with HIV infection. Kidney Int. 2002;61(1):195-202. doi: 10.1046/j.1523-1755.2002.00094.x.

18. Diouf A, Cournil A, Ba-Fall K, Ngom-Guèye NF, Eymard-Duvernay S, Ndiaye I, et al. Diabetes and Hypertension among Patients Receiving Antiretroviral Treatment Since 1998 in Senegal: Prevalence and Associated Factors. ISRN AIDS. 2012; 2012:621565. doi: 10.5402/2012/621565.

19. Wyatt CM, Winston JA, Malvestutto CD, et al. Chronic kidney disease in HIV infection: An urban epidemic. AIDS. 2007;21(15):2101-3. doi: 10.1097/QAD.0b013e3282ef1bb4.

20. Wyatt CM, Morgello S, Katz-Malamed R, Wei C, Klotman ME, KlotmanPE, et al. The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. Kidney Int. 2009;75(4):428-34. doi: 10.1038/ki.2008.604.

21. Naicker S, Fabian J. Risk factors for the development of chronic kidney disease with HIV/AIDS. Clin Nephrol. 2010;74 Suppl 1:S51-6.

22. Bourgoignie JJ, Meneses R, Ortiz C, Jaffe D, Pardo V. The clinical spectrum of renal disease associated with human immunodeficiency virus. Am J Kidney Dis. 1988;12(2):131-7.

23. D'Agati V, Suh JI, Carbone L, Cheng JT, Appel G. Pathology of HIV-associated nephropathy: A detailed morphologic and comparative study. Kidney Int. 1989;35(6):1358-70.

24. Peraldi MN, Maslo C, Akposso K, Mougenot 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(6):1578-85.

25. Weiner NJ, Goodman JW, Kimmel PL. The HIV-associated renal diseases: current insight into pathogenesis and treatment. Kidney Int. 2003;63(5):1618-31. doi: 10.1046/j.1523-1755.2003.00901.x.

26. Nochy D, Glotz D, Dosquet P, Pruna A, Guettier C, Weiss L, et al. Renal disease associated with HIV infection: a multicentric study of 60 patients from Paris hospitals. Nephrol Dial Transplant. 1993;8(1):11-9.

27. Hebert LA. Deposition of IgA-containing circulating immune complexes. Am J Kidney Dis. 1988;12(5):388-92.

28. Emancipator SN. Immunoregulatory factors in the pathogenesis of IgA nephropathy. Kidney Int. 1990;38(6):1216-29.

29. Kimmel PL, Berns JS, Stein JH, eds. Renal and Urologic Aspects of HIV Infection. New York: Churchill Livingstone; 1995. p. 77–110.

30. Beaufils H, Jouanneau C, Katlama C, Sazdovitch V, Hauw JJ. HIV-associated IgA nephropathy--a post-mortem study. Nephrol Dial Transplant. 1995;10(1):35-8.

31. Kimmel PL, Phillips TM, Ferreira-Centeno A, Farkas-Szallasi T, Abraham AA, Garrett CT. Brief report: idiotypic IgA nephropathy in patients with human immunodeficiency virus infection. N Engl J Med. 1992;327(10):702-6. doi: 10.1056/NEJM199209033271006.

32. Berliner AR, Fine DM, Lucas GM, Rahman MH, Racusen LC, Scheel PJ, et al. Observations on a cohort of HIV-infected patients undergoing native renal biopsy. Am J Nephrol. 2008;28(3):478-86. doi: 10.1159/000112851.

33. Parkhie SM, Fine DM, Lucas GM, Atta MG.: Characteristics of patients with HIV and biopsy-proven acute interstitial nephritis. Clin J Am Soc Nephrol. 2010;5(5):798-804. doi: 10.2215/CJN.08211109.

34. Zaidan M, Lescure FX, Brochériou I, Dettwiler S, Guiard-Schmid JB, Pacanowski J, et al. Tubulointerstitial nephropathies in HIV-infected patients over the past 15 years: a clinico-pathological study. Clin J Am Soc Nephrol. 2013;8(6):930-8. doi: 10.2215/CJN.10051012.