

Original Research Article

Outcomes of multi drug resistant tuberculosis under programmatic conditions: the experience

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ABSTRACT

Background: Tuberculosis is the most common cause of death from an infectious disease worldwide after HIV/AIDS. Drug resistant tuberculosis continues to be a public health crisis. India stands, one among 27 “high burden” MDR countries and has over 2 million new TB cases every year and TB kill’s nearly 1000 people every day. The WHO 2018 Global Tuberculosis Report estimated that, worldwide, approximately 3.5 percent of all new TB cases and 18 percent of previously treated cases are caused by MDR or rifampicin-mono resistant strains.

Methods: Presumptive drug resistance TB cases were subjected for CBNAAT or LPA to detect resistance patterns. About 231 cases of MDR/RR TB cases after pre-treatment evaluation started on CAT- IV regimen and both interim and final outcomes were analyzed.

Results: Out of 231cases 172(74.4%) were males and 59(25.6%) were females with age between 13-75yrs. Total of 194 cases culture conversion occurred out of which 28 cases the cultures were reverted back to positives. Final Outcomes were, cured in 84 (36.3%) cases, treatment completed in 42 (18.18%) cases, defaulters in 31 (13.4%) cases, turned to be XDR in 10 (4.32%) cases, treatment failure in 10 (4.32%) cases, 50 (21.6%) cases died, 3(1.29%) cases were transferred out.

Conclusions: Approximately 2/3rd of MDR/RR TB cases are retreatment sputum positive cases. Successful outcome observed in 54.54% of cases only. High rates of deaths and defaulters alarm the necessity of more effective implementation and surveillance of the programme.

Keywords: Multi drug resistant tuberculosis, Outcomes, Pulmonary tuberculosis, Resistance patterns standardized regimen

INTRODUCTION

Tuberculosis (TB) is a leading cause of morbidity and mortality worldwide. Tuberculosis is the most common cause of death from an infectious disease worldwide after HIV/AIDS. A major hurdle to TB control is the emergence of mycobacterium resistance to anti-tuberculosis chemotherapy.¹ Drug resistant tuberculosis continues to be a public health crisis. The best estimate is that, worldwide in 2017, 5,58,000 people

developed TB that was resistant to rifampicin (RR-TB), the most effective first line drug, and of these 82% had multidrug resistant TB (MDR-TB).¹ Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to isoniazid and rifampicin.² India stands, one among the 27 “high burden” MDR countries and has over 2 million new TB cases every year and TB kills nearly 1000 people every day. WHO currently estimates that India has about 100,000 people with MDR-TB.³

The WHO 2018 Global Tuberculosis Report estimated that, worldwide, approximately 3.5 percent of all new TB cases and 18 percent of previously treated cases are caused by MDR or rifampicin-mono resistant strains.⁴ INDIA ranks 1st in having MDR-TB cases, approximately 24%, with an incidence of 1,35,000 i.e. 10/1,00,000 population. Among them 2.8% are new cases and 12% are previously treated cases.¹ The standard treatment for MDR-TB is a 24-month regimen largely comprising second-line drugs that are less effective, more costly and associated with more number of adverse events.⁵

India's RNTCP under PMDT activities provides a standardized regimen of treatment labeled as CAT IV under DOTS-plus program and it has shown an effectiveness of 61% successful outcomes in MDR TB in resource limited countries.¹ The above data reflects the immense TB burden in INDIA and the need of urgent interventions to bring it down. In this scenario the current study was undertaken to assess different outcomes in MDR-TB patients in the region of Visakhapatnam to highlight both its success and failure under programmatic conditions, and also to see the resistance patterns.

Objectives

- To study the outcomes in multi drug resistance tuberculosis patients with standardized regimen under programmatic conditions.
- To observe the different resistance patterns among presumptive pulmonary tuberculosis patients.

METHODS

It is a prospective observational study conducted at DOTS plus center, department of pulmonary medicine, GHCCD, Visakhapatnam. All the Presumptive MDR-TB patients who attended the OPD between January 2014 to March 2016 at the above-mentioned DOTS plus site were taken into the study.

Inclusion criteria

- All Presumptive DR-TB cases who were resistant to isoniazid and rifampicin (MDR-TB) or Rifampicin (RR-TB).
- Age above 18 years.

Exclusion criteria

- Age less than 18 years
- Pregnant women
- XDR-TB
- Not willing to give consent.

Presumptive DR-TB was referred to the following patients in order of their risk i.e. TB patients found positive on any follow-up sputum smear examination during treatment with first line drugs including

treatment failures; TB patients who are contacts of DR-TB; previously treated TB patients; new TB patients with HIV co-infection. Pediatric TB non-responders were not included in the study.

A total of 231 patients were enrolled in the study after a written informed consent. Information on demographic and clinical profile of patients including co-morbidities like HIV status, diabetes, smoking habits, and alcoholism were noted. History of previous anti-tuberculosis treatment (ATT) was noted and analyzed. The diagnosis of MDR-TB was done at RNTCP accredited Intermediate Reference laboratory in this hospital, using CBNAAT, line probe assay and liquid culture wherever needed. Different resistant patterns among the presumptive MDR-TB cohort group were noted.

Prior to initiation of treatment, patients were admitted at DOTS PLUS site and pre-treatment evaluation was done after which they were started on standardized regimens (CAT- IV) as per PMDT guidelines. All the patients in the cohort group were followed till the end of the treatment. The last case enrolled was in March 2016, which completed the treatment by March 2018. All the adverse events during the treatment were noted, and necessary interventions had been taken. The status of mycobacterial cultures is generally used to guide, therapy for patients treated in resource-limited settings and is considered to be the most important interim indicator for the efficacy of multidrug-resistant TB treatment.^{6,7}

MDR - TB, cure, treatment completed, death, treatment failure, and treatment defaulter were defined as per the RNTCP guidelines.⁸

Successful outcome: Cure and completion of treatment were considered to represent successful outcome.⁸

Non-successful outcome: Defaults, death, change to category V treatment i.e. XDR TB, failure and still on treatment were considered to represent non-successful outcomes.⁸

Statistical analysis

Both interim and final outcomes of Cat IV treatment as described by the programme were noted and analyzed. Quantitative variables were summarized as MEAN±SD and qualitative variables as percentage using MS EXCEL.

RESULTS

Out of 231 cases 172(74.4%) were males and 59(25.6%) were females with age ranging between 13-75yrs with an average of 36.4±13.5 yrs. Seventeen cases (7.3%) were HIV positive. (Table 1). Among 231 cases sputum positive retreatment cases were 160(69.2%), sputum negative retreatment cases were 13(5.6%), follow up smear positive cases were 39(16.88%), HIV TB co-

infection cases 17(7.3%) and 2(0.86%) cases were contacts of MDR-TB. (Figure 1) Rifampicin resistance was observed in 109 (47.18%) cases, both INH and Rifampicin resistance was observed in 122 (52.8%) cases and additional Ethambutol resistance was observed in 6 cases (Figure 2).

Table 1: Demographic data (n=231).

Parameter	Value
Age	13-75
Males	172 (74.4%)
Females	59 (25.6%)
HIV positive	17/231 (7.3%)

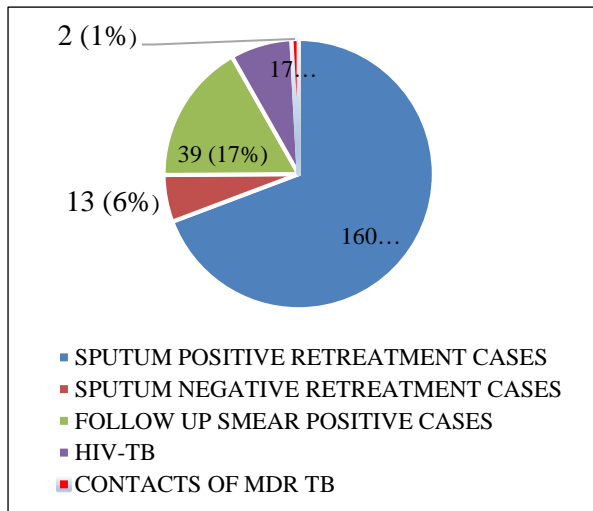


Figure 1: Categories of Presumptive MDR-TB.

Culture conversion occurred in total of 194 cases out of which 28 cases the cultures were reverted back to positive (Table-2). Sputum culture conversion occurred at 3rd month of treatment initiation, in 131(67.5%) cases, at 4th month in 24 cases (12.37%), at 5th month in 8 cases (4.1%), at 6th month in 4 cases (2%) and at 7th month in 3 cases (1.5%). 19 succumbed to death within 3 months of initiation of treatment, 13 were defaulters before culture reports, 4 had shown XDR resistance pattern and 1 case was transferred out among the rest of 37 cases.

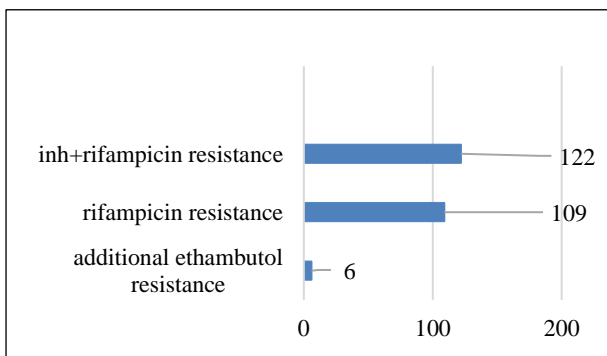


Figure 2: Drug resistance patterns.

Table 2: Interim outcomes.

Interim outcome	Number
Culture conversion	194
Culture reversion	28/194

The final outcomes noted were as follows, cured in 84 (36.3%) cases, treatment completed in 42 (18.18%) cases, defaulters in 31 (13.4%) cases, turned to be XDR in 10 (4.32%) cases, treatment failure in 10 (4.32%) cases, 50 (21.6%) cases died and 3(1.29%) cases were transferred out (Figure 3).

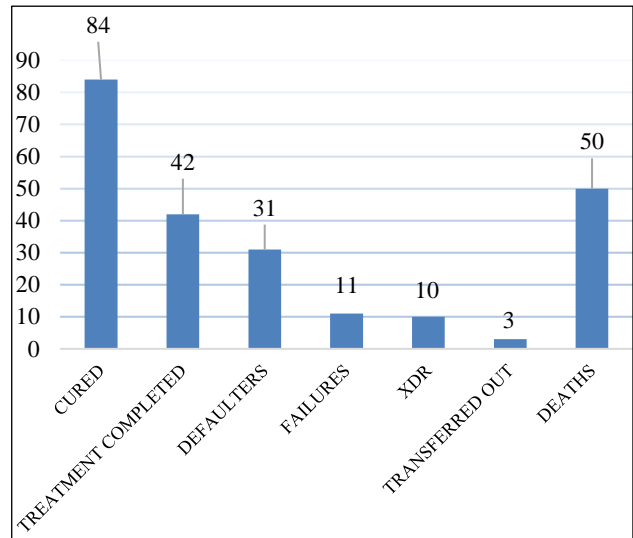


Figure 3: Final outcomes.

DISCUSSION

The emergence of MDR-TB is a global problem, which is threatening to destabilize the best efforts of TB control.^{7,9} To manage MDR-TB in poor economically and resource limited settings, WHO launched the DOTS Plus initiative to develop a global policy to provide technical assistance to DOTS programs and to enable access to second-line drugs under rational use.⁹ As the MDR patients are resistant to most of the first line drugs and require judicious and optimal combinations of second line drugs, National programs in resource-poor endemic countries may feel pressured into instituting DOTS-Plus programs for their MDR-TB patients.¹⁰

The demographic profile of MDR-TB patients in this study was similar to that of studies done by Sangita et al (2010), Sachin S Dole et al (2016), and Deepak et al (2017).¹¹⁻¹³ Majority of the patients were in the economically productive age group (20-40 years). In this study, there were few patients with HIV infection and these patients had worse outcomes than those who were HIV-negative. Adverse drug reactions were documented in nearly a quarter of the study population with gastrointestinal, psychiatric, and ototoxic reactions being

the most common. This was consistent with other recent reports.¹⁴⁻¹⁶

Majority of the cases (69.2%) were sputum positive retreatment cases which was in agreement with most of the other Indian studies and systematic reviews.¹⁷⁻¹⁹ Sputum culture conversion at 3rd month occurred in 56.7% of cases, which was low compared to other studies by Sachin S Dole et al and Deepak et al.^{12,13} But sputum culture conversion at end of 6 months was 83.9%, which was in agreement with other recent Indian studies, systematic reviews, and Meta-analysis.

In this study successful outcome was observed in 54.54% which was similar to a study done by Sachin S Dole et al, Sangita V. Patela et al study had a very low successful outcome (38.62%), and in a study by Deepak et al and in a systematic review of 36 studies the successful outcomes were 63% and 62% respectively.^{11-13,18} In this study 21.6% of cases died which was in contrast to other studies ranging from 11% to 16.4%. High death rate might be because of comorbidities and bilateral extensive i.e. far advanced disease at presentation leading to respiratory failure. The only limitation of the study was that it was a single center observational study and factors which because poor outcomes were not analyzed.

CONCLUSION

Approximately 2/3rd of MDR/RR TB cases were retreatment sputum positive cases. Successful outcome was observed in 54.54% of cases only. High mortality rate and increased number of defaulters alarms the necessity of more effective implementation and surveillance of the programme. Measures for improving nutritional status and interventions to increase the adherence to treatments might definitely improve the treatment outcomes.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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