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Clinicopathological Profile of Renal Dysfunction in People Living With HIV and Aids

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ABSTRACT

Background: To evaluate renal dysfunction in patients with HIV.

Methods: 300 patients were included to our research work for a period of one year and follow up of patients with renal involvement was done in 1st 2nd 3rd 6th and 12th month.

Results: Urea and Creatinine in AKI and CKD impairment is statistically significant. Serum Sodium in AKI and CKD is significant where Potassium in AKI and CKD is not significant in AKI but significant in CKD.Serum Calcium in AKI and CKD is not significant in AKI, significant in CKD but Serum Phosphate is statistically not significant.Proteinuria in AKI and CKD is significantly.CD4 count in AKI and CKD is significantly lower in both AKI and CKD.CD4 count is less than 200 in 22(64.7%) patients out of 34 in AKI, and 9(81.81%) out of 11 in CKD which is significant.HAART in AKI and CKD is not significant.Outcome in AKI and CKD is statistically significant.

Conclusion: AKI is more common with infection sepsis and dehydration with spontaneous recovery of renal function with treatment.Typical HIVAN was not seen where collapsing FSGS is not uncommon.Tenofovir induced renal impairment was not documented. Proteinuria, elevated creatinine could be an early marker of renal lesions.Renal biopsy is considered beneficial in patients with proteinuria especially with low CD4 count for early diagnosis and treatment.Treatment with ACEI or ARBs and Steroids can be prevent ESRD.Significant low CD4 count was observed both in AKI and CKD.

Keywords: Human immunodeficiency virus(HIV),Highly active antiretroviral theraphy(HAART),Acute kidney injury(AKI),Chronic kidney disease(CKD),HIV-associated nephropathy(HIVAN).

INTRODUCTION

Globally 37.9 million people were living with Human Immunodeficiency Virus (HIV) at the end of 2018. The prevalence of HIV varies widely between geographical regions. Approximately 2.1 million populations were estimated to be infected with HIV in India in 2018. (1)

With the prevalence of HIV increasing, the size of HIV infected population and longevity of HIV affected patients are increasing due to the Highly Active Antiretroviral therapy (HAART). Renal disease is becoming an important cause of morbidity and mortality in population with HIV infection as HIV infection has a tendency to progress to a chronic disease. (2)

Renal disorders are encountered at all stages of HIV infection. HIV-related renal impairment can present as acute or chronic kidney disease; it can be caused directly or indirectly by HIV and/or by drug-related effects that are directly nephrotoxic or lead to changes in renal function by inducing metabolic vasculopathy and renal damage. Acute renal failure is frequently caused by the toxic effects of antiretroviral therapy or nephrotoxic antimicrobial substances used in the treatment of opportunistic infections. Chronic renal disease can be caused by multiple pathophysiological mechanisms leading to HIV-associated nephropathy a form of collapsing focal glomerulosclerosis, thrombotic microangiopathy,

interstitial nephritis and various forms of immune complex glomerulonephritis.(3)

HIV-associated chronic kidney disease (CKD) vary widely between calendar periods populations and settings. Renal disease has been reported in approximately 6.0–48.5% of HIV-infected individuals in Africa; 24–83% of these cases were classic HIVAN in South Africa.(4). A cross-sectional study of 31 European countries, Israel and Argentina reported HIV-associated- CKD in 3.5–4.7% of HIV-infected individuals (5). Renal histological findings also vary between countries. Other epidemiological studies have reported rates of 18% in Hong Kong (6), 1.1–5.6% in Brazil (7), 18% in Switzerland (8) and 20% in Iran(9). Renal histological findings also vary between countries.

HIV associated kidney disease is increasing worldwide. In developing countries like India limited financial resources and lack of infrastructure put a severe strain on existing health policies in the light of the increasing burden of HIV associated renal disease. Acute kidney injury (AKI) is an important cause of hospitalization and morbidity in human immunodeficiency virus (HIV) positive patients. However, the data on AKI in such patients is limited.

Naaz et al (10) from India reported first case of classical HIVAN from the State of Jammu and Kashmir, a low incident belt for HIV. Subsequently another study from India reported two patients of HIVAN presented with nephritic range proteinuria with renal involvement in HIV infected children. (11)

Materials and Methods:

300 patients attending our ART Clinic and Medicine OPD who were fulfilled inclusion and exclusion criteria were included our study. This was undertaken over a period of one year. Valid consent was taken from all patients. These patients were screened at different point of time each week during the study period and follow up of patients with renal involvement was done to study their response to therapy and development of chronicity in 1st month, 2nd month, 3rd month, 6th month and 12th month. Proper history and relevant systemic examination were done all our patients for proper evaluation. According to patient's profile relevant investigation (like CBC, Blood urea and creatinine, Serum Sodium and potassium, Serum Calcium and phosphate, sugar-fasting and postprandial, Urine routine, microscopic exam, ACR, 24hours urinary protein when needed, USG of kidney ureter and bladder, ECG, Echocardiography, Renal biopsy when indicated.) were done to evaluate the cases. All data were then analysed statistically.

Inclusion criteria:

Known or newly diagnosed HIV patients attending our Hospital.

Exclusion criteria:

1. Any chronic illness like diabetes, hypertension, chronic hepatitis C infection or SLE which are known to cause renal dysfunction.
2. History of prolonged drug intake known to cause renal dysfunction.
3. Any documentation of renal disease when the patient was known to have been negative for HIV.

Aims and Objectives:

1. To record and observe clinical and investigational findings which suggest renal impairment and observe its prevalence in these people living with HIV/AIDS (PLWHAs)
2. To document identifiable causes that appears to correlate with renal impairments.
3. To observe therapeutic outcomes to identified renal impairments in HIV.

RESULTS:

1. The mean age (mean± SD) of patients without renal involvement was 39.64±10.47 years, AKI 41±10.15 years and CKD 40±9.04 years.
2. Of the 300 patients 213(71%) were males, 87(29) were females. Out of which 45(15%) patients develop renal involvement (proteinuria and renal dysfunction), AKI (n=34, 75.5%), CKD (n=11, 24.5%). Among these those who develop AKI males-27, females-7, CKD males-10, female-1. With no renal involvement, Males-176, females-79.
3. The p value (0.0001 and 0.0629) of TLC in AKI and CKD respectively against no renal impairment is statistically significant in AKI not significant in CKD.

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4. The p-value (0.00001 and 0.00001) of Urea in AKI and CKD respectively against no renal impairment is statistically significant. (Table 1)
5. The p-value (0.00001 and 0.00001) of creatinine in AKI and CKD respectively against no renal impairment is statistically significant. (Table 1)
6. The p-value (0.0008 and 0.0047) of Serum Sodium in AKI and CKD respectively against no renal impairment is statistically significant.
7. The p-value (0.5730 and 0.00001) of Serum Potassium in AKI and CKD respectively against no renal impairment is statistically not significant in AKI but significant in CKD.
8. The p-value (0.2792 and 0.00001) Serum Calcium in AKI and CKD respectively against no renal impairment is statistically not significant in AKI, significant in CKD.
9. The p-value (0.2184 and 0.00001) of Serum Phosphate in AKI and CKD respectively against no renal impairment is statistically not significant.
10. The p-value (<0.0001 and<0.0001) of proteinuria in AKI and CKD respectively against no renal impairment is statistically significantly.
11. The p-value (0.0001 and 0.0001) of CD4 count in AKI and CKD respectively against no renal impairment is significantly lower in both AKI and CKD. (Table 2)
12. CD4 count is less than 200 in 22(64.7%) patients out of 34 in AKI, and 9(81.81%) out of 11 in CKD which is significant.
13. The p-value (0.4522 and 0.6003) of HAART in AKI and CKD respectively against no renal impairment is statistically not significant.
14. The p-value (0.0060 and 0.0001) of outcome in AKI and CKD respectively against no renal impairment is statistically significant.

DISCUSSION:

Renal disease in patients infected with HIV was first described by Rao et al. (12) in 1984 as a focal and segmental glomerulonephritis subsequently termed as 'HIVAN'. The prevalence of HIVAN has been reported to be from 3 to 7% and the US Renal data system has reported a steady increase in the incidence of HIVAN (13). HIVAN is best characterized by nephrotic range proteinuria, azotemia, normal-to-large kidneys on ultrasound scan, normal blood pressure, and collapsing FSGS on renal biopsy. As the prevalence of HIV is increasing the spectrum of renal disorders in HIV patients is also changing. HIVAN which used to be synonymous with HIV renal disease in the first two decades of the HIV pandemic has been replaced with much more common renal disorders namely AKI and other glomerular diseases.

Renal involvement in HIV-positive patients was more common in males in our study.

As evaluated by Prakash et al (14) AKI was noted in 138/3540 (3.9%) in HIV patients. Pre-renal, intrinsic and post-renal AKI were noted in 53.6%, 44.2% and 2.2% of cases respectively. Hypovolemia (44.2%) and sepsis (14.5%) contributed to AKI in vast majority of cases. AKI was multifactorial (volume depletion, sepsis and drugs) in 39% of patients. Mortality was 24.64%.mortality was 24.64%. We noted a highrer incidence of AKI in our study, AKI (n=34) was seen in 11.3% of the total study that comprise of 75.5% of the renal impaired population. The most common cause is associated infection (70.4%) in which tuberculosis (38.2%) predominate. Dehydration was found in 17.6% and multifactorial in 17.6%. No post renal cause was seen. Of the 34 patients, 33(97.05%) recovered and mortality was 2.9%.

In this study, the total leucocyte count was also significantly higher 6934±1688 in AKI than in CKD which is also in consistent with infection being the common cause here. Serum Calcium was significantly lower and Serum Phosphate significantly higher in CKD patients, which was not found significant in AKI.

Han et al (15) did 24-h proteinuria quantification for renal impairment and reported prevalence of 6% overt proteinuria and 8% persistent microalbuminuria in treatment naïve HIV patients in South Africa. Vijay et al from North India study (16) found higher percentage of patients (80.21%) was found to have proteinuria. In our study, transient micro-albuminuria was found in almost all the AKI patients with spontaneous recovery on treatment of the underlying sepsis infection or dehydration. Significant proteinuria was found in the CKD group with one FSGS with nephrotic range proteinuria.

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A report comparing the experience in European and North American centers (17) showed that in Black patients with HIV, FSGS was the commonest lesion occurring in about 80 per cent of renal biopsies.

Varma et al (18) from India described one patient with collapsing FSGS and four with non-collapsing FSGS out of total of 25 HIV positive patients. A pilot study from North India conducted by Vijay et al (16) found two cases showing collapsing FSGS but classical HIVAN features of microcystic tubular dilatation and interstitial cell infiltrate were not seen on light microscopy. Similarly in our study we found 4 out of 7 biopsied showed FSGS, 3 collapsing type and 1 non-collapsing FSGS. These data indicate that collapsing FSGS may not be rare in this part of the world as was previously thought but classical HIVAN is rare. The other 3 biopsy revealed 2 membranoproliferative nephropathy and 1 membranous nephropathy. 3 other patients had a small sized kidney with loss of corticulomedullary junction and Renal biopsy was not done in these patients. Other immune-complex deposits, vascular nephropathy or drug induced nephropathy were not found.

As observed by Vijay et al (16) in their study, the mean CD4 count was significantly lower in patients with renal involvement as compared to no renal involvement group. Similarly here the mean CD4 count in AKI was 223.11±204 (range 19 to 845), CKD was 120.09±86.32 (range 16 to 256) which was significantly lower ($p=0.0001$, <0.05) in both, than the population with no renal involvement 468.23±245.35 (range 48 to 1100). CD4 count was less than 200 in 22(64.7%) patients out of 34 in AKI, and 9(81.81%) out of 11 in CKD which was also significant.

A low occurrence of renal involvement was found in patients already on ART in the study by Vijay et al (16). But no significant association was found beween HAART and renal involvement in this study.

Hemodialysis was required in 1 patient of AKI who gradually recovered after a month with normal and stable renal function. 6 patients (54.54%) of CKD had progressed to ESRD requiring hemodialysis. Patients with MPGN and FSGS who have not progressed to ESRD did well on low dose steroid (0.5 mg/kg/day) and ART (till last follow up) with improvement in proteinuria and renal dysfunction. 2 patients who presented with severe azotemia requiring hemodialysis later died because of sepsis.

CONCLUSION:

From the above observations, it is concluded that:

1. Renal impairment is not uncommon in Indian patients with HIV and many of the patients already developed this at the time of diagnosis.
2. AKI is more common in patients with infection, sepsis and dehydration with spontaneous recovery of renal function with timely treatment.
3. Though typical HIVAN was not seen collapsing FSGS is not uncommon.
4. Tenofovir is a drug known to cause renal impairment but within this study period Tenofovir induced renal impairment was not documented.
5. Proteinuria and elevated serum creatinine could be an early marker of HIV associated renal lesions. So knowing the renal status of the patient by doing simple bedside tests at the time of diagnosis of HIV and before initiating ART will help in managing them and prevent the progression to further renal injury.
6. Renal biopsy is considered beneficial in seropositive patients with proteinuria especially with low CD4 count for early diagnosis and treatment of renal lesion.
7. Proper treatment with ACE Inhibitors or ARBs and Steroids can be tried to prolong the onset of ESRD.
8. Significant low CD4 count was also observed both in AKI and CKD.
9. Although from previous study, a low occurrence of renal involvement was found in patients already on ART suggesting some renoprotective effect of ART. The present study did not find a significant correlation between the two. Larger studies are necessary to confirm these findings with larger sample size and longer duration of follow up.

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Table 1: Distribution of Urea and Creatinine:

Group		Minimum	Maximum	Mean	Median	Std Dev	p-value
AKI (34)	Urea	3.90	191.00	79.90	77.50	37.93	<0.00001
	Creatinine	1.2000	6.54	2.08	1.8500	1.032	<0.00001
CKD(11)	Urea	50.00	224.00	121.36	102.00	63.58	<0.00001
	Creatinine	1.20	11.20	5.66	3.40	4.01	<0.00001
No Renal Impairment(255)	Urea	11.00	70.00	23.83	23.00	7.074	
	Creatinine	0.3000	1.80	0.80	0.90	0.21	

Table 2: Distribution of CD4

Group	Minimum	Maximum	Mean	Median	Std Dev	p-value
AKI (34)	19.00	845.00	223.12	114.00	204.98	<0.0001
CKD(11)	16.00	256.00	120.09	125.00	86.33	<0.0001
No Renal Impairment(255)	48.00	1100.00	468.24	447.00	245.36	

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Table 3: Causes and outcome of AKI and CKD:

Renal impairment (n=45, 15%)	Causes (no) (%)
AKI (n=34, 75.5%)	Sepsis/ Infection- 24 (70.4%) Tuberculosis- 13 (38.2%) RTI, Pneumonia- 8 (23.5%) HSV- 2 (5.8%) UTI- 1 (2.9%) Mutifactorial- sepsis, dehydration etc- 6 (17.6%) Dehydration- 6 (17.6%)
CKD (n=11, 24.5%)	FSGS- 4 (36.3%) Membranoproliferative Nephropathy- 2 (18.18%) Membranous Nephropathy- 1 (9.09%) Renal Biopsy not done- 3 (27.27%)
Death	AKI= 1 (2.9% of AKI) CKD= 2 (18.18% of CKD)
Hemodialysis	AKI=1 (2.9% of AKI) CKD=6 (54.54% of CKD)

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