

TUBERCULOSIS TREATMENT OUTCOMES: A FIFTEEN YEAR COHORT STUDY IN JOS NORTH AND MANGU, PLATEAU STATE, NORTH - CENTRAL NIGERIA

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Abstract

Background Tuberculosis (TB) is an infectious disease with a major global health problem; being the tenth leading cause of death worldwide, and the leading cause of death from a single infectious agent. Nigeria is among the countries with high burden of tuberculosis and the highest global mortality rate. Medication adherence has been shown to have profound effect on other treatment outcomes. Objective To examine a fifteen-year cohort of tuberculosis treatment outcomes in Jos North and Mangu Local Government Areas of Plateau State. Methods The study was done in five treatment centers which account for more than half of data for tuberculosis patients in Plateau State, North-Central Nigeria. The retrospective study was done from 2001 to 2015, where TB patient records who had completed treatment were evaluated. Treatment outcomes were classified as successful (cured, treatment completed) or unsuccessful (non-adherent, treatment failure or death) and analyzed using binomial logistic regression. Results Males composed 58.1% of the population (10,156). Mean age \pm SD was 35.5 ± 15.5 years. The overall treatment success rate was 67.4%; non-adherence/defaulting rate was 18.5%, with majority of patients defaulting at the end of intensive phase of treatment; sputum conversion rate was 72.8% and mortality rate was 7.5%. A decrease in successful treatment outcomes from 83.8% to 64.4%, with a corresponding increase in unsuccessful treatment outcomes was observed. The Predictors of medication non-adherence were patients with unknown HIV status (OR 4.29, 95% CI: 3.74-4.91, $p < 0.001$); being male (OR 1.15, CI: 1.37-1.66, $p = 0.008$) and having a history of non-adherence (OR 2.27, CI: 1.34-3.87, $p = 0.002$) and treatment failure (OR 2.83, CI: 0.98 – 8.19, $p = 0.05$). Conclusion Underlying reasons for medication non-adherence and treatment failure identified should be resolved by the patient, treatment supporter and health worker. Increased awareness and education on voluntary counseling and testing of HIV among TB patients is advocated, particularly among the male population.

Abstract

Background

Tuberculosis (TB) is an infectious disease with a major global health problem; being the tenth leading cause of death worldwide, and the leading cause of death from a single infectious agent. Nigeria is among the countries with high burden of tuberculosis and the highest global mortality rate. Medication adherence has been shown to have profound effect on other treatment outcomes.

Objective

To examine a fifteen-year cohort of tuberculosis treatment outcomes in Jos North and Mangu Local Government Areas of Plateau State.

Methods

The study was done in five treatment centers which account for more than half of data for tuberculosis patients in Plateau State, North-Central Nigeria. The retrospective study was done from 2001 to 2015, where TB patient records who had completed treatment were evaluated. Treatment outcomes were classified as successful (cured, treatment completed) or unsuccessful (non-adherent, treatment failure or death) and analyzed using binomial logistic regression.

Results

Males composed 58.1% of the population (10,156). Mean age \pm SD was 35.5 \pm 15.5 years. The overall treatment success rate was 67.4%; non-adherence/defaulting rate was 18.5%, with majority of patients defaulting at the end of intensive phase of treatment; sputum conversion rate was 72.8% and mortality rate was 7.5%. A decrease in successful treatment outcomes from 83.8% to 64.4%, with a corresponding increase in unsuccessful treatment outcomes was observed. The Predictors of medication non-adherence were patients with unknown HIV status (OR 4.29, 95% CI: 3.74-4.91, $p < 0.001$); being male (OR 1.15, CI: 1.37-1.66, $p = 0.008$) and having a history of non-adherence (OR 2.27, CI: 1.34-3.87, $p = 0.002$) and treatment failure (OR 2.83, CI: 0.98 – 8.19, $p = 0.05$).

Conclusion

Underlying reasons for medication non-adherence and treatment failure identified should be resolved by the patient, treatment supporter and health worker. Increased awareness and education on voluntary counseling and testing of HIV among TB patients is advocated, particularly among the male population.

Keywords: Tuberculosis, Medication Adherence, Treatment Outcomes, Nigeria

Introduction

Tuberculosis (TB) is a bacterial infection caused by *Mycobacterium tuberculosis*. It remains a major global health problem being the tenth leading cause of death worldwide, and the leading cause of death from a single infectious agent since 2011, ahead of the Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS).¹ Globally, 10 million people (0.13 %) were estimated to have fallen ill with TB in 2017, with 9 % of the 10 million people HIV- positive.¹ The global treatment success rate was 82 % among all new TB cases. TB treatment saved 53 million lives globally (including HIV positive TB patients) and 11 million lives were saved in Africa. Nigeria recorded a treatment success of 86 % in 2017.¹ However, Nigeria was 6th among the high TB burden countries after India, China, Indonesia, Philippines and Pakistan. Nigeria is also among the 14 countries with overlap high burden of TB, TB/HIV and multidrug resistant-TB (MDR-TB).¹ The burden of TB in Nigeria (population of 191 million people) was 63/100,000 for HIV negative TB mortality and 18/100,000 population for HIV positive TB mortality. The total TB incidence rate was 219/100,000 population, out of which of 14 % were HIV positive.¹

Mycobacterium tuberculosis is an intracellular microorganism that replicates very slowly, therefore prolonged multi-drug treatment regimen (6 months) is the recommended treatment strategy implemented through the Directly Observed Therapy (DOT).² Because of this treatment regimen, medication non-adherence remains a potential and actual challenge. Efforts have been made to identify factors influencing medication adherence,³⁻⁹ from which interventions⁹⁻¹³ have been developed to improve adherence. This is because adherence has been shown to have profound effect on other treatment outcomes.¹⁴ Another way of identifying areas for intervention is the study of the pattern of treatment outcomes over the years to identify specific areas in TB management that require intervention in order to improve these outcomes and health services. Treatment outcomes of TB patients in this study were classified as successful (cure or treatment completed) or unsuccessful (default, treatment failure or death), as defined from the World Health Organization (WHO) and National TB and Leprosy Control Program (NTBLCP) guidelines.^{1,2}

In Nigeria, studies have reported trends in tuberculosis treatment outcomes for the country,¹ and in different states within the country.^{15,16} However assessment of treatment outcomes in individual DOT centers is lacking.¹⁷ This will enable treatment centre-specific interventions to be implemented. This study was done to evaluate TB treatment outcomes and determine their predictors in five DOT centers in Jos-North and Mangu Local government areas of Plateau state, North-Central Nigeria through a fifteen year cohort study.

Methods

Study Design and Setting

A retrospective cohort study of TB patient's from five DOT centers in Jos- North and Mangu Local Government Areas of Plateau State, North-Central Nigeria was done to evaluate TB treatment outcomes. The TB centers were chosen conveniently because they account for more than 50 % of all TB cases in Plateau State. The centers include: Faith Alive Foundation Hospital (FAF), Our Lady of Apostles (OLA), COCIN Hospital and Rehabilitation Centre (CHRC) Mangu and Bingham University Teaching Hospital (BUTH), which are faith based, hospitals, Plateau State Specialist Hospital (PSSH) is a tertiary health institution owned by Plateau State Government. FAF and OLA are secondary health care institutions, while BUTH is a tertiary health care institution. Plateau State has a land mass area of 26,899 square kilometers with a population of 3,206,531 people.¹⁸

Ethical approval and permission to collect data was obtained from the various hospital's Institutional review boards/ Ethical Committees before data collection. All information obtained were treated with confidentiality. De-identified patient data were collected and used for analyses, so that anonymity of the patients was maintained throughout the study.

Data Collection

Data were collected from TB treatment cards from January 2001 to December 2015 by the researcher and a trained research assistant manually, using a pre-designed proforma before transferring to a personal computer. Incomplete data, especially those without treatment outcomes were excluded from the study therefore data from 10,156 TB patients were collected.

Data Analysis

Data checking and cleaning was done in Microsoft Excel before exporting to STATA® version 11.0 (College Station Texas, USA) for analysis. Binomial logistic regression analysis was done to determine the predictors of medication non-adherence.

Results

The mean age \pm SD was 35.5 \pm 15.5. The males were slightly more (58 %) than the females (table 1 in the Supplementary Files). Mean time-outcome \pm SD was 5.4 \pm 3.0 (time in months).

Non-adherence/defaulting rate was 18.5 %, with majority of the patients defaulting at the end of intensive phase as shown in table 2 in the Supplementary Files.

The patient enrollment in 2001 was 360 patients, which rose to a peak of 983 patients in 2013, but decreased to 721 in 2015 from figure 1 above.

Table 3 in the Supplementary Files showed that treatment success was highest in OLA hospital (86.2%); non-adherence/defaulting rate was highest in Plateau State Specialist Hospital (26.4%). Mortality rate was highest in CHRC Mangu (10.5%).

The factors associated with non-adherence from table 4 in the Supplementary Files showed that TB patients were 4 times likely to default/not adhere if they do not know their HIV status in the course of their TB treatment (CI: 3.74-4.91, $p < 0.001$). Males had a 1.15 times likelihood of medication non-adherence than females (CI: 1.37-1.66, $p = 0.008$). TB patients with a history of non-adherence and treatment failure had a 2.3 and 2.8 times higher likelihood respectively to default again from taking their anti-TB medicines (CI: 1.34-3.87, $p = 0.002$; CI: 0.98 – 8.19, $p = 0.05$).

Figure 2 above showed a steady increase in treatment success over the years was seen with a peak at 83.8 % in 2011, but dropped to a low 64.4% in 2015. A consequent reverse trend was seen in unsuccessful treatment, with a peak in 2002 (59.9%) and 30.5% in 2015.

Discussion

This study examined treatment outcomes among a cohort of TB patients retrospectively from patient records over a 15-year period. An overall treatment success rate of 67.4%, less than the Nigerian and global success rate of 86%¹ was observed. A drop in the overall treatment success rate from 83.8% to

64.4% was also observed. The predictors of unsuccessful treatment outcomes were being male, having a history of non-adherence, treatment failure and unknown HIV status.

Tuberculosis disease was distributed slightly more in males than females as similarly observed in other studies.^{19,20} The possible reasons given were; women experiencing barriers to service access, longer clinical delays in diagnosis or producing sputum of poor quality than men.²¹ A community based intervention study however reported significantly more women diagnosed with TB at community level than in the health facilities because the interventions reduced barriers to services with poor women who had previously faced difficulties travelling to health centres particularly benefitting.²¹ TB was found more in the productive age group as was similarly observed in other studies and consistent with global epidemiological findings.^{15,22-25} Majority of the patients were from Jos North Local Government Area of Plateau State, where most of the data was collected. These centers were chosen because they had records of TB patients from the inception of the Directly Observed Treatment strategy for TB in Plateau State in 2001. They also constitute about more than half of the population of TB patients in Plateau state.

CHRC Mangu, a rural DOT secondary facility had the lowest failure rate (0.2%) and defaulting rate (2.9%) but recorded the highest transfer-out (9.1%) and mortality rates (10.5%) than the urban DOT facilities. Training of health staff and treatment supporters should be encouraged so the community is more aware and educated on tuberculosis disease in order to increase case detection and decrease late reporting when the disease is advanced. Medication education and adherence counseling would further reduce treatment failure and defaulting rates. CHRC Mangu was receiving support from the Netherlands TB and Leprosy Relief. This drew a lot of patients from both Mangu and other Local Government Areas around the state because it was an active TB diagnostic and treatment centre. The Netherlands support was however withdrawn in 2016, now making Mangu more of a diagnostic and less of a treatment centre. Therefore patients diagnosed with TB in Mangu were referred to DOT centers closest to their residence for treatment; the reason behind the high transfer-out rates.

Patient Enrollment and Treatment Outcomes

The number of TB patients that accessed treatment increased from 360 patients in 2001 to 983 in 2013 (figure 1), most likely due to the increase in prevalence (from 2.2% in 1991 to 25% in 2010) of HIV disease among TB patients²⁶ and improved documentation processes. DOT expansion resulting to an increase in DOT facilities also increased the case detection rate.^{22,23} The number of TB patients that accessed TB treatment in the DOT centres however dropped between 2014 and 2015, probably due to lack of training and update of trends in TB management. The trend in treatment outcomes followed a similar pattern where the treatment success increased steadily from 2001 (52.2%) to a peak in 2011 (83.8%) but decreased to 64.4% in 2015. The Nigerian National TB and Leprosy control programme is presently training and re-training TB DOT officers to improve TB health care services.

The non-adherence/defaulting rate pattern observed a sharp increase (from 30.6% to 54.2%) in 2002, which was the highest defaulting rate observed over the years. This could be as a result of the strict compliance of DOT, where TB patients came everyday for 2-3 months (initial phase of treatment) with the DOT officers observing them take their medicines. This resulted to the high defaulting rate as the patients became tired of coming everyday (most being very sick) and most patients could not afford transportation cost to the DOT centers. Recommendations were made to modify the DOT system of accessing TB treatment.^{27,28} This probably led to the subsequent decrease in defaulting rate as contact tracing, community DOT and decrease in number of visits to the DOT center from daily to weekly is being practiced.

Factors Associated with Treatment Outcomes

Males were 1.15 times more likely to default from taking their anti TB medicines than females as similarly observed in other studies.^{17,29} A study further attributed the more likelihood of default and poor treatment outcomes in men to high risk behaviour (alcohol, substance and tobacco abuse).²⁹ Females were more likely to have successful treatment outcomes because of a greater immune response due to oestrogen, which increases interferon alpha gamma and potentiates the macrophage activation while testosterone in males inhibits immune response. However this effect is reversed in HIV positive TB patients where males tend to have a better immune response than females.³⁰

TB patients were 4 times likely to default if they did not know their HIV status in the course of their TB treatment. This finding was not consistent with that of Central Ethiopia and Abuja-Nigeria, where TB/HIV co- infected patients had less likelihood of having successful treatment outcomes.^{22,26} One plausible explanation for our finding is that HIV infected patients who have TB co-infection were likely to have received more/reinforced adherence counseling from trained adherence counselors prior to commencement of therapy thus, may be more aware of the consequences of non-adherence in TB/HIV co-infection.

TB patients with a history of defaulting/ non-adherence had a 2.3 times higher likelihood to default again from taking their anti-TB medicines, consistent with findings from other studies.^{22,25} A strengthening of adherence counseling is encouraged so that factors responsible can be identified and resolved. This is important because non-adherence and regular treatment interruptions can lead to development of resistant TB, treatment failure, relapse, longer infections or even death as similarly reported.²² Once a patient defaults from TB treatment, the likelihood of treatment failure increases most likely from the development of drug resistance, leading to poor/unsuccessful treatment outcomes. Some of the data was limited by some missing variables in patients' medical record charts and were eliminated in the course of data checking and cleaning.

In conclusion, findings from this research have revealed an increase in the number of enrolments of TB patients in Plateau State. TB treatment outcomes from five DOT facilities were evaluated to show a

decrease in tuberculosis treatment success rates in Plateau State from a fifteen year cohort study. Therefore, appropriate interventions that would detect underlying reasons for non-adherence among males, those with a history of defaulting, especially at the end of the intensive phase is advocated.

Declarations

Ethics approval and consent to participate

Ethical approval and permission to collect data was obtained from the institutional review boards/Ethical Committee before data collection:

Jos University Teaching Hospital: Institutional Health Research Ethical Committee Reference Number: JUTH/DCS/ADM/127/XIX/6058,

All information obtained were treated with confidentiality. De-identified patient data were used for analyses, so that anonymity of the patients was maintained.

Consent for Publication

Not Applicable

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interest

The authors declare that they have no competing interests.

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Author Contributions

CS and PO conceptualized the research idea, CS designed the study, MD and JA supervised the research, JM analyzed most of the data and LI read and reviewed the manuscript.

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Tables

Due to technical limitations, tables are only available as downloads in the supplemental files section.

Figures

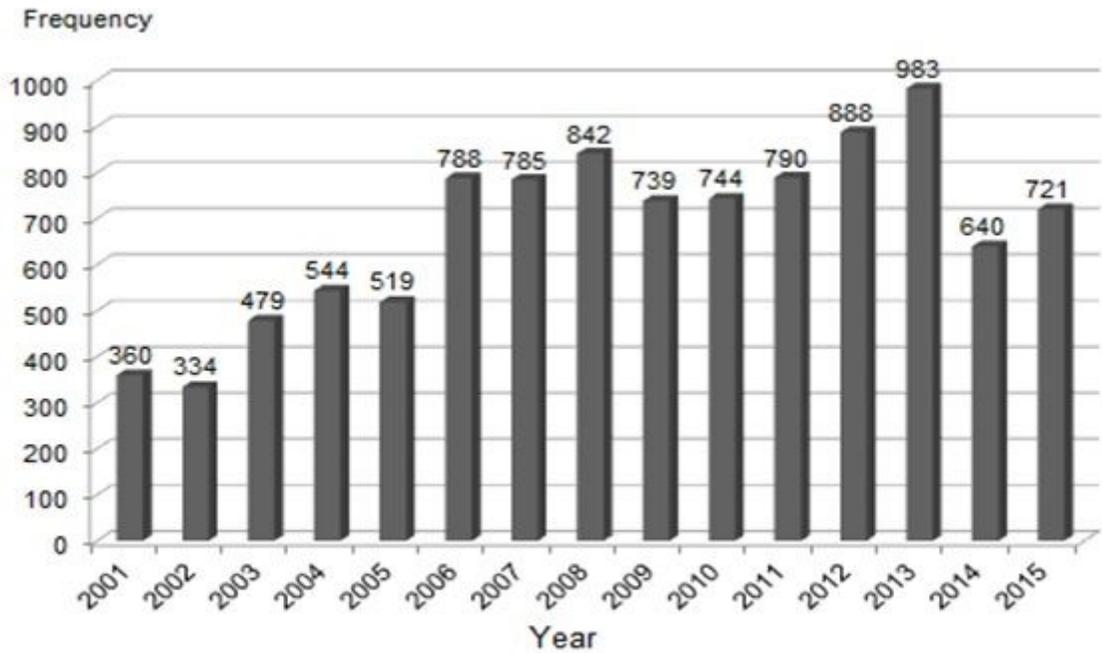


Figure 1: Tuberculosis Patient's Enrollment Trend

Figure 1

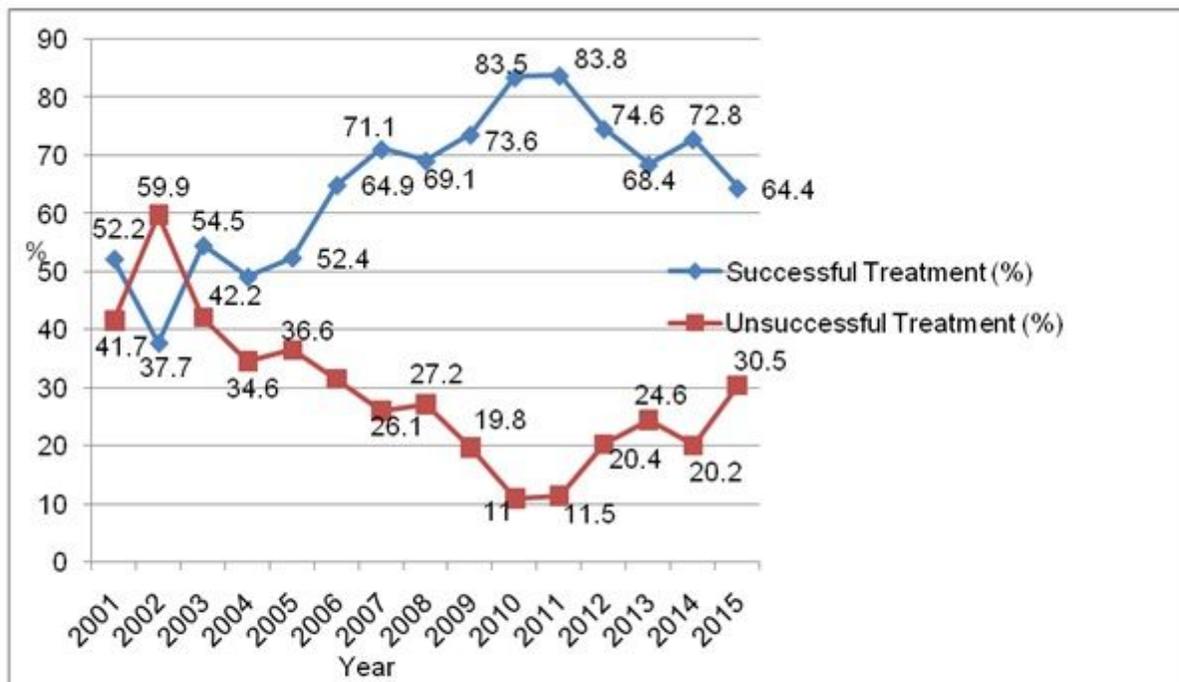


Figure 2: Trend of Treatment Outcomes

Successful treatment = Cured and Treatment Completed

Unsuccessful Treatment = Defaulted, Treatment Failure, Died and Treatment Discontinued

Figure 2

Supplementary Files

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