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Original Research Article

To Monitor Renal functions in HIV patients undergoing different HAART regimens.

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Abstract:
Background & Method: The aim of the study is to Monitor Renal functions in HIV patients undergoing different HAART regimens. The 100 newly diagnosed HIV positive patients were included in the study. Detailed history – including duration of disease, any past history of antiretroviral drug and other medications , treatment regimen started , WHO staging of the HIV disease were obtained.
Result: There was a negative correlation between Urine albumin and eGFR at the end of study and the P value is significant. Above tables shows that, albuminuria was noted in 49 patients(49%). Out of 49,23 had Trace, 14 had 1+,8 had 2+ and 4 had 3+ albuminuria.Majority of patients in <60 (Moderate to Severe) eGFR were noted 14(31.1%) trace followed by 12(26.7%) had 1+, 8(17.8%) had 2+ and 4(8.9%) had 3+.Above association between Urine Albumin and eGFR (End of study) found statistically significant ($p<0.001$).
Conclusion: This study signifies that Tenofovir based regimen is the basis for most of the decline in renal function in patients on ART. Mean Creatinine is 1.06. There is significant P value between Creatinine and eGFR. Average levels of Creatinine is significantly higher (1.30) for <60 eGFR Category. We also recommend assessment of renal function of HIV infected patients prior to initiation of HAART to guide the choice and dosing of Antiretroviral drugs.

Keywords: Renal, ART, HIV, HAART, eGFR & dysfunction.

Study Designed: Cross sectional study

1. Introduction

HIV can cause direct injury to the kidneys as manifested by HIV-associated nephropathy (HIVAN). This entity was described before the era of HAART but continues to be a significant problem despite the advent of HAART [1]. HIVAN is the third leading cause of ESRD globally. A few years ago, HIVAN was initially considered to be genetically linked to a variation in the MYH9 locus of chromosome 2, However, recent researchers have noted that the MYH9 gene is located next to the APOL-1 gene which is more significantly associated with ESRD than all previously reported variations in MYH9 gene [2]. In less developed countries, patients often present late to medical attention and may have HIVAN; however, this renal lesion can develop in patients on HAART due to poor medication adherence. Patients with HIVAN taking ART have a slower decrease in GFR and less incidents of fulminant renal failure .HAART is responsible for at least a 30% reduction in

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new ESRD cases from HIVAN .However, ART may not have a beneficial effect on the natural history of other forms of CKD, example IgA nephropathy and diabetes, which could be mistaken for HIVAN if a biopsy is not obtained[3].
This study was done with an aim to investigate the factors associated with decline in renal function by using estimated GFR by CG formula among the patients taking Highly Active AntiRetroviral Therapy (HAART) and its correlation with renal dysfunction and progression to end stage renal failure[4].

2. Material & Method

100 patients who are attending ART clinic and admitting in Medical units at Gajraraja Medical College Hospital were randomly selected as per the inclusion and exclusion criteria. Out of these, 56 were men and 44 were women. The mean age of subjects was 40.70 years with a range of 18-80 years. Written informed consent was obtained from each HIV positive patients enrolled in the study.
The 100 newly diagnosed HIV positive patients were included in the study. Detailed history – including duration of disease, any past history of antiretroviral drug and other medications , treatment regimen started , WHO staging of the HIV disease were obtained.
Patients were examined in detailed for assessing any symptoms and signs of renal failure. Blood samples were taken for screening baseline renal function for urea, creatinine. Baseline eGFR was calculated using Cockgroft – Gault equation. Patients were followed up over a period of 12 months and any opportunistic infections developed among patients during study period was noted. At the end of 12 months, patients were assessed for Urea, Creatinine by drawing blood samples and eGFR was calculated using CG formula. Urine routine and USG KUB was done.

INCLUSION CRITERIA:

1. All newly diagnosed adult HIV positive patients who are attending ART clinic and started on HAART at Jayarogya group of Hospitals Gwalior.

EXCLUSION CRITERIA:

1. Patients with Chronic renal failure
2. Patients with diagnosed systemic causes of renal diseases (eg., SLE, Systemic Sclerosis, Rheumatoid arthritis, and other rheumatological & connective tissue disorders)
3. Patients who are known Diabetic or Hypertensive or any other comorbid illness.
4. Pregnant women and children age less than 15 years
5. Patients with poor adherence (> 80 %)
6. Patients receiving other nephrotoxic drugs / NSAIDS.

3. Results

Table 1: HAART REGIMEN

HAART Regimen	No. of Cases	Percentage
TLN (A)	71	71.0
ZLN (B)	29	29.0
Total	100	100.0

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Two types of regimen were taken by the patients Tenofovir(71) andZidovudin based(29). Majority of patients are in Tenofovir based regimen.

Table2: Association between Age and eGFR

Age Group (years)	eGFR(E) (End of Study)						Total	
	Moderateto severe(<60)		Mild (60-90)		Normal(>90)			
	No.	%	No.	%	No.	%	No.	%
< 20	1	2.2%	1	2.9%	2	9.5%	4	4.0%
21-30	8	17.8%	3	8.8%	6	28.6%	17	17.0%
31-40	13	28.9%	13	38.2%	8	38.1%	34	34.0%
41-50	12	26.7%	10	29.4%	5	23.8%	27	27.0%
51-60	8	17.8%	4	11.8%	0	0.0%	12	12.0%
> 60	3	6.7%	3	8.8%	0	0.0%	6	6.0%
Total	45	100.0%	34	100.0%	21	100.0%	100	100.0%

Pearson Chi-Square = 11.361, df = 10, p value = .330, Not Significant

Symmetric Measures					
		Correlation	Asymp. Std. Error	Approx. T	P Value
Ordinal by Ordinal	Spearman Correlation	-.215	.097	-2.177	.032
Interval by Interval	Pearson's R	-.249	.084	-2.544	.013
N of Valid Cases		100			

The correlation between eGFR (E) and Age is negative.It appears almost significant with a P value of 0.032. Majority decline in eGFR occur in the age group of 31-35 with category <60 in 13 patients (28.9%).

Table 3: Comparison between eGFR across Age

eGFR (end of Study)	Mean Age	(I)	(J)	Mean Difference (I-J)	Std. Error	P value
45	42.56±13.14	Moderate to Severe (<60)	Mild	.026	2.610	1.000
			Normal	8.794*	3.035	.013
34	42.53±11.169	Mild (60-90)	Moderate to Severe	-.026	2.610	1.000
			Normal	8.768*	3.187	.019
21	33.76±7.321	Normal (>90)	Moderate to Severe	-8.794*	3.035	.013
			Mild	-8.768*	3.187	.019

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One-way ANOVA followed by Post-hoc Tukey test applied.
P value < 0.05 was taken as statistically significant
This table indicates that at eGFR (at the end of study) greater than 90 which is normal kidney function, has significantly lower average age compared to other two categories, where there has mild to moderate kidney damage occurs. However between the categories of less than 60 and 60-90, the average age levels do not seems to be significant.
So, this study shows that significant renal damage can occur in the higher age group of when compared to lower average age groups.

Table 4: Comparison between eGFR across Creatinine_(E)

eGFR (end of Study)	Mean Creatinine	(I)	(J)	Mean Difference (I-J)	Std. Error	P value
45	1.32±0.22	Moderate to Severe (<60)	Mild	.36984*	.05165	.000
			Normal	.63302*	.06006	.000
34	0.95±0.26	Mild (60-90)	Moderate to Severe	-.36984*	.05165	.000
			Normal	.26318*	.06308	.000
21	0.69±0.16	Normal (>90)	Moderate to Severe	-.63302*	.06006	.000
			Mild	-.26318*	.06308	.000

One-way ANOVA followed by Post-hoc Tukey test applied.
P value < 0.05 was taken as statistically significant
In this study, the mean creatinin of the patients was1.06±0.33, with a minimum of 0.50 and a maximum of 1.80. Table shows that, average levels of creatinineis significantly higher for <60 eGFR as compared to 60-90 and >90 eGFR levels. Also creatinine average is higher for 60-90 eGFR as compared >90 eGFR levels. Data shows that, increase in creatinine from baseline is directly proportional to decline in eGFR from 90–60 and <60.

Table 5: Association between Urine Albumin and eGFR

Urine Albumin	eGFR(End of study)						Total	
	Moderate to Severe		Mild		Normal			
	No.	%	No.	%	No.	%	No.	%
Negative	7	15.6%	24	70.6%	20	95.2%	51	51.0%
Trace	14	31.1%	8	23.5%	1	4.8%	23	23.0%
1+	12	26.7%	2	5.9%	0	0.0%	14	14.0%
2+	8	17.8%	0	0.0%	0	0.0%	8	8.0%
3+	4	8.9%	0	0.0%	0	0.0%	4	4.0%
Total	45	100.0%	34	100.0%	21	100.0%	100	100.0%

Pearson Chi-Square =50.394, p value =8, p value =.000, Significant
In the present study, there was a negative correlation between Urine albumin and eGFR at the end of study and the P value is significant. Above tables shows that, albuminuria was noted in 49 patients(49%). Out of 49,23 had Trace, 14 had 1+,8 had 2+ and 4 had 3+ albuminuria.Majority of patients in <60 (Moderate to Severe) eGFR were noted 14(31.1%)

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trace followed by 12(26.7%) had 1+, 8(17.8%) had 2+ and 4(8.9%) had 3+.Above association between Urine Albumin and eGFR (End of study) found statistically significant ($p<0.001$).

4. Discussion

In the present study, Tenofovir based regimen contributed to most of the moderate to severe decline in eGFR with 33 % of patients are under < 90 ml/min , with 56% in < 60 ml/min category. These results are comparable to other studies[5].

In the DART trial the incidence of grade 3 or 4 decreased eGFR was 1.7% for participants on TDF. These changes occurred in a median of 14 weeks after starting ART. In Western studies, incidence ranged from 1.3% changes in creatinine clearance and serum creatinine elevations in ART-experienced patients after starting TDF[6] to a cumulative incidence rate of a confirmed GFR <70 ml/min of 1.18 per year of TDF use (95% CI: 1.12; 1.25) in patients with normal baseline renal function (eGFR _90 ml/min)[7].

In a study in Senegal more patients on TDF moved from mild (60-90 ml/min/1.73 m2) to moderate renal impairment (30 - 60 ml/min/1.73 m2) after a year, compared to patients not on TDF with a rate ratio of transition from mild to moderate renal impairment of 2.74 in patients receiving TDF[8].

In a Copenhagem study by Lene Ryom et al. with total 22,603 patients. Tenofovir, Ritonavir boosted atazanavir and ritonavir boosted Lopinavir were independent predictors of confirmed eGFR <70ml/min indicated chronic renal impairment in HIV positive patients[9].

5. Conclusion

This study signifies that Tenofovir based regimen is the basis for most of the decline in renal function in patients on ART. Mean Creatinine is 1.06. There is significant P value between Creatinine and eGFR. Average levels of Creatinine is significantly higher (1.30) for <60 eGFR Category. We also recommend assessment of renal function of HIV infected patients prior to initiation of HAART to guide the choice and dosing of Antiretroviral drugs.

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