

**Pre-Treatment Loss to Follow-up of Patients with
Bacilloscopy-Confirmed Pulmonary Tuberculosis in the
National Center for the Fight Against Tuberculosis and
Respiratory Diseases in Niamey**

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Abstract

Context: Pre-treatment loss of follow-up (PTLFU) represents a major problem that hinders the management of tuberculosis. The objective of this study is to determine the prevalence of lost to follow-up patients diagnosed with smear-positive pulmonary tuberculosis (SPPT) and referred to other TB screening and treatment centers (TBSTC).

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

Results: 743 patients were diagnosed with SPPT, and 346 were referred to the TBSTC located in Niamey and Tillaberi cities. The prevalence of loss of follow-up before treatment in both Niamey and Tillaberi cities was 14.45% (50/343). Male represented 82% (41) of the cases with a sex ratio of 4.55. The mean age of our patients was 41.04 years. Patients not attending school and those with primary education represented the majority with 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 get the TB screening. During the phone call follow up, we were able to reach only 12 patients (24%) of which 7 (14%) were deceased.

Conclusion : the prevalence of PTLFU is high, therefore there is a need to reinforce the research of lost to follow up patients in order to improve tuberculosis control and management.

Keywords: Pretreatment lost to follow-up, NCFATRD, Niamey, Tillaberi

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, 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 lead to TB drug resistance (Pherson et al 2014; PNLT, 2016) and increase 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) in Africa, this rate varies from 6 to 38%, while in Asia, it varies from 4 to 28%. In Niger, 11700 cases were notified of which 91% were bacilliferous (PNLT, 2017) and 684 cases lost to treatment were recorded and 122 cases not evaluated (PNLT, 2020). In the capital, 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 patients lost to follow-up before 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 our 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: dropout of patients after diagnosis but before treatment registration.

Lost to pre-diagnosis: a patient diagnosed with TB in the laboratory, who didn't come back to get his result.

Lost to referral: TB patient diagnosed in one center and started treatment and referred to another center to continue treatment but never went after verification.

Inclusion criteria

- For lost to follow up patients at the time of diagnosis, the monitoring was done on a monthly basis, by 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 a $P \leq 0.05$.

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 our study, 743 cases of SPPT were detected. Our study involved 346 patients distributed as follows:

- 23 who did not retrieve their results (lost to follow-up): 23/346 (6.65%)
- 323 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*)

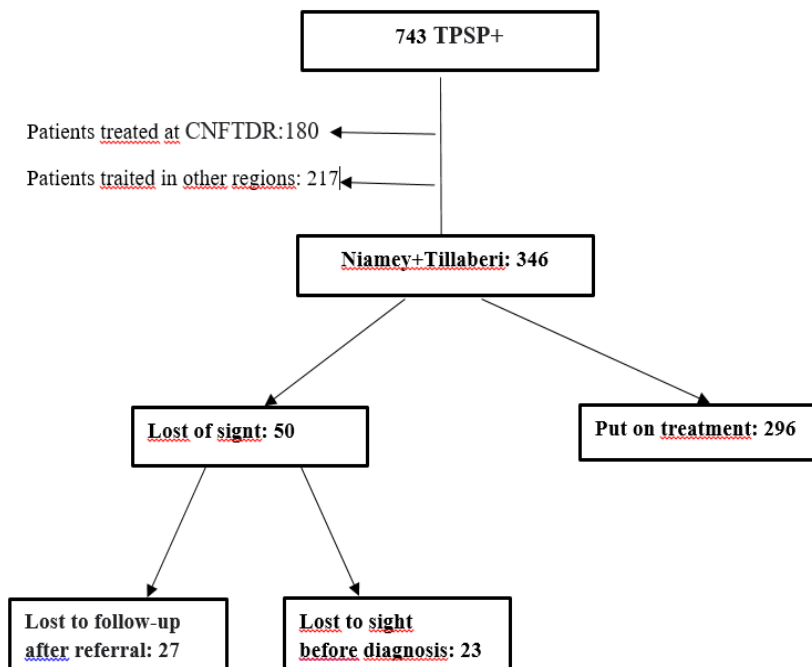


Figure 1. Patient recruitment flowchart

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

Self-employment among pre-treatment loss to follow-up represented 26%. Non-educated and primary school students accounted for 30% of pre-treatment follow up each. Nearly half (42%) of pre-treatment loss to follow-up. (pre-diagnosis and referral) had traveled 6-15 km to get TB screening (Table 1).

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

Characteristics	Patients (n=50) (%)
Sex	
Female	09 (12)
Male	41 (88)
Age, years	
< 45	35 (70)
≥ 45	15 (30)
Educational level	
Educated	35 (70)
Unschoolled	15 (30)
Region	
Niamey	38 (76)
Except Niamey	12 (24)
Type of facility	
CNFTDR	32 (64)
Public	12(23)
Private	6(13)
Traveled distance (en km)	
<5	17 (34)
5-50	23 (46)
>50	10 (20)
Reason for losing sign of no joining	
Contact unavailable	23 (61)
No contact	13 (34)
Bad contact	2 (5)

In 83% of the 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 (76%) could not be reached and were considered as lost to follow-up without information and 7 (14%) were deceased.

Among the deceased pretreatment loss to follow-up, the age range [25-34] was 43%, the mean age was 52 years with extremes of 27 and 80

years, and 5 (71%) of the deceased pretreatment loss to follow-up were male. In 61% of the cases, pretreatment lost to follow-up without information had unavailable contacts. We observed a statistically significant difference between pre-diagnosis lost to follow-up by gender and patient type $p < 0.028$ and 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 according to 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 loss to follow-up			
Pre-diagnosis	21 (91.3)	2 (8.7)	$P=0.002$
After reference	20 (74.07)	7 (25.93)	
Traveled distance (en 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 our 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

This study allowed us to determine for the first time in Niamey the prevalence of pre-treatment dropouts, their characteristics, and the associated factors in Niamey city. This study will serve as a basis for future studies. Our study, like any other work, had some limitations, including the fact that the study was carried out in one city (Niamey). Also, the unavailability of the contacts of those lost to follow-up before processing did not allow us to conduct the interviews, which prevented us from obtaining the patients' point of view.

The total prevalence of lost to follow-up before treatment was 15%. Our study had a lower prevalence than the study conducted in India (Beena et al, 2018), in the city of Chennai in 2008 which was 22.1%, and the study in Pakistan which was 21.3% in the city Quetta (Wali et al, 2017). This

difference can be explained by the fact that in our study, the sample size is smaller. Our study had a prevalence close to the study of South Africa (Botha et al, 2008), which was 16%, and to the study in Nigeria, which was 16.9% (Chukwu et al, 2012). This may be explained by the fact that our sample sizes were close. Our study also had a similar prevalence to that of the Squire SB. et al study in Malawi (Squire et al, 2005) which was 15% in Ntcheu district, and study in Botswana in Gaborone city which was 14.9% (Creek et al, 2000). Our prevalence was higher than that of the studies in India (Sai Babu et al, 2008), in Pakistan (Khan et al, 2008), and in Myanmar (Ko Ko et al, 2019) who found prevalences of 4.5%, 5.2% and 8% respectively. This difference may be explained by the fact that in each of these studies, the periods were shortened.

We found a prevalence of pre-diagnosis lost to follow-up of 6.65%. Our prevalence is lower than the studies in Cameroon (Onyoh et al, 2018), and in Pakistan (Syed et al, 2016) who had reported prevalences of 10% and 8% respectively. We can explain this difference by the fact that in our study, we had not taken into account patients who did not retrieve negative results. We found a prevalence of lost to follow-up of 8.35%.

Our prevalence is lower than that of the study in India which was 17% (Mehra et al, 2013). We can explain this difference by the fact that in this study, all diagnosed patients were referred to other centers for treatment initiation, and the study period was longer (32 months). In the study by Syed et al, in Pakistan in 2018, the prevalence of lost to follow-up was 4.9%. Our prevalence is higher than the latter. We can explain this difference by the fact that, our sampling techniques were different.

In our series, the majority of patients were male in 82% of cases. We also found a predominance of males in the lost to follow-up cases as well as in the lost to follow-up cases, with 91.3% and 74.07% of cases respectively. These results are consistent with WHO estimates that the incidence of TB will be higher among men in Niger in 2019 (OMS, 2020).

The mean age of pretreatment dropouts was 41.04 years. Our results are similar to those of Wali et al, Pakistan in 2015 and Ko Ko et al, Myanmar in 2019, in which the mean age of pre-treatment dropouts was 40 years for each study. This similarity is consistent with WHO estimates suggesting that TB affects younger adults much more (OMS, 2020). In our series, the majority of patients were male in 82% of cases. We also found a male predominance in both pre-diagnosis and referral lost sight; with 91.3% and 74.07% of cases respectively. These results are consistent with WHO estimates that the incidence of TB will be higher among men in Niger in 2019.

In our study, a little more than half of the people lost to sight before treatment were married (54% of the cases). This result shows us the

seriousness of the phenomenon in that a married person is a factor in the maintenance of the contamination within the couple, the family and the community.

Most PTLFU were from Niamey with 76% of cases. These results can be explained by the fact that the NCFATRD is the largest provider of TSCT patients according to 2016 data (CNAT, 2017). Moreover, Niamey, the capital of the country, is a city of exodus by reference (INSN, 2017): it is known that the movement of populations is a factor favoring the spread of tuberculosis.

In our series, self-employment was more represented among the pre-treatment dropouts with 26% of cases. We found that farmers and the unemployed were more represented in equal proportions (26.10% of cases) among the PTLFU. Among the reference losers, the liberal activity was more represented with 33.33% of the cases. These three professions have unstable incomes; thus, the people practicing them live in difficult 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 on tuberculosis. An equal proportion of 30% of those lost to follow-up before treatment were not in school and were in primary school. Among those lost to pre-diagnosis, those not attending school and those attending primary school were the most affected at 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 represented with 37.03% of cases. This result may suggest that people with a middle school education have a poor understanding of the risks associated with discontinuing treatment. Nearly half of the patients (42%) were within 6-15 km of the diagnostic center. These results suggest that there is a problem with patient travel 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 rest (76%) were considered lost to follow-up without information. More than half (58%) of the reachable PTLFU were deceased (14% of all PTLFU). This can be explained by the fact that some patients come in a bedridden state, so the diagnosis is made late. More than half of those lost to follow-up without information had unavailable contacts in 61% of cases. This result suggests that the information given by the patients is not reliable.

Conclusion

This study allowed us to assess the prevalence of lost to follow-up in the cities of Niamey and Tillaberi, Niger. Overall, we found a relatively high prevalence, with a slightly higher rate after referral than during the diagnosis. Pre-treatment lost sight was still a poorly understood phenomenon in the fight against TB. Despite the free treatment, this group poses 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 the need to strengthen the research for lost to follow up and increase awareness to improve tuberculosis control and management.

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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 design and draft the manuscript and read and approved the final manuscript.

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

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Human Studies

The study complied with the Niger Ministry of Health's guidelines for ethical research involving human subjects.

The research was approved by Niger's national scientific committee.

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