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Research Article

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Patients with Chronic Kidney Disease: Clinical Presentation, Outcome, and Tuberculosis Occurrence

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ABSTRACT

Background: Tuberculosis (TB) is a significant global public health concern, surpassing HIV/AIDS in mortality. Despite advancements, the prevalence and death rates of pulmonary TB have declined, while extra-pulmonary TB has unexpectedly risen. This observational study in Burla, India.

Methods: The duration of this study was from April 2021 to September 2022 and included CKD patients from a tertiary care hospital. The observational, cross-sectional design evaluated clinical data, sociodemographic factors, and TB diagnoses in a sample of 220 individuals, considering a population size of 3.5 million in western Odisha.

Results: The study revealed a high vulnerability of Chronic Kidney Disease (CKD) patients to TB, with a predominant male incidence in the 30-60 age group. Lower socioeconomic status correlated with higher TB diagnoses. Advanced CKD stages, particularly grade-4 and grade-5, were associated with increased TB susceptibility. Dialysis-requiring CKD patients demonstrated heightened vulnerability. Tubercular pleural effusion was prevalent in extra-pulmonary TB cases. Common symptoms include fever, breathlessness, and cough. Symptomatic patients with TB were prevalent, with fever being the primary symptom.

Conclusion: The study concludes that CKD patients face heightened susceptibility to pulmonary and extra-pulmonary TB. Advanced CKD stages, male gender, and lower socioeconomic status were associated with increased TB risk. Tubercular pleural effusion emerged as a common form of extra-pulmonary TB. Routine screening is crucial for early detection and effective management. Future perspectives should focus on refining screening protocols and fostering collaboration between nephrology and infectious disease specialists to enhance TB management in CKD patients.

Key-words: Tuberculosis, Chronic Kidney Disease, Pulmonary Tuberculosis, Vulnerability

INTRODUCTION

Tuberculosis is a severe global public health concern that significantly raises rates of morbidity and mortality. Before the COVID-19 pandemic, TB claimed more lives than HIV/AIDS [1-4].

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Nearly half of the 10 million new cases and 1.3 million yearly TB deaths in 2018 occurred in developing nations [5-7]. Anti-tuberculosis drugs and socioeconomic progress have led to a decline in the prevalence and death rate of pulmonary tuberculosis worldwide, yet, extra-pulmonary tuberculosis has been unexpectedly increasing [8-10]. Lung involvement is common in TB; extra-pulmonary cases make up about 12.5% of cases. Eleven to sixteen percent of extrapulmonary cases of abdominal TB involve the colon, peritoneum, and lymph nodes. Early detection of tuberculous peritonitis is necessary to lower the risk of death. In cases with intraperitoneal tuberculous abscess, a rare and deadly form of extra-pulmonary tuberculosis,

a correct and timely diagnosis is crucial for effective care [11-13].

Tuberculous peritonitis (TP), an unusual extrapulmonary infection caused by Mycobacterium tuberculosis, can account for up to 3.5% of tuberculosis infections and 31-58% of instances of abdominal TB [14,15]. High blood pressure is more common in patients with underlying medical conditions like diabetes, neoplasms, HIV/AIDS, and cirrhosis. Patients receiving kidney transplants, hemodialysis (HD), peritoneal dialysis, corticosteroids, cytotoxic, immunosuppressive, and immunomodulator drugs, and corticosteroids are also found to be at a higher risk [16]. The infection is usually caused by reactivated latent peritoneal tuberculosis, which can spread hematogenously or lymphatically from a primary pulmonary source. Occasionally, minor intestinal infections or the intake of unpasteurized milk might lead to the entry of mycobacteria from tuberculous diseases into the transmural peritoneal cavity [17]. Ayinalem A. and colleagues conducted a meta-analysis and found that the incidence of TB in patients with CKD varies from 60 per 100,000 in the United Kingdom to 19,270 per 100,000 in China. Patients undergoing hemodialysis (5611 per 100,000) and peritoneal dialysis (3533 per 100,000) had higher incidences of tuberculosis in terms of TP [18]. The incidence of TB was lower in patients undergoing renal transplants (2700 per 100,000) and those with chronic kidney disease before dialysis (913 per 100,000). It is difficult to diagnose this illness since there are no clear clinical symptoms, traditional diagnostic tests have low specificity, and radiography and ultrasound results are nonspecific. Since ascitic fluid is typically paucibacillal, it may be difficult to separate mycobacteria from it. For this reason, peritoneal biopsy is regarded as the gold standard [19]. With a case fatality rate over 50%, the prognosis for BP was dire before the introduction of tuberculostatic therapy [20].

MATERIALS AND METHODS

The study was conducted in Burla, Sambalpur district, western Odisha, India, at the Department of Pulmonary Medicine, Nephrology, and Department of Medicine within V.S.S Institute of Medical Sciences and Research (VIMSAR), Burla. The research was an observational, cross-sectional study from April 2021 to September 2022. The study population comprised patients attending the nephrology outpatient department, utilizing the hemodialysis unit, and those admitted to internal medicine and nephrology wards at VIMSAR, Burla.

Sample Size- The sample size was estimated considering a population of 3,500,000 in western Odisha, with a hypothesized outcome factor (CKD) frequency at 18% ± 5%. The confidence limits were set at 5%, and a design effect 1 for random sampling was applied. The estimated sample size calculated using the formula resulted in a required sample size of 220 individuals. This calculation used OpenEpi, Version 3, an open-source calculator called SSPropor.

Sample Technique- The study technique involves a comprehensive approach to diagnosing and analyzing the study population's chronic kidney disease (CKD). CKD diagnosis is made by treating physicians or nephrologists based on KDIGO 2012 guidelines, with data collection encompassing demographics, mode of renal replacement therapy, HIV status, comorbidities, site of TB, and the method of TB diagnosis (sputum smear, culture, histology, or tissue samples). CKD is measured using the CKD-EPI equation, considering serum creatinine value, age, sex, and race. Active tuberculosis screening is performed in all CKD patients, irrespective of respiratory symptoms, and confirmed cases are further evaluated for clinical features, sputum analysis, and chest imaging. The study employs sputum smear microscopy, CBNAAT, chest X-rays, HRCT thorax, bronchoscopy, and various diagnostic tools for extra-pulmonary TB to ensure a thorough examination of the study subjects.

Inclusion criteria- The study included all diagnosed cases of chronic kidney disease with diagnosis made by treating physicians or nephrologists following the KDIGO 2012 guidelines, regardless of chest symptoms.

Exclusion criteria

- Past History of TB
- HIV
- Diabetes mellitus
- Age <18 yrs

Statistical Analysis- Data analysis involves expressing data as percentages or counts for categorical variables and as mean±standard deviation, median, or range for continuous variables. Categorical variables are

summarized using frequencies and proportions and compared using the chi-square or Fisher's exact test. The significance level is set at a two-sided p-value <0.05. SPSS Version 29.0, IBM Statistical Package for the Social Sciences, is utilized for data analysis. Results are presented in proportions and percentages, ensuring a comprehensive statistical evaluation of the study's findings.

Ethical approval- The study conducted at V.S.S Institute of Medical Sciences and Research (VIMSAR), Burla, in Burla, Sambalpur district, western Odisha, India, obtained ethical approval from the relevant institutional review board or ethics committee. Approval was granted to ensure that the study adhered to ethical principles, safeguarded participant rights, and followed established guidelines for human research.

RESULTS

In analysing the collected clinical data from a cohort of patients, several key observations emerged, shedding light on crucial TB aspects in the CKD context. Here, we present the noteworthy findings derived from the comprehensive evaluation of relevant clinical parameters.

Table 1: Age distribution

Age Range	No. of patients	Per (%)
21-30	24	10.9
31-40	52	23.6
41-50	62	28.2
51-60	56	25.5
61-70	16	7.3
71-80	10	4.5

The age group of patients varied from 21-80 yr. with mean age of 47.02 yr and standard deviation of 12.40.

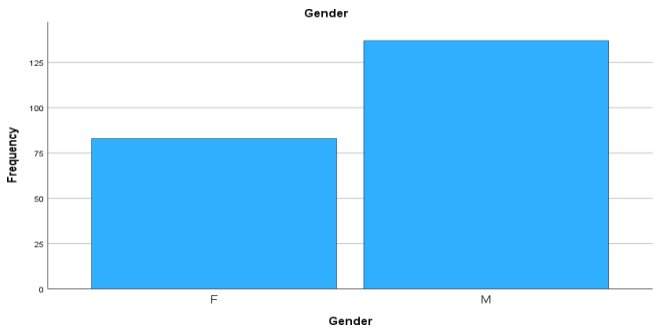

Fig. 1: Gender Distribution

Among the 220 patients included in this study, 37.7% were females (n = 83) and 62.3% weremales (n = 137). Male: female is 1.6.

Table 2: Distribution of BMI

BMI range	No. of cases	PER (%)
<18.5	59	26.8
18.5-22.9	137	62.3
23-24.9	24	10.9

A substantial portion of the patient population exhibited diverse BMI ranges, with 59 individuals (26.8%) falling below 18.5, 137 patients (62.3%) within the 18.5-22.9 range, and 24 individuals (10.9%) within the 23-24.9 range. The calculated mean BMI was 20.05 with a standard deviation of 1.98. Notably, most cases presented with a BMI considered within the normal range, contributing to the comprehensive characterization of the study cohort's anthropometric profile.

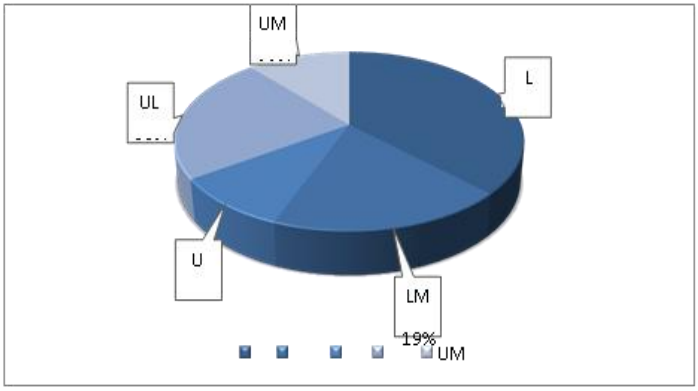

Fig. 2 Distribution of Ses

Most patients were in lower 82(37.3%) and upper lower group 51(23.2%).

Table 3: TB among study population

TB	No. of patients	PER (%)
Present	129	58.6
Absent	91	41.4

Out of 220 patients, a total 129 (58.6%) were diagnosed with TB, and 91(41.4%) patients do not have TB.

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Table 4: Types of TB among study population

Types of TB	No. of patients	PER (%)
PTB	67	31
EPTB	57	26
Disseminated TB	5	2
NEG	91	41
Total	220	100

Out of 129 patients diagnosed with TB, 67 (31%) were PTB, 57 (26%) were EPTB, 5 (2%) were disseminated TB.

Table 5: Distribution of types of TB

Type of TB	No. of patients	PER (%)
CD EPTB	56	25.5
CD PTB	17	7.7
Disseminated TB	5	2.3
MC EPTB	1	0.5
MC PTB	50	22.7
NEG	91	41.4

Among the 129 patients diagnosed with TB, a predominant portion, comprising 67 individuals, exhibited pulmonary TB. Within this subgroup, 50 cases (22.7%) were confirmed through microbiological analysis, while 17 cases (7.7%) were clinically diagnosed. Notably, 17 patients lacked an obvious tissue diagnosis but were identified as TB cases due to a high index of clinical suspicion. In the realm of extra-pulmonary TB (EPTB), encompassing 57 patients, 56 cases (25.5%) were diagnosed based on clinical evaluation, and one patient (0.5%) received microbiological confirmation. Furthermore, a smaller subset of 5 patients (2.3%) exhibited TB at multiple sites, indicative of disseminated TB. These findings highlight the diverse diagnostic modalities employed and underscore the clinical complexity associated with TB manifestations.

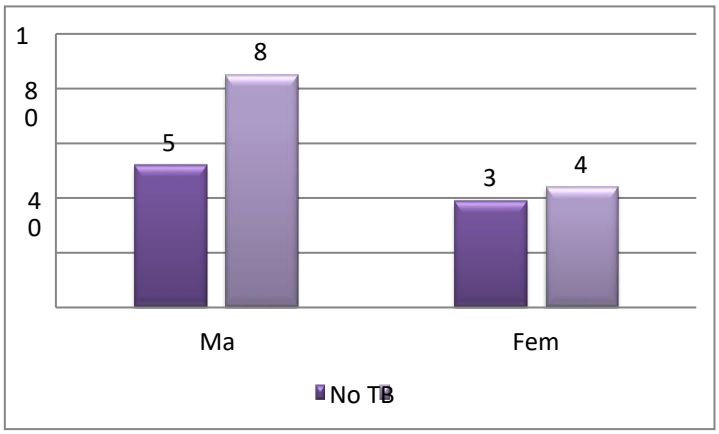

Fig. 3: Gender distribution of tuberculosis

A total 85 patients (65.9%) male and 44 (34.1%) females have been diagnosed with TB. Hence, we can conclude that Tuberculosis has more male preponderance than females.

Table 6: Age distribution of TB

Age Range (years)	TB				Total	
	Absent		Present			
	N	%	N	%	N	%
21-30	10	11.0	14	10.9	24	10.9
31-40	22	24.2	30	23.3	52	23.6
41-50	23	25.3	39	30.2	62	28.2
51-60	22	24.2	34	26.4	56	25.5
61-70	8	8.8	8	6.2	16	7.3
71-80	6	6.6	4	3.1	10	4.5
Total	91	100.0	129	100.0	220	100

As per our study, we have observed that Tuberculosis is commonly seen between the age range of 31 to 60 yrs.

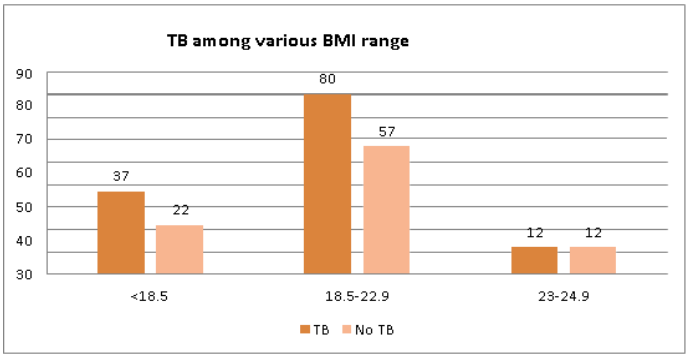

Fig. 4: Comparison of BMI in TB

Patients' BMI Range (in kg/m^2) varied from <18.5 to 24.9 with mean BMI of 20.05 and standard deviation of 1.98. As per our study, we have observed that TB is commonly seen between BMI range of 18.5-22.9 Kg/m^2.

Table 7: Comparison of socio-economic status in TB

Socio-economic status	TB				Total	
	Absent		Present			
	N	%	N	%	N	%
L	40	44.0	42	32.6	82	37.3
LM	16	17.6	25	19.4	41	18.6
U	4	4.4	17	13.2	21	9.5
UL	23	25.3	28	21.7	51	23.2
UM	8	8.8	17	13.2	25	11.4
Total	91	100	129	100	220	100

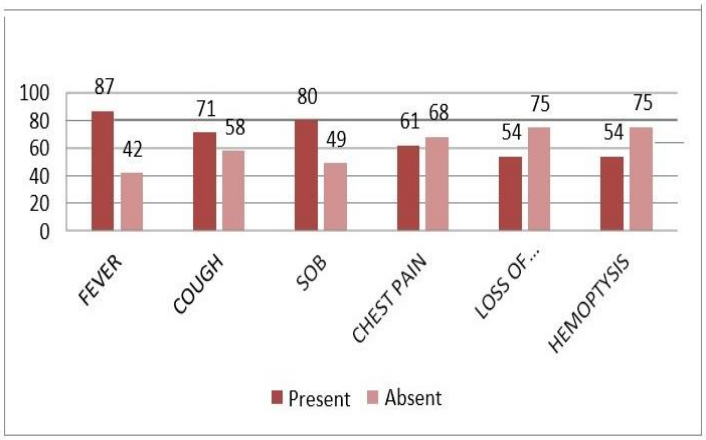

Fig. 5: Comparison of symptoms with diagnosis of TB

In the study encompassing 220 patients, a majority, constituting 90.9%, presented with symptomatic manifestations, while 9.1% were asymptomatic. Notably, among symptomatic individuals, a high percentage (98.4%) was diagnosed with TB, compared to only 1.6% of asymptomatic patients. The spectrum of TB symptoms included cough (55%), fever (67.4%), breathlessness (62%), chest pain (47.3%), haemoptysis (41.9%), and loss of appetite (41.9%). Among these, fever emerged as the most prevalent symptom, reported by 67.4% of patients, followed by breathlessness and cough. These findings underscore the importance of recognizing and evaluating symptoms in the diagnostic process of TB, particularly in the context of CKD.

DISCUSSION

The discussion section of the paper highlights the critical intersection between CKD and TB, emphasizing the global public health significance of CKD as a modern-day epidemic and the persistently high prevalence of TB in developing countries. The increased risk of TB in CKD patients undergoing chronic dialysis is attributed to various factors, including ethnicity, diabetes, HIV, vitamin D deficiency, and medications.[21,22] Notably, CKD-mediated impairment of cell-mediated immunity, particularly T-cell dysfunction, emerges as a significant contributory factor. The study's thorough examination of a sizable cohort of CKD patients at a tertiary care hospital in Burla contributes valuable insights into sociodemographic profiles, clinical features, and investigational findings, substantiated by rigorous statistical analysis and comparison with contemporary literature.

The findings reveal a substantial proportion (58.6%) of CKD patients developing TB, with a higher incidence in the 30-60 age groups and a male predominance. The study underscores the association between lower socioeconomic status (SES) and TB, possibly linked to geographical distribution and lack of awareness.[23] Furthermore, the study delves into the varied clinical presentations of TB, with fever being the most common symptom. Extra-pulmonary TB, particularly tubercular pleural effusion, is highlighted as a notable form, presenting diagnostic challenges due to nonspecific symptoms and atypical manifestations.

The discussion extends to the impact of CKD severity on TB risk, with an observed progressive increase in TB cases corresponding to worsening renal function. Dialysis, especially in grade-4 and grade-5 CKD patients, is identified as a significant risk factor, necessitating careful monitoring post-initiation.[24] Atypical clinical manifestations of TB are acknowledged, emphasizing the need for heightened awareness among healthcare providers. The study identifies varied diagnostic modalities, with microbiologically confirmed cases accounting for 23%, highlighting the challenges in accurate diagnosis.

The paper emphasizes the diagnostic complexities in differentiating TB from uremic effusion and underscores the necessity for a combined clinicopathological approach. [25] The discussion concludes by advocating for

additional research efforts to discover newer diagnostic modalities, given the high prevalence of TB in CKD, its risk factors, and the diagnostic challenges demonstrated in the study. Overall, the paper contributes substantially to understanding TB in CKD patients, shedding light on critical aspects that warrant further investigation and discussion in the broader medical community.

CONCLUSIONS

In conclusion, the study underscores the heightened vulnerability of patients with CKD to both pulmonary and extra-pulmonary TB. The middle-aged demographic, mainly individuals aged 30-60, emerged as the most affected group, with a notable male predominance attributed to health-seeking behavior. Lower and lower-middle socioeconomic status (SES) groups exhibited a higher incidence of TB diagnoses. Significantly, patients diagnosed with TB were predominantly in advanced stages of CKD, particularly in grade 4 and grade 5. Dialysis-requiring CKD patients demonstrated an increased susceptibility to TB. Tubercular pleural effusion was identified as the predominant form in extra-pulmonary TB. Clinical presentations varied, with fever being the most common symptom. The study highlights the importance of considering TB in the differential diagnosis of CKD patients exhibiting nonspecific symptoms like anorexia, fever, weight loss. Given the challenging nature of diagnosing and managing TB in CKD patients, routine screening is imperative for early detection. Looking forward, future perspectives should focus on refining screening protocols, developing targeted interventions, and enhancing collaboration between nephrology and infectious disease specialists to optimize the management of TB in CKD patients, thereby improving overall patient outcomes.

CONTRIBUTION OF AUTHORS

Research concept- Madhumita Nayak, Aurobindo Behera
Research design- Puspita Singh, Gourahari Pradhan
Supervision- Puspita Singh, Aurobindo Behera, Rekha Manjhi
Materials- Puspita Singh, Gourahari Pradhan
Data collection- Aurobindo Behera
Data analysis and Interpretation- Madhumita Nayak, Aurobindo Behera, Rekha Manjhi
Literature search- Puspita Singh, Gourahari Pradhan
Writing article- Puspita Singh, Gourahari Pradhan
Critical review- Madhumita Nayak, Aurobindo Behera, Rekha Manjhi
Article editing- Madhumita Nayak, Aurobindo Behera
Final approval- Madhumita Nayak, Aurobindo Behera, Rekha Manjhi

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