



A Study on the Prevalence of Microalbuminuria in HIV Positive Patients and Its Correlation With CD4 Count in A Tertiary Care Hospital in South India

KEYWORDS

Human Immunodeficiency Virus, Microalbuminuria, CD4 Count,

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ABSTRACT

Aim of this study was to know the prevalence of microalbuminuria in HIV infected patients and its correlation with the CD4 count. A total of 80 patients were selected and detailed examination was done. Investigations like Complete Blood Count, Blood Urea, Serum Creatinine, CD4 count, Urine Routine, Urine Microalbumin, Albumin Creatinine Ratio and 24 Hours Urine Albumin were performed. Analysis of the findings was done. Results showed microalbuminuria in 11.25% of the patients with all the cases seen in those with CD4 count < 350 cells/uL

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection is spreading worldwide in pandemic proportions. It manifests from an asymptomatic state to AIDS. Involvement of multiple organs is well documented. Renal involvement occurs due to infection per se or due to associated problems like opportunistic/co-infections, septicaemia, drug toxicity^{1,2}. Renal disease was first reported in HIV-1-seropositive individuals in 1984, and initial reports identified focal segmental glomerulo-sclerosis (FSGS) and other renal diseases. Renal involvement is seen in all stages of infection presenting as fluid and electrolyte imbalance, HIV associated nephropathy (HIVAN) progressing to End Stage renal Disease (ESRD).

Survival of patients with HIV, after HAART has been introduced, has increased and so are the number of HIV cases with Chronic Kidney Disease (CKD)³. Cohort studies suggest that approximately 30% of HIV-positive individuals have proteinuria ($\geq 1+$)⁴.

Microalbuminuria is an independent and earliest marker of renal involvement and loss of endothelial integrity. Overall microalbuminuria is seen in ~ 20% (varying from 9% to 30% in various studies) of untreated HIV infected patients^{5,6,7,8,9,10}. Microalbuminuria levels showed correlation with CD4 T cell count suggesting an association between the progression of disease and microalbuminuria^{8,9}. Present study was undertaken to confirm or refute the earlier reports.

AIM OF THE STUDY

1. To estimate the prevalence of microalbuminuria in HIV patients
2. To correlate prevalence of microalbuminuria with CD4 cell count.

MATERIALS AND METHODS

A total of 80 patients who attended the outpatient department in a tertiary care hospital who were diagnosed to be having HIV positive status were selected for the present study during the period of November 2008 – June 2009. They were divided into 2 groups according to CD4 count. 40 patients with CD4 count of ≤ 350 cells/ μ L were grouped as

Group A. Similarly 40 patients with CD4 count of > 350 cells/ μ L were grouped as Group B.

INCLUSION CRITERIA

Adult male & non pregnant female HIV infected patients before ART therapy.

EXCLUSION CRITERIA

- Children
- Patients with Overt renal disease, Diabetes mellitus, Systemic hypertension, Collagen vascular disease, Urinary tract infection, Hepatitis
- Patients on nephrotoxic agents
- Patients not willing for study

METHODOLOGY

Selected socio-demographic data like Age, Sex and occupation were noted. Clinical examination and WHO clinical staging done. Investigations like Hb, TC, DC, ESR, Urine Routine, RBS, Blood Urea, Serum Creatinine, Electrolytes, CD4 Count, Urine for Microalbumin and Albumin Creatinine Ratio, 24 Hours Urine Protein estimation were done.

Data was entered in Microsoft excel spread sheet and analyzed statistically using SPSS software version 11.5. Results were considered significant if the 'p' value was below 0.05.

RESULTS AND OBSERVATIONS

- Mean CD4 count of study group was 387.7 ± 193.78 cells/ μ L (Group A – 236.75 ± 79.77 cells/ μ L. Group B – 538.65 ± 151.53 cells/ μ L). (Table 1)
- Out of 80 patients 41 (51.25%) were males (Group A – 21, Group – B 20) and 39 (48.75%) were females (Group A -19, Group B – 20).(Table 2)
- Mean age group of study population was 33.85 ± 8.26 years (Group A – 35.65 ± 9.80 years. Group B – 32.05 ± 6.46 years)
- Heterosexual route was the most common mode of transmission of HIV infection, about 91.25%
- Mean BMI of study group was 21.66 ± 3.33 kg/m² (Group A – 19.92 ± 2.65 kg/m². Group B 22.4 ± 4.02 kg/m²)
- None of the patients in study group had symptoms pertaining to renal pathology.
- Nine patients (11.25%) (Group A - 9; Group B - 0) had Microalbuminuria. (Table 3)

- Mean value of urine microalbumin in Group A was 37.95 ± 33.75 mg/day and in Group B was 12.13 ± 5.96 mg/day. (p value = 0.000 Significant.)
- Mean urine albumin creatinine ratio of Group A was 36.78 ± 31.86 mg/gm and of Group B was 13.40 ± 5.86 mg/gm. (p value = 0.000 Significant.)
- 6 patients (7.5%) (Group A - 6; Group B - 0) had Overt proteinuria. (Table 4)
- Mean 24 hours urine protein level in Group A was 227.98 ± 104.37 mg/day and in Group B was 144.18 ± 43.42 mg/day. (Table 5)
- Eight patients (10%) (Group A - 7; Group B - 1) had elevated levels of Serum Creatinine. (Table 6)
- Significant correlation was found between microalbuminuria and CD4 count.
- No significant correlation was found between microalbuminuria and Age, Sex, Body Mass Index & WHO staging.

Table - 1

CD4 Group	Number of patients	CD4 count cells/ μ L	MeanCD4 count cells/ μ L
A	40	≤ 350	236.75 ± 79.77
B	40	> 350	538.65 ± 151.53
Total	80		387.70 ± 193.78

Table-2

SEX	CD4 GROUP				TOTAL
	A		B		
MALE	21	(52.5%)	20	(50%)	41 (51.25%)
FEMALE	19	(47.5%)	20	(50%)	39 (48.75%)

Table - 3

Microalbuminuria	CD4 Group		Total
	A	B	
Absent	31 (77.5%)	40 (100%)	71 (88.75%)
Present	9 (22.5%)	0	9 (11.25%)
Total	40 (100%)	40 (100%)	80 (100%)

p value = 0.001 Significant

Table - 4

Overt Preproteinuria	CD4 Group		Total
	A	B	
Absent	34 (85%)	40 (100%)	74 (92.5%)
Present	6 (15%)	0	6 (7.5%)
Total	40 (100%)	40 (100%)	80 (100%)

p value = 0.011 Significant

Table - 5

CD4 Group	24 Hours Urine Protein (mg/day)	
	Mean	SD
A	227.98	104.37
B	144.18	43.42

p value = 0.000 Significant.

Table - 6

Serum Creatinine	CD4 Group		Total
	A	B	
Elevated	7 (17.5%)	1 (2.5%)	8 (10%)
Normal	33 (82.5%)	39 (97.5%)	72 (90%)
Total	40 (100%)	40 (100%)	80 (100%)

p value = 0.025 Significant.

DISCUSSION

HIV infection is a pandemic of modern era. Renal disorders are encountered in all stages of HIV infection.

Microalbuminuria is the earliest marker of the renal involvement, seen in approximately 20% (8.7-30% in various studies) of untreated HIV infected patients^{5,6,7,8,9,10}.

HIVAN has become the third leading cause of ESRD among African Americans aged 20-64 years¹¹.

Ramalingam et al¹² in a study conducted in 2001 have shown that mean CD4 counts in South Indian population, both normal and HIV infected individuals are lower than in western population and have proposed a modified classification based on CD4 cell count for South Indians. The categories of CD4 count proposed were cell count > 300 , $81-300$, ≤ 80 cells/ μ L, instead of the > 500 , $201-500$, ≤ 200 recommended by CDC.

Kannagai et al¹³ in a study conducted in 2008 have shown that majority of HIV infected individuals in South India with CD4 counts of 200-350 cells/ μ L had higher viral load than that suggested by International AIDS Society.

Present study was undertaken based on above observations. There are no supportive studies showing the comparison of prevalence of microalbuminuria in CD4 counts $\leq 350/\mu$ L & $> 350/\mu$ L.

Luke DR et al⁹ observed that microalbumin levels did not correlate with age or sex. In our study also there was no correlation of microalbumin levels with age or sex.

The prevalence of microalbuminuria in HIV and AIDS patients differ in various studies. Morten Baekken et al⁶ study showed microalbuminuria in 8.7% of HIV infected patients. Lynda Anne Szczech et al⁷ study showed that microalbuminuria was present in 11% of HIV infected patients. Busch HW et al⁸ study showed microalbuminuria in 13% of HIV patients. Luke DR et al⁹ study noted 19.4% of HIV patients had microalbuminuria. Kimmel PL et al¹⁰ study showed microalbuminuria in 20 to 30% of HIV patients.

In our study the prevalence of microalbuminuria was found to be 11.25%. All the 9 patients who had microalbuminuria belonged to Group A. The mean urine microalbumin level was 37.95 mg/day (SD 33.75).

Kimmel PL et al, Umama WO et al¹⁴ noticed that, the prevalence of an increased urine albumin creatinine ratio amounting to microalbuminuria was 29.8% in the HIV infected patients. In Busch HW et al⁸ study, the prevalence rate was 13.4%. In Lynda Anne Szczech et al⁷ study, the prevalence rate was 11%.

In our study the prevalence of elevated urine albumin creatinine ratio amounting to microalbuminuria was seen in 11.25% of study group. All the 9 patients who had elevated urine albumin creatinine ratio belonged to Group A. The mean urine albumin creatinine ratio was 36.78 mg/gm (SD 31.86).

Several studies have suggested that abnormality of protein excretion without frank nephritic syndrome is common in HIV infected populations. In Agaba EL et al¹⁵ study proteinuria was detected in 25.3% Of HIV patients. In Cravley ST et al¹⁶ study the prevalence of asymptomatic proteinuria was 14% and the presence of proteinuria did not cor-

relate with viral load. Varma PP et al¹⁷ study showed overt proteinuria in 17.6% of HIV patients. In Gardener et al¹⁸ study overt proteinuria was present in 11.2% of HIV seropositive women. Lynda Anne Szczech¹⁹ et al study showed overt proteinuria in 14.1% of HIV seropositive women. Amitis Ramezaniab et al²⁰ study showed overt proteinuria in 12.3% of HIV infected persons.

In our study, 7.5% of the study group had overt proteinuria. All the 6 patients with overt proteinuria belonged to Group A. Mean urine 24 hours urine protein was 227.98 mg/day (SD 104.37).

Various studies show that there is a strong correlation between CD4 count and microalbuminuria level. Szczech LA et al²¹, Busch HW et al⁸ and Atta MG et al²² studies confirmed that microalbuminuria is commonly seen with CD4 counts \leq 200/ μ L. Busch HW et al⁸ in their study also concluded that subclinical renal involvement is not uncommon in HIV infection with T4 cell counts $>$ 200/ μ L.

In our study 9 out of 80 patients had microalbuminuria and all the patients with microalbuminuria were found to have CD4 count \leq 350/ μ L and no patients with CD4 count $>$ 350/ μ L had microalbuminuria.

CONCLUSIONS

- Microalbuminuria is significantly seen in patients with HIV.
- The prevalence of elevated urine albumin creatinine ratio amounting to microalbuminuria was 11.25% in the study group. The mean urine albumin creatinine ratio was 36.78 mg/gm.
- The microalbuminuria has strong correlation with CD4 counts, with microalbuminuria more common in those with CD4 count \leq 350/ μ L.
- Serum Creatinine levels were also elevated more in those with CD4 counts \leq 350/ μ L.
- Hence in all patients with HIV evaluation for renal problems is absolutely necessary.

LIMITATIONS

- Due to technical and financial constraints only 80 patients were selected for measurement of microalbuminuria.
- Only microalbuminuria & 24 hours urinary protein was measured.
- Renal biopsy was not attempted due to ethical reason.
- Long term follow up was not attempted.
- Effect of ART on microalbuminuria was beyond the purview of the study.
- Viral load could not be estimated due to logistical constraints.

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