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Impact of Chronic Kidney Disease on the Mortality of Tuberculosis Patients: A Cross-Sectional Study in the City of Douala

Impact de la maladie rénale chronique sur la mortalité des patients tuberculeux : étude transversale dans la ville de Douala

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Mots clés : Tuberculose, Insuffisance Rénale Chronique, Mortalité, Décès, Douala, Cameroun

ABSTRACT

Introduction. High mortality during the course of tuberculosis (TB) has been described in patients with chronic kidney disease (CKD) with scarce data in this regard from sub-Saharan Africa. Hence, we sought to determine the impact of CKD on TB-related mortality at the Douala General Hospital (DGH), Cameroon. **Methods.** We conducted a retrospective cross-sectional study of adult TB patients with CKD matched with TB patients without CKD between 2009 – 2020 at the DGH. CKD was considered in any patient with a decrease in glomerular filtration rate below 60 ml/minute for more than 3 months. Data collected included socio-demographic characteristics, comorbidities, clinical data, blood test results, and patient outcome (alive *vs*. dead). Using SPSS version 23, multiple regression analysis was used to eliminate confounders and determine independent risk factor for mortality in TB patients with CKD. **Results.** We retained 126 TB patients with CKD matched to 126 without CKD. The mean age of the patients with CKD was 44.7 ± 13 years and the sex ratio was 1.42. The most common clinical form of TB was extra pulmonary, 61.9% (78/126). The median diagnostic delay was 25 days in patients with CKD and 16 days in patients without CKD (p = 0.018). Mortality was higher in the group of patients with CKD, 33.3% versus 5.6% (p<0.0001) with 27.0% and 4.8% of deaths in the first 2 months, respectively. CKD (HR=3.4; CI=1.0 - 11.1; p<0.0001) and thrombopenia (HR=5.3; CI=0.2-9.9; p=0.013) were factors independently associated with death in TB patients. **Conclusion**. Mortality was six-times higher in TB patients with CKD compared to TB patients without CKD. Factors independently associated with mortality of tuberculous patients to be screened and managed to curb this alarming death rate include CKD and thrombopenia.

RÉSUMÉ

Introduction. Une mortalité élevée au cours de l'évolution de la tuberculose (TB) a été décrite chez les patients atteints d'insuffisance rénale chronique (IRC) avec peu de données à cet égard en Afrique subsaharienne. Par conséquent, nous avons cherché à déterminer l'impact de l'IRC sur la mortalité liée à la tuberculose à l'Hôpital général de Douala (DGH), au Cameroun. **Méthodes**. Nous avons mené une étude transversale rétrospective de patients adultes tuberculeux atteints d'IRC appariés avec des patients tuberculeux sans IRC entre 2009 et 2020 à la DGH. Les données recueillies comprenaient les caractéristiques sociodémographiques, les comorbidités, les données cliniques, les résultats des tests sanguins et les résultats des patients (vivants ou décédés). À l'aide de la version 23 de SPSS, une analyse de régression multiple a été utilisée pour éliminer les facteurs de confusion et déterminer le facteur de risque indépendant de mortalité chez les patients tuberculeux atteints d'IRC. **Résultats**. Nous avons retenu 126 patients TB avec IRC appariés à 126 sans IRC. L'âge moyen des patients atteints d'IRC était de 44,7 ± 13 ans et le sexe ratio était de 1,42. La forme clinique la plus fréquente de TB était extrapulmonaire, 61,9% (78/126). Le délai médian de diagnostic était de 25 jours chez les patients atteints d'IRC et de 16 jours chez les patients sans IRC (p = 0,018). La mortalité était plus élevée dans le groupe des patients atteints d'IRC, 33,3 % contre 5,6 % (p<0,0001) avec respectivement 27,0 % et 4,8 % de décès au cours des 2 premiers mois. L'IRC (HR=3,4 ; IC=1,0 - 11,1 ; p<0,0001) et la thrombopénie (HR=5,3 ; IC=0,2-9,9 ; p=0,013) étaient des facteurs indépendamment associés au décès chez les patients TB. **Conclusion**. La mortalité était six fois plus élevée chez les patients TB avec IRC que chez les patients TB sans IRC. Les facteurs indépendamment associés à la mortalité à dépister et à gérer pour freiner ce taux de mortalité alarmant comprennent l'IRC et la thrombopénie.

HIGHLIGHTS

What is already known on this topic

Despite the high TB-related mortality in TB patients with CKD, few studies have investigated the actual involvement of CKD in the occurrence of these deaths in our country.

What question this study addressed

Mortality of TB patients with CKD and factors that influence this mortality

What this study adds to our knowledge

Extra pulmonary TB is the most common presentation in patients with CKD and mortality is six-times higher in TB patients with CKD compared to TB patients without CKD. CKD and thrombocytopenia are independent factors associated with this high mortality.

How this is relevant to practice, policy or further research.

Special attention should be addressed to TB patients with CKD and thrombocytopenia.

INTRODUCTION

Tuberculosis (TB) remains a global public health problem, with more than 10 million people infected each year, according to Word Health Organization estimates (WHO) [1]. There is many risk factors, including chronic kidney disease, make it a concern for health services, especially in resource-limited countries, which account for the majority of tuberculosis cases. Chronic kidney disease (CKD) is defined by the Kidney Disease Improving Global Outcome (KDIGO 2012) as the presence for more than three months, of a structural or functional renal abnormality with implications for health [2]. CKD is an emerging global public health problem [3]. Indeed, according to the Global Burden of Disease Study estimates, the worldwide prevalence of CKD in 2017 was 9.1% or 697.5 million cases with 1.2 million deaths [4]. It is reportedly 3 to 4 times more common in sub-Saharan Africa (SSA) with an overall prevalence of 13.9% [5, 6].

CKD predisposed to several non-communicable diseases and infectious diseases [7, 8]. Infectious diseases are frequent and represent the second leading cause of death in CKD patients worldwide and the leading cause of death in SSA [5], resulting from deficits in cellular and humoral immunity [9-10]. TB is one of these infectious pathologies and its risk increases with the degree of impaired renal function [11, 12]. The prevalence of TB in patients with CKD varies considerably from one study to another. It is estimated to be between 4 and 13% in Asia [13, 14]; in Africa, reports from Ivory Coast, Togo, Tunisia and Mali describe a prevalence rate between 5.9% and 10.9% [15-16], [17-18]. Extra-pulmonary localizations of TB in CKD patients are more frequent and the clinical presentation is dominated by non-specific signs and symptoms leading to late diagnosis and a resultant high mortality [13].

Mortality in CKD patients having TB varies from 7-28% in Asia [14, 19], and from 20-42% in Africa [15, 18]. Many factors have been identified by previous studies as associated with this mortality including high serum urea levels, age, female gender, extra-pulmonary TB, disseminated forms of TB and HIV/AIDS immunosuppression [17, 20, 21]. Despite the high TB-related mortality in TB patients with CKD, few studies have investigated the actual involvement of CKD in the occurrence of these deaths. We proposed a cross-sectional and analytic study to determine the impact of CKD on the mortality of TB patients at a tertiary hospital in Douala, having a major referral TB care unit and Nephrology/Hemodialysis center.

MATERIALS AND METHODS

Study design and study setting

This was a retrospective and analytical cross-sectional study of the records of patients followed-up for TB between January 2009 to December 2020 in the Internal Medicine Department of the Douala General Hospital (DGH). DGH is one of the main tertiary and university teaching hospitals in Cameroon with 60 beds in the internal medicine department. The two pulmonologists of this department were responsible for the consultations and follow-ups of patients with respiratory pathologies and two nephrologists managed patients with renal disease. The internal medicine department has a dialysis unit equipped with 19 hemodialysis machines for nearly 220 end-stage CKD patients on maintenance hemodialysis during the study period. The treatment of hemodialysis patients was done adapted to their kidney function and according to the protocol of the National Tuberculosis Control Program (NTCP) and the recommendations of the World Health Organization (WHO). This protocol included at the initiation, the alternation of Rifampicin (R), Isoniazid (H) Ethambutol (E) and Pyrazinamide (Z) and RH combinations every day for 2 months, then administration of RH every day according to the patient's weight for 4 months. On hemodialysis days for patients with CKD, the anti-tuberculosis drugs were taken after the session. The anti-tuberculosis treatment of the patients without CKD followed the national protocol enacted by the National Tuberculosis Control Program: RHEZ for 02 months then RH for 04 months with clinical, biological and radiological controls at the end of the second, fifth and sixth months.

Study population and matching

All records of patients aged ≥ 18 years with TB followed-up at the DGH who developed CKD (cases) and who did not have CKD (controls) were include in the study. Records that did not contain all the relevant information such as age, sex, clinical form and/or outcome were excluded. Eligible TB patients with CKD were matched for we matched for age, sex, and TB clinical forms to TB patients without CKD.

Data collection and procedure

After obtaining the ethical clearance (N° 2619/CEI-Udo/04/2021/T) and the research authorization on the study site (N°014 AR/MINSANTE/HGD/DM/01/21), we searched the records of TB patients with CKD. We matched these records with those of TB patients without CKD, and finally, we determined the clinical and laboratory characteristics and mortality characteristics of the patients in our study population and searched for the factors associated with this mortality.

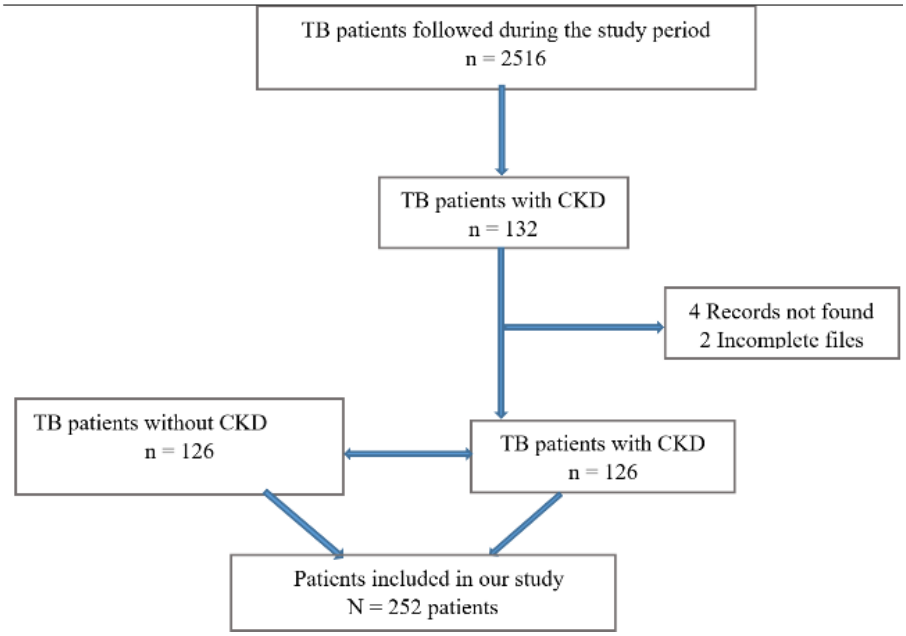

Figure 1: Flow chart explaining the recruitment of the study population
TB: tuberculosis; CKD: chronic kidney disease

The variables studied were: Sociodemographic data (age, sex, place of residence, occupation, marital status); Comorbidities and relevant past history (HIV/AIDS, hypertension, diabetes mellitus, cancer, corticosteroid therapy, immunosuppressive treatment, smoking, alcoholism); Clinical data (time to diagnosis, symptoms); clinical forms (bacteriologically confirmed pulmonary TB, non-bacteriologically confirmed pulmonary TB, extra-pulmonary TB), clinical category of TB (new patient, retreatment patient); laboratory data (HIV serology, hemoglobin level, platelet count, C Reactive Protein, sedimentation rate); and patient outcome (patient alive, patient dead, patient lost to follow-up).
The fundamental principles of medical research were respected, and the investigations were carried out in strict compliance with medical confidentiality.

Definition of operational terms
A CKD patient was one with a persistent glomerular filtration rate (GFR) of less than 60 ml/minute for more than 3 months confirmed by the nephrologist. A TB patient was one with clinical signs suggestive of TB with laboratory confirmation, or those without biological confirmation with a good therapeutic response to anti-TB treatment. A TB patient with CKD was one treated for TB with a persistent GFR below 60 ml/minute for more than 3 months and confirmed by the nephrologist. A TB patient without CKD was one treated for TB with a normal GFR. An extra-pulmonary TB patient was one with organ involvement other than pulmonary, presenting clinical signs suggestive of TB with bacteriological, histological, or biological confirmation, or with a good therapeutic response in the absence of diagnostic evidence**.** Incomplete file are medical records that do not contain all the information useful for our study, i.e., age, sex, clinical form and/or outcome**.** Diagnostic delay: delay between the consultation at the HGD and the start of treatment**.** Anemia was considered to be a hemoglobin level below 10 g/dl**.** Death was considered as any death occurring between screening and the end of anti-tuberculosis treatment from any cause.

Statistical analysis
Data were entered and processed using SPSS version 23 software. Qualitative data were expressed as numbers and percentages, quantitative data as means and standard deviations or as median with interquartile range. The comparison of qualitative data was done with the chi-square test and the comparison of quantitative data with the T-Student test. Factors associated with patient mortality were investigated using a Cox regression model with univariate and multivariate analyses. Data with a p value < 0.1 were entered into the model for multivariate analysis. Hazard ratios (HR) were calculated. A p-value less than 0.05 was considered the threshold for significance.

RESULTS
During the study period, almost 2516 patients were followed up for TB, of whom 132 (5 .24%) had chronic kidney disease and six TB cases with CKD were excluded. The final population consisted of 126 patients whom we matched as aforementioned to 126 TB patients without chronic kidney disease (Figure 1).

Socio-demographic, clinical and paraclinical characteristics of the study population
Of the 252 patients of the study population, 148 were male (58.7%) with a M/F sex ratio of 1.42. The mean age of the individuals was 44.7 years for the group of TB patients with CKD and 44.6 years for those without CKD (Table 1).
The main comorbidities found in the study population were HIV (40.5%) and hypertension (38.5%).

Table 1: Socio-demographic characteristics of the study population

Variables	Total patients n = 252 n(%)	TB patients with CKD n = 126 n(%)	TB patients without CKD n = 126 n(%)	p value
Gender				
Male	148(58.7)	74(58,5)	74(58,5)	1,000
Female	104(41.3)	52(41,3)	52(41,3)	
Age				
Mean ± SD	43 ± 12	44,7 ± 13,0	44,6 ± 12,5	0,978
Age ranges				
[18–30[	29 (11,5)	15 (11,9)	14(11,1)	
[30-40[	63 (25,0)	32 (25,4)	31 (24,6)	
[40-50[	83 (32,9)	39 (31,0)	44 (34,9)	
[50-60[	48 (19,0)	25 (19,8)	23 (18,3)	
[60-70[	16(6,3)	8 (6,3)	8 (6 ,3)	
[70-80[	10 (4)	6 (4,8)	4 (3,0)	
≥80	3(1,2)	1 (0,8)	2 (1 ,6)	

SD: standard deviation; CKD: chronic kidney disease; TB: tuberculosis;

Table 2: Distribution according to clinical category and clinical form of TB of TB patients with and without CKD (n=252)

Variables	Total patients n = 252 n(%)	TB patients with CKD n = 126 n(%)	TB patients without CKD n = 126 n(%)	p value
TB clinical category (n=252)				
New patient	227(90,1)	116(92,1)	111(88,1)	0,574
Relapse	20(7,9)	8(6,3)	12(9,5)	
Resumption of treatment	5(2,0)	2(1,6)	3(2,4)	
Clinical form of TB (n=252)				
EPT	156(61,9)	78(61,9)	78(61,9)	0,470
TPB+	44(17,5)	25(19,8)	19(15,1)	
TPB-	52(20,6)	23(18,3)	29(23,0)	

TB: tuberculosis; EPT: extra-pulmonary tuberculosis; TPB+: pulmonary tuberculosis with positive bacilloscopy; TPB-: pulmonary tuberculosis with negative bacilloscopy;

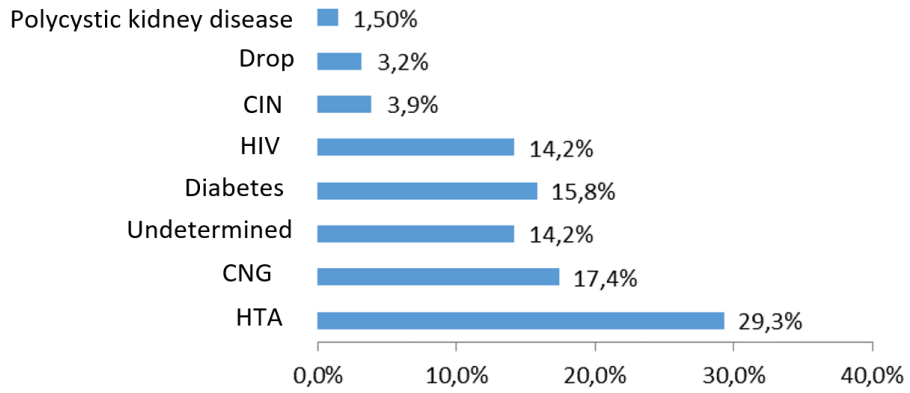

Figure 2: Distribution of CKD patients by presumed etiology of CKD

HTA : Hypertension; Chronic glomerulonephritis; HIV: human immunodeficiency virus; CIN: chronic interstitial nephritis

Table 2 presents extra-pulmonary localizations as the most frequent with serious involvement in 82.1% of patients, notably pleural TB found in 55.8% (87/156) of patients, followed by peritoneal TB in 18.6% (29/156).

Table 3 shows that almost all patients were at an advanced clinical stage of CKD: 84.1% (106/126) at stage 5 and all on maintenance hemodialysis and 15.8% (20/126) at stage 4. The median duration of CKD and hemodialysis at the time of diagnosis of TB was 24 and 19.5 months respectively.

As presents in figure 3, the most common etiologies of chronic kidney disease of the study population were hypertension (29.3%), chronic glomerulonephritis (17.4%) and diabetes (15.8%).

Table 3: Clinical characteristics of the study population

Variables	
CKD stage (n=126) n (%)	
Stage 4	20 (15,8)
Stage 5 ND	11 (8,7)
Stage 5 D	95 (75,3)
Duration of CKD in months (n=97)	
Median (SD)	24,0 (42,25)
Duration of hemodialysis in months (n = 95) Median (SD)	19,5 (36,25)

CKD: chronic kidney disease; SD: standard deviation

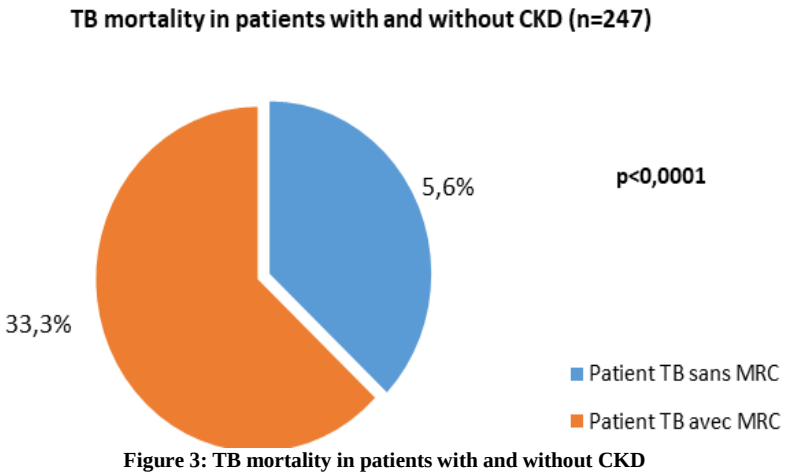

Figure 3: TB mortality in patients with and without CKD
TB: tuberculosis; CKD: chronic kidney disease

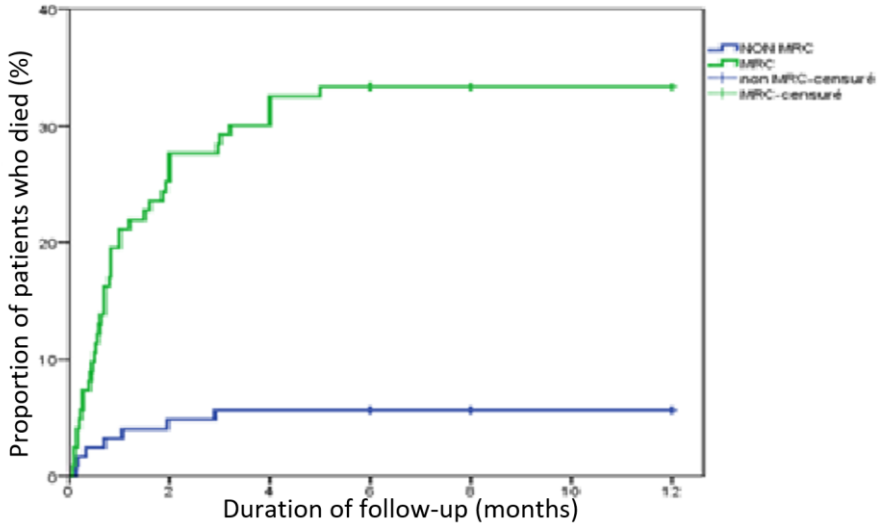

Figure 4: Survival curve of TB patients with and without CKD (n=247)

Mortality related to tuberculosis in the study population

Figure 3 below presents the mortality of tuberculosis in our population. Mortality in the group of TB patients with CKD was more than 5 times higher (33.3%) than in the group of TB patients without CKD (5.6%) with a statistically significant difference (p<0.0001).

As shown in the figure 4 below, at 2 months there were 27% deaths in the TB patients with CKD and 4.8% in the patients without CKD. That is to say 82% and 85% of deaths recorded during the first 2 months in the group of patients with and without CKD respectively (p<0.0001).

Factors associated with mortality in patients with CKD

In univariate analysis, no socio-demographic factor was significantly associated with the occurrence of death in our study population. However, CKD, hypertension, asthenia, extra pulmonary involvement, hospitalization, anemia and thrombocytopenia were significantly associated with death in the study population.

After multivariate analysis, as presented in table 4 below, the factors independently associated with the occurrence of death of individuals during TB were CKD (p<0.0001) and thrombocytopenia (p=0.003).

Table 4: Multivariate analysis of factors associated with death in TB patients (n=247)

Variables	HR Adjusted* (IC 95%)	p value
CKD	**3,4 (1,0 - 11,1)**	**0,037**
HTN	1,8 (0,2 – 12,5)	0,529
Asthenia	2,0 (0,3 – 12,2)	0,447
TEP	2,2 (0,4 – 11,5)	0,324
Hospitalization at diagnosis	3,1 (0,7 – 13,6)	0,117
Thrombopenia	**5,3 (1,4 – 20,1)**	**0,013**
Thrombocytosis	1,6 (0,2 – 9,9)	0,578
Anemia	1,3 (0,3 – 4,7)	0,632

*HR: Hazard ratio CI: confidence interval; CKD: chronic kidney disease; HTN: Hypertension; PET: extra pulmonary tuberculosis; TEP: extra pulmonary tuberculosis; *Adjusted for significant variables in univariate analysis*

DISCUSSION

The objective of our work was to determine the impact of chronic kidney disease on TB-related mortality at the Douala General Hospital, Cameroon. Mortality was significantly higher in the group of TB patients with CKD

(32.5%) than in the group of TB patients without CKD (5.6%) p<0.0001. Chronic kidney disease and thrombocytopenia were independent factors associated with mortality in patients with TB in our study.

In the general population, the most common clinical form of TB is the pulmonary form, and the frequency of extra-pulmonary TB localizations has been reported in previous studies to vary from 20 to 40% of cases [22, 23, 24]. In the present study, the most frequent clinical form in TB patients with CKD was the extra pulmonary form (61.9%). This result was comparable to that of Jebali et al in Tunisia, Tékpa et al in Central Africa, Pradhan et al. and Unsal et al. in Turkey who found respectively 78%, 74.09%, 69.1% and 65.4% of extra pulmonary forms in patients with CKD [17, 19, 25]. However, it differs from that of Kouamé et al. in Ivory Coast in which the most represented clinical form in TB patients with CKD on hemodialysis was the pulmonary form (94.91%). This could be explained by the study methods used with the inclusion criteria of consenting hemodialysis patients who presented a cough with sputum that was much more suggestive of a pulmonary location [15]. The median diagnostic delay in TB patients with CKD was 25 days. This result is comparable to that of 28 days found by Nakamura et al. in Japan [26], However, it differs from the 72 days found by Yao et al. in Ivory Coast and the 113 days found by Jebali et al. in Tunisia in patients with CKD which was longer than in our study [15, 17]. This difference can be explained by the fact that the current study took place in a tertiary hospital with all the internal medicine specialists. It is closed to the diagnostic time found in a meta-analysis conducted in 2017 by Getnet et al, which was 30-366 days. [27] This was for the general TB population, with no emphasis on the presence or absence of underlying chronic kidney disease. This diagnostic delay remains higher with a significant difference (p=0.018) than that of patients without CKD which was 16 days. This diagnostic delay is a real challenge in low- and middle-income countries worldwide. In TB patients with CKD, it can also be explained by the fact that the diagnosis of extra pulmonary forms is more difficult [28], the clinical signs of TB being often assimilated to a uremic syndrome explaining the delay in diagnosis [15].

Anemia and thrombocytopenia were the most frequent laboratory abnormalities found in our population. These abnormalities were more frequent in patients with CKD than in those without CKD: 66.1% versus 31.0% (p<0.0001) for anemia and 26.4% versus 10.5% (p=0.003) for thrombocytopenia. This result is similar to that of Lundin et al. in the United States, who found 62.5% anemia in their patients. Anemia is a common complication of tuberculosis. A meta-analysis study in 2019, found mild or moderate anemia in 43% of patients [29], and in HIV/TB co-infected patients, hematologic abnormalities of different lines are frequently described. [30] Anemia is a complication that affects most patients with advanced chronic kidney disease. It is of multifactorial origin with erythropoietin deficiency as the main cause [31]. There are also functional abnormalities of platelets in CKD that can lead to thrombocytopenia. In addition, dialysis patients use heparin which can also be responsible for hemolysis [32].

Mortality from tuberculosis varies between studies. In Europe, a systematic review found a mortality of 5-12% in the general population [33]; in previous African studies, mortality ranged from 8-18.6% [34, 35]. It was higher in the present study population, 33.3% in TB patients with CKD. Indeed, patients with CKD represent a particular risk group for the occurrence of tuberculosis and for death related to tuberculosis [36, 37]. Our result was comparable to that of Jebali et al. in Tunisia and Nakamura et al. in Japan who found a mortality of 36.5% and 36.8% respectively in patients with TB and CKD [17, 26]. Ramilitiana et al. in Antananarivo, and Cissé et al. in Senegal found a lower mortality rate of tuberculosis in patients with CKD than ours, i.e., 29.0% and 20.0% respectively [35, 38]. On the other hand, Yao et al. in Ivory Coast, the mortality was 42% [15]. This result was also higher than ours and this could be explained on the one hand by the delay in diagnosis, which was high in this study, i.e., about 74 days against 25 days in our study and the delay in diagnosis is a factor associated with death recognized in tuberculosis [39]. On the other hand, this difference can be explained by the small size of the population in this study which was 7 patients against 126 patients in our study.

The mortality in the group of TB patients without CKD was 5.6%. This result was similar to that of Baghaei et al. in Tehran who found a mortality of 3.6% in the same group [37]. Mortality was more than 5 times higher in the group of TB patients with CKD compared to those without CKD i.e. 32.5% versus 5.6% with a statistically significant difference. This result is similar to that of Baghaei et al. who found a 4-fold higher mortality in the CKD group. CKD was associated with death in TB patients in this work with an HR of 4.87 [37]. This result could have several explanations. The high proportion of extrapulmonary forms and particularly of serosal involvement in TB in patients with CKD causes an atypical and insidious presentation often associated at the beginning of the disease with subdialysis, and the general signs assimilated to a uremic syndrome [40]. The infectious syndrome is often assimilated to a dialysis catheter infection, which is relatively frequent in this population, as Andrew et al. in the United States have also noted [41]. This insidious presentation is therefore a cause of diagnostic delay. This diagnostic delay was also observed in our study, in fact the diagnostic delay in TB patients with CKD was significantly longer (25 days) than in those without CKD (16 days). This delay in diagnosis was found to be the cause of high mortality in CKD [27].

Concerning laboratory data, this high mortality could be explained by the higher frequency of hematological abnormalities in patients with CKD [42]; in our study, anemia and thrombocytopenia were the most frequent abnormalities with significantly higher proportions in the group of patients with tuberculosis with CKD (p<0.0001 and p=0.003). Several studies have demonstrated the impact of these abnormalities in the occurrence of death in patients with TB [43, 44, 45]. Death in our population being defined as any death during the course of anti-

tuberculosis treatment, this high mortality could therefore not be directly related to tuberculosis but also to comorbidities related to the CKD terrain. In the present study, diabetes mellitus was significantly higher in the group of patients with CKD with a significant p-value of 0.015 and could increase mortality in this group.

Thrombocytopenia was a factor associated with mortality of patients with CKD in our study. It was also found by Singla et al. in India in 2021 as a factor associated with early mortality in TB. Infections represent one of the major risk factors for the occurrence of thrombocytopenia [46]. Platelet destruction related to an excessive host response to infection could be the cause [47]. The platelet level would be inversely proportional to the severity of the infection [48]. This could explain the association of thrombocytopenia with mortality in our population.

There are some limitations to the current study. Firstly, the retrospective nature of the study maked it difficult to accurately pinpoint whether TB started before TB or CKD before TB. Also, because of the cross-sectional design it impossible to either infer causality or untangle bi-directional relationship of risk factors for TB-related mortality in CKD patients. We addressed these limitations by a robust statistical method using multiple regression to prevent bias in our results.

CONCLUSION

At the end of our study, the objective of which was to retain that:

- The extra pulmonary form was the most frequent clinical form of tuberculosis in the tuberculosis patient with chronic kidney disease
- Mortality was significantly high in the TB patient with kidney disease chronic compared to those without chronic kidney disease
- Chronic kidney disease, and thrombopenia has been identified as a factors associated with mortality in tuberculosis patients

Aknowlegment

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Authors' contributions

Laurent-Mireille Endale Mangamba, Adamou Dodo Balkissou: Concept development, execution of the project, drafting of manuscript; CL Mbele Onana: drafting and review of the manuscript; Vincent Ngamby: concept development and review of manuscript. Joel Notakdie Tochie: concept development and review of manuscript; Junie Carelle Emabe: data collection, concept development, review of manuscript; Hugo Bertrand Mbatchou Ngahane, Marie Patrice Halle: conceptualization, supervision of the project, data analysis and review of manuscript.

All the authors have read and agreed to the final manuscript.

Conflicts of interest

The authors declare no conflict of interest

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