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Tuberculosis treatment outcomes and associated factors in a resource poor country; A five year retrospective study

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Abstract
Background: Tuberculosis (TB) remains a global public health challenge. There is need to continuously evaluate TB treatment outcomes especially at this time of a global economic meltdown which has significant impact in resource poor countries like Nigeria.
Objectives: To determine the treatment outcomes and associated factors among patients treated at a TB treatment centre in Nigeria.
Methods: This study retrospectively reviewed the 5-year treatment outcomes of patients treated for TB at a tertiary health facility in Nigeria. All the data were retrieved from the patient's folders at the TB clinic and entered into a pro forma. Data was analysed with SPSS version 25. Chi-squared test was used to test for associations between the background characteristics and treatment outcomes with significant level placed at p-value ≤0.05. All statistically significant variables on bivariate analysis were imputed into logistic regression to determine the predictors of unsuccessful treatment outcome.
Results: A total of 483 patients were studied. More of the patients had successful outcomes (58.3%). Those aged <30 years had about 2times odds of having an unsuccessful treatment outcome when compared to those > 30years of age. Those residing in rural area has 1.5 times odds of having unsuccessful outcome when compared to those residing in the urban areas. Also HIV positive patients had about 2 times odd of having an unsuccessful treatment outcome when compared to the HIV negative patients.
Conclusions: Treatment success rates in Enugu State Nigeria was below the 85.0% recommended target set by the WHO.

Keywords: Tuberculosis, treatment outcomes, Nigeria, predictors, Enugu State

Introduction

Tuberculosis is caused by a bacteria named Mycobacterium Tuberculosis. It is a major public health concern globally accounting for the top ten causes of death [1]. It is the leading cause of death from a single infectious agent since 2011, ahead of the Human Immunodeficiency Virus (HIV) infection [1]. Globally, there are an estimated 10 million new cases of TB (0.13%), equivalent to 132 cases per 100,000 population, with 9% of the 10 million people being HIV-positive persons. TB associated mortality globally was 1.3 million, with an additional 300,000 deaths from TB among HIV positive patients in 2017 [1].

TB mortality, including HIV associated TB death in Nigeria was 155, 000 in 2017 being the second highest reported mortality globally, after India [2]. According to WHO, Nigeria is among the top 10 countries with highest estimated rates per capita of people falling ill with TB and has at least 10, 000 cases per year.[1] The prevalence of TB in Nigeria has been estimated to be as high as 219 per 100, 000 population out of which 14.0% were HIV positive [1]. The HIV-positive TB incidence rate in Nigeria is 27 per 100, 000 population, while the MDR-TB incidence rate is 11 per 100, 000 ranking among the highest in the world [1].

There are 30 TB High Burden Countries (HBCs) that collectively accounted for about 87% of the world's TB cases. Nigeria was 6th among the high TB burden countries after India, China, Indonesia, Philippines and Pakistan [1]. Nigeria is among the 14 countries with overlap of high burden of TB, TB/HIV and multidrug resistant-TB (MDR-TB). HBC is defined as around 100 or more cases per 100,000 population [3]. The HIV-positive TB incidence rate in Nigeria is 27 per 100 000 population, while the MDR TB incidence rate is 11 per 100, 000 making it rank among the highest in the world [1]. The global treatment success rate was 82% among all new TB cases [1]. TB treatment saved 53 million lives globally (including HIV positive TB patients) and 11 million lives were saved in Africa. Nigeria recorded a treatment success of 86% in 2017 [1].

TB burden in Nigeria has overwhelming negative impacts on the growth and development of the country because the majority of the affected individuals are in the productive age groups. In addition to growing morbidity and mortality TB also, leads to both direct and indirect economic losses. Direct losses from the expenses incurred during treatment (transportation); indirect losses occurring from lost earned income by TB patients [4]. In Nigeria, Directly Observed Therapy Short-course (DOTS) is the treatment modality for treating TB [5]. There are DOTS centers in all the 774 local government in areas in Nigeria where TB diagnosis and treatment are provided. There are over 5,300 TB service points and 1, 602 microscopy centers in the country [6]. These centers are located mainly within the secondary and tertiary health facilities and some comprehensive primary health facilities.

Mycobacterium tuberculosis is an intracellular micro-organism and its replication is very slow hence prolonged multi-drug treatment regimen (6 months) is the recommended treatment modality implemented through DOTS [6]. Non-adherence to medications remains a potential challenge to TB management because of the prolonged

treatment time. Studies have identified some factors influencing medication adherence [7-13], out of which interventions [13-17] have been developed to improve adherence. Non-adherence and mortality have been shown to account for 64.0% and 32.0% of unsuccessful treatment outcomes respectively [18]. This is so, because adherence has been shown to have effect on other treatment outcomes [19]. A study reported that most intervention studies targeted only adherence, but it is obvious that improving adherence would be more valuable if it improved treatment outcomes of the patient [20].

One of the targets of the Sustainable Development Goals (SDGs) is to reduce the number of TB deaths by 90% by 2030, cut new cases by 80% between 2015 and 2030, and to ensure that no family is burdened with catastrophic cost due to TB and this can be achieved by preventing new TB cases, thereby reducing the burden of TB disease and its associated morbidity and mortality [21]. Several problems mitigate against achieving the targets of TB control in Nigeria and they include limited access to healthcare services and poor quality of DOTS centers, as well as insufficient health service capacity to deliver effective TB services that will cater for the needs of patients [21]. Other multi-faceted challenges affecting the TB control programs are: poverty, poorly trained and inadequate manpower, the compounding role of HIV, weak health policies and lack of adequate infrastructure among others [22]. The SDG targets cannot be achieved in Nigeria unless there is improvement in the quality of service delivered at different levels of health care [22]. Quality of services has been reported to have an impact on the outcome of TB control in the country [23].

Current health interventions for TB prevention include: treatment of latent TB infection (LTBI), with particular attention to children aged less than five years and HIV positive TB patients, prevention of transmission of Mycobacterium tuberculosis through infection control especially among healthcare workers; and vaccination of children with the Bacille Calmette-Guérin (BCG) vaccine [1]. Many contributing factors to poor TB treatment outcomes have been reported and they include lower education, smoking, absence of Bacille Calmette-Guerin (BCG) vaccination scar, previous anti-tuberculosis treatment, not receiving directly observed treatment, advanced chest radiography findings, treatment in tertiary settings, MDR-TB and presence of extra-pulmonary TB.[24] Others include older age, male sex and HIV infection [24, 25]. Since DOTS Strategy was implemented in Nigeria, there has been improvement in treatment success rate from 15% in 1995 to 86% in 2017 and in case detection rates which improved from 4.3% to 25.8% during the same period [26] However, there are wide variations in these estimates at sub-national levels [1]. Case detection of TB cases in Nigeria is still very low [27], and evidence also continues to indicate poor treatment outcomes [23].

Unsatisfactory treatment outcomes have serious consequences in TB control, including ongoing infectivity and development of drug resistant TB and mortality [28]. Although there has been improvement in treatment success rate in Nigeria with the advent of DOTS initiative, but these improvements are still suboptimal and may mitigate against the achievement of the SDG target.

This study was conducted to retrospectively determine the 5-year treatment outcomes and associated factors among patients treated at a TB treatment centre in Nigeria.

Materials and methods

Study area

The study was conducted at the chest clinic and TB treatment center of Enugu State University Teaching Hospital (ESUTH) Park Lane Enugu Nigeria where patients with tuberculosis receive treatment.

Enugu State University Teaching hospital is centrally located within the Enugu Metropolis. It is one of the tertiary health institutions in Enugu State that provide TB treatment services to patients. It also caters for patients referred from the primary and secondary health facilities. This clinic offers TB services to patients from within and outside the state.

Study design

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

Study population

All the patients that received TB treatment and care within the 5 year period.

Inclusion criteria

Haven received TB treatment at the facility within the 5-year period

Exclusion criteria

Records with missing information on the outcome of treatment.

Data collection methods

All the data were retrieved from the patient's folders at the treatment center and entered into a pro forma. This was done between 2nd October through 30th November 2023 and a total of 483 patients were studied.

Data management

Independent variable

Background characteristics of the patients.

Dependent variable

Treatment outcome (cured, treatment completed, lost to follow up, transferred out, died)

Statistical analysis

All the data were analyzed with SPSS version 25. It was presented as frequencies and percentages. Chi-squared test was used to test for associations between the background characteristics and treatment outcomes with significant level placed at p-value ≤ 0.05. All variables with significant level of 0.2 on bivariate analysis were imputed into logistic regression to determine the predictors of unsuccessful treatment outcome.

Definition of terms

Treatment outcomes of TB patients in this study were classified as successful (cured or treatment completed) or unsuccessful (defaulted, loss-to follow-up, treatment failure or died), as defined from the World Health Organization (WHO) and National TB and Leprosy Control Program (NTBLCP) guidelines [1, 5, 29, 30]. This study used successful and unsuccessful treatment outcomes as the outcome measure.

Cured: Refers to a pulmonary TB patient who was smear or culture positive at the beginning of treatment and is smear or culture negative upon completion of treatment [5].

Completed Treatment: is a TB patient who completed treatment but without evidence (no laboratory test) at the end of treatment [29].

Successful treatment outcome: Cured and completed treatment together make up successful treatment outcomes which should increase towards 100% and reach at least 85% with good case management [5].

Unsuccessful Treatment outcome includes: Defaulted/ lost to follow-up, treatment failure or died.

Treatment Failure: Is a PTB patient who was smear or culture positive at beginning of treatment and remains positive at month 5 or later during their most recent course of treatment [5].

Lost to follow-up: Is a TB patient who did not start treatment or whose treatment was interrupted for two consecutive months or more [5].

Defaulted: Is defined by the WHO as missing more than 20% of the prescribed doses during the treatment period i.e. a treatment interruption of two consecutive months or more after at least 1 month on treatment [30]. The definition of defaulters however can vary within national programs, for example, the Federal Ministry of Health in Nigeria, defined defaulting as not taking anti-TB medications consecutively for more than 2 days intensive phase and more than two consecutive weeks continuation phase [29].

Retreatment: Is a sputum AFB positive TB patient who had a one or more month extension of intensive phase due to sputum in conversion [29].

Relapse: is a patient who was cured or completed treatment, but returned sputum positive or with clinical symptoms of TB (either a true relapse or a new episode of TB caused by reinfection) [5]. Died refers to a TB patient who died for any reason during the course of treatment. [29]

Results

A total of 483 patients were studied.

Table 1: Background characteristics of the patients

Variable	Frequency N-483	Percent
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
Place of 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 socio-demographic characteristics of the TB patients used for the study. 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%). Majority were living with their family (79.7%), are HIV negative (71.0%) and with no previous history of TB (88.8%).

Table 2: Tuberculosis treatment outcomes

Variable	Frequency (N-483)	Percent
Treatment outcome		
Cured	119	24.6
Treatment completed	163	33.7
LTF	150	31.1
Died	51	10.6
Treatment outcome re-categorized		
Successful outcome	282	58.3
Unsuccessful outcome	201	41.7

LTF; Lost-To-Follow-up

Table 2 shows that more of the patients had successful outcomes (58.3%).

Table 3: Factors associated with treatment outcomes among TB patients

Variable	Treatment outcome		X2	P value
	Successful	Unsuccessful		
Year				
2018	52(57.8)	38(42.2)	1.945	0.746
2019	54(64.3)	30(35.7)		
2020	51(59.3)	35(40.7)		
2021	56(57.7)	41(42.3)		
2022	69(54.8)	57(45.2)		
Gender				
Male	171(57.2)	128(42.8)	0.461	0.497
Female	111(60.3)	73(39.7)		
Age				
<30	103(66.9)	51(33.1)	6.720	0.010*
>30	179(54.4)	150(45.6)		
Place of Residence				
Rural	88(52.1)	81(47.9)	4.266	0.039*
Urban	194(61.8)	120(38.2)		
Educational level				
None	9(60.0)	6(40.0)	5.404	0.144
Primary completed	57(52.3)	52(47.7)		
Secondary	126(56.5)	97(43.5)		
Tertiary	90(66.2)	46(33.8)		
Occupation				
Civil/public servants	25(59.5)	17(40.5)		
Trading	72(54.1)	61(45.9)	4.362	0.499
Crafts/artisans	51(59.3)	35(40.7)		
Farmers	16(47.1)	18(52.9)		
Unemployed	69(62.2)	42(37.8)		
Students	49(63.6)	28(36.4)		
Marital status				
Single	129(62.3)	78(37.7)	3.997	0.262
Married	140(56.2)	109(43.8)		
Divorced/separated	1(25.0)	3(75.0)		
Widowed	12(52.2)	11(47.8)		

Ethnicity				
Igbo	273(59.2)	188(40.8)	3.890	0.274
Hausa	5(38.5)	8(61.5)		
Yoruba	0(0.0)	1(100.0)		
Others	4(50.0)	4(50.0)		
Living condition				
With family	226(58.7)	159(41.3)	1.775	0.620
With relatives	21(56.8)	16(43.2)		
Alone	23(52.3)	21(47.7)		
College/University	12(70.6)	5(29.4)		
HIV status				
Positive	71(50.7)	69(49.3)	4.774	0.029*
Negative	211(61.5)	132(38.5)		
Previous history of TB				
Yes	30(55.6)	24(44.4)	0.200	0.654
No	252(58.7)	177(41.3)		

* Significant values

Table 3 shows the factors associated with treatment outcomes. These factors included age (p=0.010; χ^2=38.890), place of residence [p=0.054; χ^2=7.643), ethnicity (p=0.051; χ^2=16.852) and HIV status (p=0.001; χ^2=17.455)

Table 4: Predictors of TB treatment outcomes

Variable	Adjusted Odds ratio	P value	95% CI Lower	Upper
Age (years)				
<30	1.777	0.006*	1.182	2.670
≥30	1			
Place of Residence				
Rural	1.484	0.052*	0.997	2.210
Urban	1			
Educational Level				
None	1.362	0.589	0.444	4.174
Primary completed	1.537	0.133	0.877	2.695
Secondary	1.447	0.111	0.919	2.279
Tertiary	1			
HIV status				
Positive	1.612	0.032*	1.042	2.496
Negative	1			

* Significant values

Table 4 shows predictors of treatment outcome. Age, place of residence and HIV status predicted treatment outcome. Those aged <30 years had about 2times odds of having an unsuccessful treatment outcome [p=0.006; CI (1.182-2.670)] when compared to those > 30years of age. Those residing in rural area has 1.5 times odds of having unsuccessful outcome [p=0.052; CI (0.997-2.210)] when compared to those residing in the urban areas. Also HIV positive patients had about 2 times odd of having an unsuccessful treatment outcome [p=0.032; CI (1.042-2.496)] when compared to the HIV negative patients.

Discussions

Although Tb is curable and increased access to TB treatment, the treatment outcome is still poor in Nigeria and below the WHO recommended levels [1]. The TB treatment success rate in our study was 58.3% with 24.6% cure rate. The success rate is similar to the report of a study conducted in Anambra State South East Nigeria where the success rate was 57.5% [31]. but lower than the report of other studies conducted in Oyo state South-West Nigeria [31], Plateau state North Central Nigeria [32] and the global success rate of 82.0%. [1] Other studies from Ghana [33] and Ethiopia [34] reported higher treatment success rates higher than the global success rate. The Ghanaian study suggested that improvements in diagnosis, community TB care, stigma reduction among community and health workers towards TB patients, the use of enablers' package and public–private partnership contributed to the improved treatment outcomes recorded in their study [33]. In the present study, stigmatization both at the health facility and community may account for the lower treatment success rate recorded.

Another reason for the low treatment success rate in our study may be due to the high rate of loss-to-follow-up (31.1%). Loss-t-follow-up have been shown to impact negatively on treatment success rate in a study from South East Nigeria [36]. A single patient lost to follow up remains a potential source of infection spread to the community with high risk of developing drug or multi-drug resistant TB [37]. This is so because TB is a highly infectious disease. Hence the rate of loss to follow up in our study leaves us with a cause to bother about.

It calls for strengthening of our TB programs, through improved patient-centred care and individualised treatment plans. A more comprehensive treatment model should also factor in ways of addressing associated problems such as poverty, addressing behavioural problems among high-risk patients such as HIV/TB co-infected and young male patients, psychosocial care and spiritual support already established as mediators of treatment outcome in the literature [38, 39]

The cure rate in our study was 24.6% which is very low compared to the recommended standard. The rate is similar to that of a similar study from Ogbomosho South-West Nigeria, [35] but lower than the report of other studies from Anambra, [31] and Oyo states. [31] In the latter two studies the cure rate was calculated with number of smear positives as the denominator while our study used all the TB positive cases diagnosed through any of the diagnostic ways. This may account for the higher cure rate in their study.

The mortality rate in our study was 10.6% and this was similar to the finding of another study [40] but higher than the report of other Nigerian studies. [35, 41] Socio-demographic factors may account for the differences as a recent study reported a relationship between poor socio-demographic indices and gross domestic product with excess mortality in TB patients [42, 43].

Treatment outcome success increased between 2018 and 2019 but subsequently reduced progressively from 2020 to 2022. The increase in loss- to- follow –up-cases and death

rate within the 3-year interval may explain downtrend in treatment outcome success rate.

The predictors of treatment outcomes were age, place of residence and HIV status. Patients aged <30years had about 2x odds of unsuccessful treatment outcome when compared with those ≥30years. Younger patients including children are more likely to die especially those that are HIV/TB co-infected due to severe immunosuppression. Younger patients may also default because they don't want to be associated with TB by their peers. Studies have shown that the second-to-third decades of life has been associated with high-risk behaviours such as drug abuse, alcoholism, smoking, socioeconomic struggles (poverty, poor housing) which are risk-factors for TB and TB-HIV co-infection [10, 40]. The 2016 global, regional and national burden of TB report for 1990–2016 shows a similar age distribution of TB and mortality [43] Screening young adults at job sites and recreational centers could potentially lead to early treatment and less impact.

Patients residing in the rural areas had more unsuccessful treatment outcome when compared with those residing in the urban areas. This may be due to the fact that urban dwellers are more likely to be better educated and have better knowledge of TB and its complications. They may also be of a better social class with good nutrition which will most likely give a better outcome.

In our study, being HIV positive predicted unsuccessful treatment outcome. Thus HIV/TB co-infected patients are more likely to have unsuccessful treatment outcomes when compared to HIV negative TB patients. Possible explanations may be malabsorption of TB medications and high pill burden leading to non-adherence. Also high mortality have been reported in HIV/TB co infected patients due to treatment failure or other complications of HIV infection [44] severe immunosuppression [45, 46], and other co-morbidities like cardiovascular diseases and Diabetes Mellitus [45, 47, 48, 49]. Similar studies corroborated my finding [44, 50, 51].

With the intensified application of 'the Three I's for HIV/TB' which are (1) Intensified case finding for TB, (2) Isoniazid preventive therapy (IPT) and (3) Infection control; the burden of TB among people living with HIV will be reduced [23]. Conversely, some studies reported that HIV/TB co-infected patients had better successful treatment outcomes when compared to HIV negative TB patients [32, 52, 53].

Conclusion

In other to meet the SDG goals and have a world without TB, it requires tackling social determinants of health. Treatment success rates in Enugu state were below the 85.0% recommended target set by the WHO. In the present study, age, place of residence and HIV status predicted treatment outcome. Those aged below 30 years, urban dwellers and HIV positive patients should be targeted for continuous screening, early diagnosis and treatment to improve treatment success rates.

Similar studies can also be carried out in other TB treatment centres to identify factors associated with treatment outcomes. This will help to design and implement appropriate facility-specific interventions.

Limitations

This was a retrospective study and some of the patients treated at the centre were not included in the study due to missing data on treatment outcomes. This may limit the generalizability of the study result. This study was a single-centre study only covering mainly patients from Enugu state and its environs thus, it might be difficult to generalize the results to other areas of Nigeria.

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