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Lost to follow-Up: implications for tuberculosis control in Nigeria

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Abstract
Background: Loss to Follow-Up (LTFU) from Tuberculosis (TB) treatment is a significant barrier to TB control, a major public health problem and a predictor of TB-associated deaths. Currently, research on LTFU-related factors in Nigeria is both scarce and inconsistent. The study aimed to assess the magnitude of LTFU to tuberculosis treatment and associated factors among patients that accessed care at a tertiary health facility in Nigeria.
Methods: The study was a 5-year retrospective study of patients that accessed TB care at the health facility. All the data was retrieved from the patient's folder and analyzed with SPSS version 25. Descriptive statistics was done and presented as mean and standard deviation, frequencies and percentages. Bivariate analysis was done with Chi-square test to test for the socio-demographic characteristics associated with LTFU. Significance level was placed at p-value ≤0.05.
Results: A total of 483 patient's folders were reviewed. Of these, 150 (31.1%) were LTFU. Ethnicity was the only factor that significantly affected LTFU. However, higher proportion of those LTFU were males, resides in the rural area, employed, HIV positive and with previous history of TB
Conclusion: Loss to follow-up is common in the management of patients with TB. Patients' treatment history, clinical characteristics, and socioeconomic factors can affect this treatment outcome. Targeted measures can improve patient treatment adherence, leading to reduction in LTFU and better TB control

Keywords: Tuberculosis, Loss-To-Follow-Up, Nigeria, Enugu state, treatment outcome

Introduction

Tuberculosis (TB) is a communicable disease that affects primarily the lungs as pulmonary TB as well as other organs of human body as Extra pulmonary TB. Despite decline in incidence of TB in some countries, TB still remains among the top 10 causes of mortality worldwide [1]. Globally, in 2019 approximately 10 million people developed TB while 1.4 million died with Nigeria accounting for 4.4% of these cases [2]. The World Health Organization (WHO) stated that African and Southeastern Asian regions accounted for 85% of TB deaths in both HIV-negative and HIV-positive persons [3].

Despite the expansion of DOTS services, many TB patients are still failing to complete their treatment and achieve a cure [4, 5]. This presents serious health and social implications not only for the patients themselves as it can lead to prolonged illness, development of clinical complications, development of drug resistance, and premature death, but it can also lead to the spread and outbreaks of drug-resistant bacilli in their families, communities, and health service providers [6]. Various factors have been reported to contribute to Loss-To-Follow-Up (LTFU) on TB treatment and these includes being male, alcohol abuse among men, living in rural areas, advancing age, distance from healthcare facilities, migration to another country, moving within the country, and weight loss [4, 7, 8]. The proportion of LTFU varied considerably between different countries, different types of TB, and different patient populations. Studies from different parts of the world reported different rates of LTFU; South Ethiopia (11.2%) [9], Jimma, Ethiopia (13.5%) [4], China (6.8%) [7], Georgia (12.5%) [7], Brazil (18.1%) [10], and as high as 44.9% in rural Northern Mozambique [11]. In Malaysia, the prevalence of LTFU ranged from 4.0 to 4.8% in the years 2010-2015 among the general TB population [12] but has increased to 5.6% by 2020 [13].

The estimated number of deaths from TB increased from 1.4 million to 1.6 million between 2019 and 2021 worldwide [2]. LTFU from TB treatment is a threat faced by TB control in Nigeria and remains a leading cause of these deaths [14]. The World Health Organization's (WHO) global TB report of 2021, states that the proportion of LTFU has persisted at 6% from 2012 to 2019 worldwide. With these are a significant number of LTFU cases [14] resulting in treatment failure or death, disease transmission in households and communities, and drug resistance [15]. Several challenges mitigate against the decline of TB incidence in Nigeria, including the high proportion of patients who are LTFU, nationwide socioeconomic imbalance, and high prevalence of latent TB infection.

According to the WHO's Definitions and Reporting Framework for Tuberculosis – 2013 Revision, which was updated in 2021, LTFU in patients with TB is defined as "a TB patient who did not start treatment or whose treatment was interrupted for two consecutive months or longer." [16]

A study reported that the factors for increasing LTFU in TB patients were negative attitudes toward treatment, limited social support, dissatisfaction with health services, and limited economic status [17]. Another study conducted in Namibia reported that male gender, age group 15-24 years, treatment service providers, TB intensive phase patients, and living in border/transit areas were factors for LTFU in TB patients [18]. A systematic review and meta-analysis study reported that multidrug resistance, and the anatomic location of tuberculosis were significant factors in the high prevalence of LTFU in TB patients [19]. LTFU is one of the reasons for the development of acquired Drug Resistance Tuberculosis (DR-TB). TB Patients who are readmitted after LTFU are more likely to redevelop infectious active

TB and are at higher risk of developing further drug resistant strains of tuberculosis [20]. A report on the economic challenges of TB drug non-adherence states that an estimated 52 MDR-TB patients lost to follow-up resulted in 5 patients developing XDR-TB, 3 newly infected MDR-TB and a new XDR-TB, and 3 deaths [19]. One of the leading cause of treatment failure are patients who discontinue their TB treatment too early [19]. LTFU can also increase the risk of clinical deterioration, treatment failure, and further complications in tuberculosis patients.

Knowledge of the magnitude of LTFU and its associated factors is essential for successful TB control and the optimal delivery of healthcare services in resource-poor settings.

However, there are no published data on the proportion of LTFU and its associated factors among patients enrolled in first-line tuberculosis treatment in the current study area. Therefore, this study assessed the magnitude of LTFU in tuberculosis treatment and associated factors among adults attending a public health facility in Nigeria.

Materials and methods

Study area

The study was conducted at the chest and TB clinic of Enugu State University of Science and Technology Teaching Hospital (ESUT-TH) Park Lane Enugu, Nigeria where patients with tuberculosis receive treatment. This clinic offers TB services for patients from within and outside Enugu State. It also accepts referral from primary and secondary health facilities within and outside the state.

Study design

The study was a 5 year retrospective cross-sectional study (2018-2022) of all TB cases treated at the chest and TB clinic.

Study population

All the patients that received TB treatment within the 5 year period

Inclusion criteria

Patients with confirmed TB.

Patients that received TB treatment at the center between 2018 and 2022.

Exclusion criteria

Cases with incomplete information on treatment outcomes.

Data collection methods

All the information were retrieved from the patients folders at the chest and TB clinic and entered into a pro forma

Statistical analysis

All the collected data were imputed into SPSS version 25. Descriptive statistics was done and presented as mean and standard deviation, frequencies and percentages. Bivariate analysis was done with Chi-square test to test for associations between the socio-demographic characteristics and LTFU with significance level placed at p-value ≤0.05.

Ethical clearance

Obtained from the research ethics committee of ESUTH Parklane Enugu. Anonymity was maintained by not writing names on the study materials. Confidentiality was maintained by keeping all the generated data in a safe box.

Results

A total of 483 patients were used for the study.

Table 1: Background characteristics of the TB patients

Variable	Frequency	Percent
Year		
2018	90	18.6
2019	84	17.4
2020	86	17.8
2021	97	20.1
2022	126	26.1
Age (years)		
Mean ±SD	38.91±17.39	
Age in groups (years)		
0-9	14	2.9
10-19	41	8.5
20-29	99	20.5
30-39	120	24.8
40-49	83	17.2
50-59	55	11.4
60-69	38	7.9
≥70	33	6.8
Gender		
Male	299	61.9
Female	184	38.1
Residence		
Rural	169	35.0
Urban	314	65.0
Educational level		
None	15	3.1
Primary completed	109	22.6
Secondary completed	223	46.2
Tertiary completed	136	28.2
Occupation		
Civil/public servants	42	8.7
Traders	133	27.5
Crafts/artisans	86	17.8
Farmers	34	7.0
Unemployed	111	23.0
Students	77	15.9
Marital status		
Single	207	42.9
Married	249	51.6
Divorced/separated	4	0.8
Widow/widower	23	4.8
Ethnicity		
Igbo	461	95.4
Hausa	13	2.7
Yoruba	1	0.2
Others	8	1.7
Living condition		
With family	385	79.7
With relatives	37	7.7
Alone	44	9.1
College/University	17	3.5
HIV status		
Positive	140	29.0
Negative	343	71.0
Previous history of TB		
Yes	54	11.2
No	429	88.8

Table 1 shows the background characteristics of the TB patients used for the study. More of the cases were seen in 2022 (26.1%). The mean age was 38.91±17.39. Most of the cases were in the 30-39 year age group (24.8%). About 2/3 of them were males (61.9%) and urban dwellers (65.0%). Most had secondary education (46.2%) and traders (27.5%). About half of them were married (51.6%) while almost all were Igbos (95.4%). About 29.0% were HIV positive while 11.2% had previous history of TB.

Table 2: Loss to Follow Up

Variable	Frequency	Percentage
LTFU	150	31.1
Not LTFU	333	68.9

Table 2 shows that the prevalence of LTFU was 31.1%

Table 3: Bivariate analysis of LTFU and socio-demographic characteristics

Variable	LTFU		X2	P value
	Yes	No		
Year				
2018	28 (31.1)	62(68.9)	4.416	0.353
2019	19(22.6)	65(77.4)		
2020	29(33.7)	57(66.3)		
2021	29(29.9)	68(70.1)		
2022	45(35.7)	81(64.3)		
Age				
<30	43(27.9)	111(72.1)	1.037	0.309
>30	107(32.5)	222(67.5)		
Gender				
Male	96(32.1)	203(67.9)	0.405	0.525
Female	54(29.3)	130(70.7)		
Residence				
Rural	56(33.1)	113(66.9)	0.525	0.469
Urban	94(29.9)	220(70.1)		
Educational level				
None	3(20.0)	12(80.0)	4.564	0.207
Primary completed	37(33.9)	72(66.1)		
Secondary	76(34.1)	147(65.9)		
Tertiary	34(25.0)	102(75.0)		
Occupation				
Employed	99(33.6)	196(66.4)	2.218	0.136
Unemployed	51(27.1)	137(72.9)		
Marital status				
Single	62(30.0)	145(70.0)	4.043	0.257
Married	79(31.7)	170(68.3)		
Divorced/separated	3(75.0)	1(25.0)		
Widowed	6(26.1)	17(73.9)		
Ethnicity				
Igbo	138(29.9)	323(70.1)	6.666	0.036*
Hausa	8(61.5)	5(38.5)		
Others	4(44.4)	5(55.6)		
Living condition				
With family	113(29.4)	272(70.6)	4.522	0.210
With relatives	15(40.5)	22(59.5)		
Alone	18(40.9)	26(59.1)		
College/University	4(23.5)	13(76.5)		
HIV status				
Positive	47(33.6)	93(66.4)	0.583	0.445
Negative	103(30.0)	240(70.0)		
Previous history of TB				
Yes	20(37.0)	34(63.0)	1.016	0.314
No	130(30.3)	299(69.7)		

* Significant value

Table 3 shows that only ethnicity significantly affected the LTFU [p=0.036] in this study.

Discussions

TB control continues to be a public health burden both in Nigeria and worldwide as its complexity remains a source of much concern. LTFU is a common finding with diseases that have long treatment time and chronic diseases. Most patients without good treatment supporters or those stigmatized can easily be loss- to-follow-up [21].

In our study, the overall LTFU was 31.1% while the remaining 68.9% were either cured, completed treatment or died during the treatment period. This was lower than what was reported in a similar study from Adamawa, Northern Nigeria (53.3%) [22], Lagos South-west Nigeria (40%) [23] and Mozambique (44.9%) [11] but higher than the report of another study from Delta state Southern Nigeria where the

LTFU was 12.9% over a five year period [24]. Other Studies from South Ethiopia (11.2%) [9], Jimma, Ethiopia (13.5%) [4], Georgia (12.5%) [7] and Brazil (18.1%) [10], also reported lower prevalence of LTFU. The differences observed in these studies may be attributed to the general challenges observed in health care services delivery, including TB control.

This calls for specific strategies to be incorporated into the medium and long-term strategic plans for TB control to reduce the burden of LTFU both nationally and at regional levels. These strategies should include building capacity in patient tracing and providing support for patients at risk of LTFU.

On bivariate analysis, only ethnicity significantly affected the LTFU rate. About 61.5% of the Hausa ethnic group of Northern Nigeria were LTFU. This was not surprising as many of them are migrant workers and can easily change place of residence. This may also be explained by the fact that many of them live alone with no constant source of income for transportation to health facilities to access their TB medications. This can be related to the report of a similar study in Northern Nigeria where 53.3% of the patients were LTFU [22].

Although, other socio-demographic characteristics did not show any statistically significant association, a higher proportion of those age >30 years were LTFU. This was consistent with the report of other studies that older patients are more likely to be LTFU than the younger ones [22, 25]. This could be explained by the fact that these elderly people may have other comorbidities, suffer from overall physiological decline with age, are less able to access health care due to distance, and are generally poorer than younger populations due to poor income. Contrary to our finding, a study from Namibia [18], Malaysia [26] and India [27] reported higher rate of LTFU among the younger patients. These younger persons may not want to be associated with TB especially among their peers and hence may stop their TB medications for fear of stigma.

More males were also LTFU compared to the females. Other studies corroborated our finding [18, 27-29]. Moreover, young males in LMICs have been reported to be at a higher risk of unemployment, HIV, alcohol and drug abuse, smoking, multiple sexual partners that predispose then to TB and poor outcomes, such as LTFU [4].

Those that live in rural areas had a higher rate of LTFU when compared to those that resided in the urban area. This can be explained by the long distance that the rural dwellers must travel before coming to access their TB medications. Studies have reported that patients who travel long distance >10km had higher risk of LTFU compared to those who travelled <10km [30, 31]. A large study conducted in Namibia reported that proximity to DOTS access points was related to a lower level of LTFU [18]. The greater the distance, the higher the LTFU rate, particularly for patients living outside the city [30]. Furthermore, economic constraints of transportation costs may also have justified how distance was associated with increasing LTFU [32]. This finding highlights the need to prioritize structural barriers and social determinants of TB care that are often overlooked in conventional TB care.

More of the patients with primary and secondary education were LTFU when compared to those with tertiary education. Other studies corroborated the finding [13, 31]. A similar study identified education as one of the individual factors that increased the risk of LTFU. Adult patients who just completed primary school had a strong positive association with LTFU. Other studies reported that a few years of schooling [33, 34]. and poor knowledge of TB [35] were associated with an increased risk of LTFU. It's also likely that this sub-group of patients may hold misconceptions or easily get deceived by misinformation about TB. Therefore, providing health education to patients that match their level of understanding could be helpful.

More of the employed patients were LTFU when compared to the unemployed. This can be due to the fact that that majority of the employed patients are being exposed to social and work stresses, which can sustain negative impacts and contribute to a high risk of LTFU. Other studies corroborated our finding [36, 37]. In contrast other studies reported that unemployment is a risk factor for LTFU [38, 39]. The reasons may be due to lack of money for transportation, the need to work despite illness, and no one supporting them to obtain their medication [40]. This shows that socioeconomic support remains an important aspect of TB treatment and control in ensuring the continuation of TB treatment. Despite the fact that anti-TB treatment is free to all TB patients, some out-of-pocket expenditures still exist, especially cost related to transportation. An average of (104.87 USD) out-of-pocket money per patient has been estimated in order to complete a 6-monthTB treatment [41]. Any intervention that could reduce the cost of TB treatment will help to improve patients' compliance with TB treatment and reduce LTFU.

Furthermore, the indirect costs incurred by TB patients on treatment include reduced income or a lower proportion of household income, which can lead to deeper poverty. A previous research reported that the costs incurred when a person does not work while on treatment account for 67% of the total costs incurred by TB patients [42].

Majority of the patients that were divorced/separated were LTFU. This can be explained by so many factors ranging from economic, psychological, social stigma, social support and depression. Similar studies reported that being single is an independent risk factor for LTFU [28, 29].

Higher proportion of patients that were living alone were LTFU when compared with those that were living with their family. It has been reported that lack of family support among TB patients was associated with over a two-fold increase in the risk of LTFU compared with those who had family support during treatment. Other studies have emphasized the importance of family and psychological support from healthcare workers to reduce or prevent LTFU from TB care [32, 43]. In countries like Nigeria, these supports including finance from family members is essential for successful TB treatment and subsequent decline in LTFU.

In our study, higher proportion of TB/HIV co-infected patients were LTFU when compared to HIV negative patients. TB and HIV co-infection has been reported to be linked to a high rate of ineffective TB treatment, including LTFU.[44] These TB patients with HIV take numerous drugs, thus, they may have poor adherence to treatment resulting in LTFU. In addition to TB treatment, patient with TB/HIV co-infection need to get HIV care and this may lead to interruption of TB treatment. This may be due to the associated difficulty in attending two clinics especially if both clinics are not located within the same hospital. Similar studies have reported some factors associated with LTFU among TB/HIV co-infected patients and they include pill

burden, believe in efficacy of TB treatment, side effects of drugs, failure of health workers to counsel patients of the potential side effects, HIV related stigma and discrimination and lack of disclosure [32, 45, 46].

More patients with previous history of TB were LTFU when compared to new cases. Other studies reported similar findings [36, 47]. This finding shows that TB cases that were LTFU previously are more likely to be LTFU again. Thus this group of patients should be given more health education, especially before the commencement of treatment. Follow up reminders should also be intensified while patients are on treatment. In addition, the higher frequency of LTFU in patients with previous history of TB may be attributed to psychological distress, lack of social support, stigma, and negative attitudes toward treatment [17, 48, 49]. These sub-group of patients are also at the highest risk for DR TB [45]. Therefore, it is essential to strengthen the management of patients that are being re-treated for TB before initiating treatment in order to reduce the incidence of drug resistant TB cases, deaths, and community transmission.

Our result findings provide important inputs to tailor interventions to the specific local needs to achieve the goal of ending TB by 2030, emphasizing factors that impact the rate of LTFU of patients on TB treatment [50].

Limitations

The limitations in this retrospective study includes the fact that some of the factors that have been previously reported to affect LTFU were not accessed in our study. These factors included distance to health facilities, patient knowledge of tuberculosis, attitude toward treatment, and treatment beliefs.

Conclusion

In conclusion, the study demonstrates a high prevalence LTFU among TB patients studied and this is above the global target of 0%. Ethnicity was significantly associated with LTFU and the group implicated are mainly unskilled migrant workers. This finding implies that main factors driving LTFU are related to socioeconomic status of the patients.

Hence socio-economic support for TB patients especially the migrant workers during their treatment period should be advocated for as this will reduce the rate of LTFU in the state. Also TB screening and education should be incorporated in workplaces and institutions that provide temporary employment (e.g. construction sites) for mobile young adults to enhance new cases detection and continuity of treatment for detected cases to improve treatment outcomes.

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