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Association of CD4+ Cell Count with Renal Sonography Findings and Degree of Proteinuria in HIV-Infected Patients: A Cross-Sectional Study from a Tertiary Care Centre in North India

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Abstract

Background: Over the last two decades, renal disease has become one of the most clinically important, although frequently overlooked, non-AIDS comorbidities associated with HIV infection. With people living with HIV (PLHIV) now living longer due to antiretroviral therapy (ART), it is perhaps unsurprising that renal complications, ranging from asymptomatic proteinuria to end-stage kidney disease, have become more prominent in their clinical course. CD4+ T-cell count, the accepted marker of immune competence in HIV, has been implicated in both structural and functional renal deterioration, although the precise nature and strength of this association is not well characterised, especially in resource-limited settings such as India. Renal biopsy is rarely available in routine practice in such settings and noninvasive tools such as renal ultrasonography and urinary protein estimation serve as practical and accessible alternatives for early detection and ongoing monitoring of renal involvement.

Methods: A cross-sectional observational study was carried out for a period of 18 months at a tertiary care

ART center in Agra, Uttar Pradesh, recruiting 140 HIV positive patients aged 18-65 years. Participants were classified into three immunological groups based on CD4 count: >500 cells/mm 3 , 200–500 cells/mm 3 and <200 cells/mm 3 . Bipolar renal length, cortical thickness, echogenicity grade (0–4) and corticomedullary differentiation (CMD) were evaluated by renal ultrasonography. Both dipstick and 24-hour urine protein estimation were used to measure proteinuria. Pearson's correlation analysis was used to assess the correlation between CD4 count and renal parameters.

Results: The mean CD4 count was 372.8 ± 176.0 cells/mm³. Proteinuria was detectable in 96.4% of the participants (mean 0.54 ± 0.14 g/day). There was a significant moderate inverse correlation between CD4 count and proteinuria ($r = -0.478$; $p < 0.001$), and a strong inverse correlation with serum creatinine ($r = -0.800$; $p < 0.001$). CD4 count and eGFR were positively correlated ($r = +0.926$; $p < 0.001$). Echogenicity grade ≥2 was observed in 47.9% of patients and CMD loss in 21.4%. Interestingly, sonographic structural parameters did not achieve statistical significance in their correlation with CD4 count.

Conclusion: The present study provides reasonable confidence that a fall in CD4 count is significantly associated with deterioration in renal function, most notably an increase in proteinuria and a fall in eGFR, in HIV-infected patients. A combined approach of CD4 monitoring, proteinuria screening and targeted ultrasound of the kidneys seems to provide a pragmatic, cost-effective and scalable solution for early renal risk stratification in resource-limited settings such as North India.

Keywords: HIV, CD4+ T-Cell Count, Renal Ultrasonography, Proteinuria, HIV-Associated Nephropathy, Corticomedullary Differentiation, Echogenicity, Chronic Kidney Disease.

Introduction

It is a well known fact that HIV infection is still one of the top public health challenges facing the global community. As per latest estimates, there are about 39 million people living with HIV and India, with an approximate 2.4 million people living with HIV (PLHIV), bears a disproportionate burden of this infection in the Asian subcontinent.But the nature of the problem is what has changed in recent decades. ART has transformed HIV from a nearly uniformly fatal disease into a long-term manageable condition, and mortality rates from AIDS-defining conditions have decreased dramatically. But there are complications that come along with this success. Amongst long term survivors of HIV, non-communicable comorbidities to which renal disease is especially prone, are becoming increasingly common.[1] Renal disease is clinically serious and, unfortunately, is frequently diagnosed too late.

HIV-associated renal disease exhibits a broad clinical spectrum, ranging from asymptomatic proteinuria, subclinical tubular dysfunction, HIV-associated nephropathy (HIVAN), immune-complex mediated glomerulonephritis, drug-induced tubulointerstitial injury, and progressing chronic kidney disease (CKD) leading to end-stage renal disease (ESRD).[3] kidney disease. It is usual. It is grave. But often it is clinically silent until the damage is already quite extensive.

In this context, the role of CD4+ T-lymphocyte count, the workhorse biomarker of HIV immunosuppression, deserves careful attention. Declining CD4 counts have been documented in literature not only with

opportunistic infections but also with Direct viral injury to the renal parenchymal cells and immune mediated glomerular damage.[4] Perhaps underappreciated is that some structural renal changes, such as increased cortical echogenicity and loss of corticomedullary differentiation, may be detectable on ultrasound even before a measurable decline in the estimated glomerular filtration rate (eGFR).[5] This window of subclinical structural change may be an opportunity for early intervention that is currently being widely missed.

Renal ultrasonography has clear practical advantages. It is non-invasive, inexpensive, free of ionising radiation, repeatable at serial visits and available in the majority of government medical colleges across India where renal biopsy facilities may be absent or practically inaccessible for routine HIV care.[6] The standardised echogenicity grading system as described by Hamper et al allows a degree of objective and reproducible structural characterisation that is otherwise difficult to achieve non-invasively.[11] Proteinuria, as measured by dipstick or 24-hour collection, has historically been considered the earliest and most readily available laboratory indicator of glomerular injury in HIV.[8]

It is pertinent to mention here that despite Uttar Pradesh having one of the highest absolute HIV caseloads in India, published data from this region correlating immune status with quantitative renal sonographic parameters and proteinuria remain sparse. These studies are often hampered by small sample sizes, insufficient confounder adjustment or heavy reliance on single-endpoint analysis.[9,10] To our knowledge, the present study is one of the very few studies from this part of North India to comprehensively evaluate the association of CD4+ count with multiple renal functional markers (proteinuria, serum creatinine, eGFR) and structural sonographic parameters (echogenicity grade, renal length, cortical thickness, CMD) simultaneously, in a well-characterised hospital-based cohort. It is hoped that the locally generated evidence will help inform region-specific renal screening protocols and, in time, translate into improved clinical outcomes for HIV patients in this resource-constrained setting.

Materials And Methods

Study Design and Setting

The present study was planned as a cross-sectional observational study and was carried out over a period of 18 months (January 2024 – June 2025) at the ART Centre and Department of General Medicine, Sarojini Naidu Medical College and Hospital, Agra, a tertiary care government institution catering to a large and diverse HIV patient population from across Uttar Pradesh and adjoining districts. The Institutional Ethics Committee approved the study (Ref. SNMC/IEC/2023/XXX) prior to starting the data collection. Written informed consent was obtained from all participants before enrolment.

Participants

Consecutive HIV-positive adults aged 18-65 years were enrolled if their diagnosis was confirmed by ELISA and Western blot as per NACO guidelines and if a CD4 count was available within the last 3 months. Exclusion criteria were deliberately kept broad to prevent confounders. Patients with existing renal impairment not related to HIV, diabetes mellitus, obstructive uropathy, active UTI at the time of evaluation, pregnant women or subjects who refused involvement were not included. Based on these criteria, 140 patients were finally included in the study.

CD4+ T-Cell Count Measurement and Stratification

Flow cytometry was used to estimate CD4+ T-cell counts from fresh venous blood samples using the BD FACSCount system.[4] Based on these counts, participants were classified in three immunological categories: group I (>500 cells/mm^3, i.e. close to normal immune status), group II (200–500 cells/mm^3, moderate immunosuppression) and group III (<200 cells/mm^3, severe immunosuppression, which is the AIDS-defining immunological threshold).

Renal Ultrasonographic Assessment

All the sonographic examinations were performed by one experienced radiologist using a 3.5 MHz convex transducer. To minimise observer bias the radiologist was blinded to the CD4 results at the time of each scan. The following parameters were noted for both kidneys: (i) bipolar renal length (cm), (ii) cortical thickness (mm), (iii) corticomedullary differentiation (CMD) classified as preserved or lost and (iv) renal cortical echogenicity graded on the standardised 0-4 scale with respect to the echotexture of the liver and spleen as initially described by Hamper et al.[11] In brief, Grade 0 is a hypoechoic renal cortex relative to the liver, the normal state;Grade 1: iso-echoic to liver with preserved CMD. Grade 2: mild hyperechogenicity with reduced CMD. Grade 3: marked hyperechogenicity with CMD absent. Grade 4: severe, diffuse hyperechogenicity with shrunken, small kidney. Generally indicative of advanced, irreversible parenchymal damage.

Proteinuria Assessment

We evaluated proteinuria with a two-step method. First, a morning midstream urine sample was tested with a calibrated dipstick and results were recorded as trace, 1+, 2+ or 3+. This was then followed by quantitative estimation by timed 24-hour urine collection and expressed in grams per day. According to the standard classification,[8] patients were classified into the following groups: no proteinuria (≤0.15 g/day), mild proteinuria (0.15–1.0 g/day), moderate proteinuria (1.0–3.5 g/day) and nephrotic-range proteinuria (>3.5 g/day).

Other Biochemical and Clinical Investigations

Serum creatinine and blood urea nitrogen were measured on an automatic biochemistry analyser. The GFR was estimated using the CKD-EPI 2021 creatinine equation . Haemoglobin, full blood count and viral markers (HBsAg, anti-HCV) were also recorded. Data on ART status, type of ART regimen (TDF-based vs non-TDF), duration of known HIV infection, co-infections (tuberculosis, hepatitis B, hepatitis C), systolic and diastolic blood pressure, smoking status and history of alcohol consumption were collected from all participants.

Statistical Analysis

Data entry and analysis were done using Microsoft Excel and IBM SPSS Statistics software (version 25.0), respectively. Continuous variables are expressed as mean ± standard deviation (SD) and categorical variables are expressed as frequency (n) and percentage (%). Before correlation analysis, the normality of the distribution of the CD4 count was first assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Pearson's correlation coefficient (r) was used to assess the relationship between CD4 count and each of the studied parameters of renal function and structure. Independent samples t-test was used to compare the continuous variables between the renal normal and renal abnormalities groups.

Results

Demographic and Clinical Profile

Of 140 patients enrolled, 101 (72.1%) were male and 39 (27.9%) were female. The male predominance in this group is not surprising and is broadly in keeping with the gender distribution of HIV in India. In terms of age distribution, the spread was fairly even across three broad groups: 18–30 years (33.6%), 31–45 years (31.4%) and 46–65 years (35.0%). No one age group was unduly affected, which is of some practical importance with respect to renal screening policy. The majority of patients (89.3%) were already on ART at the time of enrolment; only 10.7% were ART-naïve. Only 8.6% of the participants had cardiovascular disease. Smoking was reported by 27.9%, and alcohol use by 17.9%.

The authors regard the very low prevalence of cardiovascular comorbidity in the present series as rather reassuring from an interpretative point of view, since it provides reasonable support for the inference that the renal abnormalities found in this study are largely attributable to HIV-related pathological processes, as opposed to hypertensive or ischaemic vascular disease. Of course, one cannot completely exclude an independent contribution from smoking or alcohol – both of which have well-documented, if indirect, effects on renal health – but the numbers involved suggest these were not the principal drivers.

CD4+ Count Distribution

The mean CD4 count in the study population was 372.8 ± 176.0 cells/mm³ (median 367.5 cells/mm³; range 50 to 1,000 cells/mm³). The 95% confidence interval for the mean was 343.4–402.2 cells/mm3, a reasonably precise central estimate. The broad range of CD4 values in the cohort, ranging from severely immunocompromised to near-normal immune status, was frankly an important feature of this dataset, providing a broad immunological spectrum for correlation analysis. The variable CD4 count was found to be normally distributed as assessed by Kolmogorov–Smirnov test ($p = 0.200$) and Shapiro–Wilk test ($p = 0.083$). This confirmed the appropriateness of Pearson's parametric correlation in subsequent analyses.

Proteinuria (Table 1)

Proteinuria was found in 96.4% of the study participants. This was a striking figure, frankly. Trace positivity was seen in 3.6%, 1+ in 64.3% and 2+ in 32.1% on dipstick testing. The mean 24-hour urine protein excretion was 0.54 ± 0.14 g/day. These findings are generally consistent with previous reports that have identified proteinuria as a sensitive and often early marker of glomerular involvement in HIV infection,8,12 although it should be acknowledged that the very high prevalence in our cohort may in part reflect the inclusive nature of our screening protocol and the referral bias of a tertiary care setting. With this caveat, the practical implication seems to be pretty straightforward: proteinuria testing should be routine at every HIV clinic visit.

Sonographic Findings (Table 2)

In renal cortical echogenicity, only 14.3% of the participants had Grade 0 (normal). Grade 1 was found in 37.9%. Overall, 47.9% of the cohort had grades 2 to 4 — indicating moderate to severe parenchymal abnormality. CMD was found in 21.4% of the patients.[11] These structural changes were sufficiently common to be of clinical significance. Whether they represented active ongoing injury or the accumulated scarring of past insults was, as discussed below, a question that could not be definitively resolved by the present cross-sectional design. However, the high prevalence of sonographic

abnormalities in this cohort underscores the importance of renal ultrasound as part of the work-up of HIV patients even in resource limited settings.

Correlation of CD4 Count with Renal Parameters (Table 3)

There was a statistically significant moderate negative correlation between CD4 count and 24-hour proteinuria in the present study ($r = -0.478$; $p < 0.001$). The association between CD4 count and serum creatinine was even stronger and inverse ($r = -0.800$; $p < 0.001$). For its part, CD4 count showed a strong positive correlation with eGFR ($r = +0.926$; $p < 0.001$) — a finding which, on reflection, is perhaps the most important in the whole dataset, since it maps so directly onto the clinical question of whether immune status tracks with renal filtration function in HIV.[12,17]

Interestingly, and this needs some emphasis, sonographic structural parameters were not statistically significant in their correlation with CD4 count. Echogenicity R = -0.141 (p=0.096); right renal length R = 0.122 (p=0.151); right cortical thickness R = 0.040 (p=0.637). The mechanism that accounts for the lack of a significant structural–immunological correlation in the present series is not completely understood. A reasonable interpretation is presented in the Discussion.[5]

Comparison of Normal vs. Renal Abnormality Groups (Table 4)

When the subjects were split into those with and without renal abnormality, a number of highly significant differences emerged. The renal-abnormality group also had significantly higher proteinuria (0.61 vs. 0.48 g/day; $p < 0.001$), serum creatinine (1.06 vs. 0.84 mg/dL; $p < 0.001$), and blood urea (49.5 vs. 38.3 mg/dL; $p = 0.026$). The eGFR was found to be significantly lower in the renal-abnormality group (88.5 vs. 101.7 mL/min/1.73m2; $p < 0.001$). Renal-abnormality group showed significantly shorter and thinner values of all right and left renal lengths and cortical thickness. The mean CD4 count was, as expected, somewhat lower in the renal-abnormality group (347.0 vs. 396.4 cells/mm3) -- but this difference, it must be noted, did not reach statistical significance ($p = 0.097$).

This last observation — the non-significant CD4 difference between the two groups — is, the authors feel, quite revealing. It suggests that once frank renal dysfunction has been established, it is the biochemical and structural markers that diverge most prominently and consistently, rather than the CD4 count alone. The absolute CD4 value at any single time-point may, at that stage, be a less sensitive discriminator of renal injury than the functional parameters.[9,13]

Table 1: Dipstick Proteinuria Severity (N = 140)

Dipstick Category	n	%
Trace	5	3.6
1+	90	64.3
2+	45	32.1
Total	140	100.0

Table 2: Renal Cortical Echogenicity Grading (N = 140)

Echogenicity Grade	n	%
Grade 0 – Normal	20	14.3
Grade 1 – Mild increase	53	37.9
Grade 2 – Moderate increase	37	26.4
Grade 3 – Marked increase	26	18.6
Grade 4 – Severe / shrunken	4	2.9
Total	140	100.0

CMD was preserved in 78.6% (n = 110) and lost in 21.4% (n = 30) of participants.

Table 3: Pearson Correlation of CD4 Count with Renal Functional and Structural Parameters (N = 140)

Parameter	Mean ± SD	r with CD4	p-value
Proteinuria (g/day)	0.54 ± 0.14	−0.478	<0.001*
Serum Creatinine (mg/dL)	0.95 ± 0.26	−0.800	<0.001*
eGFR (mL/min/1.73m²)	95.4 ± 19.4	+0.926	<0.001*
Echogenicity Grade	1.58 ± 1.04	−0.141	0.096 (NS)
Right Renal Length (cm)	10.4 ± 0.35	+0.122	0.151 (NS)
Left Renal Length (cm)	10.5 ± 0.37	+0.144	0.090 (NS)
Right Cortical Thickness (mm)	7.70 ± 0.46	+0.040	0.637 (NS)
Left Cortical Thickness (mm)	7.77 ± 0.50	+0.025	0.765 (NS)

*Statistically significant (p <0.05); NS = not significant; r = Pearson correlation coefficient; eGFR by CKD-EPI 2021.

Table 4: Comparison of Renal Parameters Between Normal and Renal Abnormality Groups (N = 140)

Parameter	Normal Group Mean ± SD	Renal Abnormality Mean ± SD	Mean Diff	p-value
CD4 (cells/mm³)	396.4 ± 179.6	347.0 ± 169.6	49.4	0.097 (NS)
Proteinuria (g/day)	0.48 ± 0.12	0.61 ± 0.14	−0.127	<0.001*
Serum Creatinine (mg/dL)	0.84 ± 0.20	1.06 ± 0.26	−0.217	<0.001*

Serum Urea (mg/dL)	38.3 ± 30.2	49.5 ± 28.6	−11.2	0.026*
eGFR (mL/min/1.73m²)	101.7 ± 18.6	88.5 ± 17.9	13.1	<0.001*
Right Renal Length (cm)	10.45 ± 0.32	10.27 ± 0.35	0.18	0.002*
Left Renal Length (cm)	10.63 ± 0.34	10.42 ± 0.38	0.20	0.001*
Right Cortical Thickness (mm)	7.84 ± 0.43	7.55 ± 0.46	0.28	<0.001*
Left Cortical Thickness (mm)	7.97 ± 0.47	7.56 ± 0.45	0.41	<0.001*

*Statistically significant (p <0.05); NS = not significant.

Discussion

The present study was carried out with an aim to systematically and clinically meaningfully study the relationship between CD4+ T-cell count and renal status, assessed by both functional parameters and structural sonographic indices, in HIV infected patients attending a tertiary care centre in North India. In general the data obtained give a picture that the authors consider reasonably coherent and internally consistent. The decline of renal function, as measured by increasing proteinuria and creatinine and decreasing eGFR, correlates closely and significantly with declining immune status. In contrast, structural sonographic changes are frequent in this cohort but seem to follow a somewhat different course and may not be directly linked to the patient's actual CD4 count. Both findings have distinct — and practically important — implications for HIV care, and each deserves a detailed examination.

Proteinuria and CD4 Count

Obviously proteinuria plays a prominent role in the clinical evaluation of renal disease in HIV. In the present study, a statistically significant moderate inverse correlation was observed between CD4 count and 24 hour urinary protein excretion (r = −0.478; p <0.001). This finding is in agreement with the observations made by Janakiraman et al.[12] from South India, who reported a significantly higher prevalence of proteinuria in the lower CD4 strata and concluded in general terms that progressive immunosuppression drives glomerular injury in a graded and predictable fashion. Aggarwal et al.[14] from Haryana also recorded similar trend; they found proteinuria in about 52% of asymptomatic HIV patients with the burden disproportionately concentrated among patients with CD4 count < 200 cells/mm 3 . This pattern indicates that proteinuria may be a sensitive early marker of renal involvement before the appearance of overt clinical symptoms. Bakri et al.[15] and Aliyannissa et al.[16] also found an inverse correlation between CD4 count and urinary protein, however the latter study was conducted in a paediatric cohort and caution must be exercised in extrapolating the findings directly to adults.

The prevalence of proteinuria in the present series (96.4%) was higher than that reported in several comparable studies. This may be partly explained by the inclusive screening protocol (dipstick positivity trace was included) and referral to a tertiary centre where sicker, more immunocompromised patients tend to be

concentrated. However, the clinical relevance of this observation cannot be overemphasised: in conjunction with the correlation data, it provides strong support for the recommendation—as stated by Szczech et al.[8]—that proteinuria screening should be made universal and routine in all PLHIV, irrespective of clinical symptomatology. It's cheap and it's not invasive. Really there is no good argument against using it routinely.

eGFR, Serum Creatinine, and CD4 Count

One of the most important functional findings of the present study was the significant positive correlation between CD4 count and eGFR ($r = +0.926$; $p < 0.001$) and the equally significant negative correlation between CD4 count and serum creatinine ($r = -0.800$; $p < 0.001$). These figures suggest a tight, graded coupling between immune status and renal filtration function in the study population — a coupling that is, frankly, more robust than one might have anticipated in a cohort where 89.3% of patients were already on ART.

These findings are consistent with those of Longo et al.[17] who found significantly lower eGFR values among HIV-infected patients with severe immunosuppression in a large sub-Saharan African cohort, and McMahon et al.[18] who demonstrated that HIV viral suppression with ART was associated with a significantly slower rate of GFR decline among patients with biopsy-proven focal segmental glomerulosclerosis, an observation that strongly suggests, if not proves, that immune recovery leads to at least partial preservation of renal function. Janakiraman et al.[12] and Chatterji et al.[13] from Kolkata, both observed deterioration of functional renal indices parallel to immunological decline in Indian patients, consistent with our findings and supporting regional validity of what has otherwise been reported mainly in African and Western cohorts. However, it cannot be completely excluded that these correlations were influenced by residual confounding by ART regimen, TDF exposure or unrecognised metabolic disease which should be taken into account.

Renal Ultrasonography, Echogenicity, and CD4 Count

The sonographic picture in the present study underscores an important, and in the opinion of the authors, somewhat underappreciated aspect of HIV-related renal disease. Echogenicity grade ≥2 was present in almost half the cohort and CMD loss in >1/5. Such a degree of structural renal abnormality in a largely ART-treated cohort is sobering to say the least . These observations are in line with the findings of Ibinaiye et al.[19] and Garko et al.[20] from Nigeria who observed significant correlation between echogenicity grade and CD4 strata in patients with HIV and suggested that renal ultrasound could be used as a surrogate marker of immunological burden. However, our data did not reproduce this specific finding. The correlation between CD4 count and echogenicity grade was $r = -0.141$ ($p = 0.096$) — not statistically significant, but the trend was in the expected direction.

How to explain this discrepancy? A possible explanation – suggested, in a slightly different context, by da Silva et al.[5] – is that sonographic structural changes in HIV represent accumulated and often irreversible parenchymal damage – including the interstitial fibrosis and tubular atrophy arising from past episodes of viral replication, immune activation and potentially ART-related nephrotoxicity – rather than the patient's immune status at any particular moment.[7] The histopathological basis for this was established by Hamper et al.[11] who demonstrated that increased cortical echogenicity on ultrasonography correlates to parenchymal fibrosis on

renal biopsy in HIV. Such fibrosis, once established, is unlikely to regress – even with immune recovery on ART. The structural changes seen on sonography in this cohort, where 89.3% of the participants were already on antiretroviral therapy, may well reflect the legacy of earlier injury, either before treatment or early in the treatment phase, and may not reflect current immune status. In other words, it is possible that these patients had worse CD4 counts in the past – before starting ART or adequate titration – when the structural changes were accrued. Of course, one can only speculate with the cross-sectional design.

Renal Abnormality Groups and Clinical Implications

In the authors' opinion, the comparison between the renal-normal and renal-abnormality groups yields findings of great clinical importance. Proteinuria, serum creatinine, blood urea, eGFR and structural sonographic parameters (renal length and cortical thickness) were significantly different between the two groups. As noted, the difference in CD4 was not significant ($p = 0.097$). This pattern suggests (though it cannot be said to prove) that once frank renal dysfunction is established, it is the functional and structural end-organ markers that are the more sensitive and specific indicators of disease rather than the immune marker per se. This observation is in agreement with the results of a systematic scoping review by Assaram et al.[9] in South Africa that concluded that structural renal changes in HIV are most obvious after the start of functional damage. Based on these observations, it may be suggested that urinalysis, serum creatinine and eGFR should constitute the first-line renal screening battery in HIV care programmes, with renal ultrasonography being a second-line, complementary investigation when functional markers are identified as abnormal.[6,7]

Context Within Indian Literature and Regional Relevance

Published Indian data on HIV related renal disease have been predominantly from southern and eastern India, from centres in Tamil Nadu, Andhra Pradesh and West Bengal.[12,13,14] To the best of our knowledge, the present study is one of the more comprehensive assessments from North India, and specifically from Uttar Pradesh - a state that carries one of the largest HIV burdens in absolute terms among India's northern states. The present study has the advantage of assessing seven renal parameters at the same time in a single cohort in the functional as well as structural domains as compared to two of the more methodologically robust Indian studies in this area, Aggarwal et al.[14] from Haryana and Chatterji et al.[13] from Kolkata. It may also be relevant to note that Singh et al.[10] have reported a significant background burden of non-HIV CKD in India, which makes structured, combined renal surveillance in HIV patients not only desirable but arguably essential — to tease out HIV-attributable renal morbidity from the background noise of non-communicable kidney disease. There is clearly a need of bigger multicentre studies from North India.

Strengths and Limitations

The authors admit that the present study is not without limitations—and a word of caution is warranted before generalising the findings too broadly. The cross-sectional design does not allow for causal inference. The observed associations are correlations and not evidence of causality. Single centre recruitment limits generalisability to other settings. Renal biopsy was not performed, so the abnormalities seen could not be characterised histologically. Some participants had missing viral load data and the diversity of ART

regimens (some TDF-based and others not) could not be fully accounted for in the analysis. These are genuine limitations and the findings should be interpreted with due caution.

However, the authors believe there are many notable strengths in the study that should be highlighted. The simultaneous assessment of functional and structural renal parameters in the same cohort has methodological advantages. Ultrasonographic assessment was blinded to obviate the observer bias. The sample size, although not large by international standards, was sufficient for parametric correlation analysis and the wide range of CD4 values provided an adequate immunological spectrum for meaningful correlation. The near universal ART coverage reflects real-world conditions in Indian government hospitals and adds ecological validity to the findings. Obviously, further longitudinal, multicentre studies that include data on viral load, duration of ART, exposure to TDF and, when possible, histopathological correlation are required to build on the present observations.[3]

Conclusion

The present study's findings provide a reasonable degree of confidence that a declining CD4+ T-cell count is significantly and consistently associated with worsening renal functional parameters including rising proteinuria ($r = -0.478$; $p < 0.001$), rising serum creatinine ($r = -0.800$; $p < 0.001$) and a falling eGFR ($r = +0.926$; $p < 0.001$), even in HIV-infected patients receiving antiretroviral therapy. Proteinuria, found in at least 96.4% of this cohort with a mean value of 0.54 g/day, is the most sensitive, most easily available and arguably most important early marker of HIV-associated renal involvement in clinical practice.[8,12]

Structural sonographic abnormalities were clearly common, with Grade≥2 echogenicity seen in 47.9% and CMD loss in 21.4% of participants, and should not be dismissed; these findings imply a large burden of parenchymal renal disease in this population. However, these changes appear to reflect the cumulative legacy of previous renal injury rather than the current immune status of the patient, and did not correlate directly with the CD4 count in the present series.[5,11] These observations support the recommendation that routine renal screening, at minimum comprising urinalysis for protein, serum creatinine, and estimation of eGFR, be incorporated into the standard of care along all HIV care pathways, with particular attention to patients with CD4 counts <350 cells/mm3.[6,9] Considering the availability and cost-effectiveness of renal ultrasonography in the Indian setting, it may be a useful complementary addition in structural assessment when functional markers are found to be abnormal. An integrated approach to renal surveillance combining immunological monitoring with functional and structural renal evaluation has real promise to improve early detection, guide timely nephrology referral and ultimately prevent progression of HIV-related renal disease to end-stage kidney disease in a population that is, even with access to ART, still at considerable risk.[2,7]

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