

Characterization of Defaulters from Tuberculosis Treatment in a Tertiary Hospital in South Eastern Nigeria

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Abstract

Background: Tuberculosis is second only to HIV/AIDS as the greatest killer worldwide, due to a single infectious agent. Directly Observed Treatment Short-Course (DOTS) is presently the WHO recommended programme to fight tuberculosis worldwide. There is a need to understand the characteristics of patients who default from treatment for tuberculosis. This will help modify the strategies to reduce such default to the barest minimum and achieve higher levels of adherence. **Objective:** The aim of this study was to describe the characteristics of patients that defaulted from treatment for TB at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi DOTS clinic for the period 1st January 2011 to 31st December 2012. **Materials and Methods:** This was a retrospective study conducted at the DOTS clinic at Nnamdi Azikiwe University Teaching Hospital Nnewi, Anambra State, Nigeria. The records of patients who received treatment from the clinic from 1st January 2011 to 31st December 2012 (2 years) were reviewed. The data collected include patients' demographic characteristics, treatment category, patient type, baseline sputum smear result, and retroviral status. From the data, default rate was calculated and its relationship with other variables noted. Associations between patients' characteristics were determined using chi square test of independence. The significance level was set at $p = 0.05$. **Results:** A total of 765 patients enrolled for TB treatment in the DOTS clinic of the study area within the study period of 1st January 2011 and December 31st 2012. The mean age at commencement of the treatment was 33.14 years (± 18.09). The outcome of treatment showed that 260 (34%) had treatment completed, 230 (30.1%) cured, 120 (15.7%) defaulted, 103 (13.5%) died, 40 (5.2%) were transferred-out, and 12 (1.6%) failed in the treatment, giving a treatment success rate of 64.1%. Among the 120 (15.7%) patients that defaulted from treatment, majority 80 (66.7%) were males, and most 30 (25.0%) were in the 30 - 39 years age group. **Conclusion:** Defaulting starts with treatment interruption hence prompt management of interruption of treatment and default will largely help in prevent-

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ing drug-resistant TB.

Keywords

Tuberculosis, Treatment Defaulters, Tertiary Hospital, South Eastern Nigeria

1. Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, and occasionally *Mycobacterium bovis* or *Mycobacterium africanum*. It affects mainly the lungs, leading to Pulmonary TB. It could also affect other sites of the body (extra-pulmonary TB). The extra-pulmonary sites include: gastrointestinal tract, mainly the ileocaecal area, but occasionally the peritoneum, producing ascites; the central nervous system, causing tuberculosis meningitis and tuberculomas; the genitourinary system, affecting the kidneys, epididymis, fallopian tubes, leading to infertility in some females; the skeletal system causing septic arthritis and osteomyelitis; the skin giving rise to lupus vulgaris; the eyes where it can cause choroiditis or iridocyclitis; the pericardium causing constrictive pericarditis; the adrenal glands producing Addison's disease; and lymph nodes, especially in young adults and children, with hilar and para-tracheal lymph nodes being mostly affected. The affected nodes are initially firm and discreet but later they become matted and may even suppurate with sinus formation [1] [2].

TB remains one of the world's deadliest communicable diseases. It was estimated that in 2013, 9 million people developed TB, and approximately 1.5 million died from the disease. TB is present in all regions of the world [1]. Nigeria is one of the 22 high burden countries (HBCs), accounting for 80% of world's TB cases, and the 3rd among the six countries with largest number of incident cases after India and China. According to World Health Organization latest report, the prevalence of TB in Nigeria is 326 per 100,000 population, while the incidence is 338 per 100,000 population [1]. For effective management of TB, WHO recommended Directly Observed Treatment Short-Course (DOTS) policy in 1990. The Nigerian National Tuberculosis and Leprosy Control Programme (NTBLCP) adopted this DOTS strategy in 1993 [2].

The treatment of TB depends on the case definition before the commencement. New cases are treated with category 1 regimen, while retreatment of relapses, failures, return-after-default and others require category 2 regimen. The category 1 regimen involves treatment for 6 months' duration, with initial 2 months intensive phase using fixed dose combination (FDC) of four drugs (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol), and then 4 months of continuation phase using Isoniazid and Rifampicin; but if Ethambutol and Isoniazid are used then it will last for 6 months [3]-[6]. The retreatment regimen (category 2) consists of Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and Streptomycin in the intensive phase. The Streptomycin is discontinued at the end of 2 months, while Rifampicin, Isoniazid, Pyrazinamide and Ethambutol are continued for additional one month to cover the 3 months of the intensive phase. The continuation phase uses Rifampicin, Isoniazid and Ethambutol, which are given for 5 months to cover the entire 8 months period of retreatment [2] [6].

Treatment outcome of TB could be [3]: Cured—smear positive at diagnosis, who completed treatment with smear-negative at the end of 6th or 7th month of treatment and at least one previous occasion; Treatment completed—smear negative or extrapulmonary patient who completed treatment; Treatment failure—patient remains or becomes smear positive again at the end of 5th month or later during treatment; Died—patient who died for any reason during the course of the treatment; Defaulter—any patient who has interrupted for 8 consecutive weeks or more after the date of the last attendance during the course of the treatment; Transferred-out—patient who was transferred to another treatment centre in another state and whose treatment result was not known.

The emergence of resistance to drugs used to treat tuberculosis and particularly multi-drug resistant tuberculosis (MDR-TB) is significant problem and poses obstacle to effective TB control at both national and global levels. Resistance arises at various levels in the management of a patient, ranging from poor compliance, inadequate supervision, inadequate dosing, drug combinations, duration of treatment and poor training of staff [3] [4]. Drug-resistant TB can be prevented largely through effective implementation of basic DOTS policy through: uninterrupted supply of good quality anti-TB drugs for the full duration of the treatment, provision of adequate patient education throughout the course of treatment to ensure adherence to treatment, prompt management of

interruption of treatment and default, provision of anti-TB drugs in compliance with National Guidelines, free anti-TB services to the patients [4] [5]. Treatment compliance of every patient is absolutely essential in order to cure the patient and prevent drug-resistant tuberculosis. Health workers should do all in their power to ensure that patients complete treatment in the required time (adherence).

This study elicited information on the characteristics of patients that defaulted in the course of TB treatment.

2. Methodology

2.1. Study Area

The study was conducted in the Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria. NAUTH is a tertiary, referral hospital located near the major business areas of south-eastern Nigeria. It serves Anambra, Imo, Delta, Enugu and Abia States of Nigeria. It is a renowned Teaching Hospital in Nigeria which runs daily DOTS clinic in addition to other clinical departments. It is also a training centre for both undergraduates and post-graduates medical students, as well as other allied medical workers.

2.2. Study Design

It was a Retrospective study utilizing analysis of data abstracted from the treatment register of the DOTS clinic from 1st January 2011 to 31st December 2012. The data collected include patients' demographic characteristics, treatment category, patient type, baseline sputum smear result, retroviral status. From the data, default rate was calculated and its relationship with other variables noted.

2.3. Data Collection

Data was collected from the Tuberculosis clinic register. The clinic is otherwise called Directly Observed Treatment Short-Course (DOTS) clinic. A proforma was used to extract the required information about the patients.

2.4. Data Analysis

The data was analysed using Statistical Package for Social Sciences (SPSS) version 20. Chi-square test was used to determine the relationship between variables. A p-value of ≤ 0.05 was considered statistically significant. Ethical clearance for the study was obtained from the NAUTH Ethical Committee. The results were presented in figure and tables.

3. Results

A total of 765 patients enrolled for TB treatment in the DOTS clinic of the study area within the study period of 1st January 2011 and December 31st 2012. **Figure 1** shows that the mean age at commencement of the treatment was 33.14 years, with a standard deviation of 18.09.

Table 1 shows the distribution of patients by demographic characteristics, type of TB, TB/HIV status, types of patient, treatment category, and outcome of TB treatment. Majority of the patients, 445 (58.2%), were males. More than eighty one percent of the cases were less than 50 years old while only 7% were greater than 60 years old. Majority of the patients, 634 (82.9%) resided outside Nnewi town. Most of the patients, 662 (86.5%), had pulmonary TB, while 103 (13.5%) had extra-pulmonary type of TB. The baseline sputum smear microscopy result, before the commencement of the treatment, shows that 346 (45.2%) of the patients had positive sputum AFB, 283 (37.0%) had negative sputum AFB, while 136 (17.8%) could not produce sputum. Retroviral status of the patients shows that majority of the patients, 496 (61.3%) had negative retroviral status at the commencement of the treatment, while 296 (38.7%) had HIV/TB co-infection. Types of patient indicate that majority, 618 (80.8%) were new cases; 21 (2.7%) relapsed cases; 7 (0.9%) failure cases; and 18 (2.4%) were return after default (RAD) cases. Of the 765 patients, 626 (81.6%) were treated with Category 1 Regimen, while the rest, 139 (18.2%) were treated with Category 2 Regimen. The outcome of treatment shows that 260 (34%) had treatment completed, 230 (30.1%) cured, 120 (15.7%) defaulted, 103 (13.5%) died, 40 (5.2%) were transferred-out, and 12 (1.6%) failed in the treatment, giving a treatment success rate of 64.1%.

Table 1. Distribution of patients by demographic characteristics, type of TB, treatment category, patient type, TB/HIV status, and outcome of TB treatment.

Characteristics	Frequency	Percentage
Sex		
Male	445	58.2
Female	320	41.8
Total	765	100
Age (years)		
<20	173	22.6
20 - 29	143	18.7
30 - 39	170	22.2
40 - 49	137	17.9
50 - 59	86	11.2
≥60	56	7.3
Total	765	100
Residence		
Within Nnewi	131	17.1
Outside Nnewi	634	82.9
Total	765	100
Disease site		
Pulmonary	662	86.5
Extra-pulmonary	103	13.5
Total	765	100
Category of treatment		
Cat 1	626	81.6
Cat 2	139	18.2
Total	765	100
First sputum result		
Positive	346	45.2
Negative	283	37.0
Cannot produce	136	17.8
Total	765	100
Type of patient		
New case	618	80.8
Relapse	21	2.7
Failure	7	0.9
Return after default (RAD)	18	2.4

Continued

Transfer in	13	1.7
Others	88	11.5
Total	765	100
Baseline HIV status		
Positive	296	38.7
Negative	469	61.3
Outcome of treatment (result)		
Cured	230	30.1
Treatment completed	260	34.0
Failure	12	1.6
Died	103	13.5
Defaulted	120	15.7
Transferred out	40	5.2
Total	765	100

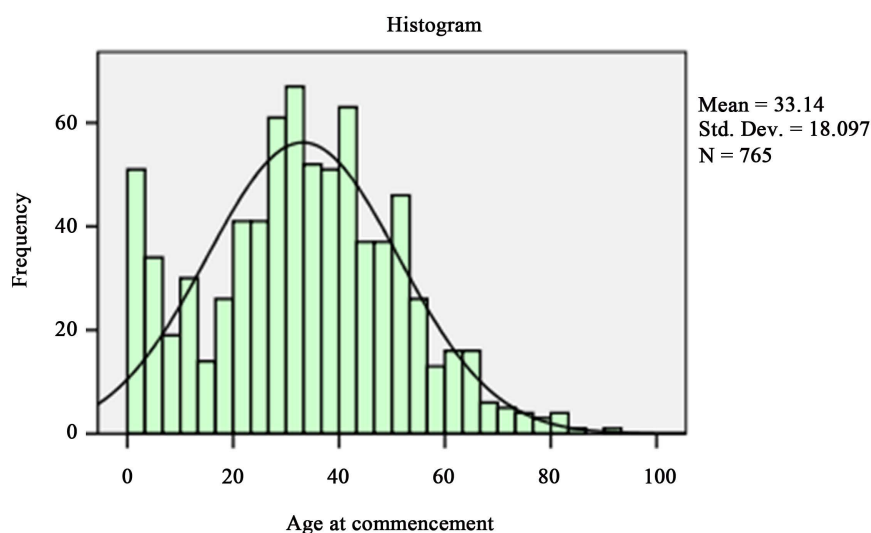


Figure 1. Age distribution at commencement of treatment (years).

The distribution of the association between patients' gender and age for TB treatment outcome is shown in **Table 2**. Among the 120 (15.7%) patients that defaulted from treatment, majority 80 (66.7%) were males, and most 30 (25.0%) were in the 30 - 39 years age group.

Table 3 shows the distribution of the association between patients' place of residence and TB treatment outcome. Patients who were residing outside the study area, Nnewi, 108 (90.0%) defaulted from TB treatment more than those who were resident in Nnewi, 12 (10.0%).

There were more TB defaulters, 98 (81.7%), among those on treatment Category 1 Regimen than those in treatment Category 2 Regimen, 22 (18.3%), as shown in **Table 4**.

Table 5 shows the distribution of the association between patients' baseline sputum AFB result and TB treatment outcome. Fifty (17.7%) of patients who tested negative to the AFB screening defaulted from TB treatment, as against the 15.0% of those who were AFB positive that defaulted from treatment.

Table 2. Distribution of the association between patients TB treatment outcome and some characteristics (sex and age).

	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
Sex							
Male	126	155	11	50	80	23	445
(%)	(54.8%)	(59.6%)	(91.7%)	(48.5%)	(66.7%)	(57.5%)	(58.2%)
Female	104	105	1	53	40	17	320
(%)	(45.2%)	(40.4%)	(8.3%)	(51.5%)	(33.3%)	(42.5%)	(41.8%)
Total	230	260	12	103	120	40	765
(%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)
{p = 0.14}							
Age (years)							
<20	20	94	3	21	29	6	173
(%)	(8.7%)	(36.2)	(25.0%)	(20.4)	(24.2%)	(15.0%)	(22.6%)
20 - 29	70	34	3	10	17	9	143
(%)	(30.4%)	(13.1%)	(25.0%)	(9.7%)	(14.2%)	(22.5%)	(18.7%)
30 - 39	62	48	1	20	30	9	170
(%)	(27.0%)	(18.5%)	(8.3%)	(19.4%)	(25.0%)	(22.5%)	(22.2%)
40 - 49	43	41	3	21	23	6	137
(%)	(18.7%)	(15.8%)	(25.0%)	(20.4%)	(19.2%)	(15.0%)	(17.9%)
50 - 59	23	27	1	18	8	9	86
(%)	(10.0%)	(10.4%)	(8.3%)	(17.5%)	(6.7%)	(22.5%)	(11.2%)
≥60	12	16	1	13	13	1	56
(%)	(5.2%)	(6.2%)	(8.3%)	(12.6%)	(10.8%)	(2.5%)	(7.3%)
Total (%)	230 (100)	260 (100)	12 (100)	103 (100)	120 (100)	40 (100)	765 (100)
{p = 0.000}							

Table 3. Distribution of the association between patients' place of residence and TB treatment outcome.

	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
Residence location							
Within Nnewi	44	52	2	17	12	4	131
(%)	19.1%	20%	16.7%	16.5%	10%	10%	17.1%
Outside Nnewi	186	208	10	86	108	36	634
(%)	80.9%	80%	83.3%	83.5%	90%	90%	82.9%
Total (%)	230 (100)	260 (100)	12 (100)	103 (100)	120 (100)	40 (100)	765 (100)
{p = 0.161}							

Table 4. Distribution of the association between patients' category of treatment and treatment outcome.

Category of treatment	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
CAT 1	207	193	8	89	98	31	626
(%)	90%	74.2%	66.7%	86.4%	81.7%	77.5%	81.8%
CAT 2	23	67	4	14	22	9	139
(%)	10%	25.8%	33.3%	13.6%	18.3%	22.5%	18.2%
Total (%)	230 (100)	260 (100)	12 (100)	103 (100)	120 (100)	40 (100)	765 (100)
{p = 0.000}							

Majority, 97 (80.8%), of the patients who defaulted from treatment were new cases of TB, as shown in [Table 6](#). However, [Table 7](#) shows that most of the defaulters, 77 (64.2%), were HIV negative.

Table 5. Distribution of the association between patients' initial sputum AFB result and TB treatment outcome.

First sputum result	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
Positive	227 65.6%	7 2.0%	10 2.9%	30 8.7%	52 15.0%	20 5.8%	346 100%
Negative	2 0.7%	166 58.7%	1 0.4%	50 17.7%	50 17.7%	14 4.9%	283 100%
Can't produce	1 0.7%	87 64.0%	1 0.7%	23 16.9%	18 13.2%	6 4.4%	136 100%
Total (%)	230	260	12	103	120	40	765 { <i>p</i> = 0.000}

Table 6. Distribution of the association between type of patient and TB treatment outcome.

Type of patient	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
New case	206 89.6%	189 72.7%	8 66.7%	87 84.5%	97 80.8%	31 77.5%	618 80.8%
Relapse	9 3.9%	2 0.8%	1 8.3%	6 5.8%	1 0.8%	2 5%	21 2.7%
Failure	4 1.7%	0 0.0%	0 0.0%	0 0.0%	3 2.5%	0 0.0%	7 0.9%
RAD	8 3.5%	1 0.4%	2 16.7%	0 0.0%	5 4.2%	2 5%	18 2.4%
Transfer-in	3 1.3%	5 1.9%	0 0.0%	3 2.9%	1 0.8%	1 2.5%	13 1.7%
Others	0 0.0%	63 24.2%	1 8.3%	7 6.8%	13 10.8%	4 10%	88 11.5%
Total (%)	230 (100)	260 (100)	12 (100)	103(100)	120 (100)	40 (100)	765 (100) { <i>p</i> = 0.000}

Table 7. Distribution of the association between patients' HIV status and TB treatment outcome.

HIV status	Cured	Treatment completed	Failure	Died	Default	Transferred out	Total
Positive	58 25.2%	104 40%	4 33.3%	72 69.9%	43 35.8%	15 37.5%	296 38.7%
Negative	172 74.8%	156 60%	8 66.7%	31 30.1%	77 64.2%	25 62.5%	469 61.3%
Total (%)	230 (100)	260 (100)	12 (100)	103 (100)	120 (100)	40 (100)	765 (100) { <i>p</i> = 0.000}

4. Discussion

Defaulting from TB treatment is one of the factors that slow the progress of meeting the target of WHO TB treatment success rate of 85%. Treatment compliance of every TB patient is therefore absolutely essential in order to cure patients, as well as prevent drug-resistant tuberculosis. This study elicited information on the characteristics of TB patients who defaulted from treatment.

The mean age of the patients was 33.14 ± 18.1 years, with 486 (63.5%) patients being less than 40 years old. Those aged less than 20 years account for 22.6%. This supports the fact that TB affects mostly people in the reproductive age group [1] [7]-[11]. However, a similar study in Switzerland reported a mean age of 62.5 ± 19.3 years [12].

Greater percentage of the patients (58.2%) are males. This is similar to the global report and other studies [1] [7] [10] [11] [13] [14]. It is worthy of note that though majority of the patients came from outside the study area, yet the association between residence and treatment outcome was not statistically significant ($p = 0.161$). Probably this may be because all the patients in our study came from the same country (tribe). Studies done in Swit-

zerland and Malaysia showed significant difference between indigenous cases and that of the foreigners [12] [15].

Out of 765 patients studied, 626 (81.8%) were treated with category 1 regimen, and the rest with category 2. Most, 618 (80.8%), of the patients were enrolled as “New Cases” and were treated with category 1 regimen. The remaining percentage of patients treated with Cat 1 regimen would have come from the “Transfer-in” group. Belete *et al.* showed similar percentage of “New Cases” in a study on treatment outcome of tuberculosis patients under directly observed treatment in Addis Ababa, Ethiopia [8]. More than 86% of the patients in this study had pulmonary tuberculosis, which is in tandem with other similar studies [10]. Omotosho *et al.* [7] in a similar study in Owo, South-Western Nigeria, reported a higher figure of 94.8%, similar to 97% reported by Atif *et al.* in a study in Malaysia [15].

In this study, 45.2% patients had positive sputum microscopy, 37% had negative smear while 17.8% could not produce sputum. Four hundred and ninety-six of the patients (61.3%) were retroviral negative, while 38.7% were TB/HIV co-infected. This is higher than the 22% TB/HIV co-infection for the entire country and also 34% for the African region reported by WHO Global report [1]. This figure is less than the 45.3% reported by the study from south-western Nigeria [7]. This is probably because this study was conducted in a referral centre, like that from South-western Nigeria. The study in Nairobi by Bernard *et al.* gave HIV co-morbidity as a predictive factor for default [10]. Though the DOTS clinic and HIV clinic are in the same centre, yet each clinic is run separately with patients receiving different appointment dates. This will increase the transport and opportunity costs [10]. A close and complex association exists between tuberculosis and HIV, with TB as leading cause of death in people with HIV [6].

The treatment success rate (cured and treatment completed) in this study is 67.6% among the smear positive cases. This is below the recommended target of 85% set by World Health Organization [1] [3] and also cure rate of 75.5% reported by Omotosho [7] as well as the treatment success rate of 86% reported nationally in 2012 [1].

The default rate of 15.7% from this study is comparable to 18.3% reported by Karanjekar *et al.* [13], but greater than 3% and 8.93% reported by Omotosho *et al.* [7] and Atif *et al.* [15] respectively. Among the 120 patients that defaulted, 43.3% had positive smear, while 41.7% were negative. In addition, majority of the defaulters, 80.8%, were new cases and were treated with TB Category 1 regimen. One-quarter of the defaulters were in the age group 30 - 39 years, with more males, 66.7%, than females, 33.3%, defaulting from TB treatment. This finding is in tandem with other studies which had reported similar higher default rate among males [7] [13].

The limitation of this study, being conducted as a retrospective survey, is the inability to elicit the views of the patients on treatment interruption and defaulting in general. Muture *et al.* in their study had stated that patients’ knowledge and beliefs about their illness, motivation to manage it and consequences of poor adherence interact to influence adherence behavior [10]. Further studies are needed to ascertain from patients why they default from TB treatment, and the ways to reduce it to the barest minimum.

5. Conclusion/Recommendations

Defaulting starts with treatment interruption hence prompt management of interruption of treatment and default will largely help in preventing drug-resistant TB. This calls for more effective patient education, supervision and support. There is also a need to maintain uninterrupted supply of good quality anti-tuberculosis drugs for the full duration of the treatment.

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List of Abbreviations

AIDS: Acquired Immuno Deficiency Virus

DOTS: Directly Observed Treatment Short-Course

FDC: Fixed Dose Combination

HBC: High Burden Countries

HIV: Human Immuno deficiency Virus

NAUTH: Nnamdi Azikiwe University Teaching Hospital

NTBLCP: National Tuberculosis and Leprosy Control Program

WHO: World Health Organisation