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ASSOCIATION OF RENAL FUNCTION WITH SERUM PARAMETERS AND CD4 COUNT IN PATIENTS ON TENOFOVIR-BASED ANTIRETROVIRAL THERAPY: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: HIV infection, primarily caused by Human Immunodeficiency Virus type 1 (HIV-1), has become a chronic condition with the advent of multi-drug antiretroviral therapy (ART). ART can lead to adverse effects, including renal dysfunction, especially in patients receiving tenofovir-based regimens.

Objectives: To determine the prevalence of renal dysfunction and identify its clinical and biochemical predictors—including serum creatinine, serum potassium, estimated glomerular filtration rate (eGFR), and CD4 count—in patients receiving Tenofovir-based antiretroviral therapy.

Methods: Cross-sectional observational study was conducted at the ART clinic of SMS Medical College, Jaipur, from March 2023 to January 2024. Study included 300 HIV patients on Tenofovir-based ART for at least six months. Demographic, clinical, and biochemical data, including renal function, serum parameters, and CD4 counts, were collected by pre-validated and pretested structured questionnaire on convenient sampling. Data analysis by SPSS vr25.

Results: Among 300 HIV patients on Tenofovir-based ART for ≥6 months, 45% had mildly decreased renal function, while 0.3% experienced kidney failure. Mean age was 37.97 years(SD 11.15), with age showing a significant association with renal function($p < 0.001$); younger participants predominantly had normal renal function, whereas older age groups had higher impairment rates. Serum potassium (mean 4.5 mmol/L) and albumin(mean 3.8 g/dL) levels were also significantly associated with renal dysfunction($p < 0.001$). Additionally, 87% of patients had undetectable viral loads, primarily among those with normal or mildly decreased renal function.

Conclusion: Age, body weight, serum potassium, and albumin levels are significant predictors of renal function in HIV patients on Tenofovir-based ART. These findings highlight need for targeted monitoring to preserve renal health in this population.

Keywords:, Renal Function, HIV/AIDS, Tenofovir (TDF) Toxicity , CD4 Count , Biochemical Markers

INTRODUCTION

Human Immunodeficiency Virus (HIV) affects over 39 million people worldwide[1]. The introduction of antiretroviral therapy (ART) has turned HIV into a manageable chronic condition[2]. Tenofovir disoproxil fumarate (TDF)-based ART is widely used for its strong antiviral activity and favourable safety profile[3], though long-term use can cause renal toxicity and tubular dysfunction[4]. Renal impairment in people living with HIV (PLHIV) arises from multiple factors, including HIV-associated nephropathy, comorbidities, and ART-related toxicity[5]. CD4+ T-cell count, a key immune marker, may influence kidney outcomes, but its role in TDF-treated patients remains uncertain[6]. This study investigates renal dysfunction prevalence and predictors to optimize ART and reduce renal complications.

MATERIALS AND METHODS

Study Design and Setting: Observational cross-sectional study was conducted at the Antiretroviral Therapy (ART) Centre of SMS Medical College, Jaipur, from March 2023 to January 2024. Ethical clearance was obtained from the Institutional Ethics Committee of Rajasthan University of Health Sciences (RUHS), Jaipur. Approval from the Clinical Trial Screening Committee (CTSC) was also secured in accordance with the institutional policy for studies involving human participants. Written informed consent was obtained from all participants, and confidentiality was maintained through the anonymization of data.

Study Population and Sampling: A total of 300 HIV-positive patients on Tenofovir Disoproxil Fumarate (TDF)-based antiretroviral therapy for at least six months were recruited using consecutive sampling. The sample size was calculated based on the expected prevalence of proteinuria in patients on long-term ART, with an added 5% margin for potential attrition. Included adults aged 18–65 years, on TDF-based ART for a minimum of six months and documented normal renal function at ART initiation. Excluded known pre-existing chronic kidney disease or comorbid chronic illnesses (e.g., diabetes mellitus, hypertension), pregnancy (due to the physiological variation in renal function during gestation) and concurrent use of nephrotoxic drugs other than TDF. Demographic and clinical data were collected using a structured proforma, including age, sex, duration of ART, weight, height, and WHO clinical staging. Body mass index (BMI) was calculated and categorized based on WHO classifications into underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥30.0 kg/m²).

Biochemical investigations included serum creatinine, urea, albumin, sodium, potassium, chloride, and random blood sugar. Immunological and virological markers—CD4 count and HIV viral load—were also assessed. Renal function was evaluated using the estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation. Renal dysfunction was defined as an eGFR <90 mL/min/1.73 m² and staged according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.

Statistical Analysis: Data were analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Descriptive statistics summarized participant characteristics. Continuous variables were presented as mean ± SD and categorical variables as frequencies and percentages. Prevalence of renal dysfunction was calculated with 95% confidence intervals. One-way ANOVA was used to compare CD4 counts across renal function stages. Given the >10% prevalence of renal dysfunction, Modified Poisson Regression with robust variance was used to identify independent predictors.

Variables with p <0.2 in univariate analysis were included in the multivariable model. A p-value <0.05 was considered significant.

RESULTS

The study population predominantly comprised younger adults, with 51% in the 18–37 age group, 42% in the 38–57 group, and only 7% aged 58–77 years. Males constituted 71% of the cohort, while females accounted for 29%. Participants' body weight ranged from 35.14 kg to 95.13 kg. However, stratification based solely on weight ranges introduced overlapping values (e.g., 55.13 kg falling into two categories), potentially affecting clarity. Percentages were also not consistently reported for all subgroups. To better assess nutritional status and its association with renal function, future analyses should categorize participants based on Body Mass Index (BMI) rather than raw weight alone, allowing clearer distinction between underweight, normal, overweight, and obese categories, and enabling integration with serum albumin levels.

Plasma viral load (VL) was available for all participants, although VL testing under the national guidelines (NACO) is typically conducted only in cases of suspected virological failure or clinical/immunological deterioration. In this study, VL was done regardless of ART duration, including those on ART for ≤6 months, possibly due to center-specific protocols or retrospective availability of records. This may limit generalizability. A clear trend was observed between viral load and CD4 count: as CD4 count declined, the proportion of individuals with viral loads >1000 copies/mL increased, suggesting a negative correlation between immune status and virological suppression (Figure 1).

Analysis of renal function status revealed that 45% of participants had mildly decreased renal function (eGFR 60–89 mL/min/1.73m²), while 0.3% met criteria for kidney failure (eGFR <15 mL/min/1.73m²). Normal renal function was observed in 42% of participants (Table 2, Figure 2). When stratified by viral load, the majority of individuals with undetectable or low VL had normal or mildly impaired renal function, while those with higher VL did not show proportionally greater renal impairment. Severe renal dysfunction remained rare across all VL strata (Table 3).

Duration of Tenofovir-based ART did not show a consistent trend in renal function outcomes. The mean ART duration was 21.02 months, but renal function varied widely across different durations (Figure 2), indicating no clear temporal association. Among biochemical parameters, serum potassium and serum albumin were significantly associated with renal dysfunction ($p < 0.001$). Participants with impaired renal function had higher serum potassium and lower serum albumin levels. In contrast, serum sodium and chloride levels showed no significant association with renal function status (Table 4 and 5).

CD4 count also differed with renal function. Participants with preserved renal function had higher CD4 counts compared to those with renal impairment. However, the differences in mean post-ART CD4 counts across renal function stages were not statistically significant ($F = 1.46$, $p = 0.225$) based on one-way ANOVA (Table 6). Multivariable analysis using Modified Poisson Regression showed that serum potassium and serum albumin were significant independent predictors of renal dysfunction. Serum sodium and chloride did not significantly influence outcomes (Table 7).

DISCUSSION

Renal Function and Serum Parameters: Our study found that 45% of participants had mildly decreased renal function, with only 0.3% experiencing kidney failure. This aligns with Mwemezi et al. [7], who reported a significant association between age and renal function. Serum albumin levels

were significantly correlated with renal function, highlighting the role of nutrition [8]. Unlike Brennan et al. [9], who reported higher renal dysfunction rates, our findings suggest a lower prevalence of severe impairment [10,11].

Body Weight and Renal Function: Higher body weight correlated with better renal function. This contrasts with Nyende et al. [12], who found no such association, but aligns with studies linking malnutrition to impaired renal function.

Duration of Tenofovir-Based ART and Renal Function: No significant trend was found between renal function and prolonged Tenofovir-based ART use, consistent with Msango et al. [13]. This contradicts studies suggesting a progressive renal decline with extended ART use.

CD4 Count and Renal Function: No significant correlation was observed between renal function and CD4 count. This differs from Kumarasamy et al. [14], who linked renal dysfunction to age and baseline eGFR. Other factors, such as body weight and serum albumin levels, may have a greater influence.

Comparison with Other Studies: Compared to Debeb SG et al. [15], our study found a higher renal dysfunction prevalence, possibly due to population differences. Our body weight findings ($p < 0.001$) contrast with Nyende et al. [16]. The link between renal function and serum albumin aligns with Gayatri L et al. [17], emphasizing the importance of nutritional assessment .

CONCLUSTION

The study concludes that older age is linked to poorer kidney function, while higher body weight may protect it. Serum potassium and albumin levels are key indicators of kidney health. No major gender differences were found, and better kidney function was associated with improved HIV treatment outcomes.

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Authentication Statement: We affirm that the manuscript is free from plagiarism. All data, images, and figures used in the manuscript are original or properly cited. This article has not been submitted to any other journal for simultaneous consideration.

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DECLARATIONS

Ethics Clearance: We certify that Ethical clearance has been obtained from the Institutional Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants where applicable. Informed consent was obtained.

IEC Approval Number: 1023 MC/EC/2023

Competing interests: The authors declare no competing interests.

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Author Contributions: M.M, AA and DM conceptualized the study, M.M and N.E designed the methodology and applied the statistical analyses, M.M and J.R conducted the data collection, D.M and J.R did the data analysis and wrote the main manuscript, A.A provided supervision. All the authors reviewed the final manuscript.

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TABLES

Table 1: Distribution of variables among study population

Variables		number (n=300)	Percentage(%)
Age Groups	18-37	153	51%
	38-57	127	42%
	58-77	20	7%
Gender	Male	213	71%
	Female	87	29%
Body wt	45.13-55.13	126	42%
	55.14-65.13	105	35%
	65.14-75.13	65	22%
	75.14-85.13	4	1.33%

Table 2: Distribution of renal functions among study population

Renal Functions	**Egfr (**mL/min/1.73m²**)**	**n = 300**	**Percentage**
Normal renal function	≥90	131	43.7%
Mildly decreased renal function	60 - 89	135	45.0%
Mildly to moderately decreased renal function	45 - 59	21	7.0%
Moderately to severely decreased renal function	30 – 44	12	4.0%

Severely decreased renal function	15 – 29	0	0%
Kidney failure	< 15	1	0.3%

Table 3: Distribution of renal functions with viral load among study population

Viral Load	Total n (%)	Normal renal function (n)	Mildly decreased renal function (n)	Mildly to moderately decreased renal function (n)	Moderately to severely decreased renal function (n)	Kidney failure (n)
TND	260 (87%)	113	121	16	9	1
50 -1000	35 (11%)	14	13	5	3	0
> 1000	5 (2%)	4	1	0	0	0

Table 4: Distribution of Renal Functions with S. Potassium among study population

Renal Function	Grand Total (n)	K+ (Mean ± SD)	P value
Normal Renal Function	131	4.04 ± 0.28	ANOVA Test F = 7.17 P = **<0.001***
Mildly decreased renal function	135	4.03 ± 0.27	
Mildly to Moderately decreased renal function	21	4.05 ± 0.27	
Moderately to severely decreased renal function	12	4.42 ± 0.43	
Kidney failure	1	5.3 ± 0	
Grand Total	300	4.06 ± 0.30	

(* signifies the P value is statistically significant)

Table 5: Association of renal functions with serum albumin among study population

Renal Functions	**Grand Total (n=300)**	**S. Albumin** (Mean ± SD)	**One way Analysis of variance (ANOVA)**
Normal Renal Function	131	4.48 ± 0.05	F = 61.56; p value = **<0.001***
Mildly Decreased Renal Function	135	4.14 ± 0.27	
Mildly to Moderately Decreased Renal Function	21	4.03 ± 0.49	
Moderately to Severely Decreased Renal Function	12	3.78 ± 0.64	
Kidney Failure	1	3 ± 0	

Table 6: Association of Renal Functions with Post ART CD4 count among study population

Renal Functions	**Grand Total (n=300)**	**Post ART CD4 count** (Mean ± SD)	**One way Analysis of variance (ANOVA)**
Kidney Failure	1	24 ± 0	F = 1.46; P value = 0.225
Mildly Decreased Renal Function	135	518 ± 48	
Mildly to Moderately Decreased Renal Function	21	541.95 ± 380.55	
Moderately to Severely Decreased Renal Function	12	383.83 ± 193.53	
Normal Renal Function	131	626.02 ± 766.26	

Table 7: Multiple logistic regression among serum electrolytes and albumin

Multiple logistic regression	**S.E**	**OR**	**p value**	**95% C.I.**

				Lower	Upper
S K+	0.625	3.402	0.050	0.999	11.583
S.Albumin	2.302	0.001	0.001	0.001	0.001

FIGURE

Figure 1: Distribution of viral load with CD4 count among study population

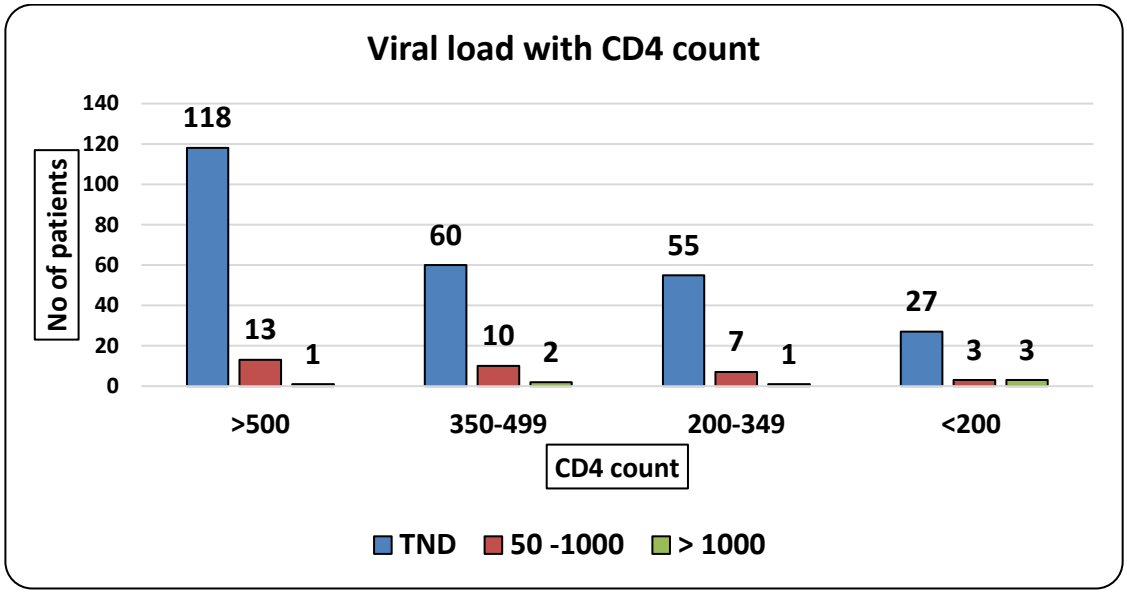


Figure 2: Distribution of Renal Dysfunctions with duration of Tenofovir based ART among study population

