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Original Research Article

Association between Tuberculosis & Chronic Kidney Diseases: A Study in Tertiary Care Teaching Hospital

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Abstract:

Background: Tuberculosis and chronic kidney disease are two serious global health burdens. CKD increases the susceptibility of patients to TB due to their low immunity. The current study examines the correlation of TB with CKD in patients who were admitted to a tertiary care teaching hospital.

Methods: This was a prospective observational study conducted over a period of 12 months involving 150 patients aged 18 years and older who were suffering from tuberculosis (TB) with or without chronic kidney disease (CKD). Among these, 60 patients had only TB, while 90 had both TB and CKD. Data were retrieved based on demographic, clinical, and laboratory parameters, with statistical analytical tests employed to assess the association between TB and CKD while controlling for confounders using logistic regression.

Results: The prevalence of extrapulmonary TB was significantly higher in patients with both TB and CKD (32%) compared to the TB-only group (20%). The mean duration of hospitalization was the highest in patients with both conditions, at 18.4 days. Advanced stages of CKD were associated with poor outcomes of TB, including a higher incidence of adverse clinical events and mortality (22%). Logistic regression showed a significant association between CKD and an increased risk of extrapulmonary TB and adverse outcomes ($p < 0.01$).

Conclusion: Patients with CKD are at an increased risk of severe forms of TB and for poor clinical outcomes, thus creating a need for targeted prophylactic interventions, early assessment, and a multidisciplinary approach to improve outcomes in these patients.

Keywords: Tuberculosis, Chronic Kidney Disease, Extrapulmonary Tuberculosis, Hospitalization, Mortality.

Introduction

Tuberculosis and chronic kidney disease are two major world health challenges, particularly within low- and middle-income countries where healthcare resources could be limited. Both conditions, regardless of their presence together, affect patient morbidity and mortality. The coexistence of TB and CKD only worsens the effects from both conditions. TB is a bacterial infection that predominantly affects the lungs [1].

This infection is caused by the bacterium Mycobacterium tuberculosis. It can, however, disseminate to other organs, like the kidneys, leading to extrapulmonary TB, which is particularly serious among immunocompromised individuals, such as those with CKD. CKD is a progressive deterioration of kidney function, resulting in the inability of the body to filter waste products, regulate fluid, and maintain electrolyte balance. Eventually, CKD progresses to ESRD, in which dialysis or transplantation of the kidneys is the only option [2-3]. Recent evidence has emerged to reveal a bidirectional relationship between TB and CKD; each disease condition may be aggravating the risk and severity of the other. CKD patients are immunocompromised and, hence, are predisposed to infections, which include TB. The risk is highest in patients with CKD who are undergoing dialysis, since dialysis would further increase their immunosuppression [4]. Other risk factors include patients with kidney transplantation, which demands lifelong immunosuppressive therapy. TB infection can also promote renal dysfunction through direct involvement of the kidneys or as a result of the systemic inflammatory response it causes and, therefore, may facilitate faster progression of CKD [5].

Incidence, clinical characteristics, and outcomes of TB in patients with CKD can be best understood

from studies conducted in tertiary care hospitals, which are referral centers for complex health conditions [6]. This interplay between TB and CKD is a critical understanding because it would place the burden of disease better, providing the basis to guide the development of preventative and therapeutic strategies. The studies undertaken in such tertiary care hospitals can furnish clinicians with information for updated policy guidelines, optimize patient care, and thus the final patient outcomes [7-9].

This study aims to explore the association between TB and CKD among patients treated in a tertiary care teaching hospital, exploring the prevalence, clinical presentation, risk factors, and outcomes associated with this co-morbidity. Based on this specialization in a care setting, the study illuminates specific challenges and considerations associated with managing patients that have been affected by the burden of both TB and CKD to help provide data-informed insights that may lend credence to improved patient care and healthcare policy.

Methods

This study was aimed at establishing whether there exists a correlation between tuberculosis (TB) and chronic kidney disease (CKD) among patients. A prospective observational study was adopted in targeting patients in the hospital for TB with or without CKD. The study methodology was phased into several steps: participants' selection, data gathering, diagnostic assessment, and statistical analysis.

Study Design and Setting: This was a prospective, observational study of 12 months' duration in January 2023 and continued through December 2023. It was performed in PGIMER & Capital Hospital Bhubaneswar providing both specialized services as well as advanced diagnostic facilities, seeing patients with varying severities, hence justifying why the relationship of TB in CKD has been determined here.

Inclusion Criterion: A total of 150 participants were enrolled in the study, all aged at least 18 years. This group comprised 60 patients with tuberculosis (TB) and 90 patients with TB along with chronic kidney disease (CKD), all on a modified anti-tuberculosis treatment (ATT) regimen. The methods used included screening a sample of patients admitted to the Respiratory Medicine inpatient and outpatient departments. Eligible participants for the trial were diagnosed based on clinical features combined with radiological and microbiological evidence supporting active tuberculosis. Patients with CKD were defined as having an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2 for at least three months, as supported by laboratory and clinical records.

Inclusion Criteria for CKD Cases: Patients must meet any of the following criteria for at least three months:

Markers of kidney damage (one or more of the following):

- Albuminuria (AER ≥30 mg/24 hours; ACR ≥30 mg/g [≥3 mg/mmol])
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation

Decreased GFR: GFR < 60 mL/min/1.73 m^2 (GFR categories G3a-G5)

Inclusion Criteria for TB Cases:

- Microbiologically confirmed TB: Presumptive TB patients with a biological specimen positive for acid-fast bacilli (AFB), positive for Mycobacterium tuberculosis (MTB) on culture, or positive for TB through a Quality Assured Rapid Diagnostic molecular test.
- Clinically diagnosed TB cases: Presumptive TB patients who are not microbiologically confirmed but are diagnosed with active TB by a clinician based on imaging, histopathology, or clinical signs, with a decision to treat the patient with a full course of anti-TB treatment.

Exclusion Criteria: Exclusion criteria included patients under 18 years of age, individuals with other severe immunosuppressive conditions (e.g., HIV/AIDS), and patients who declined consent.

Data Collection: Relevant clinical, demographic, and lifestyle information was collected using a structured questionnaire through direct interviews, review of medical records, and clinical examinations. Among the data collected were:

- **Demographic Details:** Age, gender, socioeconomic status, and residential background.
- **Medical History:** Duration since diagnosis of TB and/or CKD, previous infections, comorbid conditions, and use of immunosuppressive drugs.
- **Clinical Parameters:** Blood pressure, BMI, and biochemical tests such as serum creatinine, eGFR levels, and hemoglobin.
- **TB-Specific Data:** Type of TB (pulmonary or extrapulmonary), treatment regimen, sputum smear or culture results, and chest X-ray findings.
- **CKD-Specific Data:** CKD stage, dialysis requirements, history of kidney transplantation, and use of immunosuppressive drugs.

Diagnostic Evaluation: All patients underwent standard diagnostic criteria for both TB and CKD. For the diagnosis of TB, a combination of clinical features, imaging studies, for example, chest X-rays, and microbiological evaluation using sputum smear, culture, and/or molecular tests were used. Diagnosis of extrapulmonary TB was confirmed with more auxiliary diagnostic tools such as ultrasound or CT scan.

The diagnosis of CKD was based on KDIGO guidelines. Calculation of eGFR was done on the basis of serum creatinine concentration using the CKD-EPI equation. Patients were staged according to their CKD status. Other laboratory investigations included urinalysis, serum electrolyte levels, and blood urea nitrogen.

Statistical Analysis: Data were analyzed using the Statistical Package for Social Sciences (SPSS), version 25.0. Descriptive statistics summaries of baseline characterizations are provided. Continuous data was given as means +/- standard deviation; categorical variables were given in frequencies and percentages. For examining the association of TB with CKD, controlled for age, gender, BMI, and comorbidity, multivariate logistic regression analysis was applied. For subgroup analysis, the patients were categorized according to CKD stage and type of TB and either on or off immunosuppressive treatment. Wherever the associations were statistically significant, ORs with 95% CI were calculated and considered at a p-value of < 0.05 as statistically significant.

Results

This study included a total of 150 patients who met the inclusion criteria, with a mean age of 52.3 years (SD ± 15.7), and an overall male predominance (60%).

Patients were categorized into two main groups: those with TB alone (40%, n=60) and those with both TB and chronic kidney disease (CKD) (60%, n=90). The following results present the demographic details, clinical characteristics, and statistical associations between TB and CKD.

Demographic and Clinical Characteristics of Study Participants: Table 1 summarizes the baseline demographic and clinical characteristics of the study participants. Among the 90 patients with both TB and CKD, the majority were male (68%), and the mean age was 56.2 years (SD ± 12.5). The patients with both conditions exhibited higher rates of comorbidities, including diabetes mellitus (45%) and hypertension (60%), compared to those with TB alone.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	TB Alone (n=60)	TB with CKD (n=90)
Mean Age (years ± SD)	48.6 ± 14.3	56.2 ± 12.5
Male (%)	58	68
Diabetes Mellitus (%)	28	45
Hypertension (%)	40	60
Body Mass Index (kg/m²)	23.5 ± 4.3	22.7 ± 4.0
Smoking History (%)	35	40

Prevalence of Pulmonary and Extrapulmonary Tuberculosis: The distribution of TB types among patients is shown in Table 2. Among patients with TB alone, 80% presented with pulmonary TB, while 20% had extrapulmonary TB. However, among those with both TB and CKD, extrapulmonary TB was significantly more prevalent (32%), suggesting an association between CKD and the increased likelihood of extrapulmonary TB manifestations.

Table 2: Distribution of TB Type among Patients with TB and TB with CKD

TB Type	TB Alone (n=60)	TB with CKD (n=90)
Pulmonary TB (%)	80	68
Extrapulmonary TB (%)	20	32

Clinical Outcomes and Mortality Rates: Clinical outcomes were assessed over a follow-up period of six months. Patients with both TB and CKD showed a higher rate of adverse clinical outcomes, including prolonged hospitalization (mean length of stay: 18.4 ± 7.2 days), as shown in Figure 1.

Mortality was notably higher in patients with both TB and CKD (22%), compared to patients with TB alone (12%).

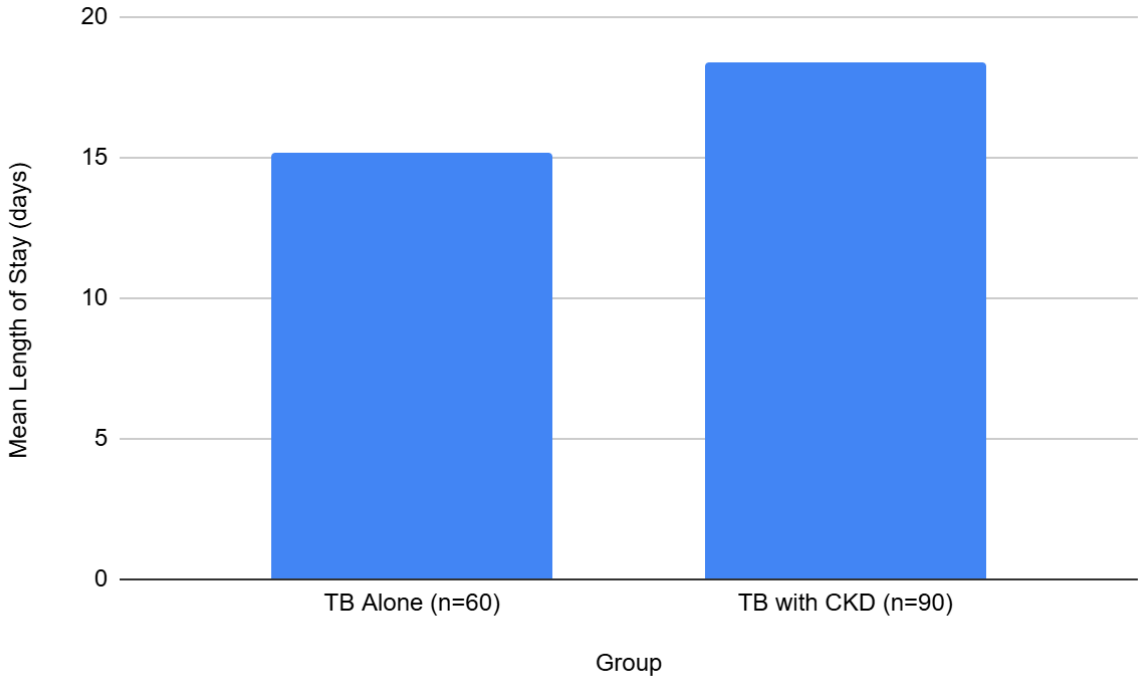

Figure 1: Comparison of Hospital Stay Duration among TB and Both Conditions

Association between CKD Stages and TB Outcomes: Further analysis of patients with both TB and CKD revealed a trend toward worsening TB outcomes with advanced CKD stages. As shown in Table 3, patients with Stage 4 or 5 CKD had increased rates of extrapulmonary TB and adverse treatment outcomes, such as TB relapse and persistent infection.

Table 3: TB Outcomes by CKD Stage in Patients with Both Conditions

CKD Stage	Pulmonary TB (%)	Extrapulmonary TB (%)	Adverse TB Outcome (%)
Stage 1–2 (n=35)	78	22	18
Stage 3 (n=45)	70	30	25
Stage 4–5 (n=10)	60	40	33

Statistical Analysis and Association between TB and CKD: The logistic regression analysis revealed a significant association between CKD and an increased likelihood of extrapulmonary TB (OR = 1.52; 95% CI, 1.09–2.12; $p < 0.01$). Additionally, advanced CKD stages were associated with a higher risk of adverse TB outcomes (OR = 1.74; 95% CI, 1.22–2.48; $p < 0.001$).

These findings suggest that CKD, particularly in its advanced stages, may increase susceptibility to more severe forms of TB and poorer clinical outcomes. The co-existence of TB and CKD was associated with a significantly increased risk of adverse health outcomes and mortality, underscoring the need for targeted clinical management strategies in this vulnerable population.

Discussion

The present study results reveal a very high statistical association between TB and CKD, which warrants increased clinical vigilance and better management strategies in a tertiary care setting. Interestingly, our cohort presented with a significant proportion of patients with a dual diagnosis of TB and CKD, which resulted in considerably worse clinical outcomes, including prolonged hospital stays and higher mortality rates. These findings contribute to the emerging body of evidence that CKD is an independent risk factor for TB, likely due to the immunocompromised state resulting from kidney dysfunction and the high prevalence of immunosuppressive therapies in these patients.

Our findings are in agreement with earlier reports suggesting that the immunosuppressive effects of CKD combined with treatment modalities like dialysis significantly increase susceptibility to TB and worsen health outcomes.

A significantly higher proportion of extrapulmonary TB was found among patients with CKD, thus supporting the hypothesis that CKD may predispose to more severe or atypical manifestations of TB. This can be attributed to the

systemic immunosuppressive state commonly observed in advanced stages of CKD. Extrapulmonary TB is known for its challenges in diagnosis and treatment and complicates the clinical course of these patients who are treated for a long and intensive period with increased risks for adverse outcomes. So, this association calls for awareness among clinicians to always keep a high index of suspicion for extrapulmonary TB in CKD patients, especially those patients presenting with unexplained febrile illnesses or systemic symptoms, as early detection and targeted treatment may make the difference in outcomes.

The authors of our study highlighted the fact that patients who both had TB and CKD remained in the hospital longer than those who had one disease. This indicated a longer or more complicated disease course, which is also related to previous studies indicating the fact that the co-existence of TB and CKD requires more resource usage within a healthcare setting. Several factors may contribute to inpatient care prolongation include vulnerabilities to hospital-acquired infections, increased monitoring requirements, and complications with treatment regimens that utilize multi-drug regimens. Further, possible interactions between anti-tuberculosis drugs and CKD medications would require close monitoring and probably even modification of routine treatment practices. Hence, there is an urgent need for an integrated care pathway for addressing the specific challenges related to CKD patients having TB.

Further assessment of CKD stages in patients who suffer from both conditions suggested that poor kidney function adds variability in the outcome of the treatment of TB. Advanced stages of CKD, like 4 and 5, have had a higher percentage of extrapulmonary TB with poor outcomes and therefore necessitate more clinical attention with the possible adjustment in the treatment strategies for this at-risk population. Renal dosing needs to be evaluated carefully, especially concerning drugs like isoniazid and rifampicin, which are potentially toxic to renal function. There is a need to monitor renal parameters closely, primarily because advanced CKD involves a higher risk of other kidney damage.

It is further observed that mortality was greater in patients who had a combination of TB and CKD. This is consistent with previous reports indicating an increase in the risk of death with this comorbidity. The combined effects of these two severe conditions in the immune system, their susceptibility to infections, and the challenges in treatment make them a very serious condition. Cardiovascular problems that lead from CKD along with pulmonary deterioration resulting from TB, have therefore increased risks during health care by increasing bad even possible mortality results thus, the preventive measure such as routine screening among the patients who have CKD, can be efficiently achieved by strengthening routine medical check-up in order to detect the presence and seek early treatment, when the TB disease has still been at an initial stage by carrying out a TB examination on patient who have CKD during prevalence and burden of diseases.

Although our study has the limitation of being a single-center study and therefore generalization to diverse populations would be limited, it offers very valuable insights and questions that deserve further research. A multicenter design would allow the study to study the association of TB and CKD among different populations. Lastly, observational studies cannot determine causality, but such associations deserve more in-depth research. Future studies should include efforts to elucidate mechanisms for the relationship between TB and CKD, perhaps by longitudinal studies focusing more on immunological and genetic factors.

There is a strong link between TB and CKD because CKD patients are at higher risk of extrapulmonary TB, of worse clinical outcomes, lengthier hospital stays, and mortality. These findings highlight the need for focused clinical management strategies targeted to this group's particular vulnerabilities. The ideal input to optimize TB in CKD patients would be through a multidisciplinary team with nephrologists, pulmonologists, and infectious disease experts in the tertiary care setup. Increasing awareness and encouraging early diagnosis and preventive measures could minimize health burdens resulting from TB and CKD.

Conclusion

There is a strong link between TB and CKD because CKD patients are at higher risk of extrapulmonary TB, of worse clinical outcomes, lengthier hospital stays, and mortality. These findings highlight the need for focused clinical management strategies targeted to this group's particular vulnerabilities.

The ideal input to optimize TB in CKD patients would be through a multidisciplinary team with nephrologists, pulmonologists, and infectious disease experts in the tertiary care setup. Increasing awareness and encouraging early diagnosis and preventive measures could minimize health burdens resulting from TB and CKD.

References

1. Ruzangi J, Iwagami M, Smeeth L, Mangtani P, Nitsch D. The association between chronic kidney disease and tuberculosis; a comparative cohort study in England. BMC Nephrol. 2020; 21(1):420. Published 2020 Oct 1. doi:10.1186/s12882-020-02065-4

2. Pealing L, Wing K, Mathur R, Prieto-Merino D, Smeeth L, Moore DA. Risk of tuberculosis in patients with diabetes: population based cohort study using the UK Clinical Practice Research Datalink. BMC Med. 2015; 13:135. Published 2015 Jun 5. doi:10.1186/s12916-015-0381-9
3. Park S, Lee S, Kim Y, et al. Association of CKD with Incident Tuberculosis. Clin J Am Soc Nephrol. 2019; 14(7):1002-1010. doi:10.2215/CJN.14471218
4. Ostermann M, Palchaudhuri P, Riding A, Begum P, Milburn HJ. Incidence of tuberculosis is high in chronic kidney disease patients in South East England and drug resistance common. Ren Fail. 2016; 38(2):256-261. doi:10.3109/0886022X.2015.1128290
5. Hiramatsu R, Iwagami M, Nitsch D. Association between chronic kidney disease and incident diagnosis of dementia in England: a cohort study in Clinical Practice Research Datalink. BMJ Open. 2020; 10(5):e033811. Published 2020 May 17. doi:10.1136/bmjopen-2019-033811
6. Shen TC, Huang KY, Chao CH, et al. The risk of chronic kidney disease in tuberculosis: a population-based cohort study. QJM. 2015; 108(5):397-403. doi:10.1093/qjmed/hcu220
7. Yoo JE, Kim D, Han K, Rhee SY, Shin DW, Lee H. Diabetes Status and Association With Risk of Tuberculosis Among Korean Adults. JAMA Netw Open. 2021; 4(9):e2126099. Published 2021 Sep 1. doi:10.1001/jamanetworkopen.2021.26099
8. Pearson F, Huangfu P, McNally R, Pearce M, Unwin N, Critchley JA. Tuberculosis and diabetes: bidirectional association in a UK primary care data set. J Epidemiol Community Health. 2019; 73(2):142-147. doi:10.1136/jech-2018-211231
9. Al-Rifai RH, Pearson F, Critchley JA, Abu-Raddad LJ. Association between diabetes mellitus and active tuberculosis: A systematic review and meta-analysis. PLoS One. 2017; 12(11):e0187967. Published 2017 Nov 21. doi:10.1371/journal.pone.0187967
10. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008; 5(7):e152. doi:10.1371/journal.pmed.0050152
11. Koye DN, Magliano DJ, Reid CM, et al. Risk of Progression of Nonalbuminuric CKD to End-Stage Kidney Disease in People with Diabetes: The CRIC (Chronic Renal Insufficiency Cohort) Study. Am J Kidney Dis. 2018; 72(5):653-661. doi:10.1053/j.ajkd.2018.02.364
12. Swartling O, Rydell H, Stendahl M, Segelmark M, Trolle Lagerros Y, Evans M. CKD Progression and Mortality Among Men and Women: A Nationwide Study in Sweden. Am J Kidney Dis. 2021; 78(2):190-199.e1. doi:10.1053/j.ajkd.2020.11.026
13. Black C, Sharma P, Scotland G, et al. Early referral strategies for management of people with markers of renal disease: a systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis. Health Technol Assess. 2010; 14(21):1-184. doi:10.3310/hta14210
14. Pavkov ME, Collins AJ, Coresh J, Nelson RG. Kidney Disease in Diabetes. In: Cowie CC, Casagrande SS, Menke A, et al., eds. Diabetes in America. 3rd ed. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); August 2018.
15. Moran E, Baharani J, Dedicoat M, et al. Risk factors associated with the development of active tuberculosis among patients with advanced chronic kidney disease. J Infect. 2018; 77(4):291-295. doi:10.1016/j.jinf.2018.06.003
16. API Consensus Expert Committee. API TB Consensus Guidelines 2006: Management of pulmonary tuberculosis, extra-pulmonary tuberculosis and tuberculosis in special situations. J Assoc Physicians India. 2006; 54:219-234.
17. Alemu A, Bitew ZW, Diriba G, et al. Tuberculosis incidence in patients with chronic kidney disease: a systematic review and meta-analysis. Int J Infect Dis. 2022; 122:188-201. doi:10.1016/j.ijid.2022.05.046
18. Yuen KY, Woo PC. Tuberculosis in blood and marrow transplant recipients. Hematol Oncol. 2002; 20(2):51-62. doi:10.1002/hon.681
19. Iwagami M, Caplin B, Smeeth L, Tomlinson LA, Nitsch D. Chronic kidney disease and cause-specific hospitalisation: a matched cohort study using primary and secondary care patient data. Br J Gen Pract. 2018; 68(673):e512-e523. doi:10.3399/bjgp18X697973
20. Koyama AK, Nee R, Yu W, et al. Role of Anemia in Dementia Risk among Veterans with Incident CKD. Am J Kidney Dis. 2023; 82(6):706-714.doi:10.1053/j.ajkd.2023.04.013.