

## Retraction

The article "Treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis drugs at tertiary care hospital a Himachal Pradesh, India" is retracted by the Editor-in-Chief, due to violation of the policies and practices of International Journal of Community Medicine and Public Health.<sup>1</sup> The article is retracted due to dispute in authorship.

## REFERENCES

1. Kumari A, Sharma PK, Bansal R. Treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis drugs at tertiary care hospital at Himachal Pradesh, India. *Int J Community Med Public Health* 2020;7:3119-22. DOI: <http://dx.doi.org/10.18203/2394-6040.ijcmph20203387>.

## Original Research Article

DOI: <http://dx.doi.org/10.18203/2394-6040.ijcmph20203387>

# Treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis drugs at tertiary care hospital at Himachal Pradesh, India

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Received: 22 May 2020

Accepted: 03 July 2020

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## ABSTRACT

**Background:** MDR-TB treatment defaulter are potentially harmful to community as these can relapse and spread infection, developed resistance to second line anti tubercular drugs and may result in to extensive drug resistant tuberculosis (XDR-TB) and major challenges for successful outcome. Objective was to study treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis drugs at tertiary care hospital at Himachal Pradesh.

**Methods:** It was prospective observational study carried out after approval from institutional ethics committee. A total 104 MDR/RR-TB case enrolled for study from November 2012 to October 2013. Data were collected in predesigned proforma and entered in to Microsoft excel worksheet 2007 and analyzed with the help of SPSS software version 17. Chi-square test was applied to find out the association between independent variable and outcome of MDR-TB and  $p < 0.05$  was considered statistically significant.

**Results:** Among all 104 patients initiated on treatment 73.07% patients were alive, completed intensive phase and switch to continuation phase of treatment, 14.42% patients were died, 5.76% defaulted, 0.96% patient was transferred out and 5.76% patients were turned out XDR-TB and switched to regimen of XDR-TB treatment.

**Conclusions:** Treatment and control of MDR-TB require sound infrastructure and well equipped laboratory facilities to provide quality and prompt diagnosis. Lack of knowledge, awareness, long duration of treatment and defaulters are major challenges for successful outcome.

**Keywords:** Second line antitubercular drugs, Treatment outcome, MDR-TB

## INTRODUCTION

Multidrug-resistant tuberculosis case is defined as a suspect who is sputum culture positive and whose TB is due to *Mycobacterium tuberculosis* that are resistant in-vitro to isoniazid and rifampicin with or without any other anti-tubercular drugs based on drug sensitivity testing (DST) results from Revised National TB Control Programme (RNTCP) accredited Culture and DST

laboratory.<sup>1</sup> As per RNTCP if patient is only rifampicin resistance should also managed as MDR-TB case.<sup>1</sup>

Drug resistant TB has been known from the time of anti-tuberculosis drugs were first introduced for treatment of tuberculosis.<sup>2</sup> 2016 globally as estimated 60000 new cases of multidrug and rifampicin resistant tuberculosis (MDR/RR-TB) emerged.<sup>3</sup> MDR/RR-TB cause 2400 death occur in 2016 and most of case and death occur in

Asia and about 6.2% MDR-TB case have additional drug resistance extensively drug resistant –TB (XDR-TB).<sup>3</sup> Drug resistance is entirely man made problem due to inadequate chemotherapy.<sup>4</sup> Treatment of MDR-TB required long duration and associated with adverse drug reactions and timely and intensive monitoring and management of adverse drug reactions are essential component of drug resistant tuberculosis controlled programme.<sup>2</sup> Poor management of adverse drug reactions increase risk of default, irregular adherence to treatment and may result in death and permanent morbidity.<sup>2</sup> Treatment and control of MDR-TB require sound infrastructure and well equipped laboratory facilities to provide quality and prompt diagnosis.<sup>5</sup> Major challenges for successful treatment outcome could be lack of knowledge, education and awareness among patients, long duration of treatment and defaulters. The disease is not only medical problem or public health problem but also social and economic problem. With this background, present study was conducted on treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis at tertiary care hospital.

## METHODS

The present study was conducted at DOTS-plus centre at Dr Rajendra Prasad Govt medical college, Tanda, Himachal Pradesh. It was prospective observational study carried out after approval from institutional ethics committee. A total 104 MDR/RR-TB case enrolled in to study from November 2012 to October 2013 under DOTS plus centre on second line anti-tubercular treatment involved six district of Himachal Pradesh who fulfill inclusion and exclusion criteria.

MDR/RR-TB register patients were given written informed consent were included in the study. MDR/RR-TB patients not given written informed consent were excluded from the study.

Patients were enrolled for study after given written informed consent and approval from institutional ethics committee. Pretreatment analysis were done for based line investigation as per PMDT guideline like blood sugar, liver function test, complete hemogram, serology testing for HIV infection, renal function test, thyroids function test and pure tone audiometry (PTA). After pretreatment analysis patients were started on second line antituberculosis drugs DOTS plus centre as per PMDT guideline. Outcome of patients of MDR-TB patients categorized in to cure, treatment completed, treatment failure, death, transfer out, defaulter, treatment stopped due to ADR or any other reason and switched to regimen XDR-TB as per programmatic management of drug resistant TB (PMDT) guideline 2012.<sup>1</sup> Follow up of patients were done at DOTS Plus centre till patients excluded from study. Follow up sputum smear and culture done at 3, 4, 5, and 6 months and reports were collected from DOTS Plus site at Dr. RPGMC, Tanda.

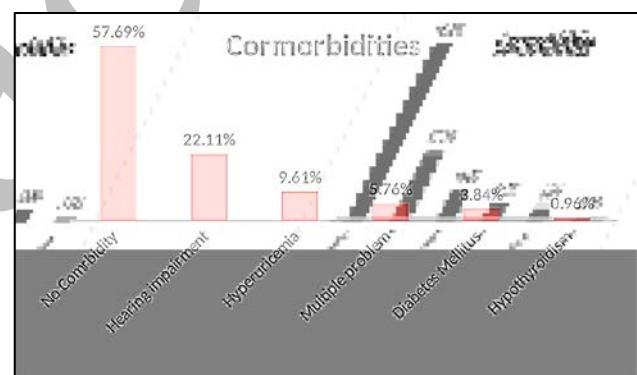
Data were collected in predesigned proforma for complete hemogram, blood sugar, liver function test, serology testing for HIV infection, renal function test, thyroids function test, ESR and pure tone audiometry (PTA), weight at before starting treatment and at the end of 6 month, comorbidity associated with MDR-TB patients, outcome of patients of MDR-TB patients in intensive phase, sputum smear and culture reports of 3,4,5,6 month.

## Data analysis

Data were entered in to Microsoft excel worksheet 2007 and analyzed with the help of SPSS software version 17. Chi-square test was applied to find out the association between independent variable and outcome of MDR-TB and  $p < 0.05$  was considered statistically significant.

## RESULTS

During pre-treatment analysis 90.38% were anemic and ESR was raised in almost all patients. Co-morbidities were observed during pretreatment analysis hearing impairment in 22.11% patients, hyperuricemia in 9.61%, multiple problems in 5.76% patients, diabetes mellitus 3.84% and hypothyroidism in 0.96% patient (Figure 1).



**Figure 1: Co-morbidities observed during pre-treatment analysis of MDR-TB patients.**

## Outcome of patients at end of intensive phase

Among all 104 patients initiated on treatment 73.07% patients were alive, completed intensive phase and switch to continuation phase of treatment, 14.42% patients were died, 5.76% defaulted, 0.96% patient was transferred out and 5.76% patients were turned out XDR-TB and switched to regimen of XDR-TB.

## Association between independent variable and outcome of MDR-TB

Attempt was made to find out the association between independent variable and outcome of MDR-TB. It was observed that variable like age, gender, comorbidity and weight may affect treatment outcome of patients.

**Table 1: Association between independent variable and outcome of MDR-TB.**

Independent variable	Outcome of MDR-TB		Chi Square Test
	Completed IP	Not completed IP	
Age	<40 45 (43.3%)	11 (10.6%)	$\chi^2$ 3.269
	>40 31 (29.8%)	17 (16.3%)	p (<0.05)*
Gender	Male 57 (54.8%)	22 (21.2%)	$\chi^2$ 0.143
	Female 19 (18.3%)	6 (5.8%)	p (0.705)
Co morbidity	Absent 47 (45.2%)	13 (12.5%)	$\chi^2$ 1.992
	Present 29 (27.9%)	15 (14.4%)	p (0.118)
Weight	<35 kg 13 (12.5%)	8 (7.7%)	$\chi^2$ 1.669
	>35 kg 63 (60.6%)	20 (19.2%)	p (0.001)*

IP- Intensive phase, p\* &lt;0.005%

**Table 2: Results of culture examination during follow up of MDR-TB patients.**

Culture result	Months of follow up			
	3	4	5	6
Positive	8 (7.96%)	7 (6.73%)	6 (5.76%)	6 (5.76%)
Negative	38 (36.53%)	33 (31.73%)	32 (30.76%)	41 (39.42%)
Leakage of sputum during transportation	6 (5.76%)	5 (4.80%)	1 (0.96%)	-
Not available	52 (50%)	59 (56.73%)	65 (62.5%)	57 (54.80%)
Total Patients (n)	104	104	104	104

n - Total No of MDR-TB patients, not available -patients had expired or defaulter, transfer out and could not evaluated due to technical and administrative reason.

Significant association was found between age, weight and outcome of MDR-TB (Table 1).

Bacteriological outcome of patients: 39.42% patients were sputum culture negative and 5.76% patients were sputum culture positive and 54.80% patients culture report were not available during follow up due to patients had expired or defaulter, transfer out and could not evaluated due to technical and administrative reason at the end of sixth month (Table 2).

## DISCUSSION

MDR-TB is major challenges for successful outcome. The disease is not only medical problem or public health problem but also social and economic problem. Treatment and control of MDR-TB require sound infrastructure and well equipped laboratory facilities to provide quality and prompt diagnosis.

Present study 14.42% patients were died compared to RNTCP annual status report 2014, as per 6 month interim report on MDR-TB 10% patients were died in India and 13% died in Himachal Pradesh.<sup>6</sup> Death rate of present study was more compared to RNTCP 6 month interim report 2014. Out of 14.42% patients 10.6% death occurred within 3 month of start of treatment; this could be because of advance disease and late presentation at time of diagnosis. In present study 5.76% patients defaulted, out of these 3.84% patients defaulted due to social reason and 1.9% patients left treatment because of the belief that it has side effects. The default rate in our study was less as compared to RNTCP 2014 in India; 6

month interim report on MDR-TB documents 10% default in India.<sup>6</sup> Another study conducted by Patel et al default rate 15.5% (high) compare to present study.<sup>7</sup> MDR-TB treatment defaulter are risk to community as these can relapse and spread infection, developed resistance to second line anti tubercular drugs and may result in to extensive drug resistant tuberculosis (XDR-TB)

39.42% patients were sputum culture negative and 5.76% patient's sputum culture positive and suspected as XDR TB and sputum was sent for second line drug sensitivity test. Patients were turned out XDR-TB and switched to regimen of XDR-TB. A Study conducted by Patel et al 43.4% patients were culture negative and 12.4% patients' remains smear and culture positive at six month which is more compare to present study it could be in present study 50.80% patients culture report were not available during follow up due to patients had expired or defaulter, transfer out and could not evaluated due to technical and administrative reason at end of six month (Table 2). Sputum smear and culture conversion from positive to negative is early interim indicator of efficacy of treatment and program effectiveness. From public point of view reducing the time of sputum conversion is an important measure of control infection.<sup>8,9</sup>

## Limitation

This was an observational study on patients treated under intensive phase of RNTCP-PMDT regimen; continuation phase was not included due to time constraint. Sputum smear and culture at 3rd, 4th, 5th and 6th month was not

done for all patients due to newer diagnostic methods like LPA and Gene Xpert MTB/Rif assay were adopted by RNTCP when the study was mid-way. This has affected the profile of outcome.

## CONCLUSION

MDR-TB is not only medical problem or public health problem but also social problem. This may lead to death, permanent morbidity, defaulter and irregular adherence. This can be prevented by early and rapid detection of case, used of combined effective treatment, early detection of ADR and their management and organization of training to health care professional, patients and family member.

## ACKNOWLEDGMENT

Author would like to thank State TB cell RNTCP HP for funding for study. Guide and co-guide for their support and guidance throughout study period.

*Funding: By State TB cell RNTCP Himachal Pradesh, India*

*Conflict of interest: None declared*

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

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**Cite this article as:** Kumari A, Sharma PK, Bansal R. Treatment outcome of multi-drug resistant tuberculosis patients on second line anti-tuberculosis drugs at tertiary care hospital at Himachal Pradesh, India. *Int J Community Med Public Health* 2020;7:3119-22.