

A STEP TOWARDS CONTROL OF MULTIDRUG RESISTANT TUBERCULOSIS: HOSPITAL BASED STUDY FROM NASHIK INDIA

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ABSTRACT

Introduction: The Global TB report (2012), estimates 73,000 MDR TB patients living in India, among them only 1,660 cases were notified and 68.4% cases were put on treatment. Hence, this study was conducted with objective to assess the treatment outcome of multi drug resistant Tuberculosis patients enrolled in DOTS plus (Cat-VI) site.

Methodology: It is a retrospective case series of MDR-TB cases conducted at Dr. Vasantryo Pawar Medical College, Hospital & Research Centre, Nashik (Maharashtra). Information was collected on age, gender, HIV status, previous treatment of TB, weight of patient, refused to take treatment for Cat IV. Outcome was recorded in terms of cure rate, rate of failure, defaulter, treatment completed, switch to Cat V and death.

Results: Among the study subject, majority of study subjects were male (65%) and highest proportion (49%) of MDR-TB was in 25-44 years of age. Out of 353 patient 241 (68.4%) were still on Cat IV in which 35% patient's on intensive phase and 65% put on continuation phase while 12.8%, 13.5%, 4%, 1.1%, 3.6% & 0.5% patient were found to be defaulted, died, refused to take treatment, treatment completed, transfer out & switch to Cat V, respectively.

Conclusion: In the present study, the majority of study subjects (99.4%) were previously treated for TB, we identified number of operational challenges in the treatment of MDR-TB like rate of defaulter, refuse to take treatment & deaths among MDR-TB patient was high. There is need to study correlates of these factors in details also need of operational research to improve MDR-TB treatment in India is considered as priority.

Key words: Outcome, Multi drug resistance, Tuberculosis, Treatment

INTRODUCTION

In the recent years, Multi-Drug Resistant Tuberculosis (MDR-TB) is being discussed globally for the reason of increase morbidity and mortality along with the challenges faced in treatment completion. MDR-TB as it is known, the Tuberculosis bacteria is resistant to at least one of the first line drugs Isoniazid and Rifampicin.¹ Drug resistance surveillance data indicate

that in 2013, approximately 480,000 people developed MDRTB worldwide. Among TB patients reported by national TB programmes in 2013, there were an estimated 300 000 cases of MDR-TB. More than half of these cases were in India, China and the Russian Federation.²

Government of India, through Revised National Tuberculosis Control Programme (RNTCP) has proposed measures to implement and address the growing burden through its National Strategic Plan 2012-2017.³ One of the key measure was to gather epidemiological and programmatic evidence to burden of MDR-TB in India. In this context, programme identified and operationalized DOTS-Plus sites exclusively for management of identified patients. Though DOTS-Plus sites were operational, from 2007,

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there are limited evidences to show the outcome of the treatment management at these sites. The paper here describes the outcome of those MDR_TB patients who were enrolled in DOTS Plus site of Dr. Vasantrao Pawar Medical College, Hospital & Research Centre, Nashik (Maharashtra).

METHODOLOGY

Study Design: The study was a retrospective case series of MDR-TB cases conducted at Dr. Vasantrao Pawar Medical College, Hospital & Research Centre, Nashik (Maharashtra). Which is the first private Tertiary care Institute where DOTS-Plus was started. Total sample size was 353 cases included in study from Jan 2012 to March 2014.

Data collection: Information was collected on age, gender, HIV status, previous treatment of TB, weight of patient, refused to take treatment for Cat IV. Outcome was recorded in terms of cure rate, rate of failure, defaulter, treatment completed, switch to Cat V and death.

Ethical approval: Data collection was done with prior permission from District Tuberculosis Officer, Nashik and Medical Director, Dr. Vasantrao Pawar Medical College, Hospital & Research Centre, Nashik.

Statistical analysis: Data was entered in Microsoft excel file & analyzed using Epi_info software package. The frequencies are expressed in percentages. Chi-square test was used to test the association. P-value <0.05 was taken as significant.

Operational definitions used for this study as per RNTCP guidelines are⁴

- **Cured:** An MDR-TB patient who has completed treatment and has been consistently culture negative (with at least 5 consecutive negative results in the last 12 to 15 months). If one follow-up positive culture is reported during the last three quarters, patient will still be considered cured provided this positive culture is followed by at least 3 consecutive negative cultures, taken at least 30 days apart, provided that there is clinical evidence of improvement.
- **Treatment completed:** An MDR-TB patient who has completed treatment according to guidelines but does not meet the definition for cure or treatment failure due to lack of bacteriological results.

- **Death:** An MDR-TB patient who dies for any reason during the course of MDR-TB treatment
- **Treatment failure:** Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12-15 months are positive, or if any of the final three cultures are positive.
- **Treatment default:** An MDR-TB patient whose MDR-TB treatment was interrupted for two or more consecutive months for any reasons.
- **Transfer out:** An MDR-TB patient who has been transferred to another reporting unit (DOTS Plus site in this case) and for whom the treatment outcome is not known. Till the time the DOTS Plus services are available across the country, the Cat IV patients can be transferred out only to those districts, within or outside the state, where these services are available. If a Cat IV patient moves from one district to another, both of which are covered by the same DOTS Plus site, transfer out will not be required.
- **Treatment stopped due to adverse drug reactions:** A patient on MDR-TB treatment who develops severe adverse reactions and could not continue the MDR-TB treatment in spite of the management of the adverse reactions as per the defined protocols and decision has been taken by the DOTS-Plus site committee to stop treatment.
- **Treatment stopped due to other reasons:** A patient on MDR-TB treatment who could not continue the MDR-TB treatment for any other medical reason (than adverse drug reactions), and a decision has been taken by the DOTS-Plus site committee to stop treatment.
- **Switched to Category V treatment:** A Category IV patient who during treatment is identified as an "XDR-TB suspect" and who is found to have XDR-TB on testing by an NRL, who subsequently has had their Category IV treatment stopped and RNTCP Category V treatment initiated.
- **Still on treatment:** An MDR-TB patient who, for any reason, is still receiving their RNTCP CAT IV treatment at the time of the submission of the RNTCP DOTS- Plus Treatment Outcome Report.

RESULTS

Among the study subject, highest proportion (49%) of MDR-TB was in 25-44 years of age followed by 27.5% in 15-24 years. It was minimum in the age group of 0-14

years. Proportion of MDR-TB was 230 (65%) among males as compared to 123 (35%) in females. The significant difference between age among MDR-TB patients except in the age of 25-44 years of age was ($p < 0.05$). There is a significant difference in the gender among MDR-TB patients is mentioned in table 1.

Table 1. Age & gender wise distribution of MDR-TB patient.

Age in years	Gender		Total	P-value
	Male	Female		
0-14 year	1 (0.5)	2 (1.7)	3 (0.9)	0.58
15-24 years	53 (23.0)	44 (35.8)	97 (27.5)	0.01*
25-44 years	109 (47.3)	64 (52.0)	173 (49.0)	0.20
45-54 years	35 (15.2)	9 (7.3)	44 (12.5)	0.03*
55 years & above	32 (14.0)	4 (3.2)	36 (10.1)	0.01*
Total	230 (65.1)	123 (34.3)	353 (100)	0.001*

*statistically significant, figure in parenthesis are percentage.

Most of the patients 351 (99.4%) had a history of previous treatment for tuberculosis. Only 2 (0.6%) patients were new to anti-tubercular drugs.

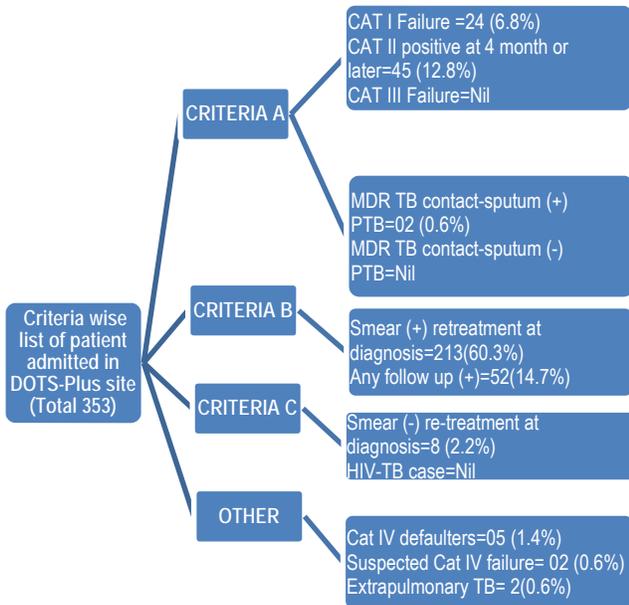


Figure 1. Criteria wise list of patient admitted in DOTS-Plus site

Outcome of MDR-TB treatment: Out of 353 patient 241 (68.4%) were still on Cat IV in which 35% patient's on intensive phase and 65% put on continuation phase while 12.8%, 13.5%, 4% 1.1%, 3.6% & 0.5% patient were found to be defaulted, died, refuse to take treatment, treatment completed, transfer out & switch to Cat IV, respectively. (See figure 2).

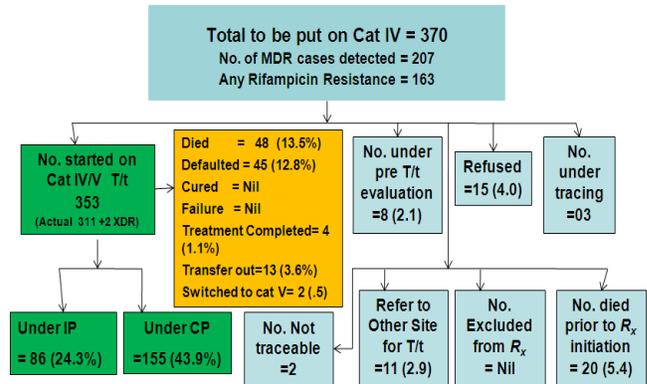


Figure 2. Outcome of MDR-TB patient at DOTS-Plus site

DISCUSSION

Government of India, implemented DOTS Plus under RNTCP program for the control of MDR TB. Despite of various activities in the present study we found that, rate of defaulter (12.8%) and death (13.5%) were high but treatment failure (Nil) was not reported. As per WHO Global supplementary report on MDR TB only 48% of the MDR-TB patients in the 2011 cohort of detected cases were successfully treated. 16% died, 24% did not have their treatment outcome documented or interrupted treatment, and 12% were not cured despite receiving treatment² while Jain K et al. found that, 13% of patients were failure, 23% defaulter, and 19% died.⁵ As per N. Lytvynenko et al. (Ukraine), Cured (19%), treatment completed (1%), failure (16%), died (2%), and lost to follow up (16%).⁶ Most of the studies have similar findings except treatment failure. The difference may be because of study design, place and implementation of program. The present study also reported switch to category V from Cat IV as well as refuse to take treatment.

In the present study, we found that MDR-TB was mainly seen in young age & male population. The proportion of drug resistance among younger age groups is more likely to be indicative of recent transmission than

among older age groups, which are more likely to be harboring older infections. Data on drug resistance stratified by age groups and sex but stratification cannot show effectiveness of programme.

Another interesting observation was that none of the patients with MDR-TB was HIV co-infected in the present study. This finding is in agreement with previous studies, although there are studies which contradict this finding.⁵⁻¹⁰ (shown in table 2)

Table 2. Comparisons of finding of present studies with published research articles

Study	Setting	MDR Cases (n)	HIV status	Prevalence of XDR-TB (%)
In Present study	Tertiary care Centre, Nashik	231	All HIV-negative	1 (0.5)
Mondal and Jain, 2007	Tertiary care centre, Lucknow	68	All HIV-negative	5(7.4)
Jain et al, 2007	Tertiary care centre, Mumbai	326	All HIV-negative	36 (11)
Thomas et al, 2007	Field trial, Chennai	66	All HIV-negative	1(1.5)
Sharma et al, 2009	AIIMS, New Delhi, tertiary care hospital	211	All HIV-negative	5(2.4)
Ramchandran et al, 2009	Gujrat, Field study	216	All HIV-negative	7(3.1)
Singh et al, 2007	Tertiary care center, New Delhi	12	All HIV -infected	4 (33,3)

Strength of this study: this is the first study from India, assessing the treatment outcomes of MDR-TB (DOTS-Plus). Data collection & data entry was done by well qualified & trained staff. **Limitation of study:** end result of treatment outcome (cure) was unknown at the end of study.

This is secondary data analysis and only recorded information was used. Tuberculosis is major public health problem and MDR-TB is emerging threat in

India. India is the second largest burden country after China. Government of India taken various innovative approaches to control the problem of TB and MDR-TB under RNTCP program but on the other side treatment of MDR-TB can take more than 2 years for cure; drugs are more toxic and expensive, less effective as compared to first line. There will be need to make shorter and effective drug regimen.

CONCLUSION

In this study we have identified number of challenges in treatment of MDR-TB like high rate of defaulter, deaths & refused to take treatment. There will be need to assess the treatment outcome of DOTS-Plus at both intensive phase as well as continuation phase. Operational research to improve programmatic management of MDR-TB in India is considered as priority.

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