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Determinants of Treatment Delay among Pulmonary Tuberculosis Patients: A Cross-Sectional Study in Six Provinces of the DRC

Philippe Ngwala Lukanu[1,2], Papy Lusameso[1], Angel Matota Shoma[1], Jeanne Tshibungu[1], Isabelle Kufundu[1], Patrick Kinkani[1], Matthieu Ntumba[1], Jean-Marie Kanyonga[1], Max Lomba Ngoma[1], Nicolas Mihuhi[1], Jean Pierre Lubaki Fina[2], Albert Ntumba Kalonji[1], Aliocha Natuhoyila Nkodila[1,2]

[1]Family Medicine Department, School of Medicine, Protestant University of Congo, Lubumbashi, DRC
[2]Pirmary Health Care in Rural Area, SANRU, Kinshasa, DRC
Email: phlukanu@yahoo.fr

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Abstract

Background: A late diagnosis of tuberculosis has serious consequences for the spread and outcome of the disease. Delayed diagnosis is an important indicator of the quality of a tuberculosis control program. The aim of this study is to identify the determinants of delay in tuberculosis treatment for patients with positive pulmonary tuberculosis followed at TB diagnosis and treatment health centers in Democratic Republic of the Congo (DRC). **Methods:** A facility-based cross-sectional study was designed to analyze data from a representative sample of patients with positive pulmonary tuberculosis followed at Tuberculosis Diagnosis and Treatment Health Centers (TBDTHC) in 6 provinces of the DRC. We used logistic regression to identify the determinants of the delay in tuberculosis treatment. The level of statistical significance was $p < 0.05$. **Results:** The TB Local Network (TBLON) project recruited a total of 1365 patients in 6 TB management provinces. More than half (58.7%) of the participants were male, and 45.8% were aged between 19 and 39. About 2.9% were HIV positive and 8.6% MDR-TB. The management of more than half of the patients (53.3%) took more than 2 days. Determinants of delay in treatment were patients' formal and informal occupations (aOR: 4.87, 95% CI: 3.19 - 7.45; aOR: 1.90, 95% CI: 1.23 - 2.93); single and married status (aOR: 3.75, 95% CI: 1.58 - 8.93; aOR: 6.04, 95% CI: 3.30 - 11.05); provenance from a public institution (aOR: 7.79 IC 95%: 2.55 - 10.83); and TBMR status (aOR: 3.89, 95% CI: 2.28 - 6.66). **Conclusion:** This study highlights the persistence of treatment

delays among TB patients in the DRC and identifies key sociodemographic and systemic determinants, including marital status, occupation, type of health facility, and MDR-TB status. Addressing these delays will require strengthened referral systems, improved MDR-TB diagnostic protocols, and targeted community awareness interventions to ensure early treatment initiation and limit disease transmission.

Keywords

Tuberculosis, Treatment, Delay, Democratic Republic of Congo

1. Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the leading causes of morbidity and mortality worldwide. One third of the world's population is infected with tuberculosis bacillus. Every day, 25,000 people develop active tuberculosis, and 5000 die from the disease [1] [2]. The tuberculosis bacillus infects one third of the world's population. Therefore, limiting the bacillus's transmission in these countries is the only way to control this epidemic. The primary objective of tuberculosis management program is to prevent further transmission of the disease through early diagnosis and treatment [3] [4]. Effective treatment is a foundational aspect of achieving TB eradication by the target date. Delays in treatment can adversely affect the health of TB patients and their families, negatively impact treatment outcomes, and contribute to the ongoing spread of tuberculosis [5] [6]. Patients with untreated TB pose a risk to the community, particularly to vulnerable groups, such as children under five. Numerous studies have analyzed delays in initiating tuberculosis treatment. They have shown that delays in starting TB patients on treatment exist in most countries. Treatment implemented according to *Mycobacterium tuberculosis* drug susceptibility test results considerably reduces the frequency of coughing and the number of bacteria in sputum. Patients following effective treatment are generally considered non-infectious within a few days or weeks [4]. The aim of this study is to determine factors associated with delay in tuberculosis treatment among patients followed at TB Diagnosis and Treatment Health Centers (TBDTHC) in six provinces in the RDC.

2. Patients and Methods

2.1. Study Design

We carried out a facility-based cross-sectional study among patients with positive pulmonary tuberculosis followed in 6 provinces in the Democratic Republic of the Congo (Kasai Oriental, Kasai Central, Lomami, Sankuru, Tanganyika, and Sud Kivu).

2.2. Study Population

The target population comprised patients with positive pulmonary tuberculosis

registered in six provinces of the Democratic Republic of Congo. About 1365 patients were registered in 2021-2022 at the TB Diagnosis and Treatment Health Centre (TBDTHC) in these six provinces in the RDC. The inclusion criteria were all files from patients with a positive pulmonary tuberculosis diagnosis during the study period without consideration of age or sex. Files from patients with negative pulmonary tuberculosis or extrapulmonary tuberculosis were excluded from the analysis.

The sample selection results in a two-stage sampling process. The first stage comprised the selection of TB Diagnosis and Treatment Health centers (TBDTHC) in the six selected provinces in the RDC. The number of TB Diagnosis and Treatment Health centers (TBDTHC) to be selected in the study was calculated using the SSPropor software with the formula DEFF = 1 + δ (n − 1) and δ = interclass correlation; n = common size of the cluster). To evaluate a combined measure (TB care time), a p-value of 50% was used with a 5% confidence level to make sure the sample accurately represents the total number of TBDTHC. The calculation resulted in a sample size of 185 TBDTHCs. The selection of the TBDTHC was done through a systematic sampling approach. It involved: 1) listing TBDTHC by province, 2) randomly ordering them, 3) applying a survey step by dividing the total number of TBDTHC by the sample size (557 total TBDTHC divided by 185 gave a survey step of 3), and 4) selecting TBDTHC based on the survey step (**Figure 1**).

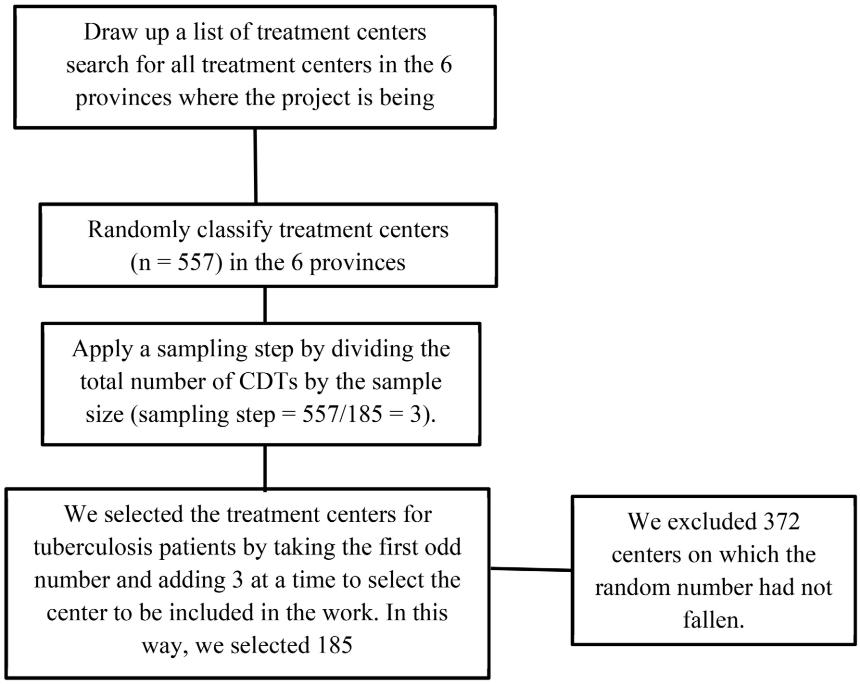

Figure 1. Flow chart for systematic treatment centers included in the study.

At the second stage, comprising the selection of patients' files, all the files from registered patients in 2021-2022 for positive pulmonary tuberculosis were included in the study.

2.3. Data Collection

The outcome variable of interest for this study was the delay in treatment to start tuberculosis treatment. It was defined as the onset of treatment more than two days after the diagnosis. The independent variables assessed in the study were sociodemographic, clinical, and treatment related.

2.4. Statistical Analysis

Data was encoded, entered, verified, and cleaned using Excel 2010 and analyzed with SPSS for Windows version 24. Descriptive statistics were presented as means (with standard deviation) for normally distributed continuous variables and as medians (with interquartile range) for non-normally distributed data. Categorical variables were expressed as absolute (n) and relative frequencies. Statistical tests included the student's t-test, Mann-Whitney U test, Pearson's chi-square, or Fisher's exact test for comparing means, medians, and proportions between groups. The Kruskal-Wallis test was used to compare median treatment times across more than three groups. Logistic regression was employed in a multivariate analysis to identify determinants of delay in treatment in positive pulmonary tuberculosis patients, calculating odds ratios at 95% confidence intervals. A p-value of <0.05 was considered statistically significant.

3. Results

A total of 1365 PTB registers were selected from 185 randomly chosen TBDTHC across 122 health zones in the 6 provinces involved in the TBLON project. Kasai Oriental accounted for 28% of the patients across 19 health zones; Tanganyika had 20% of the patients in 11 health zones; Sankuru had 16.3% of the patients in 16 health zones; South Kivu also had 16.3% but spread over 34 health zones; Lomami included 14% of the patients in 16 health zones; and Kasai Central covered 11% in 26 health zones (Figure 2).

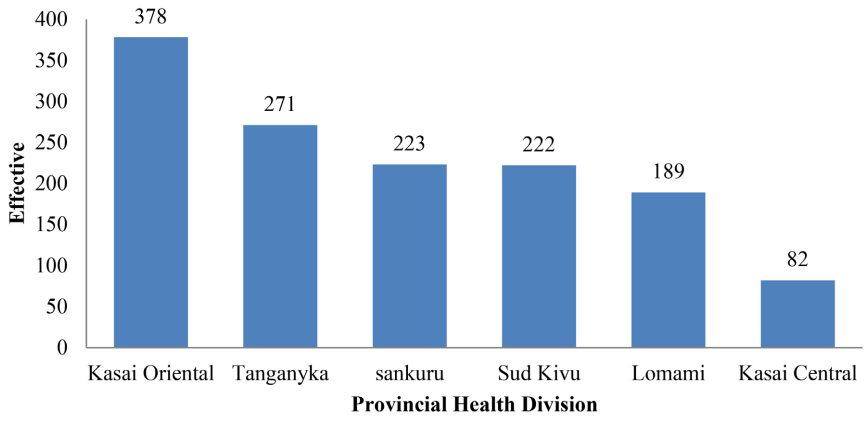

Figure 2. Distribution of TB patients in the province covered by the TBLON project.

In all provinces, men were more prevalent than women, with the 19 - 39 age group being the most affected. Community Health Workers (CHW) contributed

31% to the efforts, while the private sector contributed 2% (Table 1). The prevalence of TB/HIV co-infection was 2.5%, with the provinces of Lomami, South Kivu, and Tanganyika showing the highest rates. Sankuru province displayed an unusual pattern, as all 223 PTB registers tested negative for HIV. In 79.4% of PTB-diagnosed cases, both sputum samples tested positive, highlighting the importance of microscopic diagnosis in countries with limited resources where molecular TB testing isn't accessible (Table 2).

Table 1. Sociodemographic characteristics of the entire study population and by province.

Variable	Over all n = 1365	Kasai Central n = 82	Kasai Oriental n = 378	Lomami n = 189	Sankuru n = 223	Sud Kivu n = 222	Tanganyka n = 271	p
Gender								**<0.001**
Male	801 (58.7)	41 (50.0)	220 (58.2)	101 (53.4)	103 (46.2)	150 (67.6)	186 (68.6)	
Female	564 (41.3)	41 (50.0)	158 (41.8)	88 (46.6)	120 (53.8)	72 (32.4)	85 (31.4)	
Age								0.814
1 - 18 years	118 (8.6)	7 (8.5)	30 (7.9)	21 (11.1)	12 (5.4)	28 (12.6)	20 (7.4)	
19 - 39 years	625 (45.8)	48 (58.5)	168 (44.4)	85 (45.0)	90 (40.4)	92 (41.4)	142 (52.4)	
40 - 59 years	484 (35.5)	25 (30.5)	134 (35.4)	63 (33.3)	98 (43.9)	84 (37.8)	80 (29.5)	
≥60 years	138 (10.1)	2 (2.4)	46 (12.2)	20 (10.6)	23 (10.3)	18 (8.1)	29 (10.7)	
Occupation								**0.001**
Formel	19 (1.4)	0.0	5 (1.3)	0.0	4 (1.8)	8 (3.6)	2 (0.7)	
Informel	513 (37.6)	0.0	240 (63.5)	0.0	114 (51.1)	96 (43.2)	63 (23.2)	
Unemployed	158 (11.6)	0.0	41 (10.8)	0.0	105 (47.1)	4 (1.8)	8 (3.0)	
Marital Status								**<0.001**
Single	33 (2.4)	0.0	18 (4.8)	0.0	0.0	15 (6.8)	0.0	
Married	131 (9.6)	0.0	42 (11.1)	0.0	0.0	89 (40.1)	0.0	
Divorced	115 (8.4)	0.0	114 (30.2)	0.0	0.0	1 (0.5)	0.0	
Provenance								0.025
Self consultation	811 (59.4)	64 (78.0)	205 (54.2)	134 (70.9)	116 (52.0)	107 (48.2)	185 (68.3)	
CHW Oriented	422 (30.9)	18 (22.0)	147 (38.9)	55 (29.1)	87 (39.0)	87 (39.2)	28 (10.3)	
Public health facility	105 (7.7)	0.0	0.0	0.0	20 (9.0)	28 (12.6)	57 (21.0)	
Private health facility	27 (2.0)	0.0	26 (6.9)	0.0	0.0	0.0	1 (0.4)	
Special Population								**<0.001**
Prisoners	28 (2.1)	0	2 (0.5)	0.0	0.0	0.0	26 (9.6)	
Minors	44 (3.2)	0	18 (4.8)	0.0	3 (1.3)	12 (5.4)	11 (4.1)	
Contact Case	230 (16.8)	9 (11.0)	157 (41.5)	0.0	0.0	46 (20.7)	18 (6.6)	
Displaced population/refugees	94 (6.9)	0	92 (24.3)	0.0	0.0	0.0	2 (0.7)	

Table 2. Clinical characteristics of the entire population and by province.

Variable	Over all n = 1365	Kasai Central n = 82	Kasai Oriental n = 378	Lomami n = 189	Sankuru n = 223	Sud Kivu n = 222	Tanganyka n = 271	p
HIV Status								**<0.001**
Positive	34 (2.5)	1 (1.2)	7 (1.9)	6 (3.2)	0	10 (4.5)	10 (3.7)	
Negative	1004 (73.6)	43 (52.4)	166 (43.9)	158 (83.6)	215 (96.4)	162 (73.0)	260 (95.9)	
Indeterminate	327 (24.0)	38 (46.3)	205 (54.2)	25 (13.2)	8 (3.6)	50 (22.5)	1 (0.4)	
TB Patient								**<0.001**
PTB	1248 (91.4)	82 (100.0)	377 (99.7)	189 (100.0)	223 (100.0)	222 (100.0)	155 (57.2)	
Multi drugs TB resistance	117 (8.6)	0	1 (0.3)	0.0	0.0	0.0	116 (42.8)	
Positive lab results								**<0.001**
Positive to sample 1	257 (18.8)	5 (6.1)	24 (6.3)	189 (100.0)	14 (6.3)	3 (1.4)	22 (8.1)	
Positive to sample 2	24 (1.8)	5 (6.1)	7 (1.9)	0.0	5 (2.2)	7 (3.2)	0.0	
Positive for all 2 samples	1084 (79.4)	72 (87.8)	347 (91.8)	0.0	204 (91.4)	212 (95.5)	249 (91.9)	
Treatment Issue								**0.003**
Healed	1016 (74.4)	81 (98.8)	324 (85.7)	183 (96.8)	0.0	207 (93.2)	221 (81.5)	
Deceased	39 (2.9)	1 (1.2)	7 (1.9)	1 (0.5)	0.0	5 (2.3)	25 (9.2)	
Failure	8 (0.6)	0.0	0.0	0.0	0.0	1 (0.5)	7 (2.6)	
Indeterminate	279 (20.4)	0.0	41 (10.8)	5 (2.6)	223 (100.0)	4 (1.8)	6 (2.2)	
Completed Treatment	23 (1.7)	0.0	6 (1.6)	0.0	0.0	5 (2.3)	12 (4.4)	

3.1. Median Treatment Time

Figure 3 illustrating the median time for treatment showed that overall, this treatment time was 2 days (IQR: 1 - 3). This median time was higher for patients diagnosed in Lomami province, with a statistically significant difference ($p < 0.001$).

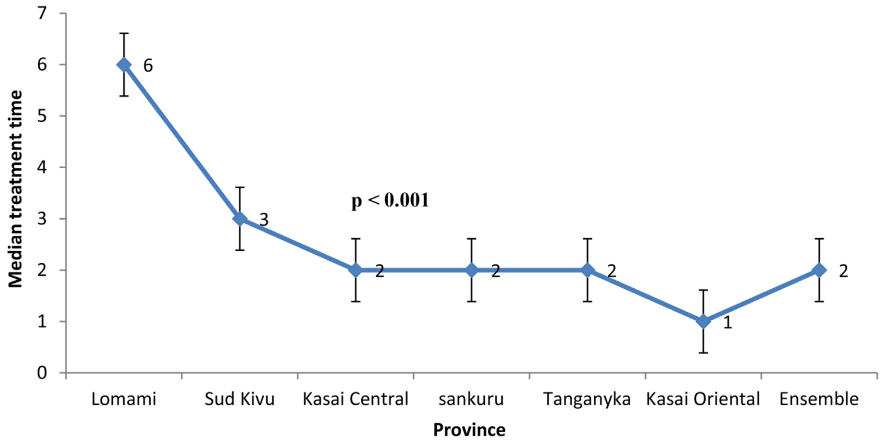

Figure 3. Median treatment time for all and by province.

It was noted that patients with treatment failure and death had a significantly higher median time to treatment ($p < 0.001$) (Figure 4).

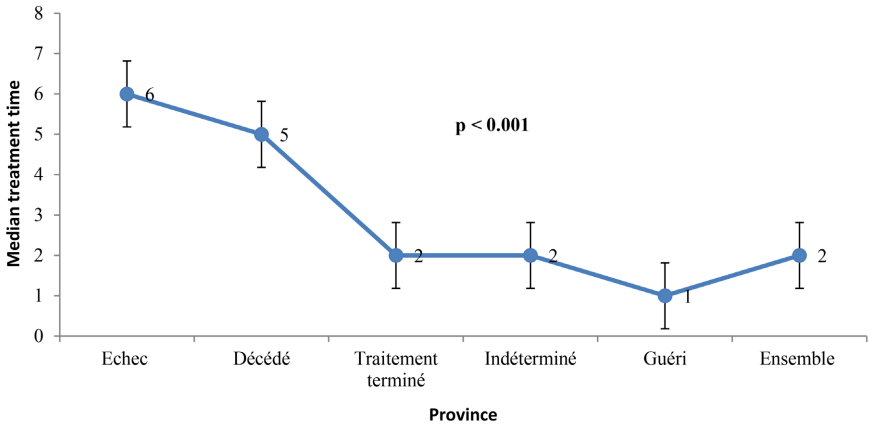

Figure 4. Median time to treatment as a function of patient outcome.

3.2. The Prevalence of Delays in Tuberculosis Treatment

The majority of PTB registers began TB treatment out of the recommended timeframe of 0 - 1 day (Figure 5). When looking at the data by region, Kasai Central, Sankuru, and Kasai Oriental provinces demonstrated strong performance, with rates of 89%, 75.8%, and 67.5%, respectively (Figure 6).

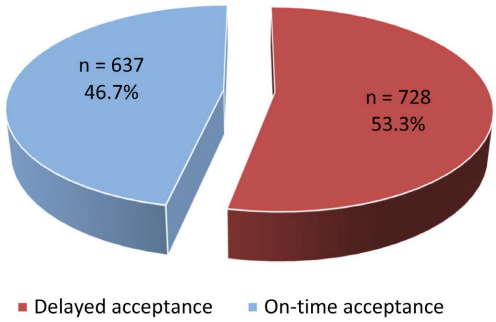

Figure 5. Patients treatment deadline.

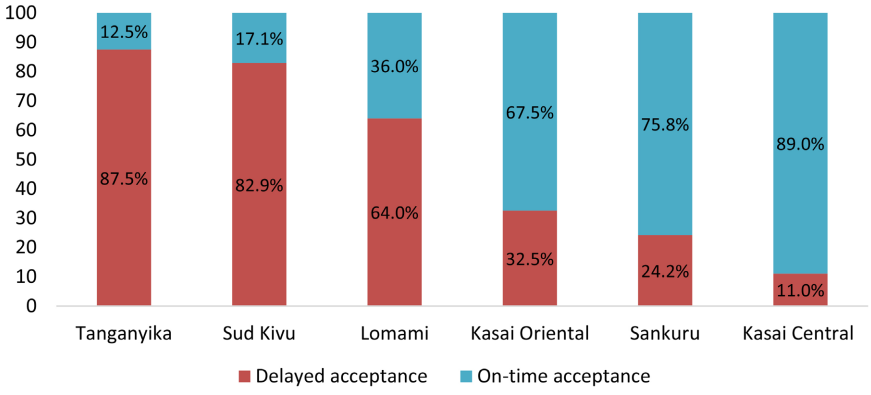

Figure 6. Sociodemographic characteristics and treatment deadline.

3.3. Determinants of Delay in Tuberculosis Treatment

Associated factors with delay in tuberculosis treatment were unemployment, informal occupation, single or married participants, receiving care from a public health facility, and having multidrug-resistant PTB (Table 3).

Table 3. Associated factors with treatment delay among PTB patients.

Facteur associé	Univariate analysis		Multivariate analysis	
	p	cOR (95% CI)	p	aOR (95% CI)
Sexe				
Female		1		1
Male	**0.012**	1.32 (1.06 - 1.64)	0.700	1.05 (0.83 - 1.33)
Occupation				
Unemployed		1		1
Formal	**<0.001**	3.78 (2.60 - 5.48)	**<0.001**	4.87 (3.19 - 7.45)
Informal	**<0.001**	2.23 (1.52 - 3.26)	**0.004**	1.90 (1.23 - 2.93)
Marital Status				
Divorce		1		1
Single	**0.004**	3.24 (1.46 - 7.22)	**0.003**	3.75 (1.58 - 8.93)
Married	**<0.001**	5.36 (3.10 - 9.24)	**<0.001**	6.04 (3.30 - 11.05)
Provenance				
Private health facility		1		1
CHW Oriented Patients	**0.010**	3.16 (1.32 - 7.56)	0.126	2.21 (0.80 - 6.11)
Self consultation	**0.014**	3.02 (1.25 - 7.30)	0.066	2.62 (0.94 - 7.34)
Public health facility	**<0.001**	8.25 (3.14 - 21.68)	**<0.001**	7.79 (2.55 - 23.83)
Displaced/refugees		1		1
Prisoners	**0.027**	2.73 (1.12 - 6.66)	0.362	0.62 (0.22 - 1.75)
Minors	**0.002**	3.45 (1.58 - 7.51)	0.160	1.86 (0.78 - 4.43)
Contact Case	0.406	1.23 (0.76 - 1.99)	0.907	1.04 (0.57 - 1.88)
TB Patient				
PTB		1		1
Multi Drugs resistance TB	**<0.001**	4.46 (2.74 - 7.24)	**<0.001**	3.89 (2.28 - 6.66)

TB: Tuberculosis, cOR: Crude Odds Ratio, aOR: adjusted Odds Ratio.

4. Discussion

This study evaluated the delay between diagnosis and treatment initiation among tuberculosis patients in 185 TBDTHC. Most patients included in our study were adults, and most of them were men, which is consistent with other studies, notably

in Ethiopia [7] [8]. This demographic profile highlights gender disparities in access to healthcare services for tuberculosis patients, particularly in detection and treatment. The low proportion of children (9.6%) reflects persistent challenges in diagnosing TB in paediatric populations.

The average treatment duration observed in our study was 2 days. This period appears to be very short compared to most studies that have noted longer delays [8]-[10]. The difference can be explained by the fact that the DRC national TB program (NTP) has excellent program coverage, which has greatly contributed to improving access to the package of care for tuberculosis patients. This difference can also be explained by methodology; in fact, in our study we analyzed the delay between diagnosis and treatment initiation, whereas other studies evaluated the delay by considering the time interval between the start of symptoms, diagnosis and TB treatment initiation. Delay seems to be long in our study for patients with multidrug-resistant PTB (MDRPTB), which can be explained by the specific lab test to be done before MDRPTB treatment initiation.

The overall prevalence of TB-HIV co-infection in the intervention zones was 2.5%, higher in Sud Kivu, Tanganyika, and Lomami provinces. Consequently, prevalence was null in Sankuru province. This prevalence is very low by African standards. In sub-Saharan Africa (SSA), where HIV prevalence is high, the prevalence of TB/HIV co-infection varies from 16% to 80% depending on the country [11] [12]. However, in Western countries where the prevalence of HIV infection is low, the prevalence of co-infection varies from 3% to 6% [13] [14]. This low prevalence of TB-HIV co-infection could be explained by the poor diagnosis of HIV in TB patients or by problems with the supply and management of HIV diagnostic tests. In most African countries, TB diagnosis and treatment are free of charge. However, national TB control programs will only be effective if they consider TB/HIV co-infection, which includes systematic and free HIV screening, assessment of immune status, and initiation of ARV treatment when necessary. In the DRC, especially in provinces where the TB/HIV project has not been implemented, screening for HIV infection is not yet systematic due to the cost of screening borne by TB patients, although progress is being made with the establishment of a Provincial TB/HIV Surveillance and Management Committee in each province. Furthermore, the prevalence of co-infection found in most of the provinces in this study is in line with the targets of the Global Plan to Stop TB and HIV by 2030 [15], except for the provinces of South Kivu, Lomami and Tanganyika, where this prevalence is still above the overall prevalence. The persistence of TB-HIV co-infection in these provinces may be due to sexual violence resulting from inter-ethnic conflicts and wars. It was noted that HIV prevalence was zero in Sankuru province, a finding that could be linked to specific problems with data collection or screening protocols in this province. To confirm these results, it would be better to conduct a longitudinal study with a standard diagnostic method for all patients and a large sample size to boost the chance of finding a case of HIV in tuberculosis patients in Sankuru province. In our study, we found that waiting too long to start treatment was strongly linked to how serious the illness was and other related

problems [10]. In our study, we found a significant association between delayed treatment initiation and clinical severity as well as related issues. A long delay in treatment can result in severe clinical symptoms, which may lead to patient hospitalization, extensive disease progression, and ultimately death. In Guinea-Bissau [16]-[18], the proportion of clinical severity was higher among patients who had long and very long delays. In Ghana study [19], a higher risk of hospitalization for TB patients was associated with longer treatment delay. This finding aligns with studies conducted in Guinea-Bissau, Ghana, Italy [20] and Spain. The studies in Italy [21] and Spain [22] indicated that delayed TB patients initiating treatment had resulted in more severe clinical presentations and extensive disease conditions.

This study identified several determinants of delayed patient management. Among these determinants are patient occupation, whether formal or informal; single or married status; patient transfer from a private to public health facilities; and multidrug-resistant TB status.

The occupation of patients could explain the delay in treatment by several direct or indirect mechanisms: the stigmatization of patients who work. Some authors have already demonstrated that the stigma surrounding tuberculosis can discourage patients from seeking treatment [23]. Working patients often don't have the time to be aware of and follow the advice to seek treatment before the disease is diagnosed. So, it's crucial to develop strategies to raise awareness and reduce stigma among patients with either formal or informal occupations to promote early care for these patients [23].

Regarding married or single marital status in the delayed management of tuberculosis, it turns out that the delay among single people is linked to a lack of support and access to information on tuberculosis management. Consequently, the stress and responsibilities that hinder early care seeking may account for the delay in tuberculosis treatment among married individuals [24].

The process through which a public health worker refers patients for late treatment of tuberculosis remains unclear. Indeed, health workers who are unable to manage tuberculosis patients due to limited technical resources refer all their patients to higher health structures, and the impact of patients who, for one reason or another, have not presented themselves to the health system either for lack of means of transport or for some other reason. Therefore, we recommend developing a counter-referral mechanism to effectively monitor these patients [25].

Finally, we revealed that multidrug-resistant tuberculosis (MDR-TB) is a determinant of delays in the management of TB patients. Several reasons were given for this relationship: the fact that patients who have been in treatment for a long time may neglect it once they are asked to continue a new course of tuberculosis treatment. If patients no longer have the means of survival to initiate treatment, they will certainly have advanced reasons for starting TB treatment late [10].

5. Limitation of the Study

Despite the identification of determinants of delay in the management of tuber-

culosis patients, this study did not consider clinical and biological variables such as viral load, tuberculosis prior to antiretroviral treatment, sputum positivity and others. Moreover, given the cross-sectional nature of the study, it is difficult to establish the cause and effect of the determinants found in it. We need a longitudinal study to confirm or refute our determinants.

6. Conclusion

The findings of this study reveal that more than half of pulmonary TB patients experienced a delay in treatment initiation, driven by social, institutional, and clinical factors. Married and single patients, those with informal or formal employment, patients referred from private to public health facilities, and those diagnosed with MDR-TB were significantly more likely to experience delays. These results underline the need for targeted interventions, such as strengthening referral pathways, decentralizing MDR-TB diagnostic services, and enhancing patient education. Involving community health workers and improving coordination between TB diagnosis and treatment centers may help reduce delays and improve TB control outcomes in the DRC. These results underline the need for targeted interventions, such as strengthening referral pathways, decentralizing MDR-TB diagnostic services, and enhancing patient education. Involving community health workers and improving coordination between TB diagnosis and treatment centers may help reduce delays and improve TB control outcomes in the DRC.

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Author Contributions

Conceptualization, PLN. and PL; Methodology, LNP; Validation, JPFL., SA., and Z. Z.; Writing—Original Draft Preparation, LNP, NNA.; Writing—Review & Editing, ANK, JPLF; Supervision, IF, PK, MN, JMK, MLN, NM; Project Administration, JT, AMS.; Funding Acquisition, PLG.

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Data Availability

The datasets during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance to relevant guidelines and regulations.

Consent for Publication

Not Applicable.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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