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Clinical, Diagnostic, and Evolutionary Profiles of TB Patients Followed up in Kisangani, Democratic Republic of the Congo: A Short Report

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Abstract

Background: Tuberculosis disproportionately affects disadvantaged populations. Individuals with comorbidities such as HIV and diabetes are more vulnerable to developing TB. Tshopo Province presents disparities in health outcomes across different health zones, indicating challenges in care management. The objective of this study was to describe the clinical, diagnostic, and evolutionary profiles of TB patients followed up at Kisangani's Tuberculosis Diagnostic and Treatment Centers. **Materials and Methods**: This was a retrospective descriptive study conducted from January 2020 to June 2023 involving 1204 TB patients followed up in the TB diagnostic centers of Kisangani. The data were collected via Kobotoolbox, processed in Excel, and analysed via Stata. **Results**: The study population consisted primarily of young adult males, with a predominance of pulmonary tuberculosis (62.79%) and classic TB symptoms (cough, fever, night sweats). Despite a high treatment success rate (95.51%), TB remains a major cause of mortality among treatment failure patients, particularly in the presence of HIV coinfection. **Conclusion**: Tuberculosis remains a major public health problem in Kisangani, primarily affecting young adults. Despite encouraging treatment success rates, TB-related mortality rates remain high, highlighting the need to strengthen prevention, screening, and integrated HIV-TB care strategies.

Keywords

Clinical Profile, Biological Profile, Therapeutic Profile, Evolutionary Profile,

Tuberculosis, Kisangani, Democratic Republic of the Congo

1. Introduction

Tuberculosis is a bacterial disease caused by M. tuberculosis. At the beginning of this third millennium, it remained one of the world's leading public health challenges, with one-third of the world's population being infected [1]. Since the advent of HIV/AIDS, its incidence has increased, with changes in its classic features, both clinically and epidemiologically [2].

The WHO's End TB Strategy, adopted by the World Health Assembly in May 2014 and taking into account the United Nations Sustainable Development Goals (SDGs), aims for a 95% reduction in mortality and a 90% reduction in the incidence of the disease by 2035, with intermediate targets every five years [3].

In 2022, the WHO region with the highest number of new tuberculosis cases was Southeast Asia (46% of all new cases), followed by Africa (23%) and the Western Pacific Region (18%) [4].

The DRC has a high burden of tuberculosis, with an estimated incidence rate of 318 per 100,000 people. It ranks among the 22 most affected countries worldwide, fifth in Africa and 11th globally [5]. The country accounts for almost 3% of all reported global TB cases, ranking among the eight countries that together contribute to more than two-thirds of the world's TB burden. The situation is further complicated by the dual threat of HIV/TB coinfection and drug-resistant TB, placing it among the WHO's top ten priority countries for TB control [6]. Despite the implementation of TB control strategies, the Democratic Republic of the Congo, like most African countries, faces enormous challenges in the fight against tuberculosis [7], including underreporting of cases, high mortality rates among vulnerable groups, and the high prevalence of TB/HIV coinfection [8], the logistical challenges in expanding the coverage of tuberculosis control activities, the situation of screening and diagnostic methods, which still rely on smear microscopy and have lower sensitivity than the rapid diagnostic test recommended by the WHO [9]. Despite these challenges, the treatment success rate in the DRC has evolved over time, from 88% in 2017 [10] to 95% by 2021 [11]. These results highlight disparities in outcomes across different health zones in the country.

The PNLT 2022 report underscores ongoing disparities in tuberculosis treatment outcomes, suggesting challenges in patient management. Despite a target of successfully treating 90% of notified TB cases, the data from Kisangani in 2018, where 1064 new cases and 52 relapses were reported among 1,068,315 residents (equivalent to 99.59 new cases and 4.8 relapses per 100,000), indicate a significant gap between the target and reality [12]. Studies conducted in Kisangani, DRC, shed light on the challenges associated with tuberculosis and HIV co-infection. MUSAFIRI *et al.* (2010) observed that TB patients co-infected with HIV experienced frequent treatment relapses and had poor knowledge of TB symptoms [11]. Separately, the research by Kabudri *et al.* (2007-2016) indicated a TB recurrence rate varying from 3.65% to

9.6% in the city's treatment centers, averaging around 7.3%. These authors attributed this frequent recurrence to a combination of factors such as high population density in socio-economically disadvantaged areas with poor housing, widespread poverty, high HIV co-infection, limited access to health services, inadequate infrastructure and poorly defined local environmental and behavioural determinants [13]. From this perspective, the present study was conducted in Kisangani to describe the clinical, diagnostic, and evolutionary profiles of tuberculosis patients followed up at Kisangani's Tuberculosis Diagnostic and Treatment Centers. The data from this study provides a preliminary basis for a more in-depth cohort study.

2. Materials and Methods

2.1. Study Sites

This study was conducted in the city of Kisangani, the capital of Tshopo Province in the northeastern Democratic Republic of Congo, covering an area of 1910 km^2. The city comprises six urban communes (Makiso-Kisangani, Kabondo, Mangobo, Tshopo, and Lubunga). Kisangani's health infrastructure includes five health zones (Makiso-Kisangani, Kabondo, Mangobo, Tshopo, and Lubunga), 89 health areas, and 110 integrated health facilities, along with private medical centers and training institutions. For tuberculosis control, the city has 74 treatment centers and 21 screening and treatment centers (including two with GenXpert) out of the 78 centers in Tshopo Province.

2.2. Study Design

This study employed a retrospective cross-sectional design, analyzing data from patients diagnosed with and treated for drug-sensitive tuberculosis in Kisangani's CDTs between January 2020 and June 2023. The study population included individuals aged 15 years and older who were followed up during treatment. All available patient records from the five health zones of Kisangani were included.

2.3. Sample Size

The sample size consisted of 1204 tuberculosis patients followed up in the CDTs of the five health zones of Kisangani city.

2.4. Sampling Technique

In order to obtain the best results and enable the analysis of specific subgroups, we conducted an exhaustive data collection in all the diagnostic and treatment centers of the five health zones in the city of Kisangani. This approach aimed to capture all eligible cases within the study period, minimizing selection bias. After initial data collection, records of 2008 tuberculosis patients followed up in the CDTs from January 2020 to June 2023 were recorded. Manual sorting was then rigorously performed to ensure adherence to the inclusion criteria. This led to the exclusion of 643 records that did not include the variables of interest. In accordance with the inclusion criteria, focusing on adults, 161 records of patients aged

between 1 and 15 years were not included in this study. This meticulous process led to the selection of a final sample of 1204 patients.

The inclusion criteria were as follows: tuberculosis patients aged over 15 years who were receiving treatment during the study period and whose sociodemographic and therapeutic data were complete.

The study excluded patients based on the following criteria: i) unknown TB laboratory results (to ensure accurate diagnosis), ii) transfer to another facility (to maintain complete follow-up within our sites), iii) confirmed multidrug-resistant (MDR) or extensively drug-resistant (XDR) tuberculosis (as the focus was drug-sensitive TB), and iv) age younger than 16 years (to concentrate on the adult population).

Sampling Approach and Participant Selection

The selection of participants for this retrospective study followed a rigorous process, illustrated by the attached flow chart (Figure 1). Initially, 2465 records of potentially eligible patients, registered at the Diagnostic and Treatment Centers (CDTs) in Kisangani between January 2020 and June 2023, were identified.

A pre-selection of records was done at the CDTs to retain documents with complete data, and patients were followed up on during the study period.

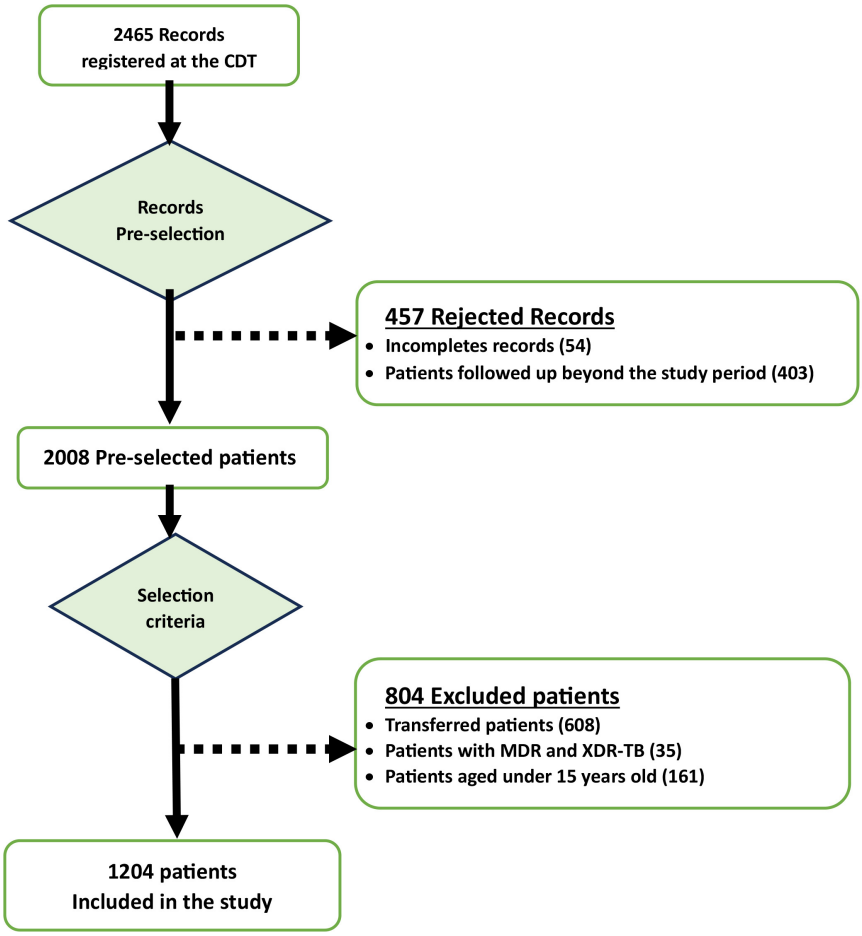

Figure 1. Flow chart of participant inclusion in the study.

Overall, 457 (18.5%) incomplete files were excluded from the study, either because of a lack of information relating to the relevant data in the study (54, *i.e.* 2.2%), or because the period during which they were managed did not correspond to the study period, which was intended to consider only patients whose follow-up time was fully included in this period (403, *i.e.* 16,3%).

Following this initial pre-selection stage, 2008 patients records were retained for further evaluation according to the predefined selection criteria.

The inclusion and exclusion criteria resulted in the removal of 804 more patients. This was due to: (i) patient transfer to other facilities (to ensure consistent follow-up in the studied Kisangani CDTs and avoid bias), (ii) presence of MDR/XDR-TB (as these require separate analysis), and (iii) age under 15 years (to focus on the adult population).

Following a rigorous selection process, the final analysis included 1204 patients. This comprehensive data collection across all Kisangani CDTs, combined with strict inclusion/exclusion criteria, aimed to achieve a representative sample of drug-sensitive TB patients followed up in the region during the study, ensuring data quality and relevance.

2.5. Diagnostic Criteria

The CDTs used the diagnostic criteria according to PATI6 to diagnose TB [14].

- **Bacteriologically confirmed TB**: Defined by at least one positive sputum smear out of two samples, regardless of HIV status, or any biological sample positive by microscopy, molecular test, and/or culture.
- **Clinically diagnosed TB (TB/C):**

- For suspected smear-negative pulmonary TB in HIV-negative individuals;
- Suspected smear-negative pulmonary TB in HIV-positive individuals;
- Clinical diagnosis can also be based on strong suspicion from chest X-rays without bacteriological confirmation.

2.6. Data Collection

This was a document review of tuberculosis patient files, including treatment records, laboratory registers and tuberculosis notification registers at the CDTs in the city of Kisangani. Data were collected using a form developed with KoboToolbox.

Data quality was ensured through several validation steps: i) double data entry on 10% of records with electronic comparison for discrepancies, ii) resolution of discrepancies by the principal investigator using original documents, iii) regular supervision of data collectors for protocol adherence and problem clarification, and iv) data validation checks including range and consistency checks, and identification/correction of missing data and outliers using patient records. Analyzed variables covered i) clinical and diagnostic profiles (age, sex, consultation reason, admission diagnosis, patient category, comorbidities) and ii) evolutionary profiles (DOTS, treatment completion, outcomes, success, cause of death, biological monitoring).

2.7. Statistical Analysis

All data collected via Kobotoolbox (Kobocollect) software and processed via Excel 19 were analyzed via Stata 13.1. To describe the clinical, diagnostic and evolutionary profiles, we used proportions, with their 95% confidence intervals, for the qualitative variables and means with their standard deviations for the quantitative variables.

Ethical considerations

Approval for the study was obtained from the ethics committee of the Faculty of Medicine and Pharmacy of the University of Kisangani, whereas authorization to conduct this study was obtained from the Provincial Health Division of Tshopo before data collection in the five health zones of the city of Kisangani. Anonymity and confidentiality were guaranteed.

3. Results

3.1. Clinical and Diagnostic Profiles of Tuberculosis Patients

The clinical and diagnostic profiles of the tuberculosis patients included in the study can be found in Table 1.

An analysis of the data in Table 1 highlights the predominance of pulmonary tuberculosis among patients who were predominantly young adults and male, with a mean age of 39.4 ± 16.1 years, and who presented with the classic triad of tuberculosis symptoms (cough, fever, night sweats). In terms of comorbidities, HIV/AIDS was the most frequently identified coinfection. The underreporting of HIV cases can be attributed to a lack of adequate screening, given that nearly half of the tuberculosis patients were not tested.

3.2. Evolutionary Profile

The data in Table 2 demonstrates a high level of treatment adherence, with most patients completing their treatment as prescribed. The overall treatment success rate was 95.51%. Among those who did not succeed in treatment, nearly 75% of deaths were attributed to tuberculosis.

Table 1. Clinical and diagnostic findings in the study population.

Variables	Modalities	Health Zones					Sample size N = 1204	% [IC 95%]
		Kabondo (284) % [IC 95%]	Lubunga (114) % [IC 95%]	Mangobo (211) % [IC 95%]	Makiso (243) % [IC 95%]	Tshopo (352) % [IC 95%]		
Age of patients (years)	Mean ± SD	38.5 ± 15.3	42.5 ± 16.9	37.7 ± 15.9	39.3 ± 15.6	40.2 ± 16.6	39.4 ± 16.1	
Age range % ($IC_{95\%}$)	16 - 25 years	25.70 [20.6; 30.8]	19.30 [11.9; 26.7]	28.91 [22.8; 35.0]	22.22 [17.0; 27.4]	24.15 [19.7; 28.6]	295	24.5 [19.3, 29.7]
	26 - 35 years	22.89 [17.9; 27.9]	22.81 [15.0; 30.6]	24.64 [18.8; 30.5]	25.93 [20.5; 31.4]	21.59 [17.3; 25.9]	282	23.42 [18.1, 28.7]
	36 - 45 years	19.37 [14.7; 24.0]	14.04 [7.7; 20.4]	17.06 [12.0; 22.1]	19.75 [14.8; 24.7]	20.45 [16.3; 24.6]	227	18.85 [13.9, 23.8]

Continued

	More than 45 years	32.04 [26.7; 37.4]	43.86 [34.5; 53.2]	29.38 [23.2; 35.6]	32.10 [26.4; 37.8]	33.81 [29.0; 38.6]	400	33.22 [28.4, 38.0]
Sex % ($IC_{95\%}$)	Masculine	61.97 [56.2; 67.8]	67.54 [58.5; 76.6]	69.67 [63.3; 76.0]	66.67 [60.6; 72.8]	60.51 [55.2; 65.8]	775	64.37 [61.6, 67.2]
	Feminine	38.03 [32.2; 43.8]	32.46 [23.4; 41.5]	30.33 [24.0; 36.7]	33.33 [27.2; 39.4]	39.49 [34.2; 44.8]	429	35.63 [32.8, 38.4]
Reason for consultation % ($IC_{95\%}$)	Cough, fever, night sweats	73.24 [67.8; 78.7]	89.47 [83.1; 95.8]	63.03 [56.6; 69.5]	55.97 [49.6; 62.3]	78.69 [74.4; 83.0]	856	71.09 [68.4, 73.8]
	3A	26.06 [20.9; 31.2]	7.89 [3.0; 12.8]	35.07 [28.7; 41.5]	43.62 [37.4; 49.9]	20.17 [16.0; 24.4]	334	27.74 [24.9, 30.6]
	others	0.35 [0.0; 1.0]	2.63 [0.0; 5.6]	1.89 [0.0; 4.1]	0.41 [0.0; 1.2]	1.14 [0.0; 2.4]	14	1.16 [0.6, 1.7]
Diagnosis at admission % ($IC_{95\%}$)	TP+	71.48 [66.0; 77.0]	46.12 [36.9; 55.4]	65.88 [59.5; 72.2]	51.03 [44.7; 57.4]	66.48 [61.4; 71.6]	756	62.79 [59.9, 65.7]
	TP-	28.52 [23.0; 34.0]	44.74 [35.5; 54.0]	30.33 [24.0; 36.7]	45.27 [39.0; 51.6]	27.27 [22.7; 31.8]	402	33.39 [30.1, 36.7]
	EPT	0.00	6.14 [1.6; 10.7]	3.79 [1.1; 6.5]	3.70 [1.1; 6.3]	6.25 [3.5; 9.0]	46	3.82 [2.7, 4.9]
Patient category	New patient	96.13 [93.9; 98.4]	94.74 [90.3; 99.2]	95.73 [92.9; 98.6]	96.71 [94.7; 98.7]	95.17 [92.8; 97.5]	1153	95.76 [94.7, 96.8]
	Retreatment case	3.87 [1.6; 6.1]	5.26 [0.8; 9.7]	4.27 [1.4; 7.1]	3.29 [1.3; 5.3]	4.83 [2.5; 7.2]	51	4.24 [3.1, 5.4]
HIV Test realized	Yes	44.72 [39.0; 50.4]	7.89 [3.0; 12.8]	58.29 [51.8; 64.8]	30.45 [24.8; 36.1]	55.68 [50.3; 61.0]	529	43.94 [41.1, 46.8]
	No	55.28 [49.6; 61.0]	92.11 [87.2; 97.0]	41.71 [35.2; 48.2]	69.55 [63.9; 75.2]	44.32 [39.0; 49.6]	675	56.06 [53.2, 58.9]
Type of comorbidity	HIV/AIDS	4.22 [1.8; 6.6]	0.87 [0.0; 2.5]	0	11.52 [7.2; 15.8]	10.23 [6.9; 13.6]	77	3.74 [2.9, 4.6]
	HTA	0	0	0	0.41 [0.0; 1.2]	0.57 [0.0; 1.6]	3	0.25 [0.0, 0.5]
	Diabetes	0	0	0	0.82 [0.0; 2.0]	0.28 [0.0; 0.8]	3	0.25 [0.0, 0.5]
	Not specified	0	0	0.47 [0.0; 1.3]	0	0	1	0.08 [0.0; 0.2]

Table 2. Distribution of cases based on patient evolution.

Variables	Modalities	Health Zones					Sample size N = 1204	% **[IC 95%]**
		Kabondo (284) % **[IC 95%]**	Lubunga (114) % **[IC 95%]**	Mangobo (211) % **[IC 95%]**	Makiso (243) % **[IC 95%]**	Tshopo (352) % **[IC 95%]**		
TDO approach followed	Yes	100.00	100.00	100.00	93.00 [89.3; 96.7]	97.74 [95.9; 99.6]	1179	97.92 [97.0, 98.8]
	No	0	0	0	7.00 [3.3; 10.7]	2.27 [0.4; 4.1]	25	2.08 [1.2, 3.0]
Treatment competed on time	Yes	97.89 [95.8; 99.9]	100.00	98.58 [96.8; 100.0]	89.51 [85.1; 93.9]	93.47 [90.8; 96.2]	1147	95.27 [94.0, 96.6]

Continued

	No	2.11	0.00	1.42	10.29	6.53	57	4.73 [3.4, 6.0]
Therapeutic outcomes	Cured	69.37 [63.8; 74.9]	49.12 [39.8; 58.4]	65.40 [59.1; 71.7]	50.62 [44.3; 56.9]	63.35 [58.3; 68.4]	737	61.21 [57.6, 64.8]
	Treatment completed	28.52 [23.3; 33.7]	50.88 [41.6; 60.2]	33.18 [27.0; 39.4]	39.51 [33.4; 45.6]	30.68 [26.0; 35.4]	413	34.30 [30.9, 37.7]
	Lost of followed-up	0.00	0.00	0.00	5.35 [2.3; 8.4]	0.85 [0.0; 2.0]	16	1.33 [0.7, 1.9]
	Died	2.11 [0.1; 4.2]	0.00	1.42 [0.0; 3.2]	4.53 [1.8; 7.3]	5.11 [2.8; 7.4]	38	3.16 [2.2, 4.2]
Treatment success	Yes	97.89 [95.8; 99.9]	100.00	98.58 [96.8; 100.0]	90.12 [85.8; 94.4]	94.03 [91.5; 96.6]	1150	95.51 [94.3, 96.7]
	No	2.11 [0.1; 4.2]	0.00	1.42 [0.0; 3.2]	9.88 [5.6; 14.2]	5.97 [3.4; 8.5]	54	4.49 [3.3, 5.7]
Causes of death during treatment								
	TB related death	2.11 [0.1; 4.2]	3.51 [0.0; 7.4]	1.42 [0.0; 3.2]	3.70 [1.1; 6.3]	1.42 [0.0; 3.2]	27	2.24 [1.4; 3.1]
	Death related to comorbidity	1.06 [0.0; 2.5]	0.89 [0.0; 2.6]	0.95 [0.0; 2.7]	0.00	0.85 [0.0; 2.0]	9	0.75 [0.3; 1.2]
	Other causes	0.00	0.89 [0.0; 2.6]	0.00	0.41 [0.0; 1.2]	0.00	2	0.17 [0.0; 0.4]
Biological follow-up	Yes	69;37 [63.8; 74.9]	49.12 [39.8; 58.4]	65.40 [59.1; 71.7]	50.62 [44.3; 56.9]	64.49 [59.5; 69.5]	741	61.54 [58.0, 65.1]
	No	30.63 [25.1; 36.2]	50.88 [41.6; 60.2]	34.59 [28.3; 40.9]	49.38 [43.1; 55.7]	35.51 [30.5; 40.5]	463	38.46 [34.9, 42.0]

4. Discussion

This study examined the profile of tuberculosis patients followed up in the CDT of Kisangani city. The results revealed that the majority of patients were young adult males, with a mean age of 39.4 ± 16.1 years, who were primarily suffering from pulmonary tuberculosis and were often coinfected with HIV. Despite a high treatment adherence rate and a treatment success rate of 95.51%, tuberculosis remains a significant cause of death among patients with comorbidities. In addition, statistically significant variations were observed in the clinical presentation of tuberculosis upon admission across the different health zones of Kisangani ($\chi^2(8) = 52.3604$, $p < 0.05$), as well as in the documented prevalence of comorbidities among these zones.

The higher occurrence of classic tuberculosis symptoms in predominantly rural areas could be attributed to specific bacterial strains and living conditions, delayed diagnosis due to limited access to care, varying clinical suspicion among healthcare professionals, a lack of resources to identify unusual forms, and uneven rates of co-infections like HIV across zones. Analyzing the clinical, radiological, and evolutionary profiles of pulmonary tuberculosis in elderly individuals, Bouytse K. *et*

al. concluded that older adults with bacteriologically confirmed pulmonary tuberculosis (BCPTB) presented with an atypical clinical picture, leading to delayed diagnosis; frequently accompanied by comorbidities (diabetes, heart disease) [15].

Significant inter-zonal differences were also evident in the therapeutic success rates. The overall therapeutic success rate for tuberculosis in Kisangani is high (95.51%), with Lubunga and Kabondo leading, likely due to the effective implementation of DOTS. This success could be attributed to the quality of the TB control program, which adheres to guidelines and utilizes the DOTS approach, access to care, and patient characteristics.

The mean age of 39.4 years observed in our tuberculosis patient cohort in Kisangani is notably higher than the mean ages reported in previous studies conducted in Senegal (35.5 years) [16] and Tunisia (36.02 years) [17]. This relatively advanced age could indicate a greater vulnerability to tuberculosis within the Kisangani population due to factors such as potentially poorer living conditions, a naturally weakening immune system associated with age, and the increased acquisition of comorbidities like HIV, diabetes, and hypertension.

In this study, the majority of patients (71.09%) presented with the three cardinal symptoms of tuberculosis (fever, cough, night sweats), aligning with established literature on typical TB presentation. However, this proportion is higher than that reported by B.H. Mbatchou Ngahane *et al.* [18]. This discrepancy might suggest variations in the epidemiological profiles of the study populations, potentially reflecting differences in the timing of diagnosis, access to healthcare, or even subtle variations in the circulating M. tuberculosis strains and their associated clinical manifestations between the study locations.

The results of this study are situated in a complex epidemiological context, marked by a high prevalence of HIV-tuberculosis coinfection in Africa and particularly in the DRC. This coinfection, recognized as a major risk factor for treatment failure, has been identified in studies by Mébiny-Essoh *et al.* [19] and Fortes Déguénonvo L. *et al.* [20].

Furthermore, a retrospective cohort study conducted by Izudi J in Uganda highlighted a negative association between HIV coinfection and tuberculosis treatment success (HR 0.88 95% CI 0.82 - 0.95) [21]. These results are consistent with those of our study and reinforce the idea that HIV coinfection is an independent risk factor for treatment failure. This assertion is complemented by the study conducted by Mamadou *et al.* [22], which revealed a treatment success rate (81.28%) associated with a high mortality rate (10.42%), of which 40.4% of deaths occurred in patients coinfected with tuberculosis and HIV.

The results of this study present a treatment success rate (95.51%) that not only exceeded the WHO target but also reached the target set for 2025 (greater than 90%). These positive results are attributable to the efforts of the National Tuberculosis Control Program, particularly in early detection, implementation, and follow-up of patients with tuberculosis. Numerous studies have demonstrated the effectiveness of the current treatment regimen for drug-susceptible tuberculosis. Indeed, the majority of patients treated for six months recover completely without

complications or disease recurrence [23].

In contrast to our encouraging results, other studies conducted in sub-Saharan Africa reported treatment success rates below the target set by the WHO, highlighting the complexity of the situation and the existence of varied local contexts [23]. Torres, NMC *et al.* highlighted that despite significant progress in the fight against tuberculosis, global treatment success rates do not fully meet the target set. The authors attributed this situation to biases in case notifications and difficulties in managing tuberculosis patients, particularly in low-resource countries [24], which could be the case in the Democratic Republic of the Congo.

5. Conclusion

Despite an overall high tuberculosis treatment success rate in Kisangani, notable differences exist between health zones, suggesting potential issues in care management. The National Tuberculosis Control Programme should: i) increase community awareness of early detection, including through the use of community-based organisations; ii) improve the capacity of front-line staff to deal with atypical clinical presentations; and iii) extend HIV testing to all TB patients. Future research should examine the causes of treatment failure and inter-zonal disparities in treatment success.

Limitations

The retrospective nature of our study design-imposed limitations on our analysis, as we relied on existing data that may have been incomplete or of variable quality. Disruptions in the reagent supply, particularly for HIV diagnosis, further hinder our ability to assess the impact of HIV coinfection on tuberculosis outcomes. To address these limitations, we recommend conducting prospective studies that would facilitate rigorous and systematic data collection. To address these limitations, we will design a prospective study with rigorous and systematic data collection and more options for analysis of risk factors for treatment failure.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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