

Original Research Article

Analysis of treatment outcome in multi-drug resistant tuberculosis patients treated under programmatic conditions

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ABSTRACT

Background: Programmatic management of MDR-TB has taken over the un-standardized and unsupervised treatment practice in India. However, despite being implemented in whole of country, the data on the program surveillance is scarce. Hence the present study was sought to evaluate the treatment outcome in patients with MDR TB in Chandigarh being treated under programmatic conditions.

Methods: A retrospective study was carried out by enrolling all MDR-TB patients registered between January 2012 to December 2014. Medical records of 140 patients were scrutinized for necessary information on demographic, clinical parameters and previous TB treatment. Treatment outcomes to Cat IV anti-TB therapy, any interruptions in treatment, adverse drug reactions, culture conversion etc. were evaluated from the records.

Results: Of the 140 patients, 77 (55%) were declared cured, 11 (7.9%) completed treatment, 23 patients (16.4%) died, 13 (9.3%) defaulted on treatment, 5 (3.6%) had treatment failure and 11 (7.9%) were shifted to Cat V therapy. On comparison, BMI, haemoglobin, treatment outcome in previous ATT, treatment adherence and time to sputum culture conversion were significantly different in different treatment outcome groups.

Conclusions: The treatment success rate of MDR-TB patients have shown improvement under programmatic conditions. Interventions to improve BMI and treatment adherence might further help to improve the success rate.

Keywords: Programmatic conditions, MDR-TB, Treatment outcome

INTRODUCTION

The emergence of drug resistance in tuberculosis (TB), particularly multidrug resistant TB (MDR-TB) is a significant public health problem worldwide. Globally, there was an estimated 480000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100000 people with rifampicin-resistant TB (RR-TB) in 2015, who were also eligible for MDR-TB treatment.¹ As per WHO 2016 data, India has around 80000 registered which is among the highest in the world.¹ Hence, Revised National TB Control Program (RNTCP) introduced the programmatic management of drug resistant TB (PMDT) services in 2007 for the management of MDR-TB.

DOTS-Plus program follows a standardized regimen of treatment (labeled as Cat IV) which has shown feasibility and effectiveness with 61% successful outcome in MDR-TB in resource limited countries. However, in real life conditions, the picture is dismal with WHO reporting a treatment success rate of only 46% in India.¹

It is evident that there is a great scope of improvement in the program. Few studies from different parts of the country have yielded variable results in terms of treatment outcome of MDR-TB.²⁻⁴ Regular surveillance of the program highlighting both its success and failure is important to find weak areas which need intervention for better program outcome.

Chandigarh is amongst the first few states of India where PMDT services were started in 2012. It has a designated drug resistant TB (DRTB) centre at Govt. Medical College and Hospital (GMCH) which caters to the population of Chandigarh as well as adjoining 5 districts of Haryana. No study has been undertaken to assess the performance of the DOTS-Plus program in this region. Hence, the present study was undertaken to assess different treatment outcome among MDR-TB patients being treated under programmatic conditions.

METHODS

It was a retrospective study conducted at department of Pulmonary medicine, GMCH, Chandigarh. All MDR-TB patients (residents of Chandigarh) who were registered between January 2012 and December 2014 at the above-mentioned DOTS plus site and initiated on Cat IV regimen of RNTCP were recruited in the study. The study was approved by institutional ethics committee of GMCH. Informed consent was not required as whole data was retrieved from the medical records of patients who had already completed treatment or had some labeled outcome

The diagnosis of MDR-TB was done at RNTCP accredited Intermediate Reference laboratory using liquid culture, line probe assay or cartridge based nucleic acid amplification test (CBNAAT) according to the standard guidelines.⁵ Information on demographic and clinical profile of patients including smoking and alcohol abuse, co-morbidities (diabetes and HIV Status), history of previous anti-tuberculosis treatment (ATT), routing investigations done as a part of pre-treatment evaluation was extracted from the treatment card and patient's record available at the DRTB centre and office of State TB officer. Further details on the current course of Cat IV ATT particularly any interruption in the treatment, adverse drug reactions, time of culture conversion, final outcome, weight gain etc. were also retrieved.

Multidrug resistant TB is defined as tuberculosis resistant to both isoniazid and rifampicin, first line anti-TB drugs. Different outcomes to Cat IV treatment viz. cure, treatment default, treatment completed, death and treatment failure were defined as per RNTCP-PMDT guidelines.⁵

For analysis, successful outcome was represented by cure and completion of treatment. Adverse outcome in previous ATT regimens was labelled in the event of default or failure in any of the previous anti-TB therapy. A patient was said to adherent to treatment when he had taken $\geq 90\%$ of the total prescribed dose

Different treatment outcome was calculated as numbers and percentages. Further, different parameters mentioned above were compared among different outcome groups.

Statistical analysis

Quantitative variable was summarized as mean+ SD and qualitative variable as percentages. Analysis of variance (ANOVA) and Chi-square test were used to compare continuous and nominal variables respectively among patients of different outcome arms. p-value was considered significant at <0.05 .

RESULTS

Total 152 patients registered over a period of 3 years who had been declared with one of the treatment outcome. Out of these, 12 patients were transferred out during the course of treatment. Remaining 140 patients were taken for final analysis. Majority of the patients comprised of young age with low body mass index (BMI). Table 1 shows the demographic and clinical characteristics of the patient cohort.

Table 1: Demographic and clinical characteristics of patients.

Parameter	Value Mean \pm SD or n (%)
Age (years)	30.7 \pm 13.8
Male/female	80/60
Weight (kg)	42.3 \pm 10.4
BMI	16.5 \pm 3.8
Diabetes	11 (7.9%)
HIV positive	4 (2.7%)
Smokers	27 (19.3%)
Alcohol abuse	16 (11.4%)
Hemoglobin (gm/dl)	11.2 \pm 2.09

BMI: Body mass index

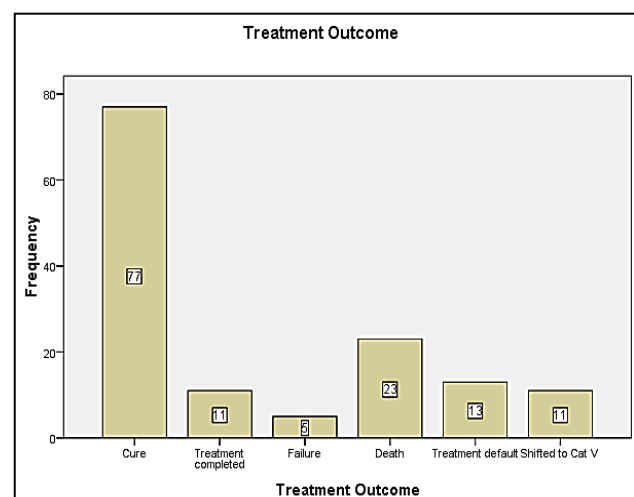


Figure 1: Distribution of patients in each of the treatment outcome arms.

Treatment outcome

Out of 140 patients, 88 (63%) had a successful outcome after complete course of ATT (cured or treatment

completed). Remaining 52 patients had an unsuccessful outcome (death, default, failure or switched to Cat V) (Table 2). The patients with successful outcome had a weight gain of 8.2 ± 6.11 kg which was significantly higher than those with unsuccessful outcome (p -value < 0.001). Figure 1 shows number of patients in each of the treatment outcome arms.

Table 2: Treatment outcome among MDR-TB patients.

Treatment outcome	Number of patients	% of patients
Cure	77	55
Treatment completed	11	7.8
Death	23	16.4
Treatment default	13	9.2
Treatment failure	5	3.5
Switched to Cat VATT	11	7.8
Total	140	

Ninety-eight patients (70%) showed sputum culture conversion at 3 months of ATT whereas 112 (81.4%) converted by 6 months. However, out of remaining 26 patients who remained positive, 14 patients died, 7 defaulted and 5 had treatment failure. Thirty-seven (26.4%) patients suffered from adverse drug reactions. Gastro-intestinal intolerance (vomiting and jaundice) (15), swelling and joint pain (12), neurological and psychiatric disturbances due to cycloserine (7) and loss of hearing (5) were the common side effects noted.

Different demographic, clinical and treatment related variables were compared among different treatment outcome groups. It was seen that baseline parameters like BMI and hemoglobin level and outcome in previous ATT were statistically different among different outcome groups. Among current treatment related variables, there was statistically significant difference in treatment adherence and time to sputum culture conversion among different treatment outcome groups (Table 3).

Table 3: Comparison of parameters among different treatment outcome groups.

Parameter	Cure/treatment completed (N=88)	Death (N=23)	Default N=13)	Failure (N=5)	Switched to Cat V (N=11)	P value
Age	30.3 ± 13.1	33.7 ± 17.9	33.4 ± 11.5	28.6 ± 21.2	25 ± 6	0.46
Males	52 (59)	8 (34.7)	11 (84.6)	3 (60)	6 (54.5)	0.06
BMI	17.1 ± 3.7	14.6 ± 4.1	17.1 ± 3.5	14.9 ± 3.6	15.4 ± 3.1	0.05
Diabetes	5 (5.6)	4 (17.3)	1 (7.7)	1 (20)	0	0.29
Smoker	17 (19.3)	5 (21.7)	2 (15.3)	1 (20)	2 (18.1)	0.9
Alcoholic	11 (12.5)	1 (4.3)	2 (15.3)	0 (0)	2 (18.1)	0.51
Hemoglobin	11.6 ± 1.9	9.32 ± 1.4	11.9 ± 2.56	10.0 ± 1.97	11.93 ± 1.55	< 0.001
No of previous ATT courses						
1	46	10	5	3	5	0.87
>1	36	12	6	2	5	
Outcome in previous ATT						
Adverse	51	20	9	4	10	0.01
Successful	31	2	2	1	0	
Sputum culture conversion						
At 3 months	75	9	3	4	7	0.02
>3 months	10	1	4	1	3	
Treatment adherence (%)	81 (92)	13 (56)	3 (23)	4 (80)	10 (90)	< 0.001

Quantitative data is indicated as mean+SD and qualitative data as n (%); ATT: anti-TB treatment; BMI: body mass index.

DISCUSSION

The present study was conducted to evaluate a 3-year retrospective data on the treatment outcome of MDR TB under programmatic conditions. The study showed convincing results with 63% success rate in treating MDR-TB. The results also indicated a significant difference in different clinical and treatment related parameters among different outcome groups.

Under DOTS-Plus program, patients received a standardized regimen comprising of six medicines for first 6-9 months of intensive phase and four drugs for 18 months of continuation phase. Our study achieved a treatment success rate of 63% which is consistent with recently published meta-analysis.⁶⁻⁸ On the other hand, 2 western Indian studies with similar design showed a lower success rate of 38-45%.^{3,4} Similar studies from other Asia countries have also shown variable success rates ranging from 37%-70%.^{9,10} Though the treatment

outcomes have improved over a period of time but they are far from the WHO targets of 75-90% success rate. This calls for need to review DOTS plus program and improve upon the factors that are predictors of poor outcome.

In spite of treatment, 16.4% of patients (n=23) in our cohort died during the course of treatment (Table 2). The figure is better than those quoted in the previous 2 Indian studies (19%³ and 30%⁴) but is higher than the results of recent 2 meta-analysis (11% and 12.6%).^{6,7} Seventy five percent of the deaths in our study occurred within 6 months of start of treatment. Possible reasons include bilateral extensive disease leading to respiratory failure, adverse drug reactions and super-added infections. Early detection of complications by the DOTS provider and timely referral to DRTB centre might help in decreasing mortality. Our study showed a treatment default rate of 9% which is significantly better than 21%⁴ and 23%³ as achieved in previous Indian studies. Treatment default rate is an important parameter to judge performance of the program as minimizing it not only improves treatment outcome but also prevents further spread of MDR-TB strain in the community. Patient education and treatment supervision are 2 important components of management that can help to deal with it.

Sputum culture conversion is an important indicator of treatment response that also determines the duration of intensive phase. Our patient cohort achieved a conversion rate of 81.4% which is comparable to different studies reported across globally.¹⁰⁻¹² Around 70% of patients in our study had a sputum culture conversion at 3 months. However, 22 patients (22%) out of them still had an unsuccessful end treatment outcome. This emphasizes the need for close monitoring, counselling and care by DOT care provider. Previous studies have shown baseline sputum smear positivity, baseline resistance to fluoroquinolones, previous treatment failure or default and low BMI as predictors of delayed culture conversion.^{13,14} However, these were not evaluated in our study.

The results in present study showed a statistically significant difference in BMI among different treatment outcome arms (P=0.05). On Post Hoc analysis the difference in BMI was significantly seen between cured patients versus those who died (mean difference 2.49 kg/m²; p = 0.007). Similar to our study, the association between poor outcome and BMI has also been mentioned in previous studies.^{7,15} Ironically, there are no comparative studies or guidelines on optimal nutritional intervention that could improve the outcome in MDR TB patients. Alcohol abuse has been associated with poor outcome including default and death in previous studies.^{16,17} However the significant difference in alcohol addiction among outcome groups was not seen in our study probably due to less number of patients with alcohol addiction. It is important to mention here that, in our study, patients who had adverse outcome in the

current Cat IV ATT course (death, default, failure) had a frequent history of adverse outcome (failure, default to treatment or shift to Cat IV) in previous anti-TB therapies. Interestingly diabetes has not been seen to impact second-line TB treatment outcomes, but increase the risk of adverse events to treatment.^{7,18} We also observed similar findings in the study.

Present study gave a ground scenario of the treatment outcome of MDR-TB patients treated under programmatic conditions in our geographical region. However, there were few limitations in our study. It was a single centre observational study in which the data was retrieved from the treatment cards and other records. Information on certain parameters like alcohol abuse, smoking, mild adverse drug reactions were missing for some patients thus undermining their statistical value. Follow up information on the transferred-out patients (n=12) was incomplete as a result they had to be excluded in statistical analysis.

CONCLUSION

Present study revealed that the treatment success rates in MDR-TB under programmatic management have shown improvement over the recent years but are still far from WHO targets. The results also suggest that interventions to improve patient nutrition as well as measures to ensure treatment adherence might help to improve the performance of the program and treatment success rates.

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Conflict of interest: None declared

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

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