Journal of Pre-Clinical and Clinical Research 2022, Vol 16, No 2, 34-37
www.jpccr.eu

ORIGINAL ARTICLE

Timing and reasons for lost to follow-up among patients on 6-month standardized anti-TB treatment in Nigeria

Abiola Victor Adepoju[1,A,D], Ademola Adelekan[2,C,E], Olusola Adedeji Adejumo[3,D-F]

[1] *Jhpiego Nigeria (an affiliate of John Hopkins University), Nigeria*
[2] *Bluegate Research Institute, Ibadan, Nigeria*
[3] *State Ministry of Health, Lagos, Nigeria*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abiola Victor Adepoju, Ademola Adelekan, Olusola Adedeji Adejumo. Timing and Reasons for Lost to Follow-up among patients on 6-month standardized anti-TB treatment in Nigeria. J Pre-Clin Clin Res. 2022; 16(2): 34–37. doi: 10.26444/jpccr/150601

Abstract

Introduction and Objective. Loss to follow-up (LTFU) along the TB care cascade is a barrier to TB control because of sustained TB transmission including resistant strains, high mortality and increased spread of DRTB strains. Understanding common reasons for LTFU and their timing could help target interventions to improve adherence to TB treatment.

Materials and method. A cross-sectional study using pre-tested questionnaires were administered by phone interviews to 90 TB patients receiving treatment between January – December 2020 who were LTFU while on TB treatment in 31 health facilities across three States in South West Nigeria. The focus of the interviews was to determine the reasons why they were LTFU. Interviewers contacted treatment supporters when patients could not be reached. Clinical and socio-demographic information, such as age, sex and HIV status were extracted from treatment registers

Results. The mean age of patients was 42.6 years (16–90) and SD=17.2. The majority 73 (81%) of LTFU were male, while Ogun State had the highest number – 35 (38.9%), LTFU was highest during the first month on treatment – 60 (66.7%), among HIV negative – 63 (70%), and those who had not been treated previously for TB – 85 (94.4%). The most common reason for LTFU among TB patients on treatment was death – 23(25.6%), followed by lack of transport – 16 (17.8%), and religious beliefs – 12 (13.3%).

Conclusions. The study suggests a high mortality among patients receiving treatment who may have been classified as LTFU. Interventions to reduce mortality and increase coverage of TB treatment facilities, thus bringing care closer to patients, is necessary. It is suggested that 30-day adherence calendars should be used to improve adherence counselling in the first one month on treatment to minimize early LTFU among TB patients.

Key words

tuberculosis, lost to follow-up, directly observed therapy short course, anti-TB drugs

INTRODUCTION AND OBJECTIVES

Nigeria is one of the high burden countries for TB, TB/HIV and multi-drug resistant TB, with an estimated annual incident of TB cases of 407,000 [1]. The 2019 National TB Programme Annual Report stated that 106,533 of the estimated 407,000 TB cases (26% treatment coverage) were notified, giving a gap of 300,467 cases yet to be notified including 40,479 missed HIV positive incident TB cases [1]. To eliminate TB as a major public health problem, Nigeria initially adopted directly observed treatment short-course (DOTS) strategy in 1993 with achievement of 99% geographic coverage [1–2]. DOTS strategy is a combination of active case detection, the use of DOTS by dedicated health workers, government commitment, guaranteed supply chain for anti-TB drugs, and efficient recording and reporting systems. The objective of DOTS is to cure the patient, interrupt the chain of TB transmission to others, and prevent development of DR-TB strains [3–4]. These have been difficult to achieve as a result of several barriers mitigating against the patient and health systems thus resulting in drop-outs while TB patients are receiving a standardized anti-TB regimen. One of the challenges of DOTS is the long term of treatment with six months for all drug sensitive TB, with the exception of osteoarticular TB (bone, joint and meningitis) which takes 12 months, while DRTB treatment could be of shorter or longer duration [4]. DOTS helps to prevent primary and secondary TB resistance but the commitment required often poses enormous challenge for adherence and prevention of LTFU.

A patient is said to be LTFU if there is interruption of treatment for two consecutive months or more [4]. Lost to follow-Up (LTFU) is a major barrier to TB control efforts and constitute an economic burden. It is also a significant cause of increased transmission of drug-resistant strains, mortality and TB reactivation [3]. Also, LTFU was a major reason for failed TB treatment, DRTB, relapse and future retreatment after completing treatment [5]. In Nigeria, a high proportion of patients with drug-resistant TB, estimated at 4.3% among new cases and 25% among previously-treated cases, were previously documented [6]. Earlier studies in southern and eastern India identified several reasons for LTFU when patients are on first-line anti-TB medications. Highlighted reasons include inadequate patient-provider interaction, long distance of DOTS facilities, gender,

Address for correspondence: Abiola Victor Adepoju, Jhpiego Nigeria (an affiliate of John Hopkins University), Federal Capital Territory, Wuye, Abuja, Nigeria
E-mail: schrodinga05@yahoo.com

Received: 01.05.2022; accepted: 01.06.2022; first published: 17.06.2022

alcoholism, anti-TB drug side-effects [7–9], while in central India illiteracy and insufficient TB knowledge were reported as reasons for LTFU [9]. Globally, measures have been taken to prevent or minimize the incidence of LTFU. For example, most countries have a policy to engage community health extension workers (CHEWs) as DOTS providers for reasons that are not far-fetched, as they are closer to the community and will be able to provide adherence support, including follow-up visits. These efforts have been relatively successful as many TB patients receiving treatment still fail to complete DOTS as scheduled [10–11]. In order to prevent the reversal of gains made by TB control programmes, implementation studies evaluating timing and reasons for LTFU from the perspective of TB patient or their treatment supporter will be necessary. Identifying these reasons and time in which LTFU occur will help to design time sensitive strategies aimed at improving adherence to and completion of TB treatment. This study aimed to determine the timing and reasons for LTFU while patients are on first-line anti-TB treatment in Nigeria.

MATERIALS AND METHOD

Cross-sectional study design. Questionnaires were designed, pre-tested and administered by phone to 90 participating TB patients (or their treatment supporter) who were LTFU while receiving standardized six-month anti-TB drugs between January-December 2020 across 31 health facilities in Lagos, Ogun and Osun States in South-West Nigeria. The study took place in February 2022. The questionnaire elicited responses to various reasons for LTFU. Clinical and demographic information of LTFU patient, such as age, gender, education, place of residence, HIV status, date treatment started, treatment outcome and date assigned were extracted from the TB treatment register. For TB patients who could not be reached, the treatment supporters were contacted and interviewed to discuss the LTFU patients on phone.

Study Setting. The 31 health facilities in this study are a mix of primary, secondary and tertiary hospitals providing DOTS services in three states, Ogun, Lagos and Osun, all in southwest Nigeria. In 2021, Osun state has a population of 731,000 [12], Lagos is the most populous metropolis in Nigeria with a population of over 20 million [12], while Ogun State has a population of 543,723 in 2021 [13]. Both states share extensive border with constant cross-border migration. Selected health facilities have been engaged by the National TB, Buruli Ulcer and Leprosy Control Programme and receive support from the United States Agency for International Development (USAID) for TB Control. Patients diagnosed with DSTB in Nigeria are placed on six months of anti-TB medications, with the exception of osteoarticular TB (TB of the bone, joint and meninges) in which medications are taken for 12 months. Treatment outcome is documented at the end of treatment or as LTFU once a patient has abandoned treatment for two or more consecutive months.

Participants. All TB patients aged 18 years or over registered across the 31 facilities between January-December 2020, and were found to be LTFU in the course of treatment, were included in the study. Exclusion criteria were osteoarticular TB treated for 12 months and DR-TB (Fig. 1).

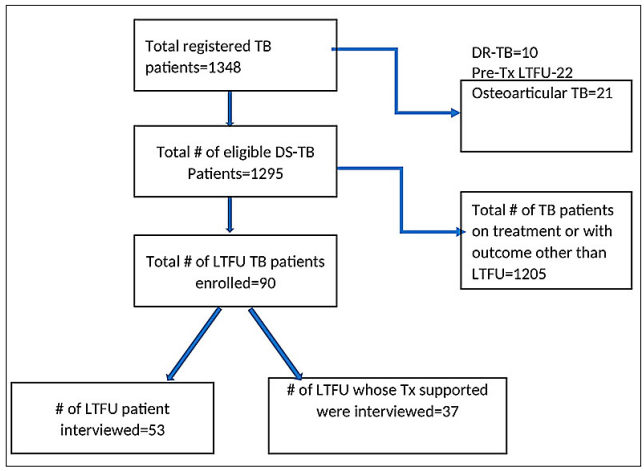

Figure 1. Flowchart showing selection of LTFU among TB patients managed with first-line anti-TB

Source of data, variable and data collection. Questionnaires were administered to collect data on reasons for LTFU among TB patients themselves, or their treatment supporter when the TB patients could not be reached. Data collection using a questionnaire was combined with data extraction from the TB treatment register to collect clinical and demographic information, as well as contact details of the treatment supporter from the treatment card (Tab. 1).

Table 1. Data Source and type of data collected from questionnaire and TB recording tools

S/N	TB treatment Register (TB Patient clinical and demographic information)	Questionnaire (Reasons for LTFU)	TB Treatment Card
1	Age, sex, occupying, type of TB, HIV status, phone number, place of residence, treatment outcome, state, LGA, date treatment started, date of assigned outcome	Death, religious belief, away from home, herbs, still had drugs, wrong phone number, change of residence, client is bedridden, spouse refused, relative is sick, at school.	Address and contact details of treatment supporter

Data analysis. Data extracted from the register and questionnaires were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS), version 23. Frequency and percentage were used to describe the proportion of different variables of interest monthly pattern and trend of LTFU across treatment months, most common reasons for LTFU while on treatment as reported by patient and treatment supporter

Ethics approval

The study was approved by the Ethics Committee of the Lagos State Ministry of Health. Permission for the study was also received from the Lagos Ogun and Osun State TB Control Programme. Informed consent was provided by the study participants prior to the interviews. Data was de-identified to preserve anonymity and no information on participant names were collected.

RESULTS

Table 2 shows the clinical and demographic characteristics of TB patients who were LTFU during anti-TB treatment. The mean age was 42.6 years (16–90) and SD=17.2. The Majority, 32/90(35.6%) were aged 35–44 years, male(81%), lived in rural areas (51.1%), with unknown educational status (33.3%), resident in Ogun state (38.9%), LTFU in the first one month of treatment (66.7%) and were HIV negative(70%).

Table 2. Sociodemographic and clinical characteristics of patient who defaulted or LTFU while receiving first line anti-TB, January-Dec, 2020, Southwest, Nigeria

Variable	Frequency	Percent
Age		
16-24	12	13.3
25-34	15	16.7
35-44	32	35.6
45-54	12	13.3
55-65	7	7.8
>65	13	14.4
Sex		
Male	73	81.1
Female	17	18.9
Place of Residence		
Rural	46	51.1
Urban	44	48.9
Level of Education		
None	22	24.4
Primary	17	18.9
Secondary	22	24.4
Tertiary	6	6.7
Unknown	23	33.3
State		
Ogun	35	38.9
Osun	22	24.4
Oyo	33	36.7
Month LTFU		
Month 1	60	66.7
Month 2	15	16.7
Month 3	7	7.7
Month 4	5	5.1
Month 5	1	1.3
Month 6	2	2.6
HIV Status		
HIV+	12	13.3
HIV-	63	70
HIV Unknown	15	16.7
Past TB Treatment		
No	85	94.4
Yes	5	5.6

Figure 2 shows the commonest reasons why patients were LTFU while on anti-TB medications. The majority, 23/90(25.6%) of the TB patients were LTFU through death, but this not known to the DOTS provider (treatment supporter reported), followed by 16/90 (17.8%) who cited lack of transportation/long distance to the DOTS facility as the second commonest reason for LTFU.

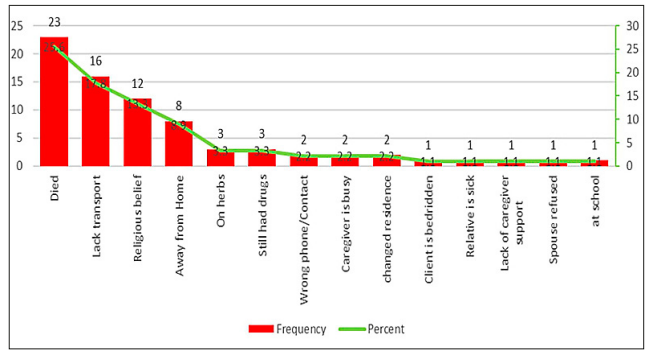

Figure 2. Common reasons for LTFU while on standardized 6-month anti-TB treatment

DISCUSSION

The study sought to determine the timing and reasons for LTFU among TB patients on standardized six-month anti-TB medications in Nigeria. It was found that four out of every five LTFU TB patients were male. Also, 67% of TB patients were lost in the first month of starting anti-TB treatment. Shockingly, the study discovered that the majority of patients initially documented as LTFU in the TB treatment register, were ultimately confirmed as dead by the treatment supporter. The commonest reason(25.6%) for LTFU was patient death (as reported by treatment supporter), followed by lack of transportation, 17.6%.

In the current study, 83.4% of patients were LTFU during the intensive phase (month 1 – 66.7%, month 2 – 16.7%). This finding is higher than the 24/55(43%) of LTFU reported in the first two months of initiating DOTS in India [14]. Also, Shaweno et al. who evaluated the difference in LTFU among patients who took anti-TB in a primary health centre versus general hospital noted that 65% of LTFU occurred during the intensive phase [15]. The higher figure in the current study could be the result of TB patients who were confirmed dead by a treatment supporter, but classified by the DOTS provider as LTFU in the treatment register. The study has serious implication for policy and practice. Patients were often regarded as LTFU once they abstained from DOTS for two months or more, and providers were unable to ascertain the true outcome, particularly when inaccessible by phone and no access to the treatment supporter. This could lead to the misclassification of death as LTFU and make it impossible to determine the true progress of TB control efforts. Effort should be made to ascertain the true outcome of LTFU by ensuring that the information from treatment supporters is always complete during the registration of TB patients and prior to treatment commencement.

In the current study, the majority (25.3%) of LTFU patients were confirmed dead by treatment supporters. TB death just after commencement of treatment remained high, taking place in the first few months of treatment in most sub-Saharan African studies [16–18]. Reporting the outcome of 1,427 TB patients, Adamu et al. noted that over 75% of deaths during anti-TB treatment occurred in the first month [17], while in another hospital study in South Africa, most of the TB deaths occurred within the first month of treatment for both new and re-treatment cases [16]. Although the presented study did not collect comorbidity data of those LTFU now confirmed dead, earlier studies cited early disease progression from comorbidity and poor adherence as major causes of early deaths [11,18]. The finding of the current study could mean that those with early deaths were diagnosed late or commenced treatment late, or had comorbidities.

In the presented study it was also found that lack of transportation/long distance to a DOTS facility was cited as

the second most relevant reason for TB patients being LTFU. This is similar to a study from Papua New Guinea (PNG) which found that patients on anti-TB treatment living more than three hours from a DOTS facility had a significantly higher chance of LTFU [19], while prolonged travel time was also cited as a major reason for poor treatment outcome in PNG [20–21]. In Ethiopia, living >10 km from a DOTS facility significantly predicted LTFU among patients on treatment [15]. Although DOTS facility overage is reasonably high in Nigeria, it is not uncommon that when a DOTS facility is available close to a patient's residence, concerns about stigma still motivate TB patients to attend a DOTS far away from home, even when it is economically unrealistic to sustain the cost of transportation to the distant DOTS facility. In the Philippines, living close to a TB service facility is a predictor of retention in care versus living abroad [22]. As many TB patients came from the lowest socio-economic class, economic considerations such as transport cost to a DOTS facility during TB treatment could help to facilitate DOTS treatment completion and cure.

Limitations of the study. The findings of this study should be interpreted with caution to avoid overestimation of mortality figures as some deaths might not be TB deaths but rather death during TB treatment. We could not also analyze the effect of other comorbidities due to the nature of the study design. Several comorbidities except HIV were not available in TB treatment register.

CONCLUSION

Despite the limitations, the study has some unique strength. Unlike previous studies which relied on TB registers, in the current study, LTFU patients and their treatment supporter (when LTFU was not reachable) were interviewed to elicit social and personal reasons leading to LTFU. This would not be possible through a study that only collected retrospective data from registers. By interviewing treatment supporters *in lieu* of LTFU patients who were not reachable, this study helped to elicit a number of LTFU who had died at home. Knowing that most LTFUs occurred in the first month of TB treatment re-iterates the need for intensified patient support, such asa daily call or SMS and a 30-day adherence calendar to help them successfully navigate this stage. Intervention should also consider the concerns about transportation and the higher percentage of LTFU among males (compared to females) while on anti-TB drugs, and address these by using male-specific strategies. A TB patient receiving treatment will need to be profiled and differentiated on a case-by-case basis with longer term appointment for stable patients with good adherence history, augmented with calls and innovations such as tele-DOTS. The impact of these differentiated models of care in DOTS treatment will need to be tested in future studies. The study has demonstrated the need to prioritize the first month of DOTS among TB patients and address gaps concerning mortality and the distance to DOTS facilities in Nigeria.

REFERENCES

1. Federal Ministry of Health. Draft Annual TB Report. www.health.gov.ng/doc/Draft-2019-NTBLCP-Annual-report-22032020.pdf (access:2021.05.01).
2. World Health Organization. Global Tuberculosis Control. https://apps.who.int/iris/bitstream/handle/10665/44425/9789241564069_eng.pdf.?sequence=1 (access:2021.04.20).
3. Xiao H. Drug-Resistant TB. In: Lu Y, Wang L, Duanmu H, editors. Handbook of Global Tuberculosis Control.Ed.2. Boston; 2016. p. 60–64.
4. Federal Ministry of Health. National tuberculosis and leprosy control programme: workers manual. 5th ed. Abuja; 2008.
5. Geremew MA, Mulualem T, Gemeda A. Survival Analysis of Loss to Follow-Up Treatment among Tuberculosis Patients at Jimma University Specialized Hospital, Jimma, Southwest Ethiopia. Journal of Stat Mech. 2015;1(1):1–7. https://doi.org/10.1155/2015/923025
6. World Health Organization. Global Tuberculosis Report. https://apps.who.int/iris/handle/10665/274453 (access:2021.05.01).
7. Babiarz KS, Suen S, Goldhaber-Fiebert JD. Tuberculosis treatment discontinuation and symptom persistence: an observational study of Bihar, India's public care system covering >100,000,000 inhabitants. BMC Public Health. 2014;14(1):418. https://doi.org/10.1186/1471-2458-14-418
8. Ruru Y, Matasik M, Oktavian A. Factors associated with non-adherence during tuberculosis treatment among patients treated with DOTS strategy in Jayapura, Papua Province, Indonesia. Global Health Action. 2018;11(1):1–4. https://doi.org/ 10.1080/16549716.2018.1510592
9. Roy N, Basu M, Das S. Risk factors associated with default among tuberculosis patients in Darjeeling district of West Bengal. India. J Fam Med Prim Care. 2015;4(1):388–394. https://doi.org/ 10.4103/2249-4863.161330
10. Herrero MB, Ramos S, Arrossi S. Determinants of non-adherence to tuberculosis treatment in Argentina: barriers related to access to treatment. Rev. bras. epidemiol. 2015; 18(2): 287–298. https://doi.org/10.1590/1980-5497201500020001
11. Aung YK, Swe PP, Kyaw Z. Differential loss to follow-up rates among adult tuberculosis patients – Findings from the largest private sector tuberculosis clinic database in Myanmar. PLoS ONE.2019;14(6):1–9. https://doi.org/10.1371/journal.pone.0218450
12. World Population. https://worldpopulationreview.com/world-cities/abeokuta-population (access 2022.05.01).
13. Macrotrends. Lagos, Nigeria Metro Area Population 1950–2022. https://www.macrotrends.net/cities/22007/lagos/population#:~:text=The%20current%20metro%20area%20population,a%203.44%25%20increase%20from%202020 (access 2022.05.01).
14. Zhou TJ, Lakshminarayanan S, Sarkar S. Predictors of Loss to Follow-Up among Men with Tuberculosis in Puducherry and Tamil Nadu, India. The American Journal of Tropical Medicine and Hygeine. 2020;103(3):1050–1056. https://doi.org/10.4269/ajtmh.19-0415
15. Shaweno T, Getnet M, Fikru C. Does time to loss to follow-up differ among adult tuberculosis patients initiated on tuberculosis treatment and care between general hospital and health centers? A retrospective cohort study. Tropical Medicine and Health. 2020;48(1):9. https://doi.org/10.1186/s41182-020-00198-8
16. Field N, Lim MS, Murray J. Timing, rates, and causes of death in a large South African tuberculosis programme. BMC Infect Dis. 2014;14(1):1–12. https://doi.org/10.1186/s12879-014-0679-9
17. Adamu AL, Gadanya MA, Abubakar IS. High mortality among tuberculosis patients on treatment in Nigeria: a retrospective cohort study. BMC Infect Dis. 2017;17(1):170. https://doi.org/10.1186/s12879-017-2249-2254
18. Bisson GP, Zetola N, Collman RG. Persistent high mortality in advanced HIV/TB despite appropriate antiretroviral and antitubercular therapy: an emerging challenge. Current HIV/AIDS Reports. 2015;12(1):107–116. https://doi.org/10.1007/s11904-015-0256-x
19. Umo I, Kulai M, Commons RJ. Factors associated with loss to follow-up among TB patients in rural Papua New Guinea. Public Health Action. 2021;21;11(4):186–190.https://doi.org/ 10.5588/pha.21.0054
20. Moses I, Main S, Commons RJ. A retrospective study of tuberculosis outcomes in Gulf Province, Papua New Guinea. Public Health Action. 2019;9(1):38–42.https://doi.org/ 10.5588/pha.18.0069
21. Sodeng K, Botu A, Semmie M. Challenges in TB diagnosis and treatment: the Kavieng Provincial Hospital experience, Papua New Guinea. Public Health Action. 2019;9(1):57–61. https://doi.org/10.5588/pha.18.0066
22. Tupasi TE, Garfin AM, Kurbatova EV. Factors Associated with Loss to Follow-up during Treatment for Multidrug-Resistant Tuberculosis, the Philippines, 2012–2014. Emerg Infect Dis. 2016;22(3):491–502. https://doi.org/10.3201/eid2203.151788