

Original Research Article

PREVALENCE AND PREDICTORS OF TUBERCULOSIS TREATMENT DEFAULT IN ABAKALIKI, NIGERIA: AN IMPLICATION FOR PATIENT CENTRED EDUCATION AND TREATMENT FOLLOW-UP

Abstract:

Introduction: Tuberculosis (TB) treatment is the most effective strategy for preventing the spread of the disease. Default in TB treatment remains an important contributor to treatment failure, resurgence of multidrug resistance (MDR-TB), prolonged infectiousness, relapse and death. TB treatment default increases the disease burden and poses a threat to its elimination. This study determined the prevalence and predictors of tuberculosis treatment default.

Methods: Records of 686 patients from TB treatment register at Federal Teaching Hospital Abakaliki from year 2012 to 2016 were analysed. Key informant interviews were conducted with nurses to elicit the factors associated with default. Ethical approval and permission were obtained respectively from the ethics committee and TB unit chief nurse. Records of treatment follow-up were grouped as “defaulter” and “non-defaulter”. Data analysis was done using SPSS software, version 20. Chi squared test of statistical significance was done at $P = .05$, and thematic analysis was done for the qualitative data.

Results: Mean age of the patients was 34.9 ± 5.7 years, and prevalence rate of default was 10.6% for the five-year period. Majority (73.1%) defaulted within the intensive phase of treatment. Common reasons for defaulting were: ‘well feeling’, ‘distance to health facility’, and high pill burden. Among the defaulters, 25% were ≤ 29 years, 52.8% were males, and 68.1% lived in rural areas. Predictors of TB treatment default were male gender (AOR =2.1; 95% CI: 1.4-7.5), and rural residence (AOR=1.8; 95% CI: 1.3-5.7).

Conclusion: Default rate was high among the patients, and it was mostly associated with the distance from the health facility. We recommend decentralization of treatment centres to rural areas; together with individual patient-centered education and counseling on treatment duration as measures to reduce defaulter rate.

Keywords: Prevalence; predictors; TB treatment default; patient education; treatment duration

1. Introduction: Tuberculosis (TB) remains a major public health problem and its control is still a global challenge especially in high-burden countries mainly due to limited resources, high co-infection with human immunodeficiency virus (HIV), and emergence drug-resistant TB^{1,2}.

Nigeria ranks 3rd among the 10 countries that accounted for 77% the total estimated gap between notification of new cases and the estimated number of incident cases in 2016, and has the second highest TB burden in Africa with an estimated prevalence rate of 161 per 100 000 population in 2012^{1,2,3}. The World Health Organisation (WHO) currently recommends a case detection rate of 70% and a treatment success rate of 85% for all TB cases¹. It is believed that achieving these targets will lead to a reduction in TB prevalence, transmission, default rate, and drug resistance to TB².

Treatment default which is defined as interruption of TB treatment for two consecutive months or more after initiation of treatment is a serious problem in tuberculosis control. It may lead to persistence of infectious source, increased mortality, increased relapse rates, and facilitate the development of resistant strains. To overcome this challenge, the World Health Organization recommends the adoption of the Directly Observed Treatment Short-Course strategy (DOTS)⁴ in which one component is directly observed treatment (DOT) by a health professional. Several studies have reported that this measure reduces the abandonment of treatment⁵. However, other studies did not observe any difference between supervised or self-administered treatment⁶.

In 2010 the WHO recommended a change in its treatment guidelines for TB from an 8-month anti-TB regimen consisting of 2 months of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E), followed by 6 months of ethambutol and isoniazid, 2RHZE/6EH; to a 6-month regimen containing 6 months of rifampicin (2RHZE/4RH)⁷. The Nigerian National TB Control Programme (NTP) adopted the current WHO guideline in January 2012⁸. Since these changes were adopted, it is unclear if the shorter treatment regimen lowers the risk of default or death during treatment. Therefore, there is a need to re-assess the determinants of treatment default and mortality among TB patients.

Factors identified to be associated with treatment default are: lack of knowledge about the disease, distance from the health post, partial or complete regression of symptoms in the first two months of treatment, the side effects associated with the medication, male gender, age, the use of toxic substances and hospitalization during treatment⁹, pre-existing pulmonary disease, previous default, TB/HIV co-infection¹⁰, absence of supervised treatment and poor quality of patient care at the health unit¹¹. Others are social and economic factors, healthcare team- and system-related factors, condition-related factors, therapy-related factors and patient-related factors. Designing

effective interventions to reduce TB treatment default and to improve treatment outcomes requires an understanding of the factors that affect treatment adherence¹². This study determined the prevalence and predictors of tuberculosis treatment default in Abakaliki, Nigeria.

2. Materials and Methods:

2.1. Study area, design and population. This study was conducted in Federal Teaching Hospital Abakaliki (FETHA) using a retrospective cohort study design, involving quantitative and qualitative methods. Within the cohort a nested case control study design was used wherein patients defaulting from treatment were considered as ‘cases’ and those completing treatment as ‘controls’.

2.2. Study Population, TB diagnosis and treatment at FETHA: Individuals who presented with cough lasting more than 2 weeks were diagnosed with sputum smear microscopic examination for acid-fast bacilli and a chest X-ray. Extra-pulmonary TB patients were individuals with a histological diagnosis of TB. All patients suspected of TB also received HIV counseling and testing. Those found to have TB were started on treatment with short course chemotherapy (SCC). Tuberculosis treatment at FETHA is based on the DOTS strategy in accordance with the Nigerian National Tuberculosis Control Program guidelines and WHO recommendations^{7, 13}.

2.3. Data collection and analysis

Institutional TB registers and patients’ case notes were used for extraction of data on patient registration status (“*new case*” vs. “*retreatment case*”), age, gender, residence, smear status, complaints documented by the Doctor during follow-up, and treatment outcome. Data were sorted into the six treatment outcomes: cured, treatment completed, defaulted, died, treatment failure and transferred out. Treatment follow-up was grouped as “defaulter” and “non-defaulter”. Five outcomes (excluding defaulters) were combined into one variable called ‘non-defaulters’. Patients who defaulted from treatment were defined as those whose treatment was interrupted for 2 or more consecutive months. The defaulters were then compared to the non-defaulters to identify factors associated with treatment default. Key informant interviews (KIIs) were conducted with the Chief Nursing Officer heading the TB unit, the local government area Tuberculosis and Leprosy Supervisor (TBLS), and 3 other Principal Nursing Officers in the unit who were involved in counseling, treatment and follow-up of TB patients, to obtain some facts

concerning treatment default from their own perspective. The interviews were conducted by three members of the study team (an interviewer, a note taker and a digital recorder operator) using an interview guide, after obtaining for recording, and each session lasted 30 and 45 minutes. Verbatim translation of the recording was done within 24 hours and cross-checked with the written notes for consistency with non-verbal expressions.

Data of 686 patients from TB treatment register at FETHA from year 2012 to 2016 were extracted and analysis was done using SPSS software, version 20. Chi squared test of statistical significance was used in the analysis and level of significance was set at p-value of less than 0.05. Thematic analysis was done for the qualitative data under six sub-theme questions, which include: How would you describe the level default from TB treatment in this hospital, is it low or high? What factors do you think are responsible for treatment default? Are there ways of predicting or suspecting those that might default before initiation of treatment? What strategies do you use to prevent or minimize treatment default? What are your challenges or constraints in preventing or minimizing treatment default? And, how do you think treatment default could be prevented?

Proportions and means ($\pm$ standard deviation) were calculated. For categorical variables, proportions were compared using the chi-squared test. Trends of default were analysed using Chisquared test. Demographic, clinical and other factors associated with treatment default were analysed using univariate analysis. Variables known to be risk factors for default and factors associated with default in the univariate analyses ($P = .05$) were selected for the logistic regression analysis. Odds ratios at 95% confidence interval (CI) were estimated using a multivariate logistic regression analysis with predictors of treatment default as an outcome variable.

2.4. Ethical considerations: Ethical approval and permission were obtained respectively from the institution's ethics committee and unit chief nurse. Consent for digital recording of the KIIs was also obtained from the interviewees. Strict confidentiality was maintained throughout.

3.0. Results:

The mean age of the respondents was 34.9 ± 5.7 years. Of the 686 clients' records, 72 (10.59%) defaulted within the five-year period, giving a prevalence rate of 10.6%. Majority (73.1%) defaulted within the intensive phase of treatment. Reasons for defaulting were 'well feeling' within the first month of treatment, distance to health facility, and high pill burden. Among the

defaulters, 59.7% were ≤ 39 years, 58.3% were males and 61.1% lived in rural areas. Predictors of TB treatment default were male gender (AOR = 2.1; 95% CI:1.4-7.5) and rural residence (AOR=1.8; 95% CI:1.3-5.7).

Table 1: Demographic and clinical profile of 686 TB patients in Ebonyi Nigeria, 2012-2016

Variable		No. (%)
Age (years)	≤ 39	266 (38.8)
	≥ 40	420 (61.2)
Gender	Male	389 (56.7)
	Female	297 (43.3)
Residence	Urban	238 (34.7)
	Rural	448 (65.3)
Disease type	Pulmonary TB	579 (84.4)
	Extra-pulmonary TB	107 (15.6)
Treatment category	New	667 (97.2)
	Retreatment	19 (2.8)
Treatment regimen	First line 1	686 (100)
	Second line 2	0 (0)

Table 2: Proportion of TB patients who defaulted during the 5-year period under review

Year	Number on treatment	Defaulters N (%)	Percentage (%)
2012	127	7	5.51
2013	160	17	10.23
2014	162	23	14.19
2015	119	14	11.77
2016	118	11	9.32
Total	686	72	100

Table 3: Time of default from treatment among defaulters

Time of default	Frequency (%)	Cumulative frequency (%)
Intensive phase	53 (73.1)	53 (73.1)
Continuation phase	19 (26.9)	72 (100)

Table 4: Univariate analysis of factors associated with TB treatment default; 2012-2016

Variable		Default (n=72) No. (%)	No default (n=614) No. (%)	Adjusted Odd Ratio (95% C.I)	P- value
Age (years)	≤ 39	43 (59.7)	223 (36.3)	2.4 (0.7-8.8)	0.07
	≥ 40	29 (40.3)	391 (63.7)		
Gender	Male	42 (58.3)	347 (56.5)	2.1 (1.4-7.5)	0.04*
	Female	30 (41.7)	267 (43.5)		
Residence	Urban	28 (38.9)	210 (34.2)	2.2 (1.5-7.6)	0.05*
	Rural	44 (61.1)	404 (65.8)		
Status	Feeling well	9 (12.5)	63 (10.2)	2.2 (1.5-7.7)	0.05**
	Feeling unwell	0 (0)	614 (100)		
Disease type	Pulmonary TB	63 (87.5)	518 (84.4)	1.7 (1.2-5.6)	0.02*
	Extra-pulmonary TB	9 (12.5)	98 (15.6)		
Treatment category	New	64 (88.9)	603 (98.2)	2.3 (1.5-7.8)	0.05*
	Retreatment	8 (11.1)	11 (1.8)		
Pill burden	Yes	3 (4.2)	69(11.2)	2.2 (1.6-7.7)	0.05**
	No	0 (0)	614 (100)		

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144 **Fisher's exact Test (FT) *Statistically significant

145 **Table 5:** Predictors of TB treatment default among patients in Ebonyi State, Nigeria

Variable	Default (n=72) No. (%)	Not default (n=614) No. (%)	Adjusted Odd Ratio (95% C.I)	P-value
Gender			2.1 (1.4-7.5)	0.04*
Male	42 (58.3)	347 (56.5)		
Female	30 (41.7)	267 (43.5)		
Residence			1.8 (1.3-5.7)	0.03*
Urban	28 (38.9)	210 (34.2)		
Rural	44 (61.1)	404 (65.8)		
Status			1.2 (0.7-1.4)	0.51
Feeling well	72 (100)	614 (100)		
Feeling unwell	0 (0)	0 (0)		
Disease type			2.6 (0.9-7.8)	0.12
Pulmonary TB	63 (87.5)	518 (84.4)		
Extra-pulmonary TB	9 (12.5)	98 (15.6)		
Treatment category				
New	64 (88.9)	603 (8.2)	1.4 (0.9 - 1.9)	0.14
	8 (11.1)	11 (1.8)		

Retreatment				
Pill burden				
Yes	3 (4.2)	69 (11.2)	1.3 (0.9 - 2.3)	0.23
No	0 (0)	614 (100)		

*Predictors

3.1. Extractions from thematic analysis of the KII

The respondents described the level treatment default as moderately high.

On the factors responsible for treatment default, one of the respondents said “Some patients come from far places because they don’t want to be treated in health facilities close to their usual residence due to stigma associated with tuberculosis disease”. Another stated, “Disappearance of symptoms and erroneous believe of being cured during the intensive phase of treatment make them to abandon their medication. Other reasons given include: delay in recovery and resorting to use of local herbal concoctions as alternative medicine; side effects of the drugs, especially in those with co-morbid conditions.

According to the respondents, the patients that frequently default are: those who do not want treatment supporter; those who are reluctant to provide their phone numbers or those of their relatives; those from far places who do not want to be transferred out; unmarried young adults; and those without fixed employment address.

Some of the strategies used by the respondents to prevent default include: individual patient counseling on treatment duration, side effects of the drugs, consequences of treatment default; transferring patients (who agree) to treatment facilities near their residence; ensuring that patients provide at least three mobile phone numbers (their own, next of kin, and treatment supporter) and verifying them immediately before initiating treatment; tracking patients that missed appointment; getting permanent home address of the patients and their treatment supporter;

Some of the challenges in preventing default are: inadequate resources for contact tracing (such as vehicle for home visit, money for phone calls), poor documentation of patients, supply of wrong residential address and mobile phone number by patients, relocation of patients to a new city, inadequate supervision by the treatment supporter

Default can be reduced to the barest minimum by: immediate verification of patients' address and phone numbers during treatment initiation; assigning members of staff familiar with the patients as treatment supporters; securing signed undertaking from treatment supporters to supervise the medication; involving Community Based Organizations in supervising treatment; and insisting that patients receive treatment at health facilities nearest to them.

4. Discussion:

This study found TB treatment default rate of 10.6% for the five years period of review. Defaulting occurred more (73.1%) in the intensive phase of treatment period and showed a downward trend the following years. Male gender and rural residence were predictors for defaulting. Early abandonment of treatment may lead to poor treatment outcomes such as treatment failure, emergence of drug resistant TB and even death. The default rate in this study was higher than the 8% found in Kenya¹² but lower than the 20% reported in Cameroon¹⁴. The reasons for these differences in default may partly be explained by the location of the study: the Kenyan and Cameroonian studies were conducted among urban dwellers, whereas this study was conducted among the urban and rural residents. The distance from the health facilities could also be a factor.

Large proportion of patients (73.1%) defaulted during the intensive phase of treatment. This finding is similar to previous findings in Uganda (where 76% defaulted at the end of the intensive phase of treatment¹⁵), Nigeria and Uzbekistan^{2,16}. However, it is at variance with the findings in Kenya and Cameroon earlier reported^{12,14}, Morocco, Moldova, Indonesia and a systematic review which showed that most patients defaulted during the continuation phase of treatment in low-and middle-income countries¹⁷⁻²⁰. This finding of large proportion defaulting in intensive phase may be a result of inadequate pre-treatment health education and poor follow-up mechanisms resulting from overworked healthcare personnel¹³. Other possible explanations include the following: early defaulters erroneously believing that they have been cured due to symptom resolution; high economic costs of travel, food, and waiting time for each visit; and drug side effects. However, it is possible that their clinical condition was worsened by co-morbidities such as HIV/AIDS or resistance of the *Mycobacterium* to anti-tuberculosis medication, and patients may lose hope for improvement after having made every effort during the first two months.

A good understanding of the peak period of treatment defaulting will help TB program managers to properly address this problem at the onset of treatment through adequate health education, adherence counseling, appropriate contact with a treatment supporter and economic support where and when necessary²¹. The current DOTS programme in Nigeria may use combination of incentives and enablers, which include education for patients and their families, referrals for other social services, as well as use of outreach teams, and tracing of defaulters. Greater efforts are required in the education of the patients and the public to increase their understanding of the importance of treatment completion for patients with tuberculosis. It has been found that inadequate knowledge is a significant factor for default. Receiving sufficient explanation on disease makes patients to understand treatment requirements, likely side effects to be encountered when using anti-TB drugs and the need to comply with treatment¹².

Good relationship between patient and health professional can improve treatment adherence, but there are several health care related factors that may negatively affect adherence. They include negative attitudes of health professionals, lack of credibility, negative attitude of the patient in relation to services, lack of medicines, and poor access to health services²².

Male sex (AOR=2.1; 95% CI:1.4-7.5) and rural residence (AOR=1.8; 95% CI:1.3-5.7) were predictors of TB treatment default in this study. This is consistent with the report in Kenya¹³. In settings where male sex is a predictor of default, men are the main economic providers for their families¹³. Thus, men tend to leave home early for work and may have difficulty complying with treatment and follow up. However, in our setting women also make economic contributions (with farming and trading) to sustain their households.

Patients residing in a rural area were more likely to default than those in urban. This may be due to the distance to this hospital (which is located in an urban area); cost of transportation when travelling from a rural area to the hospital may be a major contributor. Previous studies in other settings have documented distance to health facilities as a predictor of default^{12,14}. The health system in high burden countries suffers limited outreach services for the rural population - this is particularly seen in rural areas of Ethiopia, Indonesia, Pakistan and Nigeria². Also, the poorer socioeconomic status of rural residents may constitute a hindrance in their ability to access health services²³. Further expansion of the DOTS program and the appropriate transfer of diagnosed rural TB cases may reduce default rates.

Although this study provides important information on default rate and predictors of TB treatment default in Abakaliki, Nigeria, the analysis is limited by the use of retrospective data available from TB registers and patients' case notes. The records used did not contain information on patient income, employment status, alcohol consumption, tobacco use, nutritional status, co-morbidities, patients' knowledge of TB, distance to health facility, and patients' perception of TB services. The TB/HIV drug combination can lead to treatment default as a result of the large number and diversity of drugs, and adverse effects. These factors have been found to predict default and/or death in other settings^{17-19,23}. Some of the sampled defaulters in our study were not traced, whereas others might have died and the treatment center was not notified. This is a strong limitation of this study. Further longitudinal studies on why default occurs and what type interventions that could be most effective may improve these limitations.

Conclusion

The prevalence of TB treatment default in this study was 10.6%, and default occurred more in the intensive phase. Default can be reduced substantially by patient centered health education about the need for adherence during the intensive phase of treatment, further decentralizing locally administered DOT in a patient-centered model to patients in rural communities. Again, active tracing of defaulter must be instituted at the center, and gender differences in treatment default and other patient and health system factors affecting the timing of default should be further investigated

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