

TUBERCULOSIS TREATMENT OUTCOMES AND INTERRUPTION AMONG PATIENTS ASSESSING DOTS REGIMEN IN A TERTIARY HOSPITAL IN SEMI-URBAN AREA OF SOUTH-WESTERN NIGERIA

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ABSTRACT

Background

Tuberculosis remains one of the most infectious diseases worldwide especially with the HIV pandemic. It is a cause of high morbidity and mortality in developing countries including Nigeria. Reasons contributing to high morbidity and mortality include high defaulting rate and treatment interruption. Several studies had evaluated the treatment outcome of tuberculosis but there is paucity of published literature on the outcome of treatment interruption especially in this environment. This study thus assessed the outcome of treatments and interruption among patients assessing DOTS regimen in a tertiary hospital located in a semi urban area in south-western Nigeria.

Methodology

The study was a review of TB register of the federal medical centre, Owo from its inception in 2008 to 2011. All the patients that have completed at least one course of chemotherapy (defined as 8 months of anti-tuberculosis treatment- 2months intensive phase and 6 months continuation phase) were included. Treatment outcome and interruption were defined in accordance with World Health Organisation (WHO) recommendations. Data were analysed with SPSS version 17.

Results

A total of 400 patients were included. The mean age of patients was 36.8 ± 16.8 years and 56.3% were male. Majority, (79.7%) were adults aged 19-64 years, 12.5% were in the paediatric age group and 7.8% were elderly. Less than half, 45.3% had TB/HIV co-infection. Regarding treatment outcome of tuberculosis, 75.5% were cured, 14.8% died, 4% relapsed and 3% defaulted. A little above one-fifth, 21 (5.3%) had treatment interruption among whom 9 (42.9%) were successfully traced and completed treatment. Significantly, higher proportion of those that had treatment interruption died, 54.1% compared with their counterpart, 14.9%, ($p < 0.001$) and had relapse. (14.3% versus 3.4%, $p = 0.01$).

Conclusion

A high rate of tracking failure among patients with treatment interruption was found in the study. In addition, mortality and morbidity were higher among patients with treatment interruption. A more concerted effort is needed in tracking / tracing patients with treatment interruption in order to reduce morbidity and mortality among TB patients assessing treatment.



INTRODUCTION

Tuberculosis remains one of the most infectious diseases worldwide especially with the HIV pandemic. In spite of effective therapy, it is still a major health problem and it remains a cause of high morbidity and mortality in developing countries.

Globally, there were an estimated 9.27 million incident cases of TB in 2007. This is an increase from 9.24 million cases in 2006, 8.3 million cases in 2000 and 6.6 million cases in 1990. Most of the estimated numbers of cases in 2007 were in Asia (55%) and Africa (31%), with small proportion of cases in the

Eastern Mediterranean Region (6%), the European Region (5%) and the Region of the Americas (3%).^{1,2}

In Nigeria, tuberculosis (TB) is a serious public health problem with more than 460,000 estimated new cases in 2007.³ It ranks fourth out of the 22 countries designated by the WHO with the highest burden of TB globally behind India, China and Indonesia.¹ According to the WHO Report 2009, the number of new cases of TB in 2007 was 311 per 100,000 population and number of prevalence cases of TB was 521 per 100,000.^{1,3}

Poor compliance with treatment is thus a major impediment to effective tuberculosis (TB) chemotherapy worldwide and is one of the major causes of prolonged infectivity and poor outcomes like

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drug resistance and relapse⁴ thus accounting for one of the most serious problem in TB control. The largest cause of unsuccessful treatment was 'defaulters' which is defined as 'a patient who interrupted treatment for two months or more after the date of the last attendance during the course of treatment.'^{5, 6} Treatment interruptions on the other hand is defined as failure to report for or receive treatment for two consecutive days during the intensive phase, or failure to collect drugs for two weeks after the expected date during the continuation phase.⁶ Moreover, patients that interrupt treatment remain infectious and constitute a danger to their families and the community, a situation that is exacerbated by the organism being resistant to first line drugs.

Mycobacterium tuberculosis has shown a propensity to mutate towards drug resistance, and defaulting patients have delayed sputum conversion and almost invariably relapse, often with a drug resistant strain, thus increasing the cost of treatment and may eventually lead to death.⁷ In Nigeria, 1.8% of newly diagnosed TB patients were MDR-TB while 9.4% of MDR-TB were among previously treated TB patients.¹ Retreatment requires more expensive drugs producing a greater financial burden on either the patient or public health delivery system.⁸ The development of drug resistance may be mainly attributed to incomplete or inadequate treatment of patients with TB, inappropriate prescribing by providers, interruption of drug supply, failure to support patients on treatment, lack of infection control precautions, and poor compliance with treatment.⁹

The key elements in tuberculosis (TB) control are to detect the disease as early as possible and to ensure that those diagnosed complete their treatment and get cured.⁸ In essence, this will interrupt transmission of TB to others and prevent the tubercle bacilli from becoming drug resistant. Incomplete treatment may result in excretion of bacteria that may also acquire drug resistance and cause increased morbidity and mortality. Treatment outcome results serves as a tool to control the quality of TB treatment provided by the health care system. However, several studies have looked into treatment outcomes of tuberculosis treatment but there is paucity of published literature on the outcomes of treatment interruption. This study therefore assessed the treatment outcomes of treatment interruption among patients assessing anti-

TB in a tertiary care centre in SW Nigeria during the period 2008-2011.¹⁰

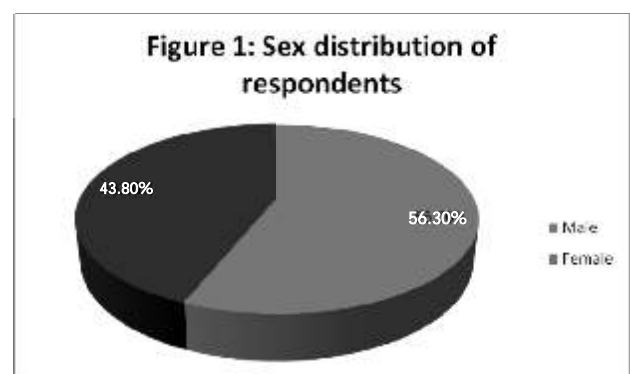
METHODOLOGY

The study was a review of TB register from its inception in 2008 to 2011. All the patients that have completed at least one course of anti-tuberculosis drugs [8 months of anti-tuberculosis treatment – two(2) months of intensive phase and six(6) months of continuation phase] were included. The study was conducted in Federal Medical Centre, Owo located in Owo local government area of Ondo State, Nigeria. The hospital provides health care at primary, secondary, tertiary level to the people within the catchment area which are Ondo, Kogi, Edo, Ekiti and Osun State. Treatment outcomes and interruption were defined in accordance with the WHO recommendations. Those that interrupted treatment for two (2) consecutive days or more during intensive phase, two (2) weeks or more during continuation phase and those that interrupted treatment for two (2) months or more after the date of the last attendance from the last treatment (defaulters) were regarded as having interrupted treatment. Data were analysed with SPSS version 17. Continuous variables were summarized using mean and standard deviation. Association between categorical variables was tested using Chi-square test at 5% level of significance.

RESULTS

A total of 400 patients who had completed a course of anti-TB were reviewed. The mean age of patients was 36.8 ± 16.8 years.

Sex distribution of patients
Above half, 56.3% were male (Figure 1)



Age distribution of patients

Table 1 shows the age group and marital status of patients. Majority, (79.7%) were adults aged 19-64 years, 12.5% were in the paediatric age group and 7.8% were elderly. Majority, 322 (80.5%) were married.

Table 1: Distribution of patients by age and marital status

AGE AND MARITAL STATUS N = 400	FREQUENCY	PERCENTAGE
Age group		
=18 (Paediatrics)	50	12.5
19-64 (Adults)	319	79.7
=65 (Elderly)	31	7.8
Marital Status		
Married	322	80.5
Single	78	19.5

Type of lesion and report of sputum AFB

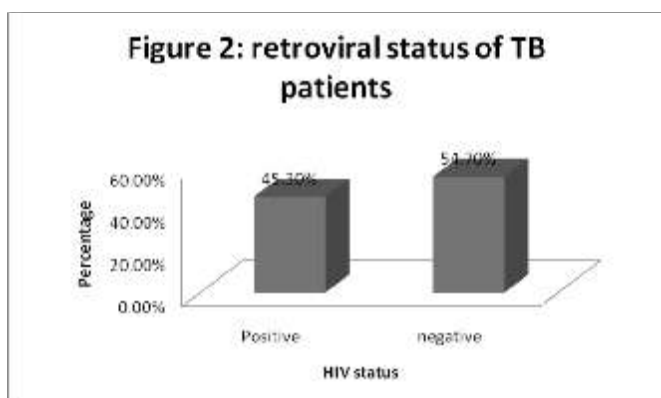
Overwhelming majority of the patients, 379 (94.8%) had pulmonary TB among whom 355 (93.7%) had positive sputum AFB (table 2).

Table 2: Distribution of patients by type of lesion and sputum AFB

Variables	Frequency	Percentage
Type of lesion (N = 400)		
Pulmonary	379	94.8
Extra pulmonary	21	5.2
Sputum AFB (N = 397)		
Positive	355	93.7
Negative	24	6.3

TB/HIV co-infection

Figure 2 shows the proportion of patients with TB/HIV co-infection. Less than half, 45.3% had TB/HIV co-infection.



Outcomes of TB treatment

About 76% were cured, 14.8% died, 4% relapsed and 3% defaulted (Table 3).

Table 3: Distribution of patients by outcome of TB treatment

Outcomes of treatment	Frequency	Percentage
Cured	302	75.5
Died	59	14.8
Relapsed	16	4.0
Defaulted	12	3.0
Transferred	7	1.8
Total	396	99

Others 4 (1%)

Treatment interruption

Table 4 shows the proportion of patients with treatment interruption. About one-fifth, 5.3% had treatment interruption among whom 9 (42.9%) were successfully traced and completed treatment.

Table 4: Distribution of patients by treatment interruption

Treatment interruption	Frequency	Percentage
Yes	21	5.3
No	379	94.7
Total	400	100

Association between treatment interruption and outcomes of treatment (death and relapse)

Significantly, higher proportion of those that had treatment interruption died, 54.1% compared with those that did not die, 14.9% ($p < 0.001$) and had relapse, 14.3% compared with those without relapse, 3.4% ($p = 0.01$).

DISCUSSION

Effective tuberculosis (TB) treatment has been shown to have a significant effect on the control of TB. Completion of treatment of active cases is therefore the most important priority of TB control programs.¹¹ Guidelines suggest a target treatment completion rate of 85% for infectious cases.¹² Any treatment outcome in which a cure is not established, i.e. sputum conversion to negative among active TB cases, will pose a danger to the community; hence, prevention of

such occurrences is necessary to maximize the efficiency of TB control programs. The mean age of patients in this study was 36.8 ± 16.8 years. This finding that TB primarily affects the young adults was consistent with previous reports in developing countries,^{13,14,15} this accounts for most of the productive years, hence, TB takes its toll on the economy of a nation. However, TB has been reported to be two-to-four times more prevalent among the elderly age group in developed countries.¹⁶

The observation that a greater percentage (56.3%) of the patients were males is consistent with other reports^{17,18} that revealed males are at an increased risk of a poor treatment outcome compared to females. This may be attributed to the prevalence of high risk behaviors among the men. Lienhardt et al, in 1998, reported that females were more likely to achieve a cure than their male counterparts.¹⁹ Similarly, Diel et al, attributed poor treatment outcomes, such as default, failure, and death, to males.²⁰

Among the 400 patients, 322 (80.5%) were married, 78 (19.5%) single, as also observed by Sweta et al,²¹ this may be due to the fact that partners tend to infect each other. 379 (94.8%) patients had pulmonary tuberculosis, while 21 (5.2%) had extrapulmonary tuberculosis, compared with 179 (89.05%) suffered from Pulmonary Tuberculosis, eight were cases of extrapulmonary Tuberculosis (EPTB); while 14 had both pulmonary as well as extra-pulmonary tuberculosis.²¹ Of those with pulmonary Tuberculosis, 355 (93.7%) were found to be smear positive, and 24 (6.3%) were found to be smear negative, this is close to what was found in other studies.^{22,23}

TB is the major opportunistic infection and leading cause of death among people living with AIDS.^{24,25} Less than half, 45.3% of patients had TB/HIV co-infection, while 54.7% were HIV negative. The rising TB/HIV epidemic no doubt impacts negatively on AIDS and TB control programs in many ways. The impact ranges from increased caseload of active TB attributable to HIV, HIV-related morbidity and mortality in TB patients, higher default rates and low cure rates, high rate of adverse drug reactions, increased risk of TB transmission and delay of access to health services for TB suspects due to the stigma of HIV/AIDS.²⁶ This result is however high compared to 28.9% positive and 71.1% negative reported by Bello in

his study on the challenges of DOTS implementation strategy in the treatment of tuberculosis in a tertiary health institution in Ilorin.¹⁵

The cure rate of 75.5% in this study is closely related to what was found in the Fatiregun et al study¹⁸ in which the cure rate was 76.6%, but below the recommended target of 85% by the WHO.¹⁴ The cure rate of 73% was what was documented among pulmonary TB patients in the Obafemi Awolowo University Teaching Hospital (OAUTH) in Ile Ife.¹³ The findings were also closely related to what was found in another study conducted at the northern Nigeria where a cure rate of 70.5% was reported among males and 78.5% among females.¹⁵ However, the University of Maiduguri Teaching Hospital DOTS program had recorded 85.5% success rate in the treatment of PTB over the studied period-three (3) years. Though the success rate reached the rate projected for Nigeria,²⁷ it was lower than 90-95% global success rate of treatment.²⁸ 59 (14.8%) died during the study period, compared with 41 (2.4%) as recorded by Yakubu et al,²³ and this could be as result of the higher cure rate in their study. Of those that died, a higher proportion was found in those that had treatment interruption. However, N Njebuome et al recorded that death rate was higher among the dually infected patients (25.7%) compared with HIV-negative patients (15.5%); the difference was also highly significant ($p = 0.000$).²²

The default rate was found to be 12 (3.0%), this is low when placed alongside with studies; it was 12.1%²³ and 22.3% in males and 14.3% in females¹⁵ respectively. This could be because the sample size in these studies were much larger than in our study, but these default rates are higher than the reported 5% global default rate.

Out of the 400 patients, 21 (5.3%) had treatment interruption, out of which an higher proportion died compared with those without treatment interruption 54.1% versus 14.9%; and 14.3% had relapse compared with 3.4% in those without interruption. Various reasons have been attributed to interruption of treatment by various studies; Kaona et al²⁹ found that 29.8% of TB patients failed to comply with anti-TB once they started feeling better.

Social problems and feeling of improvement were the top two reasons for patients to default in study by Demissie et al.³⁰ In another survey by Tissera³¹ relief

from symptoms (13%) emerged as the most common reason for treatment interruption. However, in a study by Jaggarajamma et al³², relief from symptoms was found to be the third commonest reason for discontinuation of treatment (20%).

These reasons are also very likely to hold true in our own study as most of the results obtained were very comparable.

CONCLUSION

In conclusion, treatment interruption is one of the main reasons which can affect the rate of cure and also facilitate drug resistance. We observed that there is significantly increased morbidity and mortality in patients who interrupted treatment for various reasons compared with their counterparts who did not.

Recommendations

There is a need for more direct supervision and continuous health education. A more concerted effort is also needed in tracking/tracing patients with treatment interruption in order to reduce morbidity and mortality among TB patients assessing treatment.

Limitations

Due to the retrospective nature of the study, data extracted were through the TB register.

Socio-economic status and educational background are some of the factors that we would have loved to associate with treatment interruption, but these were not captured in the TB register.

The accurate timing of interruption of treatment as well as reasons for the interruption of treatment could not be elicited from the study.

Suggestions for further studies

For subsequent studies on this subject, there's a need to establish the reasons for treatment interruption, so as to be able to stem tide of such in those just starting anti-tuberculous medications.

There's also a need to identify possible risk factors that may predispose patients to interrupting treatment having started anti-tuberculous medications and need for appropriate intervention.

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