SUCCESS OF DOTS PROGRAMME IN A TERTIARY HEALTH CARE FACILITY IN SOUTHERN NIGERIA

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ABSTRACT

This study was undertaken to evaluate the success of Directly Observed Treatment Short Course (DOTS) in a tertiary health facility located in a poor-resource setting in southern Nigeria. Case records of all TB out-patients (306) who received treatment under the DOTS programme in a tertiary health facility in Benin City between January and August 2007 were evaluated. Information collected from the case notes included their sociodemographic characteristics, clinical and treatment variables, including HIV status, medications and adherence to treatment and treatment outcomes, as well as transportation cost to their care centre. The associations between the treatment outcomes, gender and transportation cost were determined using logistic regression analysis. Most patients (85.6%) were confirmed cured at the end of the 8th month of treatment while 12.4% defaulted from treatment and 1.2% died. Each patient spent an average of USD31.42±10.68 (NGN3645±1239.28) per month as transportation cost to receive their treatment which was not associated with default from treatment ($p>0.05$). Gender was not associated with death from treatment but with default from treatment. It is concluded that although success of DOTS programme was recorded in the tertiary hospital based on WHO standards, there is need to involve private practitioners, including pharmacies, to increase access to care in the management of TB patients.

Keywords: Tuberculosis, DOTS, Treatment outcome, Nigeria.

1.Introduction

Chronic diseases such as tuberculosis (TB) are responsible for considerable morbidity and mortality. In recent times, TB has emerged as the single leading cause of death from any single infectious agent (Zeind, 1996). Despite the fact that the causative organisms (*Mycobacterium tuberculoses* and occasionally by *Mycobacterium bovis* and *Mycobacterium africanium* (Erah & Ojiebau, 2009) were identified several years ago and effective therapeutic regimens are available, the problems of TB remain worldwide, especially in Asia and Africa. As at 2006, there were an estimated 14.4 million cases out of which 9.2 million are new cases, including 4.1 million new smear-positive cases (44% of the total) and 0.7 million HIV-positive cases (8% of the total) with Nigeria ranking fifth in terms of absolute numbers of cases. Nigeria stands out as one of the countries with the poorest detection rates with as low as 11% of new cases detected in 1995 and 20% in 2006 succeeding China as the second largest reservoir of undetected cases (WHO 2008). People infected with tuberculosis very often originate from the most vulnerable sectors of society, such as those living in poverty, prisons and in poor working conditions.

Directly Observed Short Treatment Short Course (DOTS) is an internationally recommended strategy for TB control and is based on a 6-month treatment regimen with first-line drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for new patients and an 8-month treatment regimen with isoniazid, rifampicin, pyrazinamide, and streptomycin for re-treatment patients (WHO, 2003). In 2008, the World Health Organzation (WHO) reported that DOTS was being implemented in 184 countries that accounted for 99% of all estimated TB cases and 93% of the world's population as at 2006. Many anti-Tuberculosis drugs are available but in spite of the mile stone in developing these drugs and implementing the DOTS programme, the prevalence of TB is on the increase in many poor income countries, including Nigeria. Globally, a total of 4.9 million new cases, including 2.5 million new smear-positive cases (99% of the total notified globally) were reported recently (WHO, 2008). The reasons for this increase include inadequate TB control programmes, poor adherence to drugs, emergence of drug resistant TB, high rates of population growth and the HIV

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pandemic. Recently, WHO developed a new six point Stop TB Strategy which builds on the successes of DOTS while also explicitly addressing the key challenges facing TB. Its goal is to dramatically reduce the global burden of tuberculosis by 2015 by ensuring all TB patients, including for example, those co-infected with HIV and those with drug-resistant TB, benefit from universal access to high-quality diagnosis and patient-centered treatment. The strategy also supports the development of new and effective tools to prevent, detect and treat TB (WHO 2008).

Although anti-tuberculosis drugs are free for TB patients in Nigeria, transportation costs for receiving treatment are covered by the patients. Anecdotal evidence indicates that in some cases, this cost of transportation seems to exceed the available resources of the most patients who may eventually give up treatment. Over the years, treatment success has been increasing in Africa although cohorts of DOTS patients in this region, particularly Mozambique, Nigeria, South Africa, Uganda and Zimbabwe continue to have high deaths and default rates. Globally, the treatment success rate in DOTS programmes was reported to be 84.7% in 2005, which is just short of the 85% target (WHO, 2008). This has been the highest rate since reliable monitoring began, despite an increase in the size of the cohort evaluated to 2.4 million patients in 2005. Africa region had the second lowest treatment success rates (76%) being next to the European region (71%).

Although there has been earlier study to evaluate the implementation of DOTS by private medical practitioners in TB management in Nigeria (Okeke & Aguwa, 2006), the extent to which DOTS programme has brought about success in TB control in Nigeria is not well documented. The main objective of this study was to evaluate the success of DOTS in a tertiary health facility in Benin City. Specifically, we intended to measure the cure rate of TB patients, determine adherence of the patients to their anti-TB treatment and assess the cost of transportation to treatment centre and measure the association with adherence to treatment.

2.Methods

Setting

This study was carried out in a Central Hospital, Benin City - a State government owned tertiary hospital in Edo State in the southern part of Nigeria. The hospital provides teaching facilities for medical students and covers an average of 900 in-patients and 13,000 outpatients per month. It has 18 wards with 434 bed spaces with an occupancy which varies from 20% to as high as 50% and caters for the population living mostly in Edo and Delta States in Nigeria. Most of the health care services are rendered by their staff which comprises of about 120 Doctors, 35 Pharmacist and 48 nurses. The study population consisted of all out-patients attending the DOTS Center in the hospital between January and August 2007. In this centre, all TB patients were managed under the WHO DOTS-based protocol but medicines were administered to the patients in the hospital on Mondays to Fridays by two trained registered nurses on a daily basis. On Fridays, patients received their medications for the weekend for administration at home.

Study design

This was a retrospective study, involving the review of medical records of patients in the hospital. Following approval from the relevant hospital authorities, all case files of the out-patients attending the hospital (between January and August 2007) were retrieved from the available hospital records and the required data for each patient entered into a structured data collection form. Included in the study were 306 male and female out-patients diagnosed with TB, using both positive sputum smear and chest X-ray and receiving anti-TB drugs in the TB clinic in the hospital during the specified period. Excluded from the study were TB patients with serious cardiovascular and renal diseases, or psychiatric disorder. Other than available information in the case files of the patients, the care givers assisted in providing relevant information. In handling data collected, confidentiality was of the essence. The 2 nurses who administered medications to the patients were interviewed informally on reasons often given by the patients for failure to comply to their treatment.

Information in the data collection form included socio-demographic characteristics, clinical and treatment variables, including HIV status, medication and adherence to treatment, treatment outcomes, as well as cost of transportation to reach the point of care. Information on availability of drugs was obtained from the both the pharmacy department of the hospital and the DOTS personnel who provide the anti-TB drugs to the patients directly. The data collection form was pre-tested, modified and evaluated to be satisfactory in

respect of data consistency measurement. The reliability of the data was determined using Cronbach's alpha and the reliability coefficients for the data evaluated ranged from 0.78 to 0.91.

Outcomes measure

The treatment outcome was measured based on the definitions provided in Table 1. Cost of transportation of the patient to the hospital was evaluated.

Table 1: Treatment outcome definition for Tuberculosis patients under evaluation

Category	Definition
Cure	Completed treatment according to DOTS protocol (WHO, 2003) and has sputum smear test is negative at 8 months and on at least one previous occasion while completing treatment with anti-TB medications
Treatment completed	Completed treatment according to DOTS protocol
Died	Died for any reason during the course of treatment
Treatment default	Treatment was interrupted for than 2 consecutive months for any reason
Treatment failure	Patient's sputum smear test is positive at 8 months and on at least one previous occasion while completing treatment with anti-TB medications Treatment is also considered to have failed if a clinical decision has been made to terminate treatment early due to poor response or adverse events.
Transfer out	Transferred to another reporting and recording unit (care or treatment centre) and the treatment outcome is unknown

The accuracy of laboratory methods for TB was verified through quality assurance exercise performed as previously described (WHO/IUATLG, 2003).

Analysis

The data collected were entered into Microsoft Excel (Microsoft Inc, USA) and double checked for accuracy. Using SPSS for Windows version 13, proportional data were analyzed using Chi-square test or Fisher's exact test for 2x2 comparisons. Descriptive statistics (frequency and percentages) was used for the presentation of the data. The association between the dependent variable (death and default from treatment) and the independent variables (gender and transportation cost) was determined using logistic regression analysis. At 95% confidence interval, 2-tailed p-values were considered to be statistically significant when less than 0.05.

3.Results

Age and sex distribution of patients

The age and sex distribution are presented in Table 2. Patients in the age 25-34 years group accounted for the highest proportion of the patients (32.4%). Only few of them (6.2%) were less than 15 years old. There was a significant difference between the proportion of males and females among the patients (p=0.02) with more males affected as compared to the females. Twenty-seven (27) females and 22 males HIV-positive patients were identified among the study group. Available records indicated that the patients were mostly residents of Benin City and its environs.

Table 2: Age and sex distribution of patients

Age (yrs)	Males	Females
< 10	4 (1.3%)	6 (2%)
10 – 14	4 (1.3%)	5 (1.6%)
15 – 24	18 (5.9%)	34 (11.1%)
25 – 34	56 (18.3%)	43 (14.1%)
35 – 44	31 (10.1%)	21 (6.9%)
45 – 54	29 (9.5%)	14 (4.6%)
55 – 65	12 (3.9%)	7 (2.3%)
>65	16 (5.2%)	6 (2%)
TOTAL	**170**	**136**

χ^2 =16.585; df = 7; p = 0.020

Drug treatment outcome

Information obtained from the hospital pharmacy department and the nurses providing drugs directly to the TB patients indicated that there was no stock-out of anti-TB drugs throughout the study period. The outcome of treatment from anti – TB drug is given in Table 3. Treatment outcome measured indicated that over 80% of the patients were confirmed cured at the conclusion of 8th month treatment, 5.2% being also cured at 7th month of treatment. Despite this success, some of patient (1.2%) succumbed to the disease even when there was no evidence of default to treatment at the time of death. These deaths were recorded within the 1st to 3rd month of treatment. This study reveals that the 85.6% of the patients treated in this centre meets the WHO standard to declare the treatment in the centre as a success.

Although some of the patients (12.4%) defaulted from treatment at various stages i.e 2nd to 6th month, they survived up to the end of the study. Majority of these defaulters (47.4%), stopped going to the hospital for their medicines in the health facility after the 6th month of treatment. Transfer of two of the patients from the facility studied to another for continuous treatment was also recorded (Table 3).

Although the anti-TB drugs were free to all patients, the patients spent between USD 14.48

(NGN1.680) and USD68.97 (NGN8,000.00) (mean±SD; USD31.42±10.68 (NGN3645±1239.28) per month [USD, United States dollars; NGN, Nigeria Naira) as transportation cost to receive their treatment. The informal interview of the DOTS personnel (nurses) revealed that majority of patients defaulted from treatment because they could not afford to continuously pay their transportation cost and provide for their families (as appropriate) from their meager resources at the same time.

Table 3: Treatment outcomes in TB management

Variable	No of patients	No of months absent from treatment	Stage of treatment
Cured	246 (80.4%)		8th Month
	16 (5.2%)	1	7th Month
Died	1 (0.3%)	0	Pre-treatment
	1 (0.3%)	0	1st Month
	1 (0.3%)	0	2nd Month
	1(0.3%)	5	3rd Month
Defaulted*	3 (0.9%)	6	2nd Month
	9 (2.9%)	5	3rd Month
	3 (0.9%)	4	4th Month
	5 (1.6%)	3	5th Month
	18 (5.9%)	2	6th Month
Transfer out	2 (0.7%)	0	5th Month
Treatment failure	0	-	-

**Defaulted from treatment but alive*

The logistic regression analysis revealed that gender was unlikely to be related to death (Odd Ratio = 0.5278; 95% CI = 0.087-3.206). The relative risk of patient receiving treatment dying from the disease was relatively low (0.717; 95% CI = 0.244-2.107). However, there was an association between gender and default from treatment (Odd Ratio = 1.115; 95% CI = 0.56-2.215) with males more likely to default from treatment than females. There was no significant difference between the average cost of transportation by those adhering to treatment when compared with those defaulting from treatment ($p>0.05$).

Discussion

Although there are reports that only 10% of individuals infected with TB often develop clinical disease, there are many known factors that have been reported to be affecting TB development. These include age, sex, poverty, alcohol, malnutrition, diabetes and human immunodeficiency virus infection (Davies, 1999; Holmes, 1998; Nelson, 1995; Schwenk & Macallan, 2000; Hennn, 1999). Host genetic factors are also important determinants, as are evident from the different concordance rates in monozygotic and dizygotic twins and the racial difference in susceptibility to *Mycobacterium* TB infection (Kallmann & Reisner, 1943; Stead, 1990). The significantly higher proportion of males when compared to females in our data can thus be explained on the basis of earlier reports (Holmes, 1998). Watkin and Plant have demonstrated the higher prevalence of TB in men as compared to women can be related to smoking (Watkins & Plant, 2006). In this study, no attempt was made to specifically identify the reasons for the variation observed.

A pervious study by Bordgdorff (2001) showed that transmission rate of *M. tuberculosis* decrease with increasing older age. In our study group, majority of the patients were within the ages of 15 – 34. Above this age, the number recorded started to decline as previously reported.

Low cure rates occur in many countries despites attempt to implement dots as the standard of care. This is based on a previous study on "DOT and improved TB treatment outcome in Thailand" (Anuwantnonthakate, 2007) and recent report of cure rate of 57.6% in 2006 from department of health, South Africa in a media briefing. From this study, it has been seen that the WHO target of >85% treatment completion and cure rate has been met. Since supply of TB medicine in the facility was adequate as revealed from available records kept both in the Pharmacy Department and the TB Treatment Centre with good local community and staff commitment, these factors likely explain the cure rate. Although lack of access to health care in areas in which patients live far from health centers is possible reasons to non adherence to medication, Omerod (2007) reported that the main reason that WHO target of 85% for completion and cure rate is not met is that death from all causes is included as a reason for failure. This has not been the case in this study.

Previous study has shown that women are less likely to seek treatment of TB which can lead to death (Karim, 2007) even though from this study it is seen that gender showed no strong association with death (odd ratio = 0.5278).

Failure to adhere or complete treatment is a vital factor in the fight against tuberculosis and it can lead to further transmission of the disease. Although medicines and treatment options are free in the care centre studied, a relative no of patients still fail to adhere to their treatment. Poor communication between health care workers and patients, financial reasons, poor application of DOTS principles, including inadequate follow up of defaulters, poor supervision of local treatment centers and long duration of TB treatment, might be responsible

for defaulting in this study. This corresponds with the reasons reported in a research on "Risk of Default on TB treatment by patient centered adherence approach" in Senegal (Alcorin, 2007). A previous study by Johannsson, (1999) also showed that financial difficulty was the most common reason cited by patient for non-compliance in Vietnam. The timing of defaulting might be as a result of the long duration of treatment. Previous evidence (Kurk, 2008) only suggest that substantial proportion of patient appear to default in the latter stages of treatment suggesting that new TB medicines which can reduce length of treatment have potential to improve success rates of treatment.

The findings in this report are subject to certain limitations. Certain behaviors, particularly those regarded as socially unacceptable (e.g. alcohol abuse), were not recorded, and their overall impact on the cure rate could not be reflected. Also the level of income of patients was not also recorded hence the social classes of the patient could not be calculated and its association with treatment outcome not determined.

4.Conclusion

Although success of DOTS was recorded in the tertiary hospital based on WHO standards, many patients are unable to afford the cost of transportation to their treatment centres. However, default from treatment is 12.4% and deaths occurred within the first three months probably because such patients did not report for treatment on time. Although the patients spent an average of USD31.42±10.68 (NGN3645±1239.28) per month for transportation to their treatment locations, many patients are unable to bear this cost of transportation because of their poverty level.

The need to involve private medical practitioners and pharmacies in the management of TB patients have become imperative since records show that they offer better geographical access and more personalized care (Okeke & Aguwa, 2006). Curative regime that are shorter or require patient to take drug less frequently should also be developed, which will greatly facilitate adherence to medications.

References

Alcorin K, Risk of Default of Tuberculosis Treatment halved by Patient-Centered Adherence Approach In Senegal Study. Available from : http://www.aidsmap.com/en/news

Anuwatnunthakate A, Limsomboon P, Nateniyom S, Wantanaa, Mornikjat W, Komsakorn S, Moolphate S, Chiengsorn N, Kaewsa-ard S, Sombat P, Siangphoe U, Mock PA, Varma JK. Directly observed therapy and improved tuberculosis treatment outcomes in Thailand. WHO bulletin, 2007.

Borgdorff MW, Nagelkerke NJO, Dehaas EW, Suolingen DV. Transmission of Myco-tuberculosi depending on the age and sex of source case. America Journal of Epidemiology. 154(10),2001,934–943.

Davies PDO. The Effects of Poverty and Aging on the Increase in Tuberculosis. Monaldi Arch Chest Dis.,54,1999,168–171.

Erah PO, Ojieabu. Success of the Control of Tuberculosis in Nigeria: A Review. Int J Health Res. , 2(1),2009, e214p21-30.

Henn L, Nagel F, Pizzol FD. Comparison between human Imunodeficiency virus positive and negative patients with tuberculosis in Southern Brazil. Mem Inst Oswaldo Cruz., 94,1999,377–38

Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis.,2,1998,96–104.

Johansson E, Long NH, Diwan VK, Winkurst A. Attitude to compliance with TB Treatment among women & men in Vietnam. Int Journal Tuberculosis Lung Disease. ,3(10),1999,862–868.

Kallmann FJ, Reisner D. Twin studies on the genetic significance of genetic factors in tuberculosis. Am Rev Tuberc.,47,1943,549–574.

Karim F, Islam MDA, Chowdhury A, Johansson E, Diwan V. Gender difference in delay in diagnosis and treatment of tuberculosis. Health Pol Plan. ,22(5),2007,329–334.

Kurk ME, Schwalbe NR, Aguiar CA. Timing of default from TB treatment: a systematic review. Trop Med Int Health.,13(5),2008,703–712.

Nelson S, Mason C, Bagby G, Summer W. Alcohol, tumor necrosis factor, and tuberculosis. Alcohol Clin Exp Res.,19,1995,17–24.

Okeke TA, Aguwa EN. Evaluation of the implementation of DOTS by private medical practitioners in the management of TB in Enugu, Nigeria. Tanzania Health Research Bulletin. ,8(2),2006, 86-89.

Ormerod PL. The evidence based treatment of TB: Where and why are we failing. 2006. Available from: http://thorax.bmj.com/cgi/content/full/63/1/388. Accessed on Sept.11, 2008.

Schwenk A, Macallan DC. Tuberculosis, malnutrition and wasting. Curr Opin Clin Nutr Metab Care. ,3,2000,285–291. .

Stead WW, Senner JW, Reddick WT, Lofgren JP. Racial differences in susceptibility to infection by Mycobacterium tuberculosis. N Engl J Med.,322,1990,422–427.

Watkins RE, Plant AJ. Does smoking explain sex differences in the global tuberculosis epidemic? Epidemiol Infect. ,134,2006,333-339

World Health Organization. Treatment of Tuberculosis. Guidelines for National Programmes. 3rd edition. Geneva: The Organization, 2003. Publication WHO/HTM/TB/2003.313. Available from: http://www.who.int/tb/publications/ cds_tb_2003_313/en/index.html.

World Health Organization. Global Tuberculosis Control. WHO Report 2008. The Organization, Geneva, 2008.

Zeind CS, Gourley GK, Corbett CE. Tuberculosis. In: HerfindaL ET (ed). Textbook of Therapeutics, drug & disease management. Williams & Wilkins publishers, Maryland USA. 1996, pp. 1283 – 1297.