

A STUDY OF THE RENAL PROFILE IN ART NAÏVE HIV/AIDS PATIENTS

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ABSTRACT:

Background : As HIV/AIDS has emerged to be the first modern pandemic with ever increasing prevalence globally, the present study was undertaken to study the renal profile in patients living with HIV/AIDS, not started on ART.

Materials and Methods: This was a hospital based observational study where 277 cases were studied in details with the aims and objectives of studying the renal manifestations in ART naïve patients with HIV/AIDS and its relationship with CD4 counts. A detailed history, clinical examination and relevant investigations were done in patients above 15yrs of age who were not on ART.

Results and Observations: Out of 277 seropositives, 40 had proteinuria (14.44%) on urine examination. The mean serum creatinine of the total study population was found to be 0.92 ± 0.83 mg/dl while 14 cases (5%) had serum creatinine more than 1.5mg/dl. A decrease in eGFR ($<60\text{ml/min}/1.73\text{m}^2$) was seen in 28 (10.1%) cases. Out of 178 cases with CD4 count more than 200cells/mm^3 , renal dysfunction was found in 12 cases (6.7%), whereas the cases with CD4 count less than or equal to 200cells/mm^3 , 19 out of 99 cases (19.2%) had renal dysfunction which is statistically significant

Conclusion: In the present study, which included ART naïve patients with HIV/AIDS, predominant renal involvement was in the form of proteinuria followed by raised serum creatinine levels and reduced eGFR. A negative correlation was found between renal dysfunction and CD4 counts.

KEY WORDS: HIVAN (Human immunodeficiency virus associated nephropathy),
Renal dysfunction in HIV, CD4 count

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INTRODUCTION

As the fourth leading cause of death around the world and the first leading cause of death in Africa, HIV/AIDS continues to affect 36.7 million people worldwide.¹ The national adult HIV prevalence in India is 0.26%. The total number of People Living with HIV (PLHIV) in India is estimated at 21.17 lakhs of which children account for 6.54% in 2015.²

The clinical consequences of HIV infection encompass a spectrum ranging from an acute clinical syndrome associated with primary infection to a prolonged asymptomatic stage to advanced disease. The spectrum of illnesses changes as the CD4+ T cell count declines.

Diseases of the kidney or genitourinary tract may be a direct consequence of HIV infection, due to an opportunistic infection or neoplasm, or related to drug toxicity. In the pre-ART era, HIV associated nephropathy (HIVAN) was characterised by rapid progression to end-stage renal disease(ESRD) leading to the need for dialysis. With the advent of ART, the natural course of disease has changed increasing the importance of prompt diagnosis and treatment.

Despite improved outcomes among persons living with HIV who are treated with antiretroviral therapy, they remain at increased risk for acute and chronic kidney diseases and are important contributors to morbidity and mortality in PLHIV.

Patients with HIVAN typically present with heavy proteinuria and rapidly progressive kidney failure and definitive diagnosis requires kidney biopsy, which reveals focal glomerulosclerosis and tubular microcyst formation with tubulointerstitial inflammation and fibrosis.³ HIV type 1(HIV-1) infected patients are at a greater risk of developing acute and chronic renal diseases. HIV-1 associated nephropathy is now the 3rd leading cause of end stage renal disease in 20-64 years of age in the United States. These patients typically have

proteinuria followed by a reduction in the glomerular filtration rate(GFR) that progresses to end stage renal disease in few weeks or months. Overall microalbuminuria is seen in ~20% of untreated HIV infected patients, significant proteinuria is seen in closer to 2%. The presence of microalbuminuria has been associated with an increase in all-cause mortality rate.⁴

Absolute CD4 counts are accepted as the best indicator of immunologic competence of patients with HIV infection and they are an indirect reflection of HIV viral load and activity. The CD4+ T cell count in patients with HIVAN is usually <200 cells/mm³, but has been reported in patients with higher counts. Lower CD4 counts is also associated with increased risk of AKI in HIV infected patients.⁵

AIMS AND OBJECTIVES

1. To study the incidence of renal dysfunction in ART naïve HIV/AIDS patients.
2. To study the different types of renal dysfunction.
3. To study the correlation between renal dysfunction and CD4 count.

MATERIALS AND METHODS

Study location: This study was conducted at tertiary care hospital. 277 cases were collected from the ART Plus Centre, Department of Medicine and Nephrology departments (both outpatient and inpatient).

Study design: This was a hospital based observational study conducted between 1st July 2016 to 30th June 2017. Approval was taken from the institutional ethical committee. Proper and written informed consent was taken from all the patients included in the study.

Inclusion criteria:

1. HIV positive adult patients (as per NACO guidelines) above 15years.
2. Patients not on ART.

Exclusion criteria:

1. All HIV positive children below 15 years (as per NACO guidelines).
2. Patients with pre-existing renal parenchymal disease due to diabetes, long-standing hypertension, cardiac failure and collagen vascular disease.

3. Patients who are on antiretroviral therapy.

Patients with serum creatinine ≥ 1.5 mg/dl were labelled as having renal dysfunction. Patients with renal dysfunction and/or spot proteinuria $> 1+$ or 24-h urinary protein ≥ 500 mg were classified as having renal involvement.⁶ The Cockcroft and Gault equation which estimates creatinine clearance on the basis of serum creatinine level, age, sex and weight was used. The formula is as follows:

$$eCrCl = \frac{140 - \text{age(yrs)} \times \text{weight (kg)}}{72 \times \text{s. creat (mg/dl)}} \quad (\times 0.85 \text{ for females})$$

$$72 \times \text{s. creat (mg/dl)}$$

RESULTS

Out of 277 seropositives, 40 had proteinuria (14.44%) on urine examination. Of these, 36 had $\geq 1+$ spot proteinuria, 2 each had $\geq 2+$ and $\geq 3+$ proteinuria. The mean 24 hour urinary protein estimation done in these cases (n=40) was found to be 856.02 ± 372.88 mg/day. Proteinuria > 1 g/day was found in 4 cases (10%).

Table 1: INCIDENCE OF PROTEINURIA

RANGE OF PROTEINURIA	NUMBER OF CASES	PERCENTAGE(%)	Mean 24 hours Urinary protein (9mg/d)
$\geq 1+$	36	12.99	748.13 ± 98.3
$\geq 2+$	2	0.72	1374 ± 246.07
$\geq 3+$	2	0.72	2280 ± 113.14

The mean serum creatinine of the total study population was found to be 0.92 ± 0.83 mg/dl. When serum creatinine > 1.5 mg/dl was considered as renal dysfunction, the mean creatinine levels of that group (14/277) was found to be 3.05 ± 2.92 mg/dl (95%CI=1.37-4.74), which is statistically significant ($p < 0.0001$).

Table 2: ANALYSIS OF SERUM CREATININE

CATEGORY	MEAN CREATININE
TOTAL STUDY GROUP	0.92 ± 0.83 mg/dl

CASES WITH RENAL DYSFUNCTION	3.05±2.92 mg/dl
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The total number of cases with decreased creatinine clearance ($<60\text{ml/min}/1.73\text{m}^2$) was seen in 28 (10.1%) cases. CKD stage G3 (moderate to severe renal dysfunction) i.e, Cr. Cl. between 30- 59ml/min/1.73m² was seen in 23 cases. However, stage G4 (Cr cl =15-29ml/min/1.73m²) was seen in 7 cases and G5 (Cr cl <15 ml/min/1.73m²) was seen in 1 case only.

Table 3: ANALYSIS OF CREATININE CLEARANCE

CREATININE CL. (ML/MIN),	CKD STAGE	NUMBER OF CASES	PERCENTAGE(%)
≥90	G1	160	57.8
60-89	G2	86	31.0
30-59	G3	23	8.3
15-29	G4	7	2.5
<15	G5	1	0.4

(Range=5-252.10ml/min, mean=103.10ml/min)

Out of 178 cases with CD4 count more than 200cells/mm³, renal dysfunction was found in 12 cases (6.7%). Whereas of the 99 cases with CD4 count less than or equal to 200cells/mm³, 19 cases (19.2%) had renal dysfunction which is statistically significant (P value=0.01; relative risk=0.602; 95%CI=0.38-0.94). The mean CD4 count in patients with renal involvement was 227.2 ± 233.63 cells/mm³ while in those without renal involvement was 331.7 ± 223.4 cells/mm³ (P value <0.0001; relative risk=2.87; 95% CI= 2.07-3.81).

Table 4: RENAL DYSFUNCTION IN RELATION TO CD4 COUNTS

Table 4(a)

<u>CD4 COUNT</u>	<u>TOTAL NO. OF CASES</u>	<u>CASES WITH RENAL DYSFUNCTION (%)</u>
>200 cells/mm ³	178	12 (6.7%)
≤200 cells/mm ³	99	19 (19.2%)

(p value=0.01)

Table 4(b)

CATEGORY	MEAN CD4 COUNT
With renal involvement	227.2±233.63 cells/mm ³
Without renal involvement	331.7±223.4 cells/mm ³

(p value<0.0001)

DISCUSSION

In the present study, out of 277 seropositives, 40 had proteinuria (14.44%) on urine analysis. Of these, 36 had $\geq 1+$ spot proteinuria, 2 each had $\geq 2+$ and $\geq 3+$ proteinuria. This is consistent with the study by Gupta V et al⁶ in North India who reported 58 patients out of 392 ART naïve cases to have proteinuria (14.79%). Similarly, Varma P P et al⁷ also reported 25/142 (17.6%) HIV positive cases to have proteinuria or abnormal urinary sediment. Janakiraman H et al⁸ studied 104 HIV positive patients, albuminuria was observed in 29 (27%) patients. Similarly, Prakash J et al⁹, reported proteinuria of 1+ or more in 112 (38.2%) patients in his study. The discrepancy in the incidence of proteinuria with the present study was probably due to the difference in sample size. The mean 24 hour urinary protein in the cases with spot proteinuria (40/277) was found to be 856.02±372.88 mg/day, in the present study. However, in the study of Gupta V et al⁶ the mean 24 hour proteinuria was found to be 1561±906 mg/day in patients with proteinuria (n=130). The difference with the present study might be due to difference in sample size and inclusion of patients on ART in his study. No patient in the present study had nephrotic range proteinuria. Proteinuria $> 1\text{g/day}$ was found in 4 cases (10%) in the present study which was similar to Prakash J et al⁹, who found 16 (14.2%) patients to have proteinuria of more than 1g/24h.

The mean serum creatinine of the total study population was found to be 0.92±0.83 mg/dl. When serum creatinine $> 1.5\text{mg/dl}$ was considered as renal dysfunction, the mean creatinine levels of that group (14/277) was found to be 3.05±2.92 mg/dl, which was higher than the total study population. In a study by Atta MG et al¹⁰, the patients with biopsy proven HIV-associated nephropathy and

not on ART had a significantly higher mean creatinine level ($7.8 \pm 2.9 \text{ mg/dl}$; $P < .001$) at the time of biopsy than those on ART. This was similar to the study by Gupta V et al⁶ where among a group of 392 ART naïve patients, 74 (18.9%) had renal involvement. Patients with renal dysfunction had a mean serum creatinine of $4.60 \pm 3.17 \text{ mg%}$ (range 1.7-10.5).

In the present study, the total number of cases with moderate to severe renal dysfunction i.e, Cr. Cl. between $30-59 \text{ ml/min}/1.73\text{m}^2$ was found to be 23 (8.3%). However, Cr cl = $15-29 \text{ ml/min}/1.73\text{m}^2$ was seen in 7 cases and Cr cl $<15 \text{ ml/min}/1.73\text{m}^2$ was seen in 1 case only. Overall, patients with creatinine clearance $<60 \text{ ml/min}$ were 28 (10.1%). Similarly, the prevalence of CKD in Chinese patients was found to be 5.6% by Cheung CY et al.¹¹

In the present study, out of 178 cases with CD4 count more than 200 cells/mm^3 , renal dysfunction was found in 12 cases (12/178; 6.7%). Whereas of the 99 cases with CD4 count less than or equal to 200 cells/mm^3 , 19 cases (19/99; 19.2%) had renal dysfunction ($P \text{ value}=0.01$) which is statistically significant. Janakiraman H et al⁸ studied 104 HIV positive patients, and reported that albuminuria was observed in 29 (27%) patients, and it revealed a significant negative correlation with CD4 count ($p < 0.01$). HLF Kamga et al¹² also found that creatinine clearance in HIV positive patients with CD4 count below 200 cells/mm^3 was low while serum creatinine levels were higher though it was not statistically significant.

In the present study, the mean CD4 count in patients with renal involvement was $227.2 \pm 233.63 \text{ cells/mm}^3$ which was lower than those without renal involvement. The patients with ART naïve HIV-associated nephropathy had a lower mean CD4 count ($161 \pm 130 \text{ cells/mm}^3$) at the time of biopsy.¹⁰ In another recent study the mean CD4 count of ART naïve patients was significantly lower in patients with renal involvement as compared to those without renal involvement (180 ± 154 vs $302 \pm 201 \text{ cells/mm}^3$).⁶

CONCLUSION

In the present study, which included ART naïve patients with HIV/AIDS, predominant renal involvement was in the form of proteinuria followed by raised serum creatinine levels. Creatinine clearance and thus GFR is reduced in HIV/AIDS patients and a negative correlation was found between renal involvement and CD4 counts. Although, proteinuria was present in some HIV/AIDS patients in our study population, this parameter alone is not indicative of HIVAN.

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