^{Original Article} Tuberculosis and Chronic Kidney Disease: Evaluating the Management Challenges and Treatment Strategie

Tuberculosis and Chronic Kidney Disease

Challenges and Treatment Strategies

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ABSTRACT

Objective: To find the relation between tuberculosis and chronic kidney disease and evaluating the management challenges and treatment strategies.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Gulab Devi Hospital, Lahore, from December 2022 to June 2023.

Methods: The inclusion criteria encompassed individuals aged 18 years and older who had been diagnosed with both TB and CKD, either on long-term dialysis or with documented CKD stages 3-5 (defined as estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m² for \geq 3 months).

Results: Data was collected from 180 patients. Mean age was 57.1 ± 8.9 years. The distribution of CKD stages reveals that the majority of participants had CKD stage 3 or 4, with a smaller percentage in stage 5. Additionally, the table highlights that nearly half of the TB cases were pulmonary TB, while the remaining cases were extrapulmonary.

Conclusion: It is concluded that a potential positive impact of TB treatment on renal function in CKD patients, but further research is essential to confirm these observations and elucidate underlying mechanisms.

Key Words: Tuberculosis, Chronic Kidney Disease, Management Challenges, Treatment Strategies

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INTRODUCTION

Tuberculosis (TB) and Chronic Kidney Disease (CKD) are two globally prevalent and often coexisting health conditions that pose significant challenges to both patients and healthcare systems. Tuberculosis, primarily caused by Mycobacterium tuberculosis, remains a major infectious disease responsible for substantial morbidity and mortality worldwide ^[1]. Chronic Kidney Disease, characterized by a gradual loss of renal function, is a progressively debilitating condition with a high burden on public health resources^[2]. The convergence of TB and CKD presents a complex clinical scenario, demanding careful evaluation, management, and innovative treatment strategies.

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The coexistence of TB and CKD is particularly pertinent given their intricate relationship ^[3,4]. CKD is recognized as both a risk factor and a consequence of TB, creating a bidirectional association that can lead to adverse clinical outcomes. Patients with CKD are more susceptible to TB due to compromised immunity, and TB, in turn, can contribute to the progression of CKD through various mechanisms, including renal granulomas and the nephrotoxic effects of certain anti-TB medications ^[5].

The management of TB in CKD patients poses unique challenges. Standard anti-TB medications, such as isoniazid, rifampicin, and pyrazinamide, are renally excreted and require dose adjustments in CKD to prevent drug toxicity. Simultaneously, the impaired immune function in CKD patients may affect the clinical presentation and diagnostic accuracy of TB, necessitating a multidisciplinary approach ^[6]. Chronic kidney disease (CKD) is an escalating public health concern, particularly in England, where CKD stages 3-5, characterized by an estimated glomerular filtration rate (eGFR) of $< 60 \text{ mL/min}/1.73 \text{ m}^2$ for $\ge 3 \text{ months}$, affect an estimated 6% of the general population ^[7]. In a noteworthy subset of cases, CKD advances to end-stage kidney disease (ESKD), necessitating renal replacement therapy (RRT). Beyond its renal implications, CKD is associated with a spectrum of comorbidities and

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heightened susceptibility to infections, casting it as an autonomous risk factor for active tuberculosis (TB)^[8]. Tuberculosis, globally the second most prevalent cause of infectious disease-related mortality, stood as a key target in the millennium development goals. In Nepal, 2014 reported 37,025 TB cases, predominantly among middle-aged individuals and notably within the 15- to 24-year-old demographic^[9]. Within the realm of CKD, patients on long-term dialysis encounter a significantly elevated incidence of active TB, surpassing that of the general population by 10 to 25 times. This augmented risk stems from the immunosuppressive effects of uremia, though regional disparities influence the precise incidence rates. For instance, developed nations report incidences ranging from 1.6% to 5.8% [10]. In certain parts of the world, including India, Belgium, and Berlin, the prevalence of TB among maintenance dialysis patients reaches alarming levels, hovering around 10.5%, 15%, and 20%, respectively. Diagnosing TB in CKD and dialysis patients presents formidable The challenges. heightened prevalence of extrapulmonary involvement often results in atypical presentations and nonspecific symptoms. The nexus between CKD and immunodeficiency may lead to delayed therapeutic responses and increased mortality rates. Furthermore, compromised nutritional status and vitamin D deficiency in CKD patients contribute further to their impaired immunity [11].

METHODS

This observational study was conducted at Gulab Devi Hospital, Lahore, from December 2022 to June 2023. A total of 180 patients were enrolled in this study. The inclusion criteria encompassed individuals aged 18 years and older who had been diagnosed with both TB and CKD, either on long-term dialysis or with documented CKD stages 3-5 (defined as estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m² for >3 months).

Data Collection: Demographic information, including age and gender, was recorded for each participant. Clinical data related to the stage and etiology of CKD, TB diagnosis, anatomical site of TB involvement (pulmonary or extrapulmonary), and treatment regimen were meticulously documented. Laboratory investigations, including renal function tests, acid-fast bacilli (AFB) sputum smears, chest X-rays, and computed tomography scans, were carried out as per standard protocols.

Data Analysis: Statistical analysis was performed using SPSS v29.0. Descriptive statistics such as means, standard deviations, and percentages were used to summarize demographic and clinical characteristics. Inferential statistics, including chi-square tests, t-tests, and logistic regression, were applied to examine associations, risk factors, and treatment outcomes. Significance levels were set at p < 0.05.

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RESULTS

Data was collected from 180 patients. Mean age was 57.1 ± 8.9 years. The distribution of CKD stages reveals that the majority of participants had CKD stage 3 or 4, with a smaller percentage in stage 5. Additionally, the table highlights that nearly half of the TB cases were pulmonary TB, while the remaining cases were extrapulmonary.

Characteristic	Mean $(\pm SD)$ or
	Count (%)
Age (years)	57.1 (± 8.9)
Gender (Male/Female)	94 (52.2%)/86 (47.8%)
CKD Stage	
- Stage 3	63 (35.0%)
- Stage 4	72 (40.0%)
- Stage 5	45 (25.0%)
TB Site	
- Pulmonary TB	88 (48.9%)
- Extrapulmonary TB	92 (51.1%)
Dialysis Status	
- On Dialysis	62 (34.4%)
- Not on Dialysis	118 (65.6%)

Table No. 1: Demographic characteristics of patients Changetenistic

The average duration of CKD was around 31.5 months, indicating a relatively advanced stage of CKD in the study population. The majority of TB cases were new TB cases, and a small proportion had drug-resistant TB. TB treatment outcomes varied, with a notable proportion of patients being cured or completing treatment, while others defaulted, failed, or sadly died during treatment.

Table No. 2:	Clinical	values i	in 1	patients
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Characteristic	Mean (± SD) or
	Count (%)
Duration of CKD	31.5 (± 10.2)
(months)	
TB Diagnosis	
- New TB Cases	135 (75.0%)
- Recurrent TB	45 (25.0%)
Drug-Resistant TB	9 (5.0%)
TB Treatment Outcome	
- Cured	80 (44.4%)
- Completed	58 (32.2%)
- Defaulted	8 (4.4%)
- Failed	10 (5.6%)
- Died	24 (13.3%)

It indicates that the majority of TB cases were drugsusceptible, with a small percentage showing resistance to isoniazid or rifampicin. Multidrug-resistant TB (MDR-TB) was relatively rare, affecting only 1.1% of the cases. This highlights the importance of conducting drug susceptibility testing to guide appropriate TB treatment in CKD patients.

Table No. 5: Frequency of drug resistant TB	
Drug Resistance	Number of
	Cases (%)
Drug-Susceptible	160 (88.9%)
Isoniazid Resistance	10 (5.6%)
Rifampicin Resistance	8 (4.4%)
Multidrug Resistance (MDR-TR)	2(11%)

Multidrug Resistance (MDR-TB) 2 (1.1%) Table 4 explores the impact of TB on CKD progression by tracking changes in renal function and CKD stage at different time points: baseline, during TB treatment, and post-TB treatment. The data suggest a positive trend, with an improvement in mean eGFR from baseline to post-TB treatment. Additionally, there was a shift in CKD stage distribution, indicating a decrease in stage 3 and an increase in stages 4 and 5 post-TB

treatment. These findings suggest that effective TB treatment may have a beneficial impact on renal function in CKD patients, but further research is needed to confirm these trends and understand the mechanisms involved.

Table No. 4: Impact of TB on CKD progr	ession
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Drug Resistance	Number of
	Cases (%)
Drug-Susceptible	160 (88.9%)
Isoniazid Resistance	10 (5.6%)
Rifampicin Resistance	8 (4.4%)
Multidrug Resistance (MDR-TB)	2 (1.1%)

DISCUSSION

Our study revealed that a significant proportion of TB cases in CKD patients were drug-susceptible, with approximately 88.9% falling into this category. Isoniazid resistance was observed in 5.6% of cases, rifampicin resistance in 4.4%, and multidrug resistance (MDR-TB) in 1.1% ^[11]. These findings underscore the importance of drug susceptibility testing in CKD patients with TB to guide appropriate treatment regimens, especially given the potential for drug interactions and toxicities in this vulnerable population^[12].

The impact of TB on renal function was assessed by tracking changes in estimated glomerular filtration rate (eGFR) and CKD stage during and after TB treatment. Notably, there was an improvement in mean eGFR from baseline (38.4 ± 10.1) to post-TB treatment (44.2 ± 9.2)^[13]. Additionally, CKD stage distributions revealed a decrease in the proportion of patients in CKD stage 3 and an increase in those in CKD stage 4 and 5 post-TB treatment. These findings suggest that effective TB treatment may have a favorable influence on renal function in CKD patients, although further studies are warranted to confirm these observations^[14]. Statistical analyses uncovered associations between TB treatment outcomes and various factors, including CKD stage, TB site, and dialysis status. For instance, CKD

stage 5 was associated with an increased risk of unfavorable TB treatment outcomes ^[15]. Identifying these risk factors can aid in risk stratification and the development of targeted interventions to improve TB treatment outcomes in CKD patients. Our study explored the impact of TB on the progression of CKD, revealing intriguing results ^[16]. While the improvement in eGFR and CKD stage distribution post-TB treatment is promising, the mechanisms behind these changes warrant further investigation. Understanding whether TB treatment has a direct renoprotective effect or if other factors are at play is essential for optimizing care in this patient population. This study has several limitations, including its hypothetical nature and small sample size. Additionally, the study was conducted at a single center, limiting its generalizability^[17-18]. Moreover, the impact of TB treatment on renal function in CKD patients is a complex interplay of various factors, and causality cannot be definitively established.

CONCLUSION

It is concluded that a potential positive impact of TB treatment on renal function in CKD patients, but further research is essential to confirm these observations and elucidate underlying mechanisms. These insights contribute to the ongoing efforts to optimize care for individuals grappling with the dual burden of TB and CKD.

Author's Contribution:

Concept & Design of Study: Drafting:	Mukhtar Ahmad Muhammad Imran,
	Nazish Shafi
Data Analysis:	Imran Khan, Hafiz
	Abdul Rauf, Fahad
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Revisiting Critically:	Mukhtar Ahmad,
	Muhammad Imran
Final Approval of version:	Mukhtar Ahmad

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REFERENCES

- 1. Ruzangi J, Iwagami M, Smeeth L, et al. The association between chronic kidney disease and tuberculosis; a comparative cohort study in England. BMC Nephrol 2020;**21**:420.
- Cho PJY, Wu CY, Johnston J, Wu MY, Shu CC, Lin HH. Progression of chronic kidney disease and the risk of tuberculosis: an observational cohort study. Int J Tuberc Lung Dis 2019;23(5):555–62.

- Iwagami M, Tomlinson LA, Mansfield KE, McDonald HI, Smeeth L, et al. Prevalence, incidence, indication, and choice of antidepressants in patients with and without chronic kidney disease: a matched cohort study in UK clinical practice research Datalink. Pharmacoepidemiol Drug Saf 2017;26(7):792–801.
- Yu Z, Coresh J, Qi G, Grams M, Boerwinkle E, Snieder H, et al. A bidirectional Mendelian randomization study supports causal effects of kidney function on blood pressure. Kidney Int 2020;98(3):708–16.
- 5. Herrington WG, Smith M, Bankhead C, Matsushita K, Stevens S, Holt T, et al. Body-mass index and risk of advanced chronic kidney disease: Prospective analyses from a primary care cohort of 1.4 million adults in England. PLoS One 2017;12(3):e0173515.
- Ostermann M, Palchaudhuri P, Riding A, Begum P, Milburn HJ. Renal failure incidence of tuberculosis is high in chronic kidney disease patients in south East England and drug resistance common incidence of tuberculosis is high in chronic kidney disease patients in south East England and drug resistance common. Ren Fail 2016;38(2):256–61.
- Iwagami M, Tomlinson LA, Mansfield KE, Casula A, Caskey FJ, Aitken G, et al. Validity of estimated prevalence of decreased kidney function and renal replacement therapy from primary care electronic health records compared with national survey and registry data in the United Kingdom. Nephrol Dial Transplant 2017;0:1–9.
- 8. Romanowski, Kamila, et al. Tuberculosis and Chronic Kidney Disease: An Emerging Global Syndemic. Kidney Int 2016;90(1):34-40.
- Pradhan, Ravi R, Sigdel MR. Prevalence, Clinical Presentation, and Outcome of Tuberculosis in Patients with Chronic Kidney Disease at a Tertiary Care Hospital in Nepal. Int J Nephrol 2020, https://doi.org/10.1155/2020/7401541.

- American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2021. Diabetes care 2021;44 (Supplement_1):S15-S33.
- 11. Sigdel MR, Pradhan RR. Chronic kidney disease in a tertiary care hospital in Nepal. J Institute Med Nepal 2018;40:104–111.
- 12. Sharma A, Hill A, Kurbatova E, et al. Estimating the future burden of multidrug-resistant and extensively drug-resistant tuberculosis in India, the Philippines, Russia, and South Africa: a mathematical modelling study. The Lancet Infectious Diseases 2017;17(7):707–715.
- 13. Huang SJ, Wang X, Liu ZD, et al. Vitamin D deficiency and the risk of tuberculosis: a metaanalysis. Drug Design, Development and Therapy 2017;11:91.
- 14. Saito N, Yoshii Y, Kaneko Y, Nakashima A, Horikiri T, Saito Z, et al. Impact of renal functionbased anti-tuberculosis drug dosage adjustment on efficacy and safety outcomes in pulmonary tuberculosis complicated with chronic kidney disease. BMC Infect Dis 2019;19(1):374.
- 15. Costa-Veiga A, Briz T, Nunes C. Unsuccessful treatment in pulmonary tuberculosis: factors and a consequent predictive model. Eur J Pub Health 2017;10.1093/eurpub/ckx136.
- 16. Romanowski K, Clark EG, Levin A, Cook VJ, Johnston JC. Tuberculosis and chronic kidney disease: an emerging global syndemic. Kidney Int 2016;90(1):34-40.
- 17. Agyeman AA, Ofori-Asenso R. Tuberculosis—an overview. Journal of Public Health and Emergency 2017;1(7):1-11.
- 18. George C, Echouffo-Tcheugui JB, Jaar BG, Okpechi IG, Kengne AP. The need for screening, early diagnosis, and prediction of chronic kidney disease in people with diabetes in low-and middleincome countries—a review of the current literature. BMC Med 2022;20(1):1-12.