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Active tuberculosis among patients with presumptive tuberculosis with chronic kidney disease in a high tuberculosis burden country, Ethiopia: a multi-center study

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ABSTRACT

Objectives: To assess tuberculosis (TB) and associated factors among patients with presumptive TB with chronic kidney disease (CKD).

Methods: A prospective cross-sectional study was conducted from January to December 2023 among 381 patients with CKD attending six hospitals found in five regions of Ethiopia. Sputum and urine specimens were collected and examined for TB using smear microscopy, culture, and Xpert MTB/RIF Ultra assay. Data were analyzed using SPSS version 27. Descriptive statistics and logistic regression models were executed.

Results: More than half (206, 54.1%) were male, with a mean age of 45.08 years. A total of 94.0% (358) were pre-dialysis patients with CKD, and 90% (343) had additional comorbidity. TB was detected in 12.9% (49), with 10.5% (40) bacteriologically confirmed and 2.4% (9) clinically diagnosed TB. Previous or current cigarette smoking (adjusted odds ratio [aOR]; 2.82), decreased appetite (aOR; 5.97), night sweats (aOR; 2.21), diabetes comorbidity (aOR; 3.01), positive dipstick albuminuria (aOR; 5.55), less than 1-year follow-up in the renal unit (aOR; 9.49), body mass index <18.5 kg/m^2 (aOR; 6.69), and hemodialysis (aOR; 4.41) were all associated with TB.

Conclusions: TB is a substantial cause of morbidity among patients with CKD in Ethiopia, necessitating programmatic intervention. Thus, active TB screening and surveillance among patients with CKD in Ethiopia is important.

Introduction

Tuberculosis (TB) is a global public health problem affecting 10.6 million individuals and taking the lives of 1.3 million individuals each year [1]. It is also a major public health problem in Ethiopia, which is included among the high TB burden countries [1]. Although one-fourth of the global population is estimated to be infected with *Mycobacterium tuberculosis complex* (MTBC), only 5-10% of individuals develop active TB during their lifetime [1]. However, the risk is considerably higher among certain groups of the population with diminished immune systems, including individuals with chronic kidney disease (CKD) [2], which is a progressive loss in renal function over months or years [3].

Patients with CKD have a higher TB risk than the general population [4]. A study conducted in Taiwan reported that the risk of *MTBC* infection relative to the general population was 4.5 times [4]. In a recent global pooled estimate, the incidence of TB in patients with CKD was 3718 per 100,000 patients with CKD, which is far from the general population [5]. Despite the low number of studies assessing the burden of TB in patients with CKD in sub-Saharan Africa, the findings revealed that TB comorbidity in patients with CKD is becoming a challenge. A study done in South Africa reported that 17% of patients with CKD had TB with an incidence rate of 4505 per 100,000 patient-years [6]. Likewise, in Ethiopia, a high TB prevalence (27%) has been reported among patients undergoing maintenance hemodialysis [7].

Currently, the incidence of CKD is increasing alarmingly. According to the global disease burden study, 697.5 million cases of all-stage CKD were recorded in 2017, with a prevalence of 9.1% [3]. Most of the burden is concentrated in the lowest quintiles of the socio-demographic index, which are also vulnerable to TB [3]. In Africa, the pooled prevalence of CKD is 10.1% [8]. The burden of CKD is also increasing in Ethiopia [9,10]; however, the burden of TB in this population is not well-explored. Based on a single published study conducted in Addis Ababa, 27% of patients on maintenance hemodialysis had TB [7]. Addressing individuals vulnerable to TB for TB screening would help to reduce the

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disease's double burden and its transmission and allow early management. Thus, this study assessed TB and its associated factors among patients with presumptive TB with CKD attending selected hospitals in Ethiopia.

Methods

Study design, setting, and period

A hospital-based prospective cross-sectional study was conducted from January to December 2023 among patients with CKD visiting the selected six hospitals located in five regions for medical care: Addis Ababa (Minelik II Comprehensive Specialized Hospital, and St. Paul's Hospital Millennium Medical College), Dire Dawa (Dilchora Referral Hospital), Oromia (Adama Hospital Medical College), Sidama (Adare General Hospital), and Southern Ethiopia (Arbaminch General Hospital).

Population and enrollment procedure

TB screening was conducted prospectively for consecutive patients with CKD aged 15 years or older who visited the selected hospitals during the study period. The study included those who had signs and symptoms suggestive of TB and volunteered to participate. We excluded patients with CKD with severe disease who were unable to produce the required specimens.

Sample size estimation and sampling method

We estimated the sample using a single proportion formula considering a 95% confidence level, 5% level of significance, 35.7% of TB prevalence among patients with CKD in Egypt [11] because there were no published data from Ethiopia before our data collection period, and 8% non-response rate. Accordingly, 381 patients with CKD were included. The study sites were selected due to the availability of services for the management of CKD and their high patient load. The study participants were recruited consecutively until the sample size was fulfilled.

Data collection procedure

Data were collected by trained clinicians and medical laboratory professionals working on the care and support of patients with CKD in the study sites. From each study hospital, three health professionals (two clinicians and one laboratory professional) were trained on the objectives of the study; case enrollment procedure; data collection procedure; and sample collection, storage, and transportation procedures. Patient-related socio-demographic, behavioral, clinical, and environmental data were collected using a pre-tested questionnaire.

Laboratory investigations

Sputum and urine specimens were collected from each study participant and transported to the National TB Reference Laboratory, Ethiopian Public Health Institute for laboratory testing. The specimens were decontaminated using a 3% N-acetyl-L-cysteine–sodium hydroxide decontamination method [12]. From the sediment, we prepared a smear, stained using Ziehl Neelsen staining, and examined it under the microscope. The remaining sediment was re-suspended with 2 ml of phosphate buffer solution, and 2-4 drops (~100 µl) and 0.5 ml sediment were inoculated to Lowenstein Jensen slant (solid culture) and mycobacterial growth indicator tube (liquid culture), respectively. The media were incubated at 35-37°C until growth was detected or up to 56 days for solid culture and up to 42 days for mycobacterial growth indicator [12]. In addition, the Xpert MTB/RIF Ultra assay (Cepheid, Sunnyvale, CA, USA) was conducted [13]. Identification of MTBC was conducted using the combination of colony characteristics, smear microscopy, and SD-Bioline [14].

Data quality assurance

Data were collected using a pre-tested questionnaire. The data collectors in each participating health facility were chosen and trained on the objectives and procedures. The questionnaire and samples were linked using a study-unique patient identifier. Each test procedure involved internal quality control, and preventive maintenance was performed for each instrument. Furthermore, the test procedures and result interpretations were carried out following the standard operating procedures. Finally, the laboratory results were reviewed by a second investigator.

Data processing and analysis

Data were entered into Epi Info version 7.2 and analyzed using SPSS version 27. We used descriptive statistics to characterize the study variables. We used a logistic regression model to determine the factors associated with TB. An odds ratio (OR) along with 95% confidence interval (CI) was determined. Variables with $P < 0.25$ in the bi-variable analysis were subjected to a multivariable logistic regression model to identify the independently associated variables. Those variables with $P < 0.05$ in the adjusted model were considered to have a statistically significant association.

Operational definitions

Patients with CKD: Encompasses patients with all degrees of decreased kidney function, from damaged at risk through mild, moderate, and severe chronic kidney failure.

CKD staging: The CKD staging was based on the estimated glomerular filtration rate (eGFR) calculated using the modification of diet in renal disease formula eGFR = $175 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 1.212 \times (0.742 \text{ only if female})$ [15] with stage 1: having eGFR ≥90 ml/min/1.73 m^2, stage 2: having eGFR 60-89 ml/min/1.73 m^2, stage 3a: having eGFR 45-59 ml/min/1.73 m^2, stage 3b: having eGFR 30-44 ml/min/1.73 m^2, stage 4: having eGFR 15-29 ml/min/1.73 m^2, and stage 5: having eGFR <15 ml/min/1.73 m^2 [16].

End-stage renal disease: Patients with stage 5 CKD.

Pre-dialysis CKD: A significant impairment of kidney function that will ultimately lead to either death or inclusion in kidney replacement therapy (dialysis and/or transplantation).

Hemodialysis: A process of purifying the blood of a person whose kidneys are not working normally using a machine.

Current or previous cigarette smoker: Currently or previously smokes cigarettes, regardless of the amount and frequency.

Current or previous alcohol consumer: Currently or previously drinks any type of alcohol including locally prepared alcohol, regardless of the amount and frequency.

Contact with a TB patient: Any person exposed to a known person with TB disease.

High TB risk setting: A setting where people reside close to each other. It ranges from correctional facilities (prisons and jails) to homeless shelters, refugee camps, army barracks, hospices, dormitories, and nursing homes.

Results

Characteristics of study participants

Among 381 patients with CKD who participated in the study, more than half (206, 54.1%) were males. The mean age was 45.08 years (SD = 17.68), which ranges from 15-90 years. Nearly 60% (228) were from rural settings. More than half (218, 57.2%) did not have formal education, and 81.1% (309) were married. Among all participants, 11.8%

(45) were either active or previous cigarette smokers and 21.8% (83) were either previous or current alcohol consumers. One-fourth (24.9%, 95) of them were living in a room without window (Table 1).

Clinical profiles of patients with CKD

During enrollment, the frequently observed TB-suggestive symptoms were decreased appetite (341, 89.5%), weight loss (314, 82.4%), and fatigue (292, 76.6%). The other symptoms include malaise (256, 67.2%), shortness of breath (240, 63.0%), chills (241, 63.3%), cough for ≥2 weeks (212, 55.6%), chest pain (159, 41.7%), night sweats (128, 33.6%), fever (84, 22.0%), and hemoptysis (51, 13.4%). Among the assessed 11 symptoms, all the study participants had at least one TB-suggestive symptom. Specifically, only one, two, three, four, and five symptoms were observed among seven, 13, 34, 33, and 42 patients with CKD, respectively. Six or more symptoms were observed in the remaining 252 patients with CKD. The most frequent combination of symptoms was observed among 25 study participants: decreased appetite, chest pain, weight loss, chills, shortness of breath, malaise, and fatigue. The second common combination of symptoms was observed in 19 patients with CKD, which was a combination of seven symptoms which included decreased appetite, weight loss, cough, chills, shortness of breath, malaise, and fatigue. The third common combination of symptoms was observed among 19 patients with CKD with a combination of 10 symptoms: decreased appetite, chest pain, hemoptysis, weight loss, night sweats, cough, chills, shortness of breath, malaise, and fatigue.

Of all participants, 8.1% (31) had previous TB treatment history. There were 17 HIV-positive cases, and 6.8% (26) of patients with CKD were underweight (body mass index [BMI] <18.5 kg/m^2). A total of 94.0% (358) were pre-dialysis patients with CKD. The frequent CKD stage was stage 3 (212, 55.6%), and 9.7% (37) of patients with CKD developed end-stage renal disease (stage 5). Serum creatinine was ≥1.2 mg/dl in 98.2% (374) of them, and a history of hospitalization was reported in 81.6% (311). Chest X-ray was done for 188 patients with CKD, and 12.2% (23) had abnormalities suggestive of TB, and 5.9% (11) had cavitation (Table 2).

At least one comorbid disease was identified in 90.0% (343) of patients with CKD. One-third (128, 33.6%) had hypertension. The other frequently identified comorbidities were chronic obstructive pulmonary disease (91, 23.9%) and diabetes mellitus (DM) (87, 22.8%). The observed comorbidities included asthma, heart disease, pneumonia, arthritis, chronic liver disease, ascites, anemia, acute gastroenteritis, and cancer (Figure 1).

Prevalence of tuberculosis among patients with CKD

In total, among 381 patients with presumptive TB with CKD, TB was detected in 12.9% (49) of them. It was detected bacteriologically in 10.5% (40). Specifically, there were 14 (3.7%) smear-positive cases (13 from sputum and one from urine). The Xpert MTB/RIF Ultra assay detected MTB in 40 (10.5%) patients, with 27 positive cases from sputum only, seven from urine only, and six from both. TB was detected in 7.9% (30) of them using mycobacterial culture. Among the culture-positive cases, 21, four, and five were detected from sputum only, urine only, and both specimens, respectively. In addition, there were nine (2.4%) clinically diagnosed TB cases using chest X-ray and or clinical judgment.

Among the identified TB cases, 33 (67.4%) were pulmonary TB (PTB), including 25 bacteriologically confirmed and eight clinical TB cases. In addition, there were eight extrapulmonary TB (EPTB) cases (16.3%), including seven bacteriologically confirmed cases from urine specimens and one pericardial TB. Besides, there were eight disseminated TB cases (16.3%), which were confirmed bacteriologically in sputum and urine specimens (Figure 2). Overall, the prevalence of pulmonary TB, EPTB, and disseminated TB among patients with CKD was 8.7% (33), 2.10% (8), and 2.10% (8), respectively.

Table 1
Characteristics of study participants (n = 381).

Characteristics	Frequency	Percentage
Age group in years		
15-24	56	14.7%
25-34	49	12.9%
35-44	81	21.3%
45-54	78	20.5%
55-64	52	13.6%
>64	65	17.1%
Sex		
Male	206	54.1%
Female	175	45.9%
Residence		
Urban	153	40.2%
Rural	228	59.8%
Educational status		
No formal education	218	57.2%
Standard grade 1-8	100	26.2%
High school (9-12)	45	11.8%
Higher education	18	4.7%
Marital status		
Single	65	17.1%
Married	309	81.1%
Separated/divorced/widowed	7	1.8%
Occupation		
Government or NGO employed	21	5.5%
Self-employed	152	39.9%
Not have a job	44	11.5%
Housewife	120	31.5%
Student	44	11.5%
Number of rooms		
0	2	0.5%
1	66	17.3%
2	157	41.2%
≥3	156	40.9%
Number of additional household members		
0	18	4.7%
1-3	109	28.6%
4-6	200	52.5%
≥7	54	14.2%
Frequent means of transportation		
Bajaj/Taxi	191	50.15%
Bus	55	14.4%
By foot	135	35.4%
Previous or current alcohol consumer		
Yes	83	21.8%
No	298	78.2%
Previous or current cigarette smoker		
Yes	45	11.8%
No	336	88.2%
Consume raw milk		
Yes	6	1.6%
No	375	98.4%
Khat consumption		
Yes	27	7.1%
No	354	92.9%
Shisha consumption		
Yes	3	0.8%
No	378	99.2%
Frequent means of transportation		
Taxi/Bajaj	191	50.1%
Bus	55	14.4%
On foot	135	35.4%
Door/window open for the whole day time		
Yes	56	14.7%
No	325	85.3%
Living or living in high tuberculosis risk setting		
Prison	4	1.0%
Military barrack	1	0.3%
Homeless	1	0.3%
Palliative care	1	0.3%
Refuge	1	0.3%
Dormitory	1	0.3%

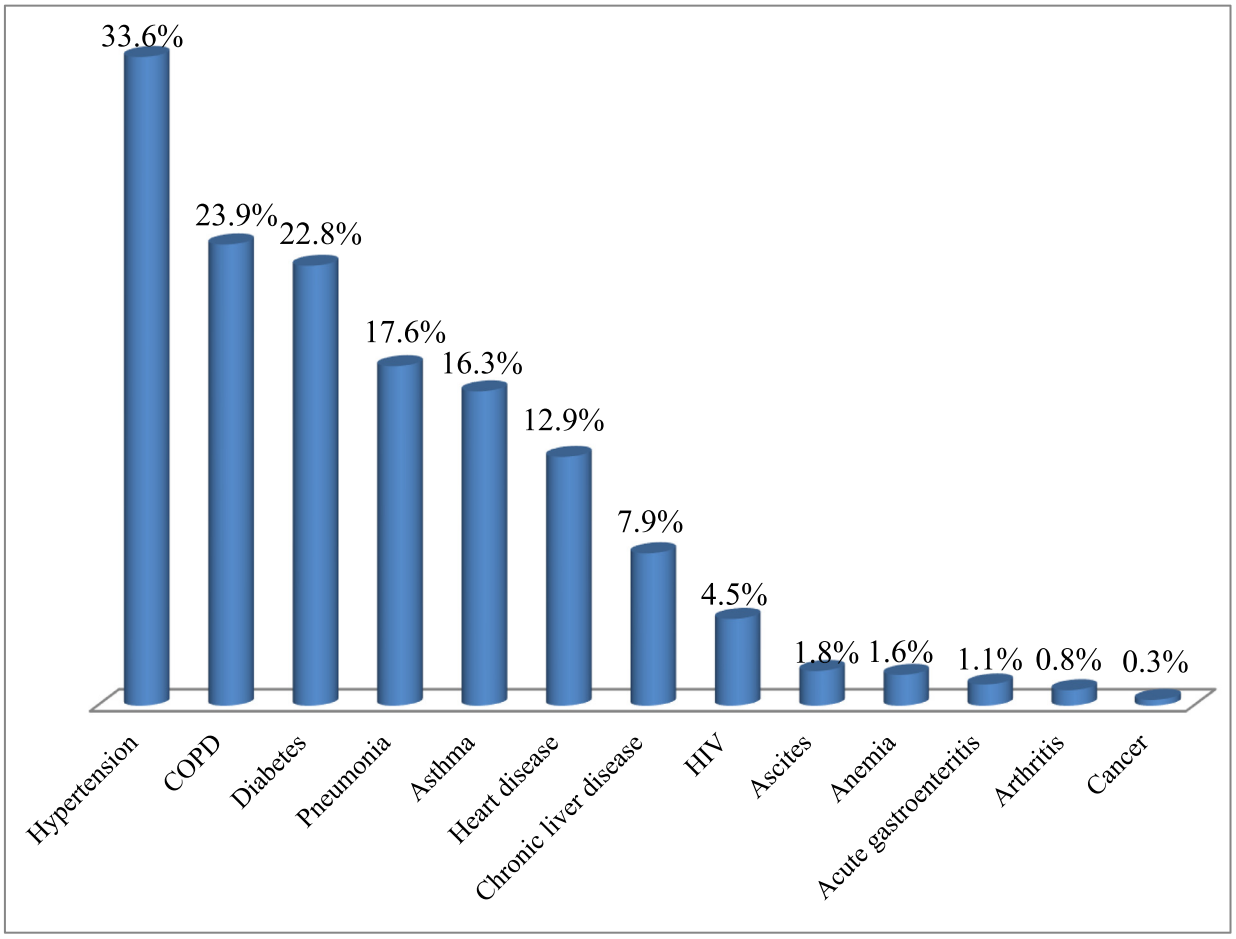

Figure 1. Proportion of patients with chronic kidney disease having the specific comorbidity.
COPD, chronic obstructive pulmonary disease.

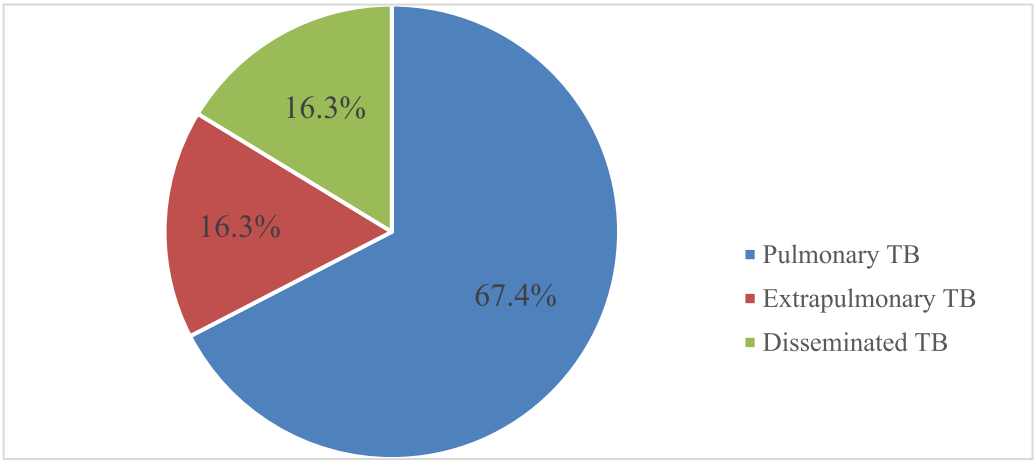

Figure 2. Type of TB detected in patients with chronic kidney disease.
TB, tuberculosis.

Tuberculosis per characteristics of patients with CKD

Among the age groups, higher TB positivity was detected in the 25-34 (10, 20.4%) and 35-44 (16, 19.8%) year age groups. Comparably, a higher proportion of TB was detected among patients with CKD residing in rural residence (rural; 15.8%, urban; 8.5%). Those patients with CKD who were either active or previous cigarette smokers had higher TB positivity (nine, 20.0%) than non-smokers (40, 11.9%). Among the nine patients with CKD in a high TB risk setting, two (22.2%) had TB compared with the 12.6% (47) TB positivity in the other group. Patients vaccinated with Bacille Calmette-Guérin with CKD had lower TB positivity (seven, 8.9%) than non-vaccinated patients (42, 13.9%). Compar-

Table 2
Clinical profiles of patients with CKD who participated in the study (n = 381).

Characteristics	Frequency	Percentage
Previous TB treatment history		
Yes	31	8.1%
No	350	91.9%
Type of previous TB		
Pulmonary	29	93.5%
Extra pulmonary	1	3.2%
Disseminated	1	3.2%
Treatment outcome of previous TB		
Cure	23	74.2%
Complete	7	22.6%
Failure	1	3.2%
HIV status		
Positive	17	4.5%
Negative	167	43.8%
Unknown	197	51.7%
TB contact history		
Yes	7	1.8%
No	374	98.2%
X-ray done		
Yes	188	49.3%
No	193	50.7%
X-ray result		
Abnormality suggestive of TB	23	12.2%
No abnormality	165	87.8%
Cavities on X-ray		
Yes	11	5.9%
No	177	94.1%
Presence of comorbidity		
Yes	343	90.0%
No	38	10.0%
Took corticosteroids		
Yes	21	5.5%
No	360	94.5%
Took immunosuppressive drugs		
Yes	2	0.5%
No	379	99.5%
Took isoniazid prophylaxis		
Yes	9	2.4%
No	372	97.6%
Hospitalization		
Yes	311	81.6%
No	70	18.4%
History of Laboratory confirmed COVID-19		
Yes	13	3.4%
No	368	96.6%
Body mass index in kg/m^2		
<18.5	26	6.8%
18.5-24.9	287	75.3%
≥25.0	68	17.8%
Dipstick albuminuria		
None	137	36.0%
Trace	80	21.0%
+1	68	17.8%
+2	96	25.2%
CKD stage		
Stage II	60	15.7%
Stage III	212	55.6%
Stage IV	72	18.9%
Stage V (end-stage renal disease)	37	9.7%
Follow-up years in renal unit		
<1	269	70.6%
1-2	76	19.9%
≥3	36	9.4%
BCG scar		
Yes	79	20.7%
No	302	79.3%
Serum creatinine in mg/dL		
<1.2	7	1.8%
1.2-3.0	304	79.8%
>3.0	70	18.4%
CKD category		
Pre-dialysis	358	94.0%
Hemodialysis	23	6.0%

CKD, chronic kidney disease; TB, tuberculosis.

atively, TB positivity was higher among patients with CKD residing in a room without a window (19%, 20.0%) than those living in a room with at least one window (30%, 10.5%) (Supplementary Table).

In general, those patients with CKD who had decreased appetite, chest pain, fever, hemoptysis, weight loss, night sweats, cough for ≥2 weeks, chills, shortness of breath, malaise, and fatigue had comparably higher TB positivity than their counterparts. Specifically, higher TB positivity was detected among patients with CKD with night sweats (20.3%), hemoptysis (17.6%), and chest pain (15.7%) symptoms (Figure 3).

Comparably, patients with HIV had higher TB positivity (three, 17.6%) than those without HIV (26, 15.6%). Among 188 patients with CKD screened using chest X-ray, 19.7% (37) had TB. A total of 10 (43.5%) and seven (63.6%) patients with abnormalities suggestive of TB and cavitation in the chest X-ray had TB, respectively. TB was detected in 13.4% (46) of patients with CKD who had comorbidity compared with 7.9% positivity among those without comorbidity. Specifically, 17.2% of patients with CKD with DM had TB compared with 11.6% TB positivity among patients without DM with CKD. Higher TB positivity was detected among patients undergoing hemodialysis (30.4%) compared with pre-dialysis patients (11.7%). Those with a hospitalization history had higher TB positivity (14.5%) than those who did not have a hospitalization history (5.7%). Besides, patients with CKD with positive dipstick albuminuria had a higher TB positivity rate than those with a negative result. In addition, when the creatinine level increased, TB positivity also increased. Furthermore, patients with CKD with less than 1 year follow-up in the renal unit had higher TB positivity than those with greater than 1 year follow-up (Supplementary Table).

When the CKD stage increased, TB positivity also increased, with 6.7%, 11.8%, 15.3%, and 24.3% among patients with stage 2, stage 3, stage 4, and stage 5 CKD, respectively (Figure 4).

Factors associated with tuberculosis in patients with CKD

A total of 26 variables that had a P <0.25 in the bi-variable logistic regression model were included in the multivariable logistic regression model. Accordingly, previous or current cigarette smoking (adjusted OR [aOR]; 2.82, 95% CI; 1.13-7.04), decreased appetite (aOR; 5.97, 95% CI; 1.04-34.36), night sweats (aOR; 2.21, 95% CI; 1.11-4.39), DM comorbidity (aOR; 3.01; 95% CI; 1.34-6.77), positive in dipstick albuminuria (aOR; 5.55, 95% CI; 2.04-15.13), less than 1 year follow-up in the renal unit (aOR; 9.49, 95% CI; 1.12-80.47), BMI <18.5 kg/m^2 (aOR; 6.69, 95% CI; 1.59-28.13), and being on maintenance hemodialysis (aOR; 4.41, 95% CI; 1.39-14.01) were independently associated with TB in patients with CKD (Table 3).

Discussion

This study finding revealed that TB is a major cause of morbidity in patients with CKD attending hospitals in Ethiopia, where 12.9% of patients with presumptive TB with CKD had TB. Previous or current cigarette smoking, decreased appetite, night sweats, presence of DM, positive dipstick albuminuria, less than one-year follow-up in the renal unit, BMI <18.5 kg/m^2, and being on maintenance hemodialysis had a statistically significant association with TB.

In the current study, 12.9% of patients with presumptive TB with CKD attending hospitals were found to have TB, indicating that TB is a significant cause of morbidity in patients with CKD in Ethiopia. Previously, high TB prevalence (27%) in patients on maintenance hemodialysis was also reported in a study conducted in dialysis centers found in Addis Ababa, Ethiopia [7]. A global systematic review and meta-analysis reported 3718 TB incidence per 100,000 patients with CKD, with the highest incidence in Africa [5]. However, the number of studies from sub-Saharan Africa where TB is endemic was few, requiring more data. Patients with CKD, mainly those on dialysis, have frequent health facility visits for their medical follow-ups and have a high chance of contracting TB cases and developing TB due to their diminished immune status.

Table 3
Factors associated with TB in patients with CKD.

Characteristics	Tuberculosis		Crude OR, 95%CI	Adjusted OR, 95%CI
	Negative	Positive		
Age-group in years				
15-24	49	7	1.41 (0.44-4.46)	1.55 (0.29-8.41)
25-34	39	10	2.52 (0.85-7.50)	1.95 (0.41-9.18)
35-44	65	16	2.42 (0.89-6.60)	3.04 (0.79-11.71)
45-54	71	7	0.97 (0.31-3.04)	1.06 (0.24-4.69)
55-64	49	3	0.60 (0.14-2.53)	0.96 (0.17-5.59)
>64	59	6	1.00	1.00
Residence				
Urban	140	13	1.00	1.00
Rural	192	36	2.02 (1.03-3.95)	1.45 (0.44-4.72)
Have windows				
Yes	256	30	1.00	1.00
No	76	19	2.13 (1.16-4.00)	2.06 (0.95-4.46)
Number of household members				
0	16	2	1.00	1.00
1-3	92	17	1.48 (0.31-7.02)	1.84 (0.33-10.30)
4-6	172	28	1.30 (0.28-5.97)	1.08 (0.20-5.73)
≥7	52	2	0.31 (0.04-2.36)	0.12 (0.01-1.25)
Frequent means of transportation				
Bajaj/Taxi	172	19	1.00	1.00
Bus	45	10	2.01 (0.87-4.63)	1.12 (0.36-3.50)
On foot	115	20	1.57 (0.81-3.08)	0.46 (0.15-1.37)
Previous or current cigarette smoker				
Yes	36	9	1.85 (0.83-4.12)	**2.82 (1.13-7.04)**
No	296	40	1.00	1.00
Door/window open for the whole day time				
Yes	52	4	1.00	1.00
No	280	45	2.09 (0.72-6.06)	1.21 (0.28-5.21)
Decreased appetite				
Yes	294	47	3.04 (0.71-13.01)	**5.97 (1.04-34.36)**
No	38	2	1.00	1.00
Chest pain				
Yes	134	25	1.54 (0.84-2.81)	1.00 (0.37-2.73)
No	198	24	1.00	1.00
Weight loss				
Yes	270	44	2.02 (0.77-5.31)	2.21 (0.70-6.97)
No	62	5	1.00	1.00
Night sweat				
Yes	102	26	2.55 (1.39-4.68)	**2.21 (1.11-4.39)**
No	230	23	1.00	1.00
Cough ≥2 weeks				
Yes	180	32	1.59 (0.85-2.97)	1.77 (0.81-3.89)
No	152	17	1.00	1.00
Chills				
Yes	206	35	1.60 (0.79-2.95)	2.06 (0.55-7.65)
No	126	14	1.00	1.00
Shortness of breath				
Yes	203	37	1.96 (0.99-3.90)	1.67 (0.65-4.34)
No	129	12	1.00	1.00
Malaise				
Yes	217	39	2.07 (0.99-4.29)	1.84 (0.60-5.62)
No	115	10	1.00	1.00
Fatigue				
Yes	251	41	1.65 (0.75-3.67)	1.73 (0.62-4.86)
No	81	8	1.00	1.00
Diabetes				
Yes	72	15	1.59 (0.82-3.09)	**3.01 (1.34-6.77)**
No	260	34	1.00	1.00
Pneumonia				
Yes	55	12	1.63 (0.80-3.33)	1.76 (0.66-4.70)
No	277	37	1.00	1.00
Hospitalization				
Yes	266	45	2.79 (0.97-2.79)	1.09 (0.24-4.98)
No	66	4	1.00	1.00
Dipstick albuminuria				
Negative	132	5	1.00	1.00
Positive	200	44	5.81 (2.25-15.03)	**5.55 (2.04-15.13)**
CKD stage				
Stage II	56	4	1.00	1.00
Stage III	187	25	1.87 (0.63-5.61)	0.75 (0.05-10.43)
Stage IV	61	11	2.53 (0.76-8.39)	1.08 (0.10-11.28)
Stage V	28	9	4.50 (1.27-15.90)	0.92 (0.13-6.68)

(*continued on next page*)

Table 3 (*continued*)

Characteristics	Tuberculosis		Crude OR, 95%CI	Adjusted OR, 95%CI
	Negative	Positive		
Follow-up years in renal unit				
<1	228	41	6.29 (0.84-47.23)	**9.49 (1.12-80.47)**
1-2	69	7	3.55 (0.42-30.01)	3.36 (0.36-31.56)
≥3	35	1	1.00	1.00
BMI in Kg/m^2				
<18.5	18	8	5.60 (1.63-19.24)	**6.69 (1.59-28.13)**
18.5-24.9	251	36	1.81 (0.68-4.79)	1.60 (0.56-4.52)
≥25.0	63	5	1.00	1.00
BCG scar				
Yes	72	7	0.60 (0.26-1.40)	0.64 (0.19-2.19)
No	260	42	1.00	1.00
Serum creatinine in mg/dL				
<1.2	6	1	1.00	1.00
1.2-3.0	270	34	0.76 (0.09-6.47)	0.42 (0.03-7.04)
>3.0	57	13	1.37 (0.15-12.36)	0.89 (0.04-18.02)
CKD category				
Pre-dialysis	316	42	1.00	1.00
Hemodialysis	16	7	3.29 (1.28-8.47)	**4.41 (1.39-14.01)**

CKD, chronic kidney disease; OR, odds ratio; TB, tuberculosis.

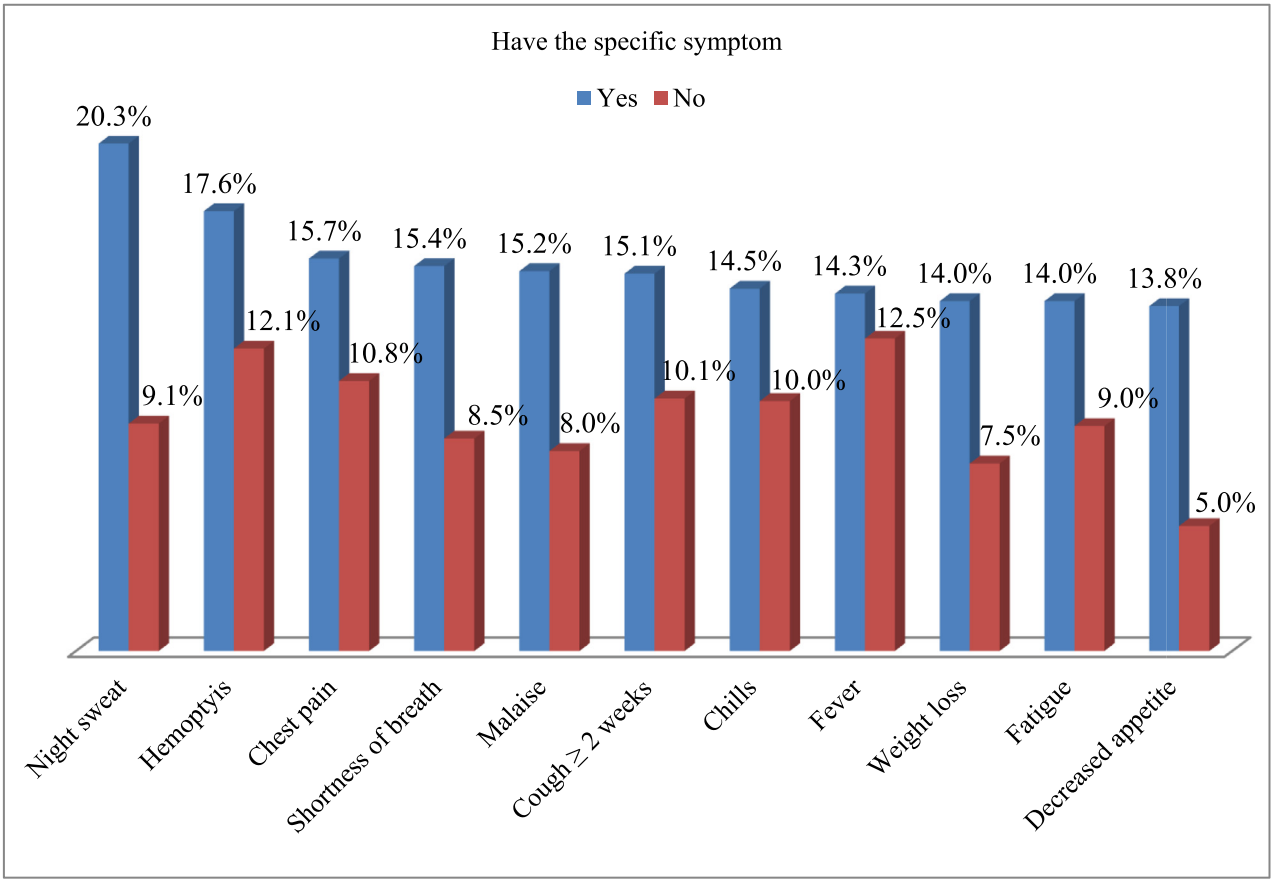

Figure 3. Tuberculosis positivity among patients with chronic kidney disease with and without the specific symptom.

Thus, systematic TB screening in patients with CKD may be important in reducing mortality in this population. Ethiopia is among the high TB burden countries; thus, it is crucial to design targeted intervention strategies such as systematic TB screening and treatment in high TB risk groups, including patients with CKD. The World Health Organization recommends TB systematic screening among people with a risk factor for TB who are either seeking health care or who are already in care, including patients with renal failure, in settings where the TB prevalence in the general population is 100 per 100,000 or higher, which includes Ethiopia [17].

In this study, 67.4% of the TB cases were PTB and 16.3% were EPTB. The PTB proportion was comparative, whereas the EPTB proportion was lower than a previous study conducted in Ethiopia, which reported 66% PTB and 28% EPTB proportion among the reported TB cases in patients undergoing hemodialysis [7]. The PTB proportion in our study and a previous study was lower than the 71% PTB proportion in the general population in Ethiopia [1]. However, EPTB was more common than PTB among patients with CKD in many previous studies [18–23]. This was revealed in a global pooled estimate where the incidence of EPTB was higher than PTB in patients with CKD [5]. In

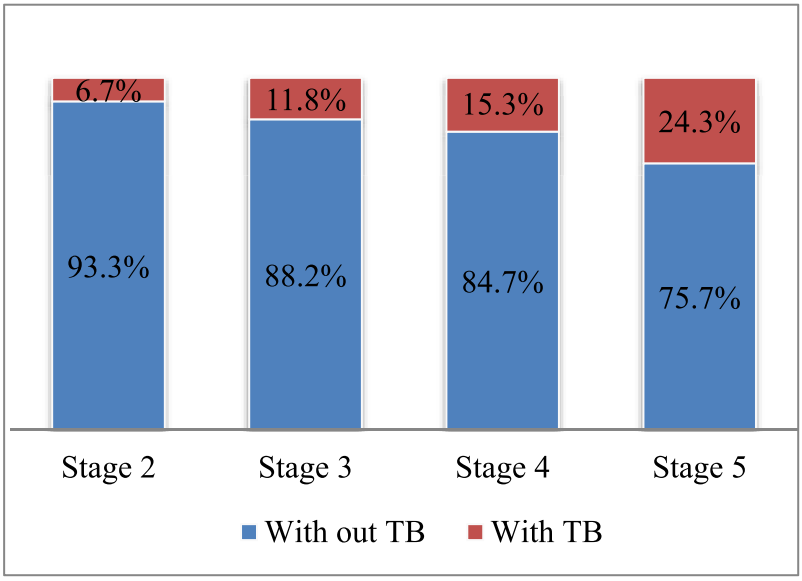

Figure 4. Tuberculosis positivity per chronic kidney disease stage. TB, tuberculosis.

our study, disseminated tuberculosis accounted for 16.3% of cases, significantly higher than the 5.6% previously reported in Ethiopia [6]. Patients with CKD have impaired immune systems, which might result high chance of mycobacterial dissemination in the body, including the renal system.

In the present study, 10.5% of patients with CKD had bacteriologically confirmed TB, which is comparably higher than the 5.6% bacteriologically confirmed TB in a previous study conducted in Addis Ababa, Ethiopia [7]. This might be due to the use of more advanced TB diagnostic technologies such as culture and Xpert MTB/RIF Ultra assay from sputum and urine specimens in our study and the retrospective nature of the previous study. Besides, our study included patients with presumptive TB with CKD, which might result in this difference. Because we did not find another published study from Ethiopia, our comparison was limited to this single study. However, a higher proportion of bacteriologically confirmed TB was reported from other settings [19]. Besides, in our study, 43.5% of patients with CKD with abnormalities suggestive of TB and 63.6% of patients with CKD with cavitation in the chest X-ray had TB. This highlights the importance of chest X-rays in increasing the yield of TB detection in patients with CKD.

Comparably, higher TB positivity was detected in the younger age group. The young age group may be exposed to environmental and behavioral factors favoring TB transmission. Likewise, in the general population, the TB risk is higher in the productive age group [1]. However, contrasting findings from other studies show higher TB positivity among older patients with CKD [18,20]. The presence of CKD and older age may synergize immunodeficiency and contribute to have high TB risk. In addition, higher TB positivity was observed in the underweight patients with CKD than the other groups, which could be due to higher immunodeficiency in this group, as reported previously [18,20].

In the present study, patients with CKD who were either previous or current cigarette smokers had nearly three times the odds of having TB compared with non-smokers. Smoking is a known risk factor for TB in the general population [1]. Smoking affects the immune system and increases susceptibility to mycobacterial infection [24]. Among the TB-suggestive symptoms, patients with CKD with decreased appetite and night sweats showed a statistically significant association with TB, which highlighted the importance of assessing for symptoms other than cough.

The findings of this study revealed that those patients with CKD with additional DM comorbidity had higher odds of having TB than patients without DM with CKD, as reported previously [18–20]. DM and renal diseases increase the risk of developing TB and the presence of both diseases at the same time may intensify the problem. Diabetes is the main underlying cause of CKD, which may complicate the problem. Multimorbidity is common in patients with CKD, where 90% of patients with CKD in the current study had additional comorbidities.

In the present study, patients with CKD with positive dipstick albuminuria had higher odds of having TB than their counterparts. Proteinuria is a marker of kidney damage and indicates a higher degree of renal impairment, which can compromise the immune system and lead to an increased risk of TB. In addition, patients with CKD with <1 year follow-up in the renal unit had higher odds of having TB than those with greater than 3 years of follow-up. However, a previous study reported a higher chance of developing TB in those with longer periods of dialysis [7,19]. The difference might have resulted from the type of patients with CKD in the study, where 94.0% of patients with CKD in our study were pre-dialysis patients with CKD. However, higher TB infection risk in those treated with hemodialysis for <12 months was also reported [18]. This highlights the importance of TB screening among patients with CKD at any period of their follow-up.

Finally, patients with CKD on hemodialysis had higher odds of having TB than pre-dialysis patients with CKD. Patients on dialysis have higher levels of kidney damage, which increases immunodeficiency and leads them to have a higher chance of developing TB. Besides, frequent visits to health care facilities for medical follow-up may increase the chance of getting mycobacteria and developing TB. This was also evidenced in a global pooled estimate [5].

In the end, because this study is a cross-sectional study, it was unable to find the TB incidence and the time to develop TB in this group of population.

Conclusion

TB is a significant cause of morbidity among patients with CKD attending hospitals in Ethiopia, necessitating programmatic intervention. Those patients with CKD who were previous or current cigarette smokers, with decreased appetite, night sweats, presence of DM, positive in dipstick albuminuria, less than 1 year follow-up in the renal unit, BMI <18.5 kg/m^2, and being on maintenance hemodialysis had higher odds of having TB than their counterparts. We recommend systematic and targeted TB screening in patients with CKD to detect TB cases as early as possible, hence reducing TB transmission and mortality in this TB-vulnerable population.

Declarations of competing interests

The authors have no competing interests to declare.

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Ethics approval and consent to participate

The study gets ethical approval from the Aklilu Lemma Institute of Pathobiology, Addis Ababa University, the Ethiopian Public Health Institute, and the St. Paul's Hospital Millennium Medical College. Written consent or assent was obtained from each study participant.

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Author contributions

The study was conceptualized by AA. AA, GD, GS, and AW conducted the laboratory examinations. AA drafted the manuscript and SM, GT, BH, NB, SHM, and BG revised the manuscript. All the authors read and approved the final manuscript.

Availability of data and materials

All the materials are available within the manuscript and supplementary files.

Consent for publication

Not applicable.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100551.

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