



Detection of Latent Tuberculosis in Patients with Chronic Kidney Disease on Renal Replacement Therapy Using Interferon Gamma Release Assay

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ABSTRACT

BACKGROUND

Latent tuberculosis infection represents an immunological response to *Mycobacterium tuberculosis* without clinical evidence of active disease. Patients with CKD (Chronic Kidney Disease), especially those on RRT (Renal Replacement Therapy), are immunocompromised and at significantly higher risk of progression from latent to active tuberculosis. Early detection of LTBI (Latent Tuberculosis Infection) in this vulnerable population is essential to reduce morbidity and mortality.

MATERIALS AND METHODS

A cross-sectional observational study was conducted at RL Jalappa Hospital from September 2022 to December 2023. Sixty patients with Stage 5 CKD on RRT for at least 90 days, without evidence of active tuberculosis, were included. Patients with prior tuberculosis or previous LTBI treatment were excluded. After informed consent and ethical clearance, blood samples were collected for IGRA (Interferon Gamma Release Assay). Additional investigations included a complete blood count, renal function tests, serum electrolytes, and a chest X-ray. Data were analyzed using SPSS version 22, with categorical variables expressed as frequencies and proportions. Chi-square and t-tests were applied where appropriate.

RESULTS

Among 60 patients, 27 (45%) tested positive for LTBI by IGRA, while 33 (55%) were negative. The mean age of IGRA-positive patients was 49.93 ± 14.7 years, with no significant age or sex association ($p > 0.05$). The mean HbA1c levels exhibited no significant difference between the groups ($p = 0.81$). Alcohol consumption showed a statistically significant association with IGRA positivity ($p = 0.001$), whereas smoking, diabetes, and hypertension did not show significant correlation. Biochemical parameters, including serum creatinine, blood urea, sodium, and potassium, showed no statistically significant differences between IGRA-positive and negative groups.



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CONCLUSION

A high prevalence (45%) of latent tuberculosis was observed among CKD patients on RRT. Routine LTBI screening using IGRA is recommended in this high-risk population. Alcohol consumption emerged as a significant associated factor. Early detection and preventive therapy may reduce progression to active tuberculosis and improve clinical outcomes.

KEYWORDS

Latent Tuberculosis, Interferon Gamma Release Assay, Chronic Kidney Disease, Renal Replacement Therapy, Hemodialysis.

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INTRODUCTION

Latent Tuberculosis Infection is defined by the presence of an immunological response to *Mycobacterium tuberculosis* antigens in the absence of clinical features of active disease. Individuals with LTBI are asymptomatic and non-infectious but remain at risk of reactivation, particularly when immunocompromised. Globally, nearly one-third of the population is estimated to harbour LTBI,^[1] making it a major public health concern. Reactivation risk is significantly higher in individuals with conditions such as CKD (Chronic Kidney Disease), HIV, diabetes, malnutrition, and those receiving immunosuppressive therapy.

Chronic kidney disease is a growing global health problem, affecting approximately 8–16% of the world's population.^[2] With progression to ESKD (End-Stage Kidney Disease), more than 2.6 million patients worldwide require RRT (Renal Replacement Therapy), including dialysis or kidney transplantation.^[3] CKD patients experience immune dysfunction characterized by impaired cellular immunity, reduced T- and B-cell function, and altered monocyte activity, increasing susceptibility to infections, particularly tuberculosis.^[4]

The risk of active tuberculosis in CKD patients has been estimated to be nearly 10 times higher than in the general population.^[5] Dialysis patients, in particular, have consistently demonstrated increased tuberculosis incidence,^[6,7] with studies reporting a 6.9- to 52.5-fold higher risk compared to healthy individuals.^[8] CKD has been independently associated with increased TB diagnosis rates in population-based studies.^[9] Furthermore, systematic screening and treatment of LTBI in patients initiating dialysis have shown a reduction in active TB incidence.^[10] Vitamin D insufficiency, common in CKD stages 3–5, may further impair immune defence against tuberculosis.^[11]

IGRAs (Interferon-Gamma Release Assays) are reliable diagnostic tools for detecting LTBI and are preferred in immunocompromised populations.^[5,12] Given the heightened vulnerability of CKD patients on RRT, early detection of LTBI is crucial to reduce morbidity and mortality.

Aims and Objectives

The study aimed to evaluate the presence of latent tuberculosis infection among patients with chronic kidney disease undergoing renal replacement therapy. The primary objective is to detect latent tuberculosis in this high-risk population using the IGRA, thereby facilitating early identification and timely preventive intervention to reduce the risk of progression to active tuberculosis and its associated morbidity and mortality.



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MATERIALS AND METHODS

Study Design

This study was conducted as a cross-sectional observational study in the Department of Internal Medicine at RL Jalappa Hospital; a teaching hospital affiliated with Sri Devaraj Urs Medical College, under Sri Devaraj Urs Higher Education and Research, a tertiary care center located in Tamaka, Kolar. The study was carried out over a period of sixteen months, from September 2022 to December 2023, during which eligible patients were evaluated to assess the prevalence of latent tuberculosis infection among individuals with chronic kidney disease undergoing renal replacement therapy.

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Inclusion and Exclusion Criteria

The study included adult patients with end-stage renal disease who had been initiated on renal replacement therapy for a minimum duration of 90 days, with no clinical features suggestive of active tuberculosis and a chest X-ray showing no evidence of active tuberculosis. Patients were excluded if they had a past history of tuberculosis, had previously received treatment for latent tuberculosis infection, or were below 18 years of age.

Sample Size Calculation

Sample size was estimated by using the proportion of latent TB infection in subjects who underwent 3HP treatment, which was 19.3% from the study by Chien using Wu et al.^[13] using the formula:

Sample Size

$$\frac{Z_{1-\alpha/2}^2 P(1-P)}{d^2}$$

Using the above values at 95% Confidence level a sample size of 54 subjects were included in the study. Considering 10% Non-response, a sample size of $54+6 \approx 60$ minimum subjects were included in the study

Data Collection Procedure

After obtaining ethical clearance from the Institutional Ethics Committee and informed consent from all participants, eligible patients meeting the inclusion and exclusion criteria were enrolled in the study. A total of 66 subjects were recruited, and detailed clinical histories along with thorough physical examinations were conducted to obtain baseline data. All participants underwent necessary laboratory investigations, including collection of 3 ml of venous blood in lithium heparin tubes for analysis. Interferon-gamma (IFN- γ) levels were measured using ELISA (Enzyme-Linked Immunosorbent Assay) as per the manufacturer's protocol (Qiagen), with optical density readings taken at 450 nm to quantify results. Proper storage and handling of samples were ensured in coordination with the Department of Microbiology to maintain specimen integrity and ensure accurate analysis.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 22 software. Categorical variables such as gender, comorbidities, IGRA results, alcohol consumption, and smoking status were expressed as frequencies and percentages. Continuous variables, including age, hemoglobin, serum creatinine, blood urea, serum sodium, serum potassium, and HbA1c, were represented as mean \pm standard deviation. The rate of detection was used to assess the prevalence of latent tuberculosis in the study population. The chi-square test was applied to determine associations between categorical variables, and Student's t-test was used to compare means between IGRA-positive and IGRA-negative groups. Logistic regression analysis was



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performed to evaluate the influence of lifestyle factors on IGRA positivity. A p-value of <0.05 was considered statistically significant.

RESULTS

IGRA Result	Frequency (n=60)	Percentage (%)
Negative	33	55%
Positive	27	45%

Table 1: Distribution of IGRA Results

Table 1 illustrates the prevalence of latent tuberculosis among CKD Stage 5 patients on renal replacement therapy. A total of 45% tested positive for IGRA, indicating a high burden of latent tuberculosis in this population.

Age Comparison			
Parameter	Negative IGRA	Positive IGRA	P-value
Mean Age (Years)	48.97 ± 15.20	49.93 ± 14.70	0.81
Sex Distribution			
Sex	Negative IGRA	Positive IGRA	P-value
Male	22	21	0.508
Female	11	6	0.508

Table 2: Demographic Characteristics (Age & Sex Distribution)

Table 2 observes no statistically significant association between age or sex and IGRA positivity, indicating that demographic factors did not influence latent TB detection in this cohort.

Comorbidity	Negative IGRA	Positive IGRA	P-value
Diabetes	22	17	0.50
Non-Diabetic	11	10	
Hypertension	33	27	0.70

Table 3: Comorbidities

Table 3 demonstrates high prevalence of diabetes and universal hypertension among CKD patients. However, no significant association was observed between these comorbidities and IGRA positivity.

Parameter	Mean ± SD
Haemoglobin (g/dL)	7.84 ± 1.47
WBC (×10 ³ /mm ³)	8.40 ± 2.21
Platelets (Lak/mm ³)	2.24 ± 0.42

Table 4: Haematological Parameters

Table 4 illustrates widespread anaemia among CKD Stage 5 patients. Haematological parameters did not show a significant correlation with IGRA results.



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Parameter	Negative IGRA (Mean ± SD)	Positive IGRA (Mean ± SD)
Serum Creatinine	3.28 ± 0.91	3.42 ± 0.95
Blood Urea	75.18 ± 19.52	79.30 ± 23.00
Serum Sodium	132.12 ± 5.87	133.07 ± 6.89
Serum Potassium	4.36 ± 0.79	4.54 ± 0.94

Table 5: Biochemical Parameters

Table 5 shows elevated renal parameters consistent with CKD Stage 5. No statistically significant differences were observed between IGRA-positive and negative groups.

HbA1c Category	Negative IGRA	Positive IGRA	P-value
Normal (<5.6%)	3	5	0.693
Pre-diabetic (5.6–6.4%)	5	3	
Diabetic (6.5–7%)	4	3	
Moderate (7.1–8%)	10	5	
High (>8%)	11	11	

Table 6: HbA1c Distribution

Table 6 observes no significant association between glycemic control and IGRA positivity, despite a high prevalence of diabetes.

Alcohol Consumption			
Alcohol	Negative IGRA	Positive IGRA	P-value
No	25	5	0.001*
Yes	8	22	0.001*
Smoking			
Smoking	Negative IGRA	Positive IGRA	P-value
No	18	10	0.334
Yes	15	17	0.334

Table 7: Lifestyle Factors and IGRA Association

Table 7 highlights a statistically significant association between alcohol consumption and IGRA positivity (p = 0.001). Smoking, however, showed no significant relationship with latent TB detection.

DISCUSSION

The present study assessed the prevalence of LTBI among patients with CKD undergoing renal replacement therapy using the IGRA. The prevalence of LTBI in our cohort was 45%, indicating a substantial burden of latent tuberculosis in this high-risk population. This finding reinforces the established association between CKD and increased susceptibility to tuberculosis.

The relationship between CKD and tuberculosis has been documented for several decades. Pradhan et al.^[6] first described the increased occurrence of TB among dialysis patients, and subsequent large cohort studies by Dobler et al.^[7] confirmed a significantly elevated TB risk in this population. Hussein et al.^[8] further demonstrated that patients with chronic renal failure and those on dialysis have a 6.9- to 52.5-fold higher risk of developing TB compared to the general population. Our observed LTBI prevalence supports these findings and highlights that Stage 5 CKD patients on RRT constitute a particularly vulnerable group.



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Immunological dysfunction plays a pivotal role in this increased susceptibility. CKD is associated with impaired cellular immunity, including reduced T- and B-cell function and compromised monocyte and neutrophil activity.^[11] Such immune dysregulation may facilitate the persistence of *Mycobacterium tuberculosis* in its latent form and increase the likelihood of reactivation. Al-Efraij et al.^[5] emphasized that CKD significantly increases the risk of active TB and underscored the importance of screening strategies in this group. Our study supports this recommendation by demonstrating a high LTBI detection rate using IGRA.

The choice of IGRA as a diagnostic modality is supported by existing literature. Agarwal et al.,^[12] reported higher IGRA positivity compared to TST (Tuberculin Skin Testing) in maintenance hemodialysis patients, suggesting superior sensitivity in immunocompromised individuals. Hayuk et al.^[14] documented LTBI prevalence of approximately 24–25% among CKD and ESKD patients, with higher rates in those undergoing hemodialysis. Yang et al.^[15] also highlighted the clinical value of IGRA in immunocompromised populations, reinforcing its applicability in CKD patients.

In our study, biochemical parameters such as serum creatinine, blood urea, sodium, and potassium levels did not show significant association with IGRA positivity. Although severe renal dysfunction contributes to immune compromise, these biochemical markers may not directly predict LTBI presence. Similar observations have been noted in CKD populations where immune dysfunction is multifactorial rather than solely dependent on biochemical severity.^[11]

Lifestyle factors demonstrated notable findings. Alcohol consumption showed a statistically significant association with IGRA positivity ($p < 0.05$). Chronic alcohol use is known to impair cellular immune responses and macrophage function, potentially facilitating latent TB infection. Comparable associations between lifestyle factors and LTBI risk in dialysis populations have been described.^[16] However, smoking did not show a statistically significant relationship with IGRA results in our cohort, suggesting that its influence may be less pronounced in the presence of CKD-related immunosuppression.

Age and sex were not significantly associated with LTBI in our study. Although male predominance was observed among IGRA-positive patients, the difference was not statistically significant. Diabetes, a well-recognized TB risk factor, also did not demonstrate significant association. While Ruzangi et al.^[9] reported increased TB risk in CKD populations, the interplay between diabetes, CKD, and LTBI may be complex and influenced by overlapping immunological mechanisms. Hypertension, though universally prevalent in our cohort, did not impact LTBI detection.

Overall, the findings of this study align with previous literature^[5-9,12,14,15] and further strengthen the evidence that CKD patients, particularly those on RRT, represent a high-risk group for latent tuberculosis. Routine LTBI screening using IGRA in this population may facilitate early identification and timely preventive therapy, thereby reducing progression to active tuberculosis, morbidity, and mortality.

Limitations

This study has several limitations. The relatively small sample size of 60 patients and its conduct at a single center may limit the generalizability of the findings to the broader CKD population. The cross-sectional design restricts the ability to establish causal relationships between latent tuberculosis and the associated clinical or lifestyle factors. Additionally, reliance on self-reported data for alcohol consumption and smoking may introduce recall bias or underreporting. The study also did not account for potential confounding variables such as duration and severity of CKD, medication use, and other comorbidities, which could influence



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LTBI risk. Larger, multicentric, and longitudinal studies incorporating these variables are needed to provide more comprehensive and generalizable conclusions.

CONCLUSION

This study demonstrates a significant prevalence of latent tuberculosis among patients with chronic kidney disease, particularly those in Stage 5 undergoing renal replacement therapy, highlighting their increased vulnerability due to immunocompromise. The use of IGRA proved effective in identifying latent infection, underscoring the importance of routine LTBI screening in this high-risk population. The coexistence of comorbidities such as diabetes and hypertension, along with prevalent anaemia and severe renal impairment, further complicates disease management. Lifestyle factors, particularly alcohol consumption, may additionally influence susceptibility, emphasizing the need for integrated clinical and behavioural interventions. Although limited by a small sample size and cross-sectional design, this study reinforces the necessity for larger, longitudinal, and multicentric research. Comprehensive and personalized management strategies that address medical, lifestyle, and psychosocial factors are essential to reduce tuberculosis risk and improve overall outcomes in CKD patients.

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