

Studying Renal Impairment In Hiv Seropositive Subject

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Abstract:

BACKGROUND AND OBJECTIVES: The number of people living with HIV/AIDS is on the rise, so are the problems like renal dysfunction which needs to be addressed. The study was aimed at providing data regarding prevalence and the association of certain modifiable and non-modifiable factors with renal function.

MATERIALS AND METHODS: This was a cross sectional study on 390 HIV positive subjects. Renal function was assessed by means of eGFR, calculated using Cockcroft-Gault equation, and proteinuria, estimated by spot urine albumin creatinine ratio (UACR). Renal dysfunction was identified by either eGFR < 60 ml/min or UACR > 30 mg/gm. The data was analyzed based on demographic characteristics, type and duration on ART, height, weight, body mass index, CD4 count.

RESULTS: 21.3% (N=83) of study population had renal dysfunction. Sixty percent of them were females. Higher mean duration of ART (40.3 months) and lower mean CD4 counts (312.6 cells/mm³) was associated with renal dysfunction. Mean height (162.6 cm) and mean weight (55.3kgs) were lower in renal dysfunction group and significant. Mean LDL cholesterol (100.3mg/dl) and serum triglycerides (197.0mg/dl) were higher among renal dysfunction group. Different types of ART regimen, BMI, blood pressure, HDL cholesterol and total cholesterol was found to have insignificant association in the study.

INTERPRETATION AND CONCLUSION: Every one in five HIV positive subjects might have renal insufficiency and more so common in females. Lower height, lower weight, increased duration of ART therapy were associated with decreased renal function and has to be screened. Different types of ART regimen, body mass index, systolic and diastolic blood pressure did not show any effect on renal function in this study. Decrease in CD4 count was shown to have positive correlation with decrease in estimated GFR. So subjects with greater immunosuppression should be screened frequently.

KEY WORDS: HIV Seropositivity; Renal Insufficiency; Proteinuria; CD4 Cell Count

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I. Introduction

Human Immunodeficiency Virus (HIV) was identified in 1983 as a causative agent for Acquired Immunodeficiency Syndrome (AIDS) ¹. This virus progressively damages cells of the body's immune system thus predisposing the infected individual to opportunistic infections, cancers, and different organ pathology.

In 1984 Rao² et al reported a renal lesion in patients infected with HIV that was characterized with severe proteinuria, biochemical features of nephrotic syndrome, and renal function impairment that rapidly progresses to end stage renal disease. Various types and severities of renal disorders have been encountered at all stages of HIV infections, ranging from mild and transient renal impairment to end stage renal disease requiring renal replacement therapy³. The CD4 cell count is used as a surrogate marker of immune status in HIV infected patients. However infection with HIV leads to destruction and depletion of CD4 cells and this predisposes the individual to various disease conditions. CD4 cell count has been used to monitor, follow up and determine the severity of HIV infection⁴.

The renal function impairment (RFI) has been encountered at various stages of HIV infection, from the stage of seroconversion to advanced AIDS. The prevalence, severity, morbidity and mortality of renal function impairment in these patients have been associated with the degree of immunosuppression^{5,6}. Various studies have reported that CD4 cell count of less than 200/ul is a poor prognostic index in HIV infected patients with renal disease^{7,8}. Early detection and intervention delays progression and in many situations reverses impairment of renal function in HIV infected patients. The CD4 cell count of HIV infected patients is assessed on presentation in most health facilities. However renal function assessment is sparse in most of the centres in attending to HIV patients. It is necessary to objectively assess the relationship between renal function and degree of immunosuppression in these patients.

Renal function is usually assessed by means of serum creatinine measurement and then estimated glomerular filtration rate calculation by Cockcroft-Gault formula or Modification of diet in renal disease equation

(MDRD)⁹. Proteinuria and persistent microalbuminuria is also used for assessing renal function. Urine albumin creatinine ratio which is a surrogate marker for microalbuminuria can detect early renal dysfunction patients. Other determinants which contribute to renal dysfunction may include comorbidities such as hypertension, diabetes, hyperlipidemia, age, sex and ethnicity¹⁰⁻¹². It might also be affected by many opportunistic infections, duration of HAART, type of drug regimen as shown in many previous studies^{13,14}. Most of the studies regarding renal impairment in HIV patients have been done outside India and data regarding prevalence and pattern of renal involvement and its correlation with various variables in this part of India is not available. So the aim of this study is to provide valuable data regarding renal dysfunction in HIVinfected individuals.

Objectives

1. To determine the prevalence of renal impairment in HIV seropositive subjects attending ART clinic.
2. To determine the association between renal impairment and variables such as age, sex, body mass index, CD4 count, duration of ART.

II. Material And Methods

Source of data

The material for the study will be collected from subjects, who are HIV seropositive and who fulfill the inclusion and exclusion criteria, attending ART clinic,

Method of collection of data

- a) **Study design:** Single centered cross sectional study in a tertiary care hospital
- b) **Sample size:** 390 (As reviewed with statistician)
- c) **Sampling Method:** Simple Random Sampling
- d) **Duration of study:** January 2022 to November 2023
- e) **Method of collection of specimens and processing:** Blood and urine sample will be collected at a single sitting with universal precautions into separate sterile containers. Blood sample will be used for testing CD4 count, haemoglobin, total count using automated counters, and used to test serum creatinine by Jaffe method. Urine sample will be tested for urine albumin creatine ratio by immunoturbidometric method.

f) Inclusion criteria

1. HIV seropositive subjects attending ART clinic.
2. Age more than or equal to 18 years.
3. Subjects either on Antiretroviral therapy or not on any drug therapy.

g) Exclusion criteria

1. Subjects with preexisting urinary tract infection.
2. Pregnancy
3. Subjects not willing to take part in the study.
4. Patients on steroid intake or antituberculous treatment.

h) Investigations

- a) Haemoglobin
- b) Urine albumin- creatinine ratio (Urine ACR).
- c) Blood urea and serum creatinine
- d) CD4 cell count
- e) Lipid profile
- f) RBS (Random Blood Sugar)
- g) LFT (Liver Function Test)
- h) White blood cell count

Data will be collected using a pretested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigation will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained. After collecting data subjects will be assessed for renal function impairment based on two criteria given below and classified into two groups, one with renal dysfunction and one with normal renal function. If a study subject satisfies any one of these two criteria, he/she will be considered to have renal function impairment or renal dysfunction.

- Criteria are 1.)** Estimated GFR <60 ml/min as calculated using Cockcroft Gault formula,
2.) Microalbuminuria or Macroalbuminuria based on urine albumin creatine ratio (UACR) >30 mg/gm.

The prevalence of renal dysfunction will be found out using this definition and the rest of the data will be used for further analysis and interpretation.

Data Analysis and Interpretation Data was entered into Microsoft excel and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 18.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables were determined. The level of significance was set at 0.05. Correlation analysis will be done wherever appropriate.

III. Result

In this study conducted in ART clinic, 390 subjects fulfilling inclusion and exclusion criteria were included. Out of them 83 subjects (21.28%) were found to have renal dysfunction according to the criteria used. Out of the 21.28% subjects with renal function impairment, 10 % had only low eGFR, 8.2% had only microalbuminuria and 3.08% had both decreased eGFR and microalbuminuria.

Table 1: Renal function distribution

	Normal renal function	307
Renal dysfunction	eGFR<60	39
	UACR>30	32
	Both	12

Figure 1: Renal function distribution

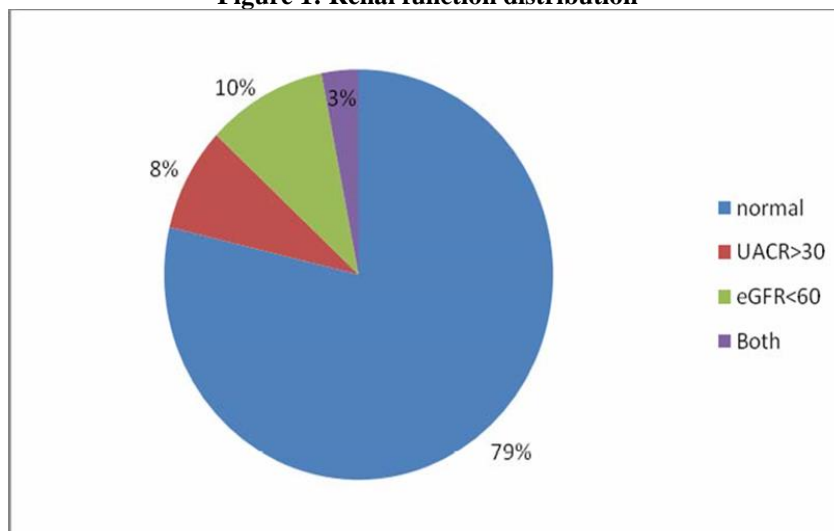
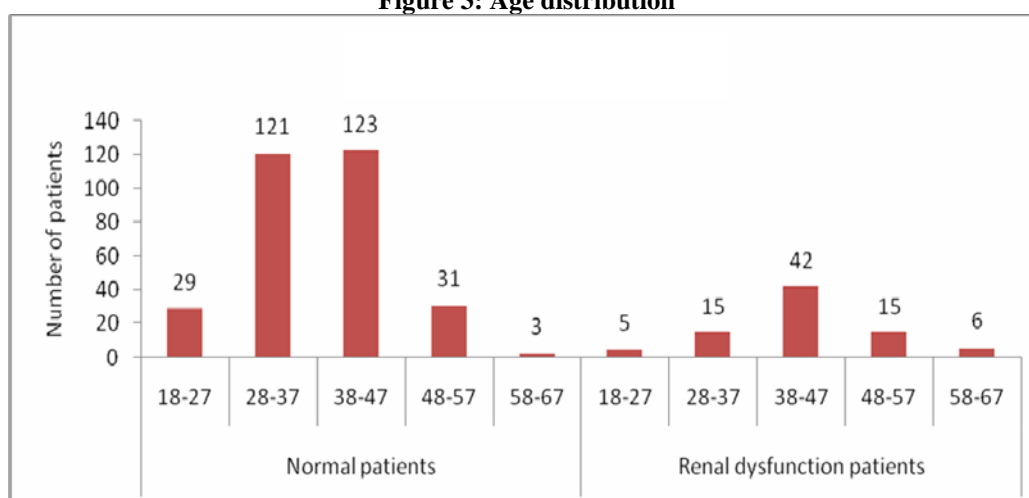


Table 2: Age distribution

Age distribution	Age categories	Number of patients	% of patients	Mean Age
Normal renal function patients	18-27	29	9.4%	23.5
	28-37	121	39.4%	32.6
	38-47	123	40.1%	41.0
	48-57	31	10.1%	51.2
	58-67	3	1.0%	63.7
Renal dysfunction patients	18-27	5	6.0%	23.8
	28-37	15	18.1%	33.7
	38-47	42	50.6%	41.0
	48-57	15	18.1%	50.1
	58-67	6	7.2%	60.5

Figure 3: Age distribution

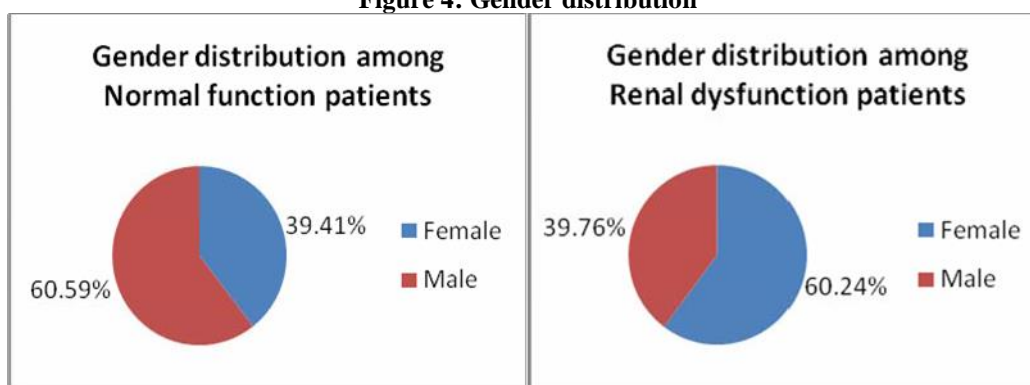


Almost 80% of subjects in normal renal function group were between age group 28 to 47 and 50.16% of the subjects in the renal dysfunction group were in the age group 38 to 47. Mean age was 42.4 years in normal function group whereas it was 41.82 years in renal dysfunction group.

Table 9: Gender distribution

Gender distribution	Gender	Number of patients	% of patients
Normal renal function patients	F	121	39.41%
	M	186	60.59%
Renal dysfunction patients	F	50	60.24%
	M	33	39.76%

Figure 4: Gender distribution

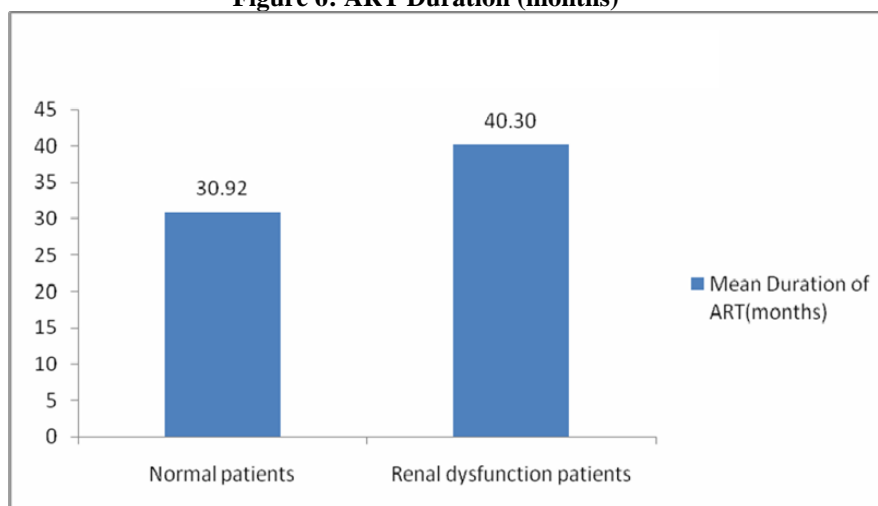


Males constituted 56.15 % (N=219) and females 43.8% (N=171). In normal renal function subjects females were 39.41 % (N=121) and 60.24% (N=50) in renal dysfunction subjects. So females show preponderance for renal impairment.

Table 11: ART Duration (months)

Duration of ART distribution	Mean Duration of ART(months)	Minimum Duration of ART(months)	Maximum Duration of ART(months)	Standard deviation	P-value
Normal function patients	30.92	0	99	27.92	0.008
Renal dysfunction patients	40.30	0	98	31.12	

Figure 6: ART Duration (months)

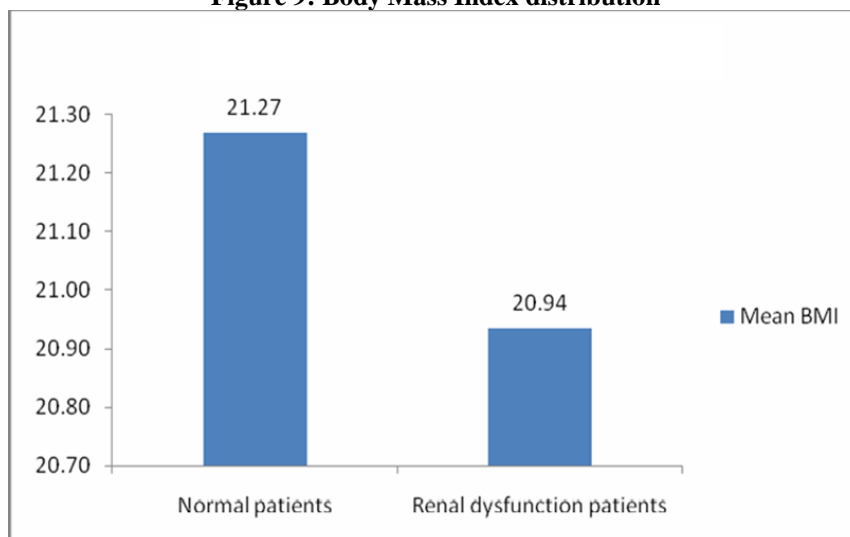


Mean ART duration between the groups is statistically different with p-value 0.008 which is less than 0.05 at 5% significance level. It indicates that the mean ART duration is statistically different in both the groups and ART duration is statistically higher among renal dysfunction patients.

Table 14: Body Mass Index distribution

BMI distribution	Number of patients	Mean BMI	Minimum BMI	Maximum BMI	Standard deviation	P-value
Normal patients	307	21.27	15.17	27.94	1.92	0.16
Renal dysfunction patients	83	20.94	16.26	25.39	1.97	

Figure 9: Body Mass Index distribution

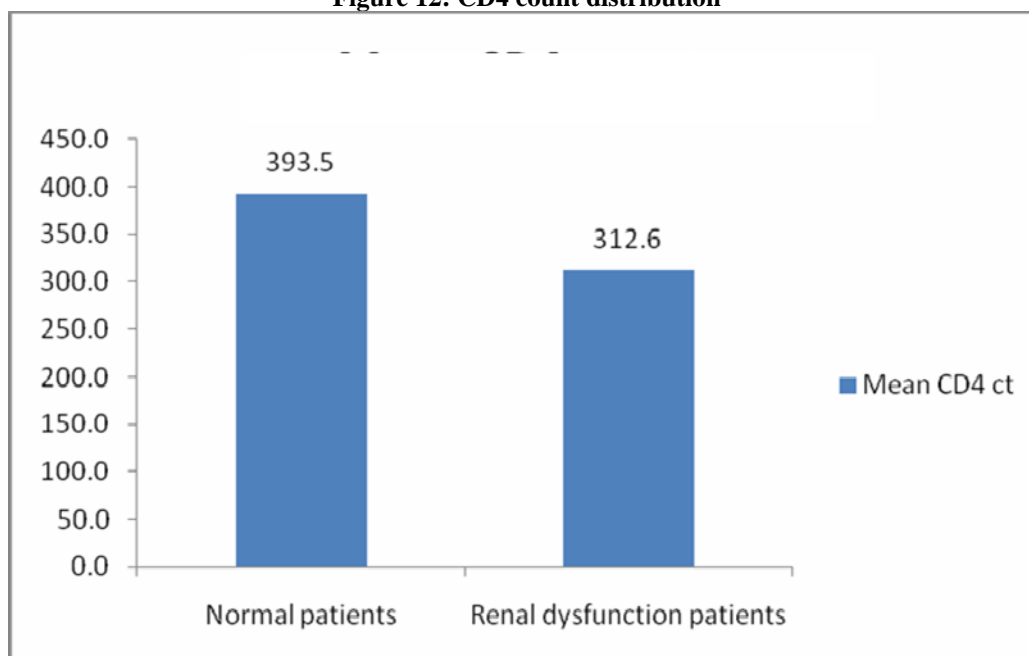


Mean BMI is statistically same among normal patients and also patients with renal dysfunction with p-value 0.16. The p-value is statistically insignificant at 5% significance level. It indicates that the mean BMI is statistically same across both the groups.

Table 17: CD4 count distribution

CD4 ct distribution	Mean CD4 ct	Minimum CD4 ct	Maximum CD4 ct	Standard deviation	P-value
Normal patients	393.49	21	1398	216.01	0.002
Renal dysfunction patients	312.61	32	1163	206.86	

Figure 12: CD4 count distribution



Mean CD4 count is statistically different among both the groups with p-value 0.002. The p-value indicates the significant difference in the mean CD4 count across both the groups. The result indicates that the CD4 count is statistically lower among patients with renal dysfunction.

Table 22: Correlation analysis of UACR, CD4 ct and eGFR

Correlation analysis results			
		UACR	eGFR
CD4 ct	Correlation value	-0.081	0.171
	P-value	0.112	0.001
	Number of patients	390	390

There is negative association between UACR and CD4 counts. The strength of association between UACR and CD4 counts is very low ($r = -0.081$, $p = 0.112$) and is statistically insignificant at 5% significance level.

The strength of association between CD4 count and eGFR is low ($r = 0.171$, $p = 0.001$) but is statistically significant at 5% significance level. So decline in eGFR is associated with decline in CD4 count.

IV. Discussion

In this study conducted in ART clinic, 390 subjects fulfilling inclusion and exclusion criteria were included. Out of them 83 subjects (21.28%) were found to have renal dysfunction according to the criteria used. Renal function impairment was identified based on two criteria, first one was estimated GFR < 60 ml/min calculated using Cockcroft Gault formula and second one was microalbuminuria based on urine albumin-creatinine ratio > 30 mg/gm. Patient was considered to have renal dysfunction if any one of the criteria was fulfilled.

Out of the 21.28% subjects with renal function impairment, 10 % had only low eGFR, 8.2% had only microalbuminuria and 3.08% had both decreased eGFR and microalbuminuria. Prevalence of renal function impairment varies from as low as 6% to high as 31% in other studies. Study by Keith Rawlings⁸¹ et al in USA had a prevalence of 6%. A study by Menezes¹⁰ et al in Brazil on HIV infected subjects with low viral load and CD4 count above 200 cells/ mm³ showed a prevalence of 8.4%. Another study by Okafor⁵ et al in Nigeria had higher prevalence of renal dysfunction in the range of 31%. Another study by Overton¹¹ et al in USA had a prevalence of 7.5%. A study by Kamga⁸² et al in Cameroon had a prevalence of 30.45%. The rest of the discussion has been done under the different factors studied.

AGE

Patients were distributed from age 18 to 66 years. Normal renal function group and renal dysfunction group were divided into 5 age classes. It was found that almost 80% of subjects in normal renal function group were between age group 28 to 47 and 50.16% of the subjects in the renal dysfunction group were in the age group 38 to 47.

Mean age was 42.4 years in normal function group whereas it was 41.8 years in renal dysfunction group. In a study conducted by Okafor⁵ et al (2007) in Nigeria showed mean age as 36.7 years in normal function subjects and 36.15 years in renal dysfunction subjects. In another study by Menezes¹⁰ et al (2009) in Brazil showed mean age in renal dysfunction patients as 45.6 (S.D =11.5) years.

GENDER

In the present study males constituted 56.15 % (N=219) and females 43.8% (N=171). In normal renal function subjects females were 39.41 % (N=121) and 60.24% (N=50) in renal dysfunction subjects. So present study shows preponderance for females for renal impairment. It is against what was shown in a study by Overton¹¹ et al (2009) in USA which showed males 60.9 % in normal function group and 67.4 % males in renal impairment group. In another study by Struik⁸³ et al (2011) in Malawi showed 67.7 % and 62.6 % females in normal function and renal dysfunction group respectively.

CD4 COUNT

In the present study mean CD4 count was 393.5(S.D=216) cells among normal renal function group and 312.6(S.D=206.9) cells among renal dysfunction group. The difference was found to be statistically significant p-value being 0.002. So lower CD4 count is associated with impaired renal function. In the study by Struik⁸³ et al lower mean CD4 count was associated with lower eGFR and in a study by Overton¹¹ et al showed low nadir CD4 count was associated with low eGFR. But in a study by Kamga⁸² et al no significant association was demonstrated between low CD4 count and low eGFR.

CD4 count showed positive correlation with eGFR ($r = 0.171$, $p\text{-value} = 0.001$) i.e. with decrease in CD4 count there will be decrease in eGFR. CD4 count showed negative correlation with Urine albumin creatinine ratio(UACR) but it was found to be statistically insignificant ($r = -0.081$, $p\text{-value}=0.112$). In a study by Okafor⁵ et al it was shown that decrease in CD4 count had positive correlation ($r=0.46$, $p\text{-value}=0.031$) with severity of renal function impairment.

V. Conclusion

1. A total of 390 HIV infected subjects were included in the study.
2. The prevalence of renal dysfunction in the study was 21.28% (N= 83). So around one fifth of HIV infected patients will have renal function impairment.
3. Around half of the renal dysfunction subjects (50.16%) were in the age group 38-47 years.
4. Though the study population was predominantly males, 60.24% of the renal dysfunction group was females.
5. HIV positive patients whether pre-ART or on different ART regimens did not have any implication on renal function.
6. There is increased chance of renal function impairment with increased duration of anti- retroviral therapy.
7. Lesser height and weight is associated with more chance of renal dysfunction.
8. Body mass index did not show any significant effect on renal function.
9. Systolic and diastolic blood pressure did not show any association with renal dysfunction in this study.
10. Lower CD4 count which indicates more immunosuppression is associated with decreased renal function and more so with decline in estimated GFR rather than proteinuria.

SUMMARY

HIV infected population and AIDS is a global health concern and more so in a populated country like India. With increasing awareness and advent of ART, the number of people living with HIV/AIDS is on the rise, so are the problems like renal dysfunction which needs to be addressed. The study was aimed at providing data regarding prevalence and the association of certain modifiable and non-modifiable factors with renal function.

A total of 390 subjects were studied and prevalence of renal dysfunction was found to be 21.28%. Around 3/5th of renal dysfunction population were females. Lower height, lower weight, increased duration of ART therapy were associated with decreased renal function. Different types of ART regimen, body mass index, systolic and diastolic blood pressure did not show any effect on renal function in this study. Decrease in CD4 count was shown to have positive correlation with decrease in estimated GFR.

LIMITATIONS OF THE STUDY

1. No attempt was made to differentiate between causes of renal dysfunction in terms of acute/chronic or reversible /irreversible in the group studied.
2. This study did a one time assessment of renal function which would have overestimated or underestimated the prevalence of renal dysfunction. Multiple assessments would have been better.

KEY TO MASTER CHART

ART	-	Antiretroviral therapy
BMI	-	Body mass index
DBP	-	Diastolic blood pressure
eGFR	-	Estimated glomerular filtration rate
HDL	-	High density lipoprotein
Ht	-	Height in cms
LDL	-	Low density lipoprotein
S.Ch	-	Serum cholesterol
S.creat	-	Serum creatinine in mg/dl
S	-	Stavudine based regimen
SBP	-	Systolic blood pressure
TG	-	Serum triglycerides
T	-	Tenofovir based regimen
UACR	-	Urine albumin creatinine ratio
Wt	-	Weight in kilogram
Z	-	Zidovudine based regimen

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