ORIGINAL ARTICLE

# Pattern of Intensive Phase Treatment Outcomes of Multi-Drug Resistant Tuberculosis in University of Port Harcourt Treatment Centre: A Review of Records from Inception till 2016

Ezinne C **IWUNZE**[1]
Ibitein N **OKEAFOR**[2]
Chinedu O **IBEH**[1]
Inumanye N **OJULE**[1]

[1]*Department of Community Medicine*
*University of Port Harcourt Teaching Hospital*
*Port Harcourt, Rivers State*

[2]*Eagles Watch Research Centre and Care Port Harcourt, Rivers State*

***Author for Correspondence***
Ibitein N OKEAFOR
*Research Support Unit*
*Eagles Watch Research Centre and Care*
*107 East-West Road,*
*Port Harcourt*
*Rivers State, NIGERIA*

*Phone: +234 815 524 1020*
*Email: eagleswatchresearch@gmail.com*

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**ABSTRACT**

**Background:** Multi-drug resistant tuberculosis (MDR-TB) is currently a global menace and poses significant risk to persons living in Sub-Saharan Africa. It occurs largely from failure of conventional treatment of tuberculosis. Its emergence further threatens TB control and prevention.
**Objective:** This study was conducted to determine the pattern of intensive-phase treatment outcomes among hospitalized MDR-TB patients in University of Port Harcourt Teaching Hospital (UPTH) treatment centre in Rivers State, South-South Nigeria.
**Methodology:** This study was a retrospective review of records of patients with MDR-TB admitted from March 2014 till 2016. Data on patients' age, sex, HIV status, treatment outcomes were extracted from the hospital book records into a computer data sheet at the UPTH treatment centre. Chi square and one-way analyses of variance (ANOVA) were performed as appropriate with statistical significance level at 0.05.
**Results:** The study had a total of 107 MDR-TB patients' records comprising 57 males (53.3%) and 50 females (46.7%). The mean age was 35.97±11.81 years. Thirty-eight percent of the female patients and 25.5% of the male patients were HIV positive. Pattern of treatment outcomes at the end of the intensive phase treatment showed that 76% of the MDR-TB patients were cured, 3% were lost to follow-up, 3% had treatment failure, and 15% died.
**Conclusion:** There is a need to further strengthen multi-drug resistant management in the face of its emergence and global epidemic through collaboration with international and non-governmental agencies.

***Key words:*** *Infectious Disease, Anti-Tuberculosis, Resistance, Treatment Success, Nigeria*

## INTRODUCTION

Tuberculosis (TB) has continued to be an important public health issue globally, resulting in illness in millions of individuals yearly.[1] It leads as one of the topmost global 10 causes of mortality, with Human

Immunodeficiency Virus (HIV) ranking below it as one of the principal causes of death of infectious origin.[1,2] The causative organism of Tuberculosis is *Mycobacterium tuberculosis*. Tuberculosis is a communicable disease which primarily affects the lungs with occasional extra-pulmonary spread.[3]

Global TB report 2016 documented its incidence as 10.4 million with 1.4 million people dying from TB worldwide.[1] Africa and Asia account for 60% of the incident cases.[1] Nigeria is one of the six high TB burden countries in the region.[1] Available and appropriate treatment is imperative for cure.[4] Global TB control and prevention has been threatened by the emergence of Drug-Resistant TB (DR-TB).[5] This crisis affects various nations with major public health impact.[5]

Drug resistance can be primary or acquired.[4] Primary drug resistance occurs when a patient is infected with a strain resistant to conventional anti-TB drugs.[4] Acquired drug resistance results from poor treatment with conventional first-line anti-tuberculosis agents.[4] Acquired drug resistance occurs when mutant strains develop due to failure of treatment with first-line anti-tuberculosis drugs.[4,6] Multi-drug resistant TB (MDR-TB) is defined as resistance to at least isoniazid and rifampicin, the two most potent first-line anti-TB drugs.[1,4] The estimate for the global prevalence of MDR-TB among newly diagnosed TB patients in 2015 was 3.9% and 21% among previously treated patients.[1] In Nigeria, its prevalence was an estimated 4.3% among newly diagnosed patients and 25% in previously treated cases.[1] In 2015, there were 480,000 incident cases of MDR-TB globally with only 20% on treatment.[1] Noteworthy, Nigeria was among the five countries that created more than 60% of this treatment gap.[1] Documented data on success rate of MDR-TB treatment in 2013 reports an estimate of 52%.[1]

The need to document data on the pattern of treatment outcomes among MDR-TB patients will expose the reality on ground and serve as a basis for instituting evidence based intervention in the management of multi drug-resistant tuberculosis especially in low-resource settings.

This study therefore aimed to determine the pattern of MDR-TB treatment outcomes in the intensive phase of patients at the MDR-TB treatment centre in Rivers State, Nigeria.

## METHODOLOGY

The study was carried out in the MDR-TB treatment centre of the University of Port Harcourt Teaching Hospital (UPTH), a tertiary health facility located in Rivers State, South-South Nigeria. The 30-bed treatment centre is solely purposed for MDR-TB management using the in-patient approach, in accordance with the National Tuberculosis and Leprosy Control Programme (NTBLCP) of Nigeria, since its inception in March 2014.[7] The centre is operated by the management of UPTH under the support and guidance of NTBLCP.[7] It receives support from the Institute of Human Virology of Nigeria (IHVN) and philanthropists. Specific TB infection control measures, which include environmental and administrative measures, were considered in the design of the centre. The patients are admitted in batches due to the limited space.

This study was a retrospective review of patients' records from inception in March 2014 till 2016. Study population comprised of all patients with MDR-TB who registered at the UPTH treatment centre. Data on patients' age, sex, HIV status, drugs and treatment outcomes were extracted from the hospital book records into a computer data sheet. Data were treated as confidential and anonymity was also maintained in line with the principles of research ethics. Ethical approval for research was obtained from the Research and Ethics Committee of the University of Port Harcourt Teaching Hospital.

Descriptive statistics was performed using frequencies and proportions for qualitative variables, while means and standard deviations were used to summarize quantitative variables. Data were explored for normality prior to choice of statistical test. Inferential statistics employed Chi square tests, to compare the differences in

proportions; and one-way Analysis of Variance (ANOVA/F test), to compare the differences in means across more than two groups. Statistical significance level was set at 0.05.

RESULTS

The study had a total of 107 MDR-TB patients' records from March 2014 to December 2016, comprising 57 males (53.3%) and 50 females (46.7%). The mean age was 35.97±11.81 years, while the median age was 35.0 years and the ages ranged from 14 years to 67 years. The ages of two patients were not specified in the record. Table 1 represents the age and sex distribution of the patients. The age category with the highest frequency was 31-40 years (33.3%). The highest proportion of males was aged 31-40 years (36.8%) while for females, it was 21-30 years (33.3%). The differences in proportions of the age categories across sex was statistically significant *(Likelihood Ratio Chi Square* = 13.38*; p*-value =0.020).

There were 105 patients' records with HIV test results; of these, 33 (31.4%) were HIV positive. Figure 1 shows the distribution of HIV status by sex. Thirty-eight percent of the female patients and 25.5% of the male patients were HIV positive.

Slightly more than three-quarter (76%) of the MDR-TB patients were cured at the end of the intensive phase treatment while 3% percent of them had treatment failure. The categories of treatment outcome of the intensive phase management of the patients are presented in Figure 2. Comparison of the mean ages of the patients across the categories of treatment outcomes showed that patients with outcomes of 'loss to follow up' had the highest mean age (39.67 ± 13.58 years) while the lowest mean age of 31.67 ± 6.66 years was noted in patients with treatment failure. The differences in the mean ages across treatment outcomes was not statistically significant (*F test* = 0.168*; p*- value = 0.954). (Table 2)

Proportions of treatment outcomes compared across the sex of the patient showed no significant difference (*Likelihood Ratio Chi Square* = 5.830*; p*- value = 0.212). Higher proportion of patients with cured (53.7%) and loss to follow-up (100.0%) treatment outcomes were males while higher proportion of patients with death as a treatment outcome were females (62.5%). (Table 2)

HIV status across treatment outcomes (Table 2) shows that almost three-quarter of patients with cured treatment outcome had HIV negative status (74.1%). Treatment failure was highest among HIV positive patients (66.7%). There was no significant difference in the proportions of the categories of treatment outcomes across HIV status in the study (*Likelihood Ratio Chi Square* = 5.421; *p*-value = 0.247).

**Table 1:** Age and sex characteristics of respondents

| **Age category in years**** | **Male N (%)** | **Female N (%)** | **Total N (%)** |
|---|---|---|---|
| ≤ 20 | 1 (1.8) | 8 (16.7) | 9 (8.6) |
| 21 – 30 | 13 (22.8) | 16 (33.3) | 29 (27.6) |
| 31 – 40 | 21(36.8) | 14 (29.2) | 35 (33.3) |
| 41 – 50 | 13 (22.8) | 6 (12.5) | 19 (18.1) |
| 51 – 60 | 7 (12.3) | 4 (8.3) | 11 (10.5) |
| > 60 | 2 (3.5) | 0 (0.0) | 2 (1.9) |
| Total | 57 (100.0) | 48 (100.0) | 105 (100.0) |

*Likelihood Ratio Chi Square =13.388; d.f=5; p value = 0.020*

***Age was not specified in the records of two patients*

**Figure 1.**HIV status by sex of MDR-TB patients

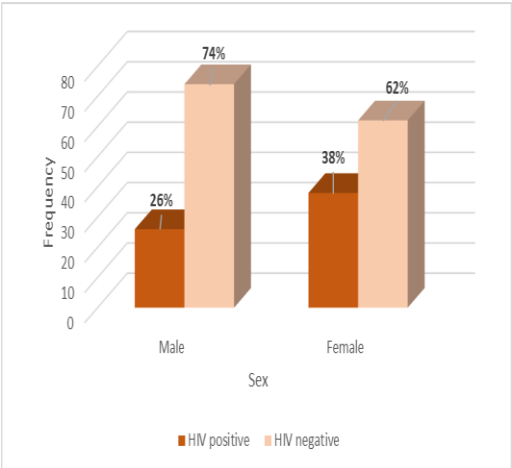

**Figure 2.**Distribution of MDR-TB treatment outcomes in the study

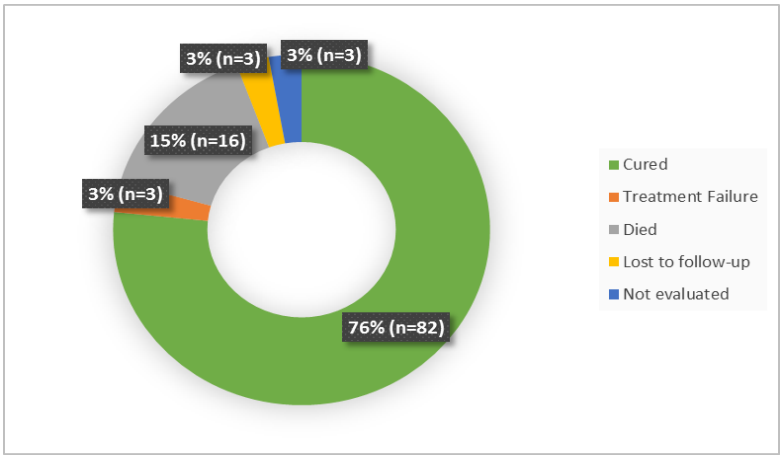


**Table 2.**Pattern of intensive phase treatment outcome by age, sex and HIV status of MDR-TB patients

| Treatment Outcomes | Age in years Mean ± Standard deviation | Sex | | HIV Status | |
|---|---|---|---|---|---|
| | | Male N (%) | Female N (%) | Positive N (%) | Negative N (%) |
| Cured*** | 35.96 ± 11.96 | 44 (53.7) | 38 (46.3) | 21 (25.9) | 60 (74.1) |
| Treatment failure | 31.67 ± 6.66 | 2 (66.7) | 1 (33.3) | 2 (66.7) | 1 (33.3) |
| Died | 36.13 ± 13.27 | 6 (37.5) | 10 (62.5) | 8 (50.0) | 8 (50.0) |
| Loss to follow up | 39.67 ± 13.58 | 3 (100.0) | 0 (0.0) | 1 (33.3) | 2 (66.7) |
| Not evaluated** | 36.00 ± 4.58 | 2 (66.7) | 1 (33.3) | 1 (50.0) | 1 (50.0) |
| *Statistical inference* | *ANOVA** = 0.168; *p value* = 0.954 | *Chi Square* **= 5.830; *p value* = 0. 212 | | *Chi Square*** = 5.421; *p value* = 0.247 | |

*One-way analysis of variance/F-test; **Likelihood Ratio Chi Square; ***One of the patients in the 'cured' and 'not evaluated' group had no HIV test result

DISCUSSION

The global MDR-TB epidemic has emerged mainly from failure of tuberculosis management and treatment.[1] This has necessitated continuous and intense research to ensure effective control and guide policies.

The study had a total of 107 MDR-TB patients' records from March 2014 to December 2016. The slight male preponderance observed in this study may be attributed to the fact that the male gender is more associated with alcoholism and substance abuse which are known promoters of tuberculosis progression.[3] This is also comparable with findings from other African studies.[5,8,9]

Most of the patients in this study were in the 31-40 years age-category which represents the working population, hence highlighting the impact of the disease on the labour force. This is in agreement with reports from other studies.[5,8] The differences in proportions of the age categories across sex was statistically significant ($p$<0.05), which contrasts the findings of a study in South West Nigeria.[10] Noteworthy, this study in South West Nigeria comprised 11 MDR-TB adolescents only.

The finding of slightly greater than three-quarters of the MDR-TB patients in this study achieving cure in the intensive phase treatment, is however higher than the cure

rate of 52% reported by Ibrahim *et al.* in Egypt.[5] Although, both studies employed the in-patient approach in MDR-TB management, the dissimilarity noted may stem from a smaller sample size of present study (107) in comparison to the study in Egypt (577). However, another study in India by Isaakidis, *et al*.[11] reported a much lower cure rate of 22%. This could have been because the study participants were ambulatory while on treatment, hence limiting close monitoring of patients. Noteworthy, the cure rate observed in this study is consistent with the finding of a nationwide cohort study by Oladimeji, *et al*.[12] and a study by Khan, *et al*.[13] Oladimeji, *et al.* accrued the commendable cure rate reported in their study to the in-patient approach recommended by the NTBLCP as well as the adoption of monthly stipends to MDR-TB patients. However, the treatment cure rate of less than 100% could be described as sub-optimal and therefore exposes the need for greater collaboration with international and non-governmental agencies.

The presence of low proportion of lost to follow-up group is in keeping with similar studies by Ibrahim, *et al*.[5] and Khan, *et al*.[13] This could be attributed to the fact that the patients were hospitalized and so were unlikely to default. However, another study that involved only admitted patients reported no loss to follow-up.[12] Other similar studies sharply contrast the low proportion of patients lost to follow-up observed in this study.[8,14,15] Unlike the present study, that of Isaakidis, *et al.* employed ambulatory approach and reported a much higher proportion of loss to follow-up of patients. Although, World Health Organization (WHO) guidelines[16,17] recommends practice of ambulatory management in the intensive phase of therapy, it is yet to be adopted in Nigeria. The NTBLCP practices an in-patient approach to encourage optimal adherence and adequate management of the patients.[18,19]

The proportion of patients in our study who had treatment failure was small, which corroborates with similar studies.[5,13] However, higher proportions of treatment failure have been observed in other studies.[14,20,21] Slightly more than a sixth of the patients in this study died in the course of their treatment; although this fraction is comparable to other studies,[5, 12,13,14] a targeted intervention at reducing mortality among MDR-TB patients while in retention is advocated.

The finding that age, sex and HIV status showed no significant relationship with treatment outcome among MDR-TB patients in this study possibly reveals that interventions targeted at promoting treatment outcomes should be instituted irrespective of the age, sex and HIV status of the patients.

**Limitations**

The retrospective review of records in this study is a limitation as some of the variables were missing. Another limitation is that the treatment outcomes for only the intensive phase of MDR-TB treatment were reported. Nonetheless, this study is the first study to the best of authors' knowledge to review treatment outcomes in UPTH MDR-TB treatment centre from inception to 2016. Hence it could serve as a baseline for further studies. Additionally, it provides information required in instituting effective interventions targeted at MDR-TB management.

## CONCLUSION

The treatment outcomes observed in the University of Port Harcourt Teaching Hospital MDR-TB treatment centre reveals a commendable cure rate. However effective measures such as strict monitoring of patients are advocated in order to minimize the loss to follow-up. Furthermore, there is need to strengthen and scale-up MDR-TB management through collaboration with international and non-governmental agencies.

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