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A Study of Correlation of Urine Microalbuminuria and eGFRwith CD4 Count in HIV Patients

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Abstract: *HIV infection is most ofteen associated with renal abnormalities. This study was conducted in 100 HIV patients including newly diagnosed and on patients on ART. The study population were divided into 4 groups according to CD4 count and GFR. About 58% of study population were in the age group of 21-40 years and 38% of study population were in the age group of 41-60 years. Most of the population in the study group were in the age group of 21-36 years. Male population is around 77% and female population is around 23% in this study population. Most of the population were on ART therapy.*
Urine microalbuminuria, macroalbuminuria,puscells,red cells and ultrasound abdomen and pelvis were performed in these patients. Urine microalbuminuria(41%) and macroalbuminuria(20%),Ultrasound evidence of increased cortical echoes(11%) and pyelonephritis/cystitis(10%) were most prevalent in study population and the p value was <0.001,statistically significant and were seen most commonly in HIV patients receiving antiretroviral therapy.other abnormalities like presence of hematuria,casts and ultrasound evidence of contracted kidney with loss of corticomedullary differentiation were seen in only few patients which were statiscally not significant.These renal abnormalities were more prevalent in stages 3 and 4 of CD4 count <200cells/microliter and in stages 3 and 4 of GFR <60ml/min//m2. There is a positive linear correlation between prevalence of urine microalbuminuriawith fall in CD4 count and GFR.

I. Introduction

HIV is a retrovirus that affects all the systems in the body,among this renal involvement is one of the leading cause of death in HIV affected individual. Diseases of the kidney and genitourinary tract may be a direct consequence of HIV infection, due to opportunistic infection,due to neoplasms or drug toxicity. Overall microalbuminuria is seen in 20% of all untreated HIV infected patients, significant proteinuria is seen closer to 2 percent. The presence of microalbuminuria has been associated with an increase in all cause mortality rate. Although the majority of the patients have CD4 count <200/ µl, HIV associated nephropathy can be an earlymanifestation of HIV infection. HIV infection increases the production of variousCytokines which are Toxic to nephrons and thereby increases therisk of renal complications. HIV infectioninduced endothelialdysfunction andvasculitisplays an important role in thepathogenesis of the complication. Rapid onset progressive renal failure leads todeath in HIV individual with 6 to 12 months of diagnosis.

As the disease progresses the CD4 count is very low which increases the renal complications leading to death. So urinemicroalbuminuriascreening should be performed in all HIV patients with low CD4 count for early detection and management of the complications.This study is being conducted to find theprevalence of urinemicroalbuminuria andeGFR in HIV patients and itscorrelation with CD4 count.

II. Materials And Methods

Study Population

This study was conducted among 100 HIV positive patients coming to ART centre, Govt.Rajaji Hospital, Madurai. URINE MICROALBUMINURIA, CD4 count, GFR and ULTRASOUND ABDOMEN AND PELVIS were done in all the participants of the study. Cases were classified as HIV patients into four groups depending upon the CD4 cell count >500 (stage1), CD4 cell count 200 – 500 (stage 2), and 50- 200 (stage 3) and <50 stage 4 and into five groups depending on GFR Stage 1 (> 90), Stage 2 (89 - 60), Stage 3 (59 - 30), Stage 4 (29 - 15), Stage 5 (< 15).

Inclusion criteria:

1. HIV patients for more than 1 year duration
2. HIV Patients with or without first line ART regimen
3. Age more than 18years
4. Gender-both male and female

Exclusion criteria:
Patients with
1. Diabetes
2. Hypertension
3. K/c/o previous renal disease
4. Congestive heart failure
5. HIV patients on second line ART regimen

Ethical clearance: Obtained
Study protocol:
 All cases were classified into 4 categories based on CD4 cell count and into five categories based on GFR.
 Urine microalbuminuria, CD4 count, eGFR and ultrasound abdomen and pelvis were done in study group.

III. Statistical Analysis

The final data was entered onto Microsoft excel sheet 2007 version and statistical analysis was done using SPSS software and chi – square test. The results were considered very significant with p value < 0.01 and significant with p value<0.05.

Results

Age in years	No of cases
<20	3
21-30	22
31-40	36
41-50	10
51-60	28
>60	1
Total	100

Gender Distribution (N=100)
Comment: Male population is around 77% and female population is around 23% in this study population.

Sex	No of cases
Male	77
Female	23

Art Status

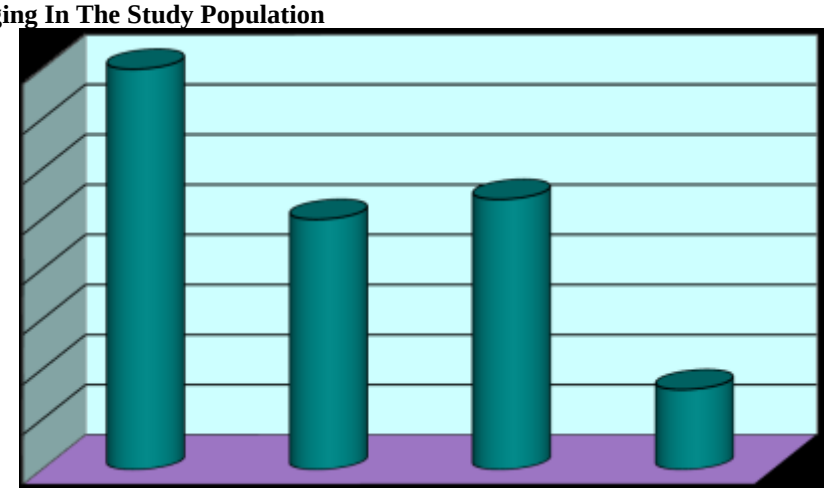
ART Status	No of Cases
On ART	86
Recently Diagnosed	14

Comment: Most of the study population were on ART

Cd4 Count
Comment: About 65% of population in the study group were in stage 1 & 2 and about 35% of population were in stage 3& 4

CD4 Count	No of cases
Stage 1 (>500)	40
Stage 2 (200-500)	25
Stage 3 (50-200)	27
Stage 4 (<50)	8

Cd4 Count Staging In The Study Population



Stage 1 (>500) Stage 2 (200-500) Stage 3(50-200) Stage 4 (<50)

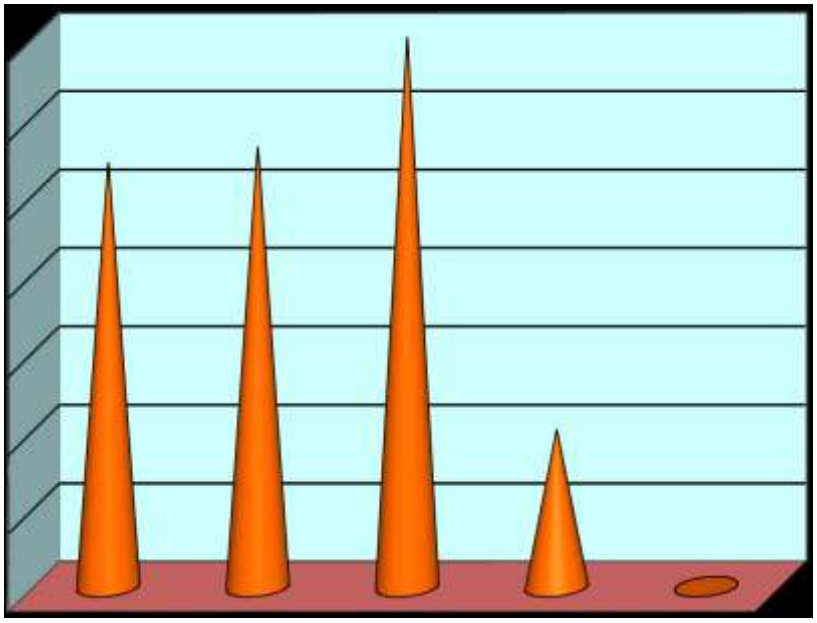
Comment:: About 65% of population in the study group were in stage 1 & 2 and about 35% of population were in stage 3& 4.

Glomerular Filtration Rate In The Study Population

GFR	No of Cases
Stage 1 (>90)	27
Stage 2 (89-60)	28
Stage 3 (59-30)	35
Stage 4 (29-15)	10
Stage 5 (<15)	0

Comment: About 55% of the study population were in stage 1 & 2 and 45% were in stage 3 & 4.

Lomerular Filtration Rate



Stage 1 (>90) Stage 2 (89-60) Stage 3 (59-30) Stage 4 (29-15) Stage 5 (<15)

Comment: Most of the study population were in stage 3 (59-60) of GFR.

Urine Microalbuminuria In The Study Population(N=100)

Urine Microalbuminuria	Noof cases

Present (+)	59
Absent (-)	41

Comment: About 41% of population in the study group were positive for urinemicroalbuminuria

Urine Macroalbuminuria

Comment: About 20% of population in the study group were positive for urine Macroalbuminuria

Urine Macroalbuminuria	No of Cases
Present (+)	20
Absent (-)	80

Pyuria

Pyuria	No of cases
Present (+)	10
Absent (-)	90

Comment: about 10% of study population were positive for pyuria.

Hematuria

Hematuria	No of cases
Present (+)	4
Absent (-)	96

Comment: About 4% of study population were positive for hematuria.

Usg -Increased Cortical Echoes

USG- Increased Cortical Echoes	No of Cases
Present(+)	11
Absent (-)	89

Comment: About 11% Of Population In The Study Group Showed Ultrasound evidence of increased cortical echoes.

Usg-Pyelonephritis/Cystitis

USG Pyelonephritis/Cystitis	No of cases
Present (+)	10
Absent (-)	90

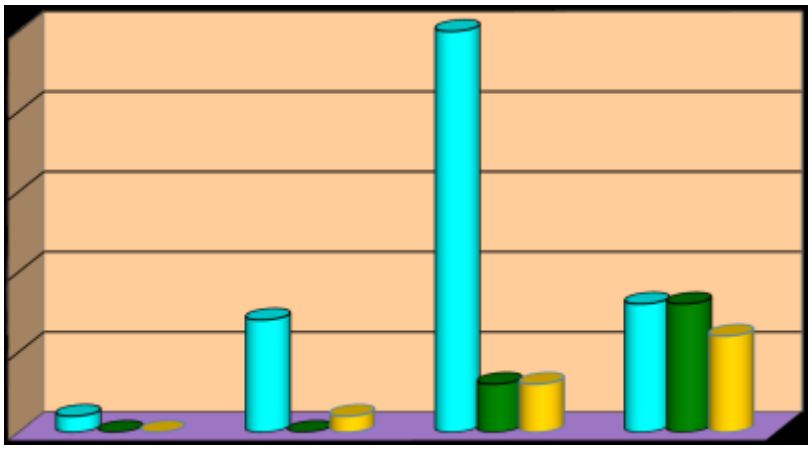
Comment: About 10% of population in the study group showed ultrasound evidence of pyelonephritis / cystitis.

Cd4 Vs Urine Microalbuminuria Vs Usg- Increased Cortical Echoes/Pyelonephritis

CD4 COUNT	No of cases	Urine- microalbinuria	USG- increased cortical echoes	USG- pyelonephritis/cystitis
Stage 1(>500)	40	1	0	0
Stage 2 (200-500)	25	7	0	1
Stage 3 (50- 200)	27	25	3	3
Stage 4 (<50)	8	8	8	6

Comment: About 65% of study population in stage 1 & 2 of CD4 count showed 8 % urinemicroalbuminuria positivity whereas 35% of study population in stage 3 & 4 of CD4 count showed 33% urine microalbuminuria positivity. P value is <0.001 Significant.

Cd4 Vs Urine Microalbuminuria Vs Usg- Increasedcortical Echoes/Pyelonephritis



Stage 1 (>500) Stage 2 (200-500) Stage 3 (50-200) Stage 4 (<50)

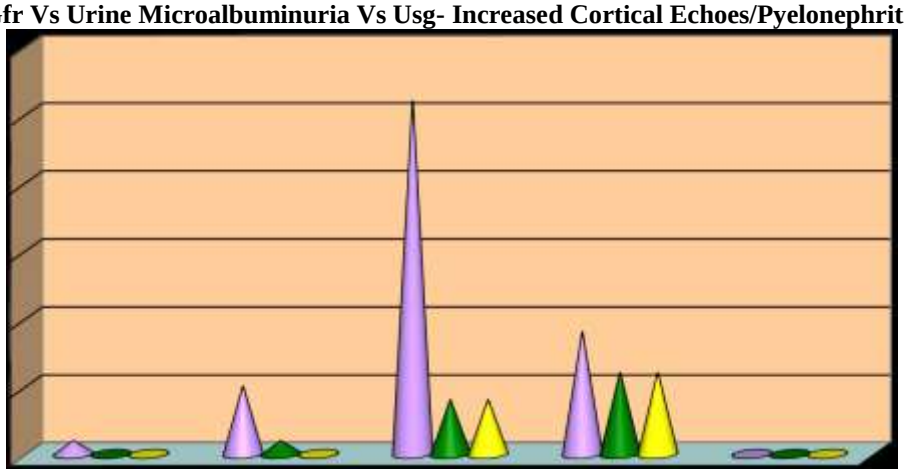
Comment: The difference in proportion of urine microalbuminuria positivity in stages 1& 2 and satge 3 & 4 is statistically significant(p<0.001).prevalence of urine microalbuminuria positivity showed a close association with decreasing CD4 count.

Gfr Vs Urine Microalbuminuria Vs Usg- Increasedcortical Echoes/Pyelonephritis

GFR	No of cases	Urine Albuminuria	USG increased cortical echoes	USG pyelonephritis/cystitis
Stage 1 (>90)	27	1	0	0
Stage 2 (89-60)	28	5	1	0
Stage 3 (59-30)	35	26	4	4
Stage 4 (29-15)	10	9	6	6
Stage 5 (<15)	0	0	0	0

Comment: About 55% of study population in stages 1 & 2 showed 6 % urine microalbuminuria positivity whereas remaining 45% of study population in stages 3 & 4 showed 35% urine microalbuminuria positivity. p value is < 0.001 significant.

Gfr Vs Urine Microalbuminuria Vs Usg- Increased Cortical Echoes/Pyelonephritis



Stage 1 (>90) Stage 2 (89-60) Stage 3 (59-30) Stage 4 (29-15) Stage 5 (<15)

Comment: The difference in proportion of urine microalbuminuria positivity in stages 1 & 2 and stages 3 & 4 is statiscally significant (p value <0.001) and the prevalence of urinemicroalbuminuria positivity showed a close association with decreasing GFR value.

gfr vs cd4 count vs urine microalbuminuria

Urine Microalbinuria	No of cases	CD4 mean	SD	P value
Present (+)	41	142.244	156.833	
Absent (-)	59	684.695	336.892	<0.001 Sig

Urine microalbuminuria	No of cases	GFR mean	SD	P value
Present (+)	42	44.732	19.634	
Absent (-)	59	83.169	19.896	0.001 sig
		Mean	SD	
CD4 count		462.29	385.13	

GFR	67.41	27.362

Pearson coefficient is 0.27(high correlation).

Comment: Prevalence of urine microalbuminuria positivity showed a close association with decreasing CD4 count and GFR value.p value is < 0.001 significant.

IV. Discussion

Renal abnormalities are common in HIV infection in late stages of disease. This study was conducted in 100 HIV patients including newly diagnosed and patients on ART attending ART clinic, Government Rajaji hospital, Madurai. The study population were divided into four groups according to CD4 COUNT and GFR. About 58% of study population were in the age group of 21-40 years and 38% of study population were in the age group of 41-60 years. Most of the population in the study group were in the age group of 21-36 years. Male population is around 77% and female population is around 23% in this study population. Most of the population were on ART therapy. Urine microalbuminuria, macroalbuminuria,puscells,red cells and ultrasound abdomen and pelvis were performed in these patients.

In this study most of the patients with HIV infection had renal abnormalities which were clinically quiescent. This suggests that urine analysis,GFR and ultrasound Abdomen and pelvis are very important in diagnosing subclinical renal abnormalities. Asymptomatic urine microalbuminuria is the most common renal abnormality observed in the study population. As the disease progresses the CD4 count is very low which increases the renal complications leading to death. so urine microalbuminuria screening sh ould be performed in all HIV patients with low cd4 count for early detection and management of the renal complications. In this study it was seen in around 41% of the population.About 65% of study population in stage 1 & 2 of CD4 count showed 8 % urine microalbuminuria positivity whereas 35% of study population in stage 3 & 4 of CD4 count showed 33% urine microalbuminuria positivity. P value is <0.001 Significant.

Out of 41% who showed urine microalbuminuria positivity, 25% were in CD4 count stage 3(50-200) with clinical spectrum ranging from asymptomatic urinemicroalbuminuria positivity to acute kidney injury/pyelonephritis. The presence of microalbuminuria is associated with increase in all cause mortality rate. HIV infection increases the production of various Cytokines which are toxic to nephrons and thereby increases the risk of renal complications. HIV infection induced endothelial dysfunction and vasculitis plays an important role in the pathogenesis of the various renal complications. In this study population around 26% who showed urine microalbuminuria positivity were in the stage of GFR(59-30).

Among 41% of study population with microalbuminuria, ultrasound abdomen and pelvis showed increased cortical echoes in 11 % of study group and evidence of pyelonephritis/cystitis in 10%.Hematuria was present inof the study group. Evidence of increased cortical echoes in ultrasound abdomen and pelvis was present in 11% of study population. The clinical spectrum of these patients is from mild symptomatic urinary tract infection to acute kidney injury. All these 11% of population were in CD4 count stage 3 & 4 (CD4 COUNT <200).p value is < 0.001 significant. Out of 11%, 10% of study group were in GFR stage 3 & 4 and remaining 1 % in GFR stage 2.

Among the study population 10% showed ultrasound evidence of pyelonephritis and cystitis. These patients also had evidence of pus cells in urine analysis. 4% among them also had hematuria.out of 10%, 9% of study population were in CD4 count stage 3 & 4 and remaining 1 % in stage 2. When correlated with GFR, all these 10% of study population were in GFR stage 3 & 4.prevalence of urine microalbuminuria positivity showed a close association with decreasing CD4 count and GFR value.

From this study we conclude that all renal abnormalities occur in the late stages of HIV patients with low CD4 count. As the CD4 count decreases renal abnormalities increases. So urine microalbuminuria is the simplest way of detecting early renal involvement in these patients and it is mandatory to screen for all HIV patients with CD4 count less than 200.

Eventhough decrease in CD4 count well correlates with the renal abnormalities, this study had some limitations.Because there may be some confounding factors like smoking ,alcohol and substance abuse ,diabetes mellitus,hypertension and dyslipidemia which can also cause these renal manifestations. Although the exact mechanism of the pathogenesis of renal abnormalities in HIV is multifactorial and poorly understood,progression of renal problems in HIV infection can be reduced by effective antiretroviral therapy .

V. Conclusion

Renal abnormalities are more common and predictable complications in late stages of HIV infection. This study was done

- To highlight the various renal abnormalities occurring in HIV infection.
- Many of these abnormalities were associated with increased morbidity and mortality in HIV patients.

 Urine microalbuminuria,macroalbuminuria,GFR,ultrasound abdomen evidence of increased cortical echoes and pyelonephritis/cystitis were the most common renal abnormalities occurring in significant number of HIV patients with low CD4 count.so thses parameters can be used as predictors of disease progression in HIV patients.

 So all HIV patients with low CD4 count(<200/microliter) and GFR<60ml/min/m2 should be screened for renal abnormalities.

 Early diagnosis and management of these complications is associated with increased survival rates and clinical outcomes in HIV patients .

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