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Full Length Research Paper

Outcome of Tuberculosis Treatment in Tertiary Hospital in South Eastern Nigeria

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Abstract

Tuberculosis (TB) is a leading cause of morbidity and mortality rate in developing countries in Asia and sub Saharan Africa. Effective treatment depends on early case detection and patients' adherence to treatment procedures. In many resource-constrained settings, tuberculosis treatment outcome is un-satisfactory. This study determined the outcome of tuberculosis treatment and factors associated with such outcomes, in a Teaching Hospital where TB Directly Observed Treatment Short-course (DOTS) strategy is adopted. A register-based historical cohort study of patients accessing care at DOTS clinic of the hospital from 1st January to 31st December 2012 was conducted. Information on the socio-demographic characteristics of patients, disease site, patient type, result of baseline sputum examination, treatment category, outcome of treatment, consent for HIV testing, result of HIV test and antiretroviral therapy were extracted. Records of 315 registered tuberculosis patients revealed 61.3% successful treatment, 1.9% treatment failure, 16.2% death, 14.6% defaulters, 5.4% transferred-out and 0.6% missing results. Outcome of tuberculosis treatment was significantly associated with gender and HIV status of patients. Majority had successful treatment outcome. Improper record keeping posed problem. Intensification of efforts at control of tuberculosis and HIV counseling and testing and training of records personnel on proper record keeping are recommended.

Keywords: Tuberculosis, Treatment outcome, Tertiary Hospital, South Eastern Nigeria.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, that most often affect the lungs. It is a curable and preventable disease (WHO, 2014). It kills 3 million people per year worldwide (Murray et al., 2005). It is still one of the leading causes of death worldwide accounting for 2.5% of global burden of disease and 25% of all avoidable deaths in developing countries (Woldeyohannes et al., 2011). It was declared a global emergency by World Health Organization (WHO) in April 1993 and as part of global efforts to control TB, the MDG 6 target 8 is to half and begin to reverse the incidence of TB by 2015 (Oluwole et al., 2013). The African region had approximately one quarter of the world's cases of TB and Nigeria has an incidence of about 108 per 100,000 and deaths of 16 per 100,000 (WHO, 2013). According to USAID, Nigeria ranks 4th among the 22 high burden countries (USAID, 2014).

The disease occurs in two forms — Pulmonary Tuberculosis (PTB) which accounts for greater than 80% of cases, and Extra-Pulmonary Tuberculosis (EPTB) which accounts for less than 20% of cases. EPTB occurs in lymph nodes, pleura, genitourinary tract, skeletal system, meninges, pericardium, gastrointestinal tract and military TB (Raviglione and O'Brien, 2012; Obionu, 2007). Definitive diagnosis of TB depends on isolation and identification of Mycobacterium tuberculosis from specimen or the identification of specific DNA sequences in a nucleic acid amplification test (Raviglione and O' Brien, 2012). However

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presumptive diagnosis TB can be made based on detection of acid fast bacilli (AFB) on microscopic examination of a specimen, radiography, serology or tuberculin skin test (Raviglione and O'Brien, 2012). Effective treatment of TB is achieved through DOTS, a strategy developed by WHO in the 1990s. Since the launch of DOTS strategy and its successor, the STOP TB strategy, a total of 56 million people had been successfully treated for TB between 1995 and 2012, hence saving about 22million lives (WHO, 2013). In Nigeria, as of 2009, there were 3,455 health facilities providing free TB and DOTS services (USAID, 2014).

Foremost challenges in TB treatment are non-adherence to treatment, treatment default, and the emergence of resistance to drugs and particularly multi-drug resistant tuberculosis (MDR-TB). These pose obstacle to effective TB control at both national and global levels. Resistance arises at various levels in the management of the patient, ranging from poor compliance, inadequate supervision, inadequate dosing, drug combinations, duration of treatment and poor training of staff (Park, 2007).

Since TB remains a major cause of mortality despite availability of effective treatment (Burton et al., 2011), monitoring the outcome of TB treatment and understanding the specific reasons for unsuccessful treatment outcome are important in evaluating the effectiveness of TB control programme (Berhe et al., 2014).

This study reviewed the outcome of tuberculosis treatment and the factors associated with such outcomes, in a Teaching Hospital where TB directly observed treatment short-course (DOTS) strategy is adopted in patient management.

MATERIALS AND METHODS

Study Design

This retrospective study utilized records of TB patients managed in the TB/DOTS clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State of Nigeria, a tertiary hospital in South Eastern Nigeria. The secondary data used was obtained from the National TB/Leprosy Control Programme register at the clinic, on patients who accessed care from 1st January to 31st December 2012. The patients were referred to the DOTS clinic from the Out Patient Department, wards, HIV care and support units of the hospital, as well as peripheral hospitals in the vicinity.

Data Collection

Data on 315 patients diagnosed with TB and registered for treatment, were obtained and entered into a proforma. The proforma contained information on the socio-demographic characteristics of the patients, disease site, type of patient, result of baseline sputum examination, treatment category, outcome of TB treatment, HIV testing, HIV result and Highly Active Anti Retroviral Therapy (HAART) treatment. All the patients were expected to have completed their drugs by August 2013.

Data Analysis

Data were entered into the Statistical Package for Social Sciences (SPSS). Frequency tables were generated and cross tabulation of variables done. Chi-square test was used to determine the relationship between variables. A p-value of ≤ 0.05 was considered statistically significant. The NAUTH Ethical Committee gave ethical clearance for this study.

Outcome of TB treatment

According to WHO, the outcomes of TB treatment include: cured (a patient who was smear positive at diagnosis, who completed 6 or 8 months of treatment and who is smear-negative at the end of 6th or 7th month of treatment and at least one previous occasion); completed treatment (a patient who was smear-positive at diagnosis and who completed treatment but in whom smear examination results are not available at the end of treatment. In addition, all smear-negative and extra-pulmonary patients who completed treatment); death (any patient who dies for any reason during the course of his/her chemotherapy); treatment failure (any patient who remains or becomes smear-positive again at the end of 5th month or later during chemotherapy); treatment default (patient whose treatment was interrupted for two consecutive months or more) and transfer out (a patient who has been transferred to another treatment centre in another State and whose treatment result is not known) (WHO, 2014).

Types of patients

Types of patients could be:

Relapse: a TB patient who previously received treatment and was declared cured or completed a full course of treatment and has once again developed sputum smear-positive TB.

Treatment failure: a smear positive patient who while on treatment remains or became smear positive again five months or later after commencement of treatment.

Return after default: a TB patient who completed at

least four weeks of Category 1 treatment and returned smear positive after at least 8 weeks of interruption of treatment.

Transfer in: a TB patient already registered for treatment in one Local Government Area/State who is transferred to another Local Government Area/State where he/she continues treatment.

Other: a TB patient who does not fit into one of the above case definition, e.g. a patient who was treated for TB outside the National Tuberculosis Control Programme network for more than 4 weeks and is smear-positive.

Treatment category

For the purpose of treatment, TB patients are broadly grouped into two: "*New*" or "*Previously* treated" i.e. *Category* I and C*ategory* II respectively.

Category I (New Cases): All new sputum smear positive and sputum smear negative, including new extra-pulmonary TB. The Category I regimen involves treatment for 6-8 months duration (2RHZE/4RH or 2RHZE/6EH), with initial 2 months intensive phase using fixed dose combination (FDC) of four drugs (Rifampicin, Isoniazid, , 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.

Category II (previously treated or re-treatment) includes cases of relapse, failure, return after default, and others. The Re-treatment regimen (Category II) involves 2SRHZE/1RHZE/5RHE and it consists of Streptomycin, Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol in the intensive phase. The Strepomycin is discontinued at the end of 2 months, while Rifampicin, Isoniazid, Pyrazinamide and Ethambutol are continued for one month more to cover the 3 months of the intensive phase. The continuation phase uses Rifampicin, Isoniazid and Ethambutol given for 5 months to cover the entire 8 months period of re-treatment (FMOH, 2010; Sunder, 2011).

Treatment of multi-drug resistance tuberculosis (MDR-TB) is regarded as Category IV.

RESULTS

Table 1 shows the distribution by patients demographic, TB/HIV status and TB treatment outcome. Age group most affected (23.2%) are those < 20years, with males (59.4%) more affected than females (40.6%). PTB occurred more than EPTB (87.3%: 12.7%). Majority of the patients (82.2%) were new cases and most (44.1%) were sputum smear positive , while 38.4% were sputum smear negative. Majority, 61.3%, of the patients had successful treatment (cured or completed treatment) outcome, 1.9% had treatment failure, 16.2% died, 14.6% had treatment default, 5.4% were transferred out and 0.6% had missing results. Ninety nine percent of the patients were tested for HIV, out of which 58.1% were found to be negative and 39.7% positive, 2.2% had missing results. A total of 45.6% of the HIV positive patients were on HAART.

Distribution by patients' demographic characteristics and TB/HIV status for TB treatment outcome is shown in Table 2. Successful treatment was highest, 69.6%, among patients aged 20-29years and lowest, 50%, among patient greater than 60 years. The latter age category also had the highest proportion of treatment failure (5%) and death (25%) ($p < 0.05$). More females (65.6%) had successful outcome than males (58.9%) and had more deaths (19.5%) than males (14.1%); while more males defaulted (16.2%) than females (12.5%) and had treatment failure (3.2%) than females (0%)($p<0.05$).

Successful treatment was slightly higher in patients with PTB (61.8%) than EPTB (60%), but treatment failure was more in EPTB (2.5%) than PTB (1.8%) ($p<0.05$). However, higher proportion of patients (68.7%) with negative HIV result had successful treatment than those with positive result (51.6%). In addition , treatment failure was higher among HIV negative patients (2.2%) than HIV positive ones (1.6%); death was higher among HIV positive (32.3%) than HIV negative patients (4.9%); and treatment default was higher among HIV negative patients (18.1%) than HIV positive ones (9.7%) ($p<0.05$).

DISCUSSION

The outcomes of TB treatment in this study indicate that 193 (61.3%) of patients had successful treatment, 46 (14.6%) defaulted, 51 (16.2%) died, 17 (5.4%) were transferred out, 6 (1.9%) had treatment failure and 2 results (0.6%) were missing. This is in contradistinction to a study in a tertiary hospital in South Western Nigeria in which out of the 78 patients studied, 36 (46.1%) had successful treatment, 24 (30.8%) had treatment default, 6 (7.7%) were transferred out, 9 (25%) died and 3 (8.3%) had treatment failure (Oluwole et al., 2013). This variation in treatment outcomes could be as a result of higher HIV co-infection resulting from undiagnosed HIV as a result of lower proportion of patients giving consent for HIV testing. The study in South Western Nigeria also recognized failure to give consent for HIV test & HIV co-infection as some of the factors that negatively affect the outcome of TB treatment (Oluwole et al., 2013).

There is a positive association between HIV status and outcome of TB treatment. Majority of patients with negative HIV result had successful treatment (68.7%)

Table 1. Distribution by patients demographic, TB/HIV status and TB treatment outcome.

Variable	Frequency	Percentage (%)
Age (years)		
< 20	73	23.2
20-29	56	17.8
30-39	62	19.7
40-49	61	19.4
50-59	43	13.7
>60	20	6.3
Gender		
Male	187	59.4
Female	128	40.6
Site of disease		
PTB	274	87.3
EPTB	40	12.7
Type of patient		
New	259	82.2
Relapse	12	3.8
Failure	2	0.6
Return-After-Default	5	1.6
Transfer-in	7	2.2
Other	29	9.2
Missing	1	0.3
Result of baseline AFB sputum exam		
Positive	139	44.1
Negative	121	38.4
Cannot produce sputum	49	15.6
Not done	5	1.6
Missing	1	0.3
Category of treatment		
Category 1	262	83.2
Category 2	53	16.8
Outcome of TB treatment		
Successful	193	61.3
Treatment failure	6	1.9
Death	51	16.2
Treatment default	46	14.6
Transfer-out	17	5.4
Missing	2	0.6
Patient tested for HIV		
Yes	312	99
No	0	0
Missing	3	1
Result of HIV test		
Positive	125	39.7
Negative	183	58.1
Missing	7	2.2
HIV patients on HAART		
Yes	57	45.6
No	57	45.6
Missing	11	8.8

Table 2. Distribution by patients demographic characteristics and TB/HIV status for TB treatment outcome

Variable	Successful (%)	Failure (%)	Death (%)	Default (%)	Transferred out (%)
Age (Years)			$X^2 = 24.96$	P = 0.20	
< 20	64.4	0.0	15.1	19.2	1.4
20-29	69.6	1.8	5.4	17.9	5.4
30-39	58.1	1.6	22.6	12.9	4.8
40-49	59.0	4.9	14.8	14.8	6.6
50-59	61.0	0.0	22.0	4.9	12.2
> 60	50.0	5.0	25.0	15.0	5.0
Gender			$X^2 = 10.61$	P = 0.31	
Male	58.9	3.2	14.1	16.2	7.6
Female	65.6	0.0	19.5	12.5	2.3
Site of disease			$X^2 = 0.40$	P = 0.98	
PTB	61.8	1.8	16.5	14.3	5.5
EPTB	60.0	2.5	15.0	17.5	5.0
Type of patient			$X^2 = 26.3$	P = 0.14	
New	59.9	1.9	17.9	15.2	5.1
Relapse	66.7	0.0	16.7	0.0	16.7
Failure	0.0	0.0	0.0	100.0	0.0
R-A-D	60.0	0.0	0.0	20.0	20.0
Transfer-in	100.0	0.0	0.0	0.0	0.0
Other	72.4	3.4	10.3	10.3	3.4
Baseline sputum result			$X^2 = 16.1$	P = 0.19	
Positive	65.9	4.3	10.9	13.0	5.8
Negative	55.0	0.0	20.8	18.3	5.8
Cannot produce sputum	65.3	0.0	20.4	10.2	4.1
Not done	60.0	0.0	20.0	20.0	0.0
Category of treatment			$X^2 = 3.01$	P = 0.56	
Category 1	61.2	1.9	17.3	15.0	4.6
Category 2	64.2	1.9	11.3	13.2	9.4
HIV Result			$X^2 = 41.74$	P = 0.000	
Positive	51.6	1.6	32.3	9.7	4.8
Negative	68.7	2.2	4.9	18.1	6.0
HIV on HAART			$X^2 = 8.98$	P = 0.62	
Yes	42.1	3.5	38.6	7.0	8.8
No	60.7	0.0	25.0	12.5	1.8

Chi-square test

than HIV positive patients (51.6%). Mortality was also higher (32.3%) among HIV positive patients than HIV negative patients (4.9%). This is in tandem with findings of similar study conducted in Federal Medical Centre, Ido-Ekiti, South Western Nigeria, in which 30.9% of patients with HIV co-infection died while 7.8% of those without HIV died. Similarly, in a study done in Durban South Africa, HIV/TB co-infected individuals were found to be more likely to die or lost to follow up within 12 months of anti-retroviral treatment (Basset et al., 2012).

The study also showed a statistically significant ($P<0.05$) association between gender and treatment outcome. Higher proportion of females (65.6%) had successful treatment outcome than males (58.9%). This

is similar to a study done in South Ethiopia, where female smear positive PTB patients had significantly higher treatment success rate (58% versus 54%; P<0.05) (Manue and Ramos, 2010). However, a study done in Addis Ababa, Ethiopia showed higher treatment success rate among males with PTB (84.4%) than females (81.4%) (Belete et al., 2013). The study also showned that more females (19.5%) died than males (14.1%) but more males (3.2%) had treatment failure than females (0%) and had defaults (16.2%) than female (12.5%). However the impact of gender in treatment outcome of TB patients has been evaluated in other studies but has revealed results that are not in tandem with these findings. There is no statistically significant association between treatment outcome and age, type of patient, site of disease, result of baseline sputum examination and treatment category in this study.

CONCLUSIONS

This study elucidates the outcomes of TB treatment in the DOTS clinic of a teaching hospital in South Eastern Nigeria and a statistically significant association between the outcomes and gender of the patient and HIV status of the patient. Efforts at TB control of should be intensified in order to meet the WHO target of reducing TB deaths by 50% by the year 2015. In addition, HIV counseling and testing should be intensified to reduce TB/HIV co-infection. Capacity building of records personnel on proper record keeping should be increased.

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