Pre-treatment Loss to Follow-up in Patients with Confirmed Pulmonary Tuberculosis in Niamey, Niger

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Abstract

Aims and Scope: Pre-treatment loss to follow-up (PTLFU) represents a major problem that hinders the management of tuberculosis. This paper focuses on determining the prevalence of lost to follow-up patients diagnosed with smear-positive pulmonary tuberculosis (SPPT) who are referred to other TB screening and treatment centers (TBSTC).

Methods: This was a prospective, descriptive, and analytical study conducted over a six-month period between March and August 2019, in patients diagnosed with smear-positive pulmonary tuberculosis at NCFATRD and referred to Niamey and Tillaberi centers. A chi-square test was used with a significance level of $P \leq 0.05$.

Findings: 743 patients were diagnosed with SPPT, and 346 were referred to the TBSTC located in Niamey and Tillaberi cities. The prevalence of loss to follow-up before treatment in both Niamey and Tillaberi cities was 14.45%

(50/343). Males represented 82% (41) of the cases with a sex ratio of 4.55. The mean age of the patients was 41.04 years. Patients not attending school, as well as those with primary school education, represented the majority of cases, accounting for 30% each. The majority of PTLFU (95.66%) were new cases of TB. Nearly half (42%) of PTLFU had traveled a distance of 6 to 15 km to receive TB screening. During the phone call follow up, only 12 patients (24%) were reached, of whom 7 (14%) were deceased.

Conclusion: The prevalence of PTLFU remains high. Therefore, reinforcing the research of lost to follow-up patients is necessary to enhance tuberculosis control and management.

Background

Tuberculosis is a serious public health problem. In 2019, 7.1 million cases were reported worldwide, including 25% of cases in Africa (OMS, 2020). The main focus of the fight against tuberculosis is the detection and treatment of the contagious form, which is the most serious epidemiological form (Horo et al., 2011). Patients diagnosed with SPPT who are not under treatment represent a significant challenge in TB management (OMS, 2020). These PTLFU patients spread the disease in the community (Rao et al., 2009; Sanchez-Padilla et al., 2015), which leads to TB drug resistance (Pherson et al., 2014; PNLT, 2016) and increased mortality rates (Beena et al., 2018). Several studies conducted in Africa and Asia showed variable rates of pre-treatment loss. In a systematic review (Pherson et al., 2014) conducted in Africa, these rates varied from 6 to 38%, while in Asia, they ranged from 4 to 28%. In Niger, 11,700 cases were detected and 91% were bacilliferous (PNLT, 2017). However, 684 of 11,700 cases were considered lost to follow-up treatment, while 122 cases were not evaluated (PNLT, 2020). In the capital city of Niger, Niamey, 90% of patients with active tuberculosis have been screened by NCFATRD (PNLT, 2019). As the diagnostic and care system are decentralized, only 30% are taken care of at this center (PNLT, 2019). The goal of this study is to determine the prevalence of TB patients lost to follow-up pre-treatment among TB patients diagnosed with smear-confirmed pulmonary tuberculosis at NCFATRD and referred to Niamey and Tillaberi TBSTC.

Methods

Study Design

Lost to pre-treatment follow-up represents a significant challenge and a vital gap in the treatment of TB. Therefore, this gap supported the purpose of the study.

Study Setting

The NCFATRD served as the study setting. This is a prospective, descriptive, and analytical study conducted over a six-month period from March to August 2019.

The study population included:
- SPPT patients diagnosed at the NCFATRD who did not receive their results.
- SPPT patients diagnosed at the NCFATRD, referred to Niamey and Tillaberi TBSTCs, and voluntarily accepted to participate.

Sample Size of the Study

The sample size was comprehensive, and participants were recruited based on the order of screening at the laboratory as well as referrals to other TBSTC.

Study Procedures
Definitions of Keywords and Phrases

Lost to pre-treatment follow-up refers to dropout of patients after diagnosis but before treatment registration.

Lost to pre-diagnosis occurs when a patient is diagnosed with TB in the laboratory but does not return to get their result.

Lost to referral occurs when a TB patient, diagnosed in one center, initiates treatment but is subsequently referred to another center for ongoing treatment and fails to attend after verification.

Inclusion Criteria
- For lost to follow-up patients at the time of diagnosis, monitoring was conducted on a monthly basis using bacilloscopy reports at the laboratory level.
- For referred patients, inclusion was done by order of registration in the reference registers after obtaining informed consent.
- Cross-referrals were completed by contacting the TBSTC managers over the phone. The PTLFU were sought by phone calls and through the community relays in collaboration with the TBSTC managers.

Collection and Analysis of Data

Data collection was completed using a pre-established form. Statistical analysis was performed by R software under the R Studio version 3.6.2 interface. Differences between groups were tested using chi-square and Fisher tests. The significance threshold was set at 95% and $P \leq 0.05$.

Ethical and Deontological Aspects

This study had the approval of the National Ethics Committee for Health Research of Niger (N°056/2022/CNERS of 21/11/22) and the head of the NCFATRD department. Verbal informed consent was obtained from the patients at the time of registration at the center. Anonymity was respected during data entry and analysis.

Results

In this study, 743 cases of SPPT were detected. The study involved 346 patients distributed as follows:

- 23 patients did not receive their results (lost to follow-up): 23/346 (6.65%)
- 323 were referred to Niamey and Tillaberi centers, 296 started the treatment, and 27 did not show up at the centers after referral (lost to referral): 27/323 (8.35%). The prevalence of those lost to follow-up before treatment at the NCFATRD was 15% (Figure 1)
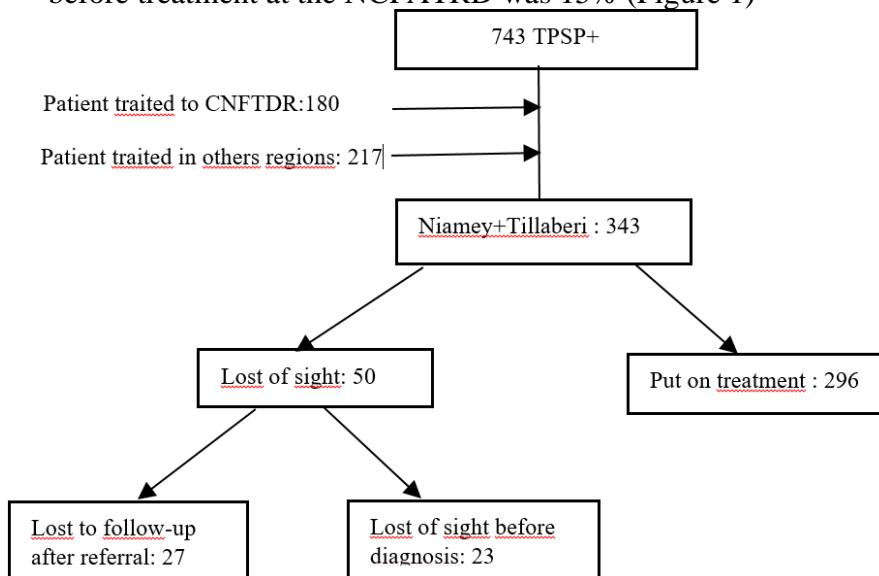

Figure 1. Patient recruitment flowchart

The majority of those lost to follow-up were male (82%). The prevalence of PTLFU was higher among the age groups of 25-34 and 35-44, with rates of 4.63% and 4.34%, respectively. The mean age of patients lost to pre-treatment follow-up was 41.04 years, ranging from 18 to 80 years.

Self-employment represented 26% among those lost to pre-treatment follow-up. Non-educated individuals and primary school students each accounted for 30% of the pre-treatment follow-up cases. Nearly half (42%) of

those lost to pre-treatment follow-up, pre-diagnosis, and referral had traveled 6 to15 km to undergo TB screening (Table 1).

Table 1. General characteristics of those lost to follow-up

Characteristics	Patients (n=50) (%)
Sex	
Female	9 (18)
Male	41 (82)
Age	
< 45	35 (70)
≥ 45	15 (30)
Educational level	
Educated	35 (70)
Unschooled	15 (30)
Region	
Niamey	38 (76)
Except Niamey	12 (24)
Type of facility	
CNFTDR	32 (64)
Public	12(23)
Private	6(13)
Distance traveled (in km)	
<5	17 (34)
5-50	23 (46)
>50	10 (20)
Reason for losing sight of no joining	
Contact unavailable	23 (61)
No contact	13 (34)
Bad contact	2 (5)

In 83% of cases, those who were lost to follow-up had only one bacilloscopy test that came back positive. In 78.26% of cases, bacilloscopy results were available within 24 to 48 hours for those lost to follow-up. During the follow-up over the phone, 38 individuals (76%) could not be reached and were considered lost to follow-up without information, while 7 (14%) were reported deceased.

Among the deceased pre-treatment lost to follow-up, the age group of 25-34 accounted for 43%, with a mean age of 52 years (ranging from 27 to 80 years). Additionally, 5 (71%) of the deceased pre-treatment lost to follow-up were male. In 61% of cases, pre-treatment lost to follow-up without information were unable to be contacted. A statistically significant difference was observed between pre-diagnosis lost to follow-up by gender and patient type (p <0.028), as well as pre-diagnosis lost to follow-up by gender and distance traveled (p =0.005) (*Table 2*).

Table 2. Characteristics of those lost to follow-up by sex

Sex	Male	Female	
Characteristics	N (%)	N (%)	
Deceased patient	2 (29)	7 (71)	*P=0.074*
Age			
< 45	30 (60)	5 (10)	*P=0.02*
≥ 45	11 (22)	4 (8)	
Type of patient			
New case	36 (72)	8 (16)	*P=0.041*
Relapse	4 (8)	1 (2)	
Recovery after abandonment	1 (2)	0 (0)	
Type of lost to follow-up			
Pre-diagnosis	21(91.3)	2(8.7)	*P=0.002*
After reference	20 (74.07)	7 (25.93)	
Distance traveled (in km)			
<5	11(22)	0	*P= 0.005*
5-50	24 (48)	5 (10)	
>50	6 (12)	4 (8)	

Discussion

The prevalence was higher in post-referral. The lost to follow-up patients were more likely to be male, married, and self-employed. Nearly three quarters of the patients were inaccessible by telephone. Also, they travelled a distance of between 6 and 15 km to be diagnosed. The mortality rate was nearly 15%.

Strengths and Weaknesses of the Study

For the first time in Niamey, this study enabled the determination,of the prevalence of pre-treatment dropouts, their characteristics, and the associated factors in the city. It will serve as a foundation for future studies. Like any other endeavour, this study had limitations, such as being conducted in only one city (Niamey). Also, the lack of available contacts for those lost to follow-up precluded interviews, thereby hindering the acquisition of patients' point of view.

The total prevalence of lost to follow-up before treatment was 15%. The study had a lower prevalence compared to the research conducted in India (Beena et al., 2018) in the city of Chennai in 2008, which reported 22.1%, and the study in Pakistan, which recorded 21.3% in the city of Quetta (Wali et al., 2017). This difference can be attributed to the smaller sample size in this study. The prevalence in this study closely mirrors that of South Africa (Botha et al., 2008), which reported 16%, and the study in Nigeria, which found a prevalence of 16.9% (Chukwu et al., 2012). This similarity may be attributed to the comparable sample sizes.

Additionally, this study also had a similar prevalence to the study of Squire SB et al. (2005) in Malawi, which recorded 15% in the Ntcheu district,

and the study in Botswana in Gaborone city, which registered 14.9% (Creek et al., 2000). The prevalence in this study was higher than that of the studies in India (Sai Babu et al., 2008), Pakistan (Khan et al., 2008), and Myanmar (Ko Ko et al., 2019), which reported prevalences of 4.5%, 5.2%, and 8% respectively. This difference may be explained by variations in sampling techniques and the comparatively shorter study period. A prevalence of pre-diagnosis lost to follow-up of 6.65% was identified. This prevalence is lower than the studies in Cameroon (Onyoh et al., 2018) and Pakistan (Syed et al., 2016), which reported prevalences of 10% and 8%, respectively. This difference can be explained by the fact that in the study, patients who did not receive negative results were not taken into account. A prevalence of lost to follow-up of 8.35% was found. This prevalence is lower than that of the study in India, which was 17% (Mehra et al., 2013).

The difference in this study can be explained by the fact that all diagnosed patients were referred to other centers for treatment initiation, and the study period lasted longer (32 months). According to Syed et al.'s (2018) study in Pakistan, the prevalence of lost to follow-up was 4.9%. The prevalence in this study is higher than the latter. This difference can be explained by the fact that sampling techniques were distinct.

In this study, the majority of patients were male (82%). In both pre-diagnosis and post reference, males comprised the majority of these cases at 91.3% and 74.07%, respectively. These results are consistent with WHO estimates, thus indicating a higher incidence of TB among men in Niger in 2019 (OMS, 2020).

The mean age of pre-treatment dropouts was 41.04 years. Similar findings were reported by Wali et al. in Pakistan in 2015 and Ko Ko et al. in Myanmar in 2019, with the mean age of pre-treatment dropouts being 40 years in each study. This similarity is consistent with WHO estimates suggesting that TB affects younger adults more than other age groups (OMS, 2020). In this study, slightly over half of those lost to follow-up treatment were married (54% of cases). This result suggests that marital status might be a contributing factor in TB transmission within household, ultimately impacting the community.

In addition, 76% of PTLFU were from Niamey. These results can be attributed to the NCFATRD being the largest provider of TSCT patients according to 2016 data (CNAT, 2017). Moreover, Niamey, the capital of Niger, experiences significant population migration (INSN, 2017), a known factor facilitating the spread of tuberculosis.

In the study, self-employment showed higher representation among the pre-treatment dropouts (26% of cases). Farmers and the unemployed were equally represented (26.10% of cases) among the PTLFU. Among those lost to referral, self-employment was more prevalent, accounting for 33.33% of

cases. These three professions have unstable incomes, leading to difficult living conditions. According to WHO, poverty is a socio-economic determinant of tuberculosis (OMS, 2020). Poverty leads to poor health status by limiting access to care (Word Bank Group, 2004). Despite the fact that tuberculosis treatment is free of charge in Niger, the fight against tuberculosis cannot be effective without increased information, education, and communication activities. An equal proportion of 30% of those lost to follow-up before treatment were either not attending school or were in primary school. Among those lost to pre-diagnosis, individuals not attending school and those attending primary school were the most affected, constituting 34.8% of cases. This result suggests that people with a low level of education may have a poor understanding of the TB diagnosis process. Among those lost to follow-up, secondary school students were more prevalent, comprising 37.03% of cases. This result may indicate that people with middle school education have a poor understanding of the risks associated with discontinuing treatment. Nearly half of the patients (42%) resided within 6 to 15 km of the diagnostic center. These results suggest an issue with patient transportation in urban areas. More than three-quarters (83%) of those lost to follow-up had only one positive bacilloscopy test. This may suggest that the TB diagnostic process is not well understood by patients or is poorly communicated. When attempts were made to trace lost-to-treatment patients by telephone, only 24% were reachable. The other 76% were considered lost to follow-up without information. More than half (58%) of the reachable PTLFU were deceased (14% of all PTLFU). This phenomenon could be attributed to late diagnosis resulting from some patients being bedridden upon presentation. Moreover, among those lost to follow-up without information, 61% were unreachable. This result suggests that contact information provided by the patients is not always reliable.

Conclusion

This study facilitated an assessment of the prevalence of lost to follow-up cases in the cities of Niamey and Tillaberi, Niger. Overall, a relatively high prevalence was found, with a slightly higher rate observed after referral than during the diagnosis. Pre-treatment dropouts remain a poorly understood phenomenon in the fight against tuberculosis. Despite the availability of free TB treatment, these patients present a significant problem for individuals (sequelae of TB, death), the community (maintenance of spread), and the National Tuberculosis Control Program (occurrence of new strains of koch bacillus, decrease in notification rate). Hence, there is a need to strengthen research on the reasons behind TB patients becoming lost to follow-up and increase awareness to improve tuberculosis control and management. A future study on counseling provided to pulmonary TB patients at the time of diagnosis should aim to minimize the number of patients lost to follow-up pre-

treatment.

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Authors' Contributions

AGIM, MBS, and AS: Research concept and design and critical revision for intellectual content of the manuscript.
SHM, SA: Assisted with participant enrollment and data acquisition.
AGIM: Submitted the manuscript for publication.
All authors contributed to the design and approval of the manuscript draft.

Data Availability: All of the data are included in the content of the paper.

Human Studies

The study complied with the Niger Ministry of Health's guidelines for ethical research involving human subjects, and it was approved by Niger's national scientific committee.

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