### **Original Research Article**

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# Prevalence of multi-drug resistant tuberculosis and factors associated with treatment outcome in three districts of Himachal Pradesh, India

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#### **ABSTRACT**

**Background:** Tuberculosis (TB) is a leading cause of morbidity and mortality in the world and especially in India. MDR TB has emerged as a major challenge in TB control in India. The prevalence of MDR TB is on the rise in India. We did this study to see the prevalence of MDR TB in 3 districts of Himachal Pradesh and to study the factors affecting treatment outcomes.

**Methods:** The period of the study was from January 2019 to December 2019. We collected data of MDR TB patients from district TB offices of Solan, Bilaspur and Hamirpur. Information from patients was collected through questionnaires while interviews were conducted with district project officer and other health officials and documents, brochures, etc. were collected from Solan, Hamirpur and Bilaspur.

**Results:** Overall prevalence rate of MDR TB in our study was 3.14%. Among new TB cases, the prevalence rate of MDR TB was 2.42% (81/3345), and among old treated cases was 9% (37/411). 31% MDR TB patients were old treated while 69% patients had no previous treatment history. The default rate was low in our study (0.84%) while 8 (6.4%) patients had treatment interruption but for less than 15 days.

**Conclusions:** The prevalence in our study is comparable to the national drug resistance survey. Early detection, timely treatment and contact tracing is vital in decreasing the MDR TB cases. Better supervision, constant monitoring, proper counselling and timely identification and management of adverse effects of the drugs will improve the treatment outcome among MDR TB patients.

Keywords: Multidrug resistant TB, Himachal Pradesh, Prevalence

#### INTRODUCTION

Tuberculosis (TB) is known to mankind since its inception. TB is among the top 10 causes of death because of a single infectious agent all over the world in adults.<sup>1</sup> The infectious agent was discovered and described by the eminent German scientist Robert Koch on 24<sup>th</sup> March, 1882. World health organization (WHO) in the year 1993 took an unprecedented step and declared TB to be a global emergency.<sup>2</sup> One million children (0-14 years of age) fell ill with TB, and 230 000 children

(including children with HIV associated TB) died from the disease in 2017. According to TB India report 2018, in Himachal Pradesh there were 15715 notified patients of TB and 1400 deaths were reported in 2017.<sup>3</sup>

Multidrug-resistant TB (MDR-TB) is form of active TB when the causative bacteria is found resistant to first line anti TB drugs i.e., Rifampicin and Isoniazid. Multidrug-resistant TB (MDR-TB) is emerging as a big health hazard and major public health crisis in the recent years. As per WHO reports there were 6 lacs in 2016, 5.58 lacs

in 2017 and 4.84 lacs in 2018 new Rifampicin resistant TB cases which is the major first-line anti TB drug; out of this 78% to 82% patients had MDR TB all over the globe.<sup>1</sup>

TB is killing more people in India than any other infectious disease. In India, every day approximately 2 deaths every 5 minutes (600 per day) are occurring and more than 6000 are developing TB disease. India is among the highest burden countries of both TB and MDR TB. A national drug resistance survey (NDRS) was conducted in India from 2014 to 2016, which showed the real burden of DRTB cases. According to this survey, 2.84% patients were MDR TB cases among the newly diagnosed TB patients, and 11.62% were MDR TB patients from the previously treated TB cases. So overall, 6.19% patients from all the diagnosed TB patients were MDR TB cases.

As MDR TB is emerging as such a big challenge in our fight to eliminate TB from India, we decided to do this study to see the prevalence of MDT TB in our region and to study the different aspects associated with its treatment in districts of Solan, Hamirpur and Bilaspur of Himachal Pradesh.

#### **METHODS**

We did this study of one-year duration in three major districts of Himachal Pradesh; Solan, Hamirpur and Bilaspur. The period of the study was from January 2019 to December 2019. The main objectives were to find out the prevalence of MDR TB, to study outcomes of different treatment regimens and any factors associated with treatment outcome.

#### Sample size

The population used for the present study was all the TB cases diagnosed (n=3756) from January 2019 to December 2019 in Districts Solan, Hamirpur and Bilaspur of Himachal Pradesh. Out of 3756 TB patients, 118 were diagnosed as MDR TB cases. Therefore 118 MDR TB cases consisted of sample size. Inclusion criteria of the study consisted of the presence of resistance to both Rifampicin and Isoniazid in a patient's sample by molecular diagnostic method or by culture and DST. We excluded cases of extensively drug resistant (XDR) TB from our study.

The above data was collected from DTOs of the 3 districts. The primary data was collected through pilot survey, personal interviews, questionnaires filled up by 118 confirmed MDR TB patients of Solan, Hamirpur and Bilaspur districts and personal observations.

The documents confirming the MDR diagnosis, treatment regimens and treatment outcome of the patients were collected from the MDR TB registers and by interviews with the DTO/DPO/health officials of the respective

districts. The patient data was collected using a standard 2-part questionnaire that was filled by the patient. The questionnaire consisted of part A for collection of the demographic and socio-economic status of the MDR TB patients and part B for collection of information about the contributing factors to MDR TB and factors that may affect treatment outcome.

#### Treatment regimen

All the patients included in the study were started on standard shorter regimen (9-11 months) for MDR TB as prescribed under government of India's guidelines for programmatic management of drug resistant TB (PMDT 2019) in India.

#### Treatment outcome

The outcome of the treatment was assigned by the treatment supporter at the end of the MDR TB treatment as per the PMDT guidelines. Treatment completed is defined as a patient who has completed treatment according to guidelines but does not meet the definition for cure or treatment failure due to lack of microbiological results.

#### Statistical tools

The values are summarized using averages, percentages, frequencies.

#### **RESULTS**

Total TB cases registered during 2019 in Solan, Hamirpur and Bilaspur districts during the year 2019 were 3756 including pulmonary as well as extrapulmonary cases. Solan is leading with the total no. of 1947 TB patients with 743 extrapulmonary cases and 1204 cases of pulmonary TB. Bilaspur had a burden of 928 TB patients with 653 pulmonary and 275 extrapulmonary cases during year 2019. Hamirpur had 881 TB cases with 594 PTB and 287 EPTB cases (Table 1).

Table 1: Total TB case notification for year 2019 in Solan, Hamirpur and Bilaspur districts.

Name of district	Pulmonary TB patients	Extrapulmonary TB patients	Total TB patients
Solan	1204	743	1947
Hamirpur	594	287	881
Bilaspur	653	275	928
Total	2451	1305	3756

The study showed that a very few patients were under the age of 16 years and comprised merely 6% of the cohort. Most patients were from age group 26-35 years and above 56-year group with 27 (22.8.%) patients from each group. Among sex wise distribution, males were predominant

with 70.3% (83) and females were 29.7% (35) with male to female ratio of 2.3 (Table 2).

Table 2: Age and sex wise distribution of MDR TB cases.

Variables	Total patients, (n=118)	Percentage (%)
Age (Years)		
Less than 16	7	5.9
16-25	22	19.5
26-35	27	22.8
36-45	18	15.2
46-55	17	14.4
Above 55	27	22.8
Sex		
Male	83	70.3
Female	35	29.7

Total MDR TB cases in Solan, Bilaspur and Hamirpur districts from 1<sup>st</sup> January, 2019 to 31<sup>st</sup> December, 2019 were 118. Out of which 21 are still on treatment. The 86 patients have completed their treatment and 9 patients died during the treatment. One patient has defaulted treatment and one patient has been switched to XDR treatment. Death rate in our study was 5%, and default rate was 0.84% during the study period as shown in the Table 3.

Overall prevalence rate of MDR TB in our study was 3.14%. Among new TB cases, the prevalence rate of MDR TB was 2.42% (81/3345), and among old treated cases was 9% (37/411). 98.3% (116/118) of the MDR TB cases were pulmonary and 1.7% were extrapulmonary TB. So, the overall prevalence of MDR TB among pulmonary TB cases was 4.73% and among EPTB cases was 0.15% (Table 4).

Table 3: Status of treatment outcome of MDR TB cases in Solan, Hamirpur and Bilaspur.

Name of district	Total MDR patients	On treatment	Completed treatment	Died	Default	Switched to XDR
Solan	63	12	47	4	0	0
Hamirpur	33	5	26	1	0	1
Bilaspur	22	4	13	4	1	0
Total	118	21	86	9	1	1

<sup>\*</sup>Source: Data collected from DTO'S of Solan, Bilaspur and Hamirpur (HP).

Table 4: Prevalence of MDR TB among new and old treated TB cases.

Case definition	Prevalence of MDR TB	Percentage (%)
New	81/3345	2.42
Old treated	37/411	9
Total	118/3756	3.14
PTB	116/2451	4.73
EPTB	2/1305	0.15

Among the MDR TB patients 37 (31%) had previous history of anti TB treatment or treatment default, but a majority of MDR TB patients 81(69%) had no prior TB treatment history.

Our study showed that most of the patients were aware of the disease and were regularly taking treatment. The 110 (93.2%) patients were taking their medicine regularly whereas only 8 (6.8%) missed their treatment doses. Main reason given by them for irregular treatment was carelessness, depressive state of mind. Among other factors for missed doses were side effects of drugs, pill burden and long duration of the treatment. Most of the patients resumed their treatment within 15 days after the intervention of healthcare providers. Poor monetary condition is not one of the factors because the treatment is available free of cost in all the government hospitals. Once the treatment started all the patients were taking only allopathic treatment. None of the patient was taking

alternative form of medicine like ayurvedic or homeopathic treatment.

A number of patients had experienced side effects during the treatment. There were 54 (45.7%) patients who had one, two or more than two side effects. Most of the patients had experienced gastrointestinal side effects, loss of appetite and drowsiness. 32.1% of the patients had gastrointestinal symptoms, 7.4% of the patients reported having a ringing sensation in the ear, 1.2% reported deafness, 9.9% had skin problems and 7.4% had experienced many other kinds of side effects too. A very few patients 2 (1.6%) who had already completed their treatment complained of having persistent breathlessness and weakness even after completion of treatment.

#### **DISCUSSION**

Tuberculosis has been a part of human experience for a long time and now with the increasing trends of MDR TB, it is becoming even more difficult to treat. Factors that commonly play a role in spreading MDR TB are socio-demographic, socio-economic, health seeking behavior, exposure to TB patients, previous TB treatment and other comorbid conditions. The present study was undertaken to find prevalence and treatment outcome of MDR TB in three districts (Solan, Hamirpur and Bilaspur) of Himachal Pradesh. The study included all the diagnosed MDR TB patients among TB patients from 1st January 2019 to 31st December 2019.

The socio-demographic profile of our study population revealed that 57% MDR TB patients were between age group 16 years to 45 years. Similar pattern of age distribution was observed by Mehari et al in their study where approximately 64% MDR TB patients were between age of 15 to 44 years.<sup>5</sup> In our study we observed that out of 118 MDR TB patients during 2019, there were 35 females (29.7%) and 83 (70.3%) were male patients. Similar observation was made by Sinha et al in their study.<sup>6</sup>

Overall prevalence of MDR TB in our study was 118 in 3756 newly diagnosed TB cases, which is 3.64%. Among new TB cases, the prevalence rate of MDR TB was 2.42%, and among old treated cases was 9% in our study. According to Sharma et al, the prevalence of MDR TB among 177 cases of newly diagnosed pulmonary TB patients in New Delhi in 2008-2009 was lower at 1.1 percent. In a recent study by Lohiya et al the prevalence of MDR TB was 3.5%, among new and 26.7% among previously treated cases respectively which is higher than our study.

Previous TB treatment factor was significantly correlated with MDR TB. In this study, the patients who had previously completed treatment or received anti-TB drugs for more than or equivalent to one month, were classified as previously treated. In our research, we had 31% patients among MDR TB patients, who were previously treated for the TB. Exactly the similar conclusions were given by Rifat et al in their study, they found previous TB treatment as one of the most common independent risk factors in the community spread of MDR-TB.9 During their research, 29.3% of MDR TB patients had the history of previous TB treatment. Major factors of previous treatment default were relief from major symptoms (fever and weight loss), drug reactions or allergies to drugs. Stosic et al observed that most of the MDR-TB patients significantly reported previous TB treatment history (OR=2.65; 95% CI=1.14-6.16) and default from treatment (OR=3.84; 95% CI=1.41-11.11) than controls, which is quite similar to our observations.<sup>10</sup>

We observed in our research that primary MDR TB patients were more than the secondary MDR TB patients. There were 69% MDR TB patients out of total 118 patients who had no previous history of TB. These interpretations were same as made by Royce et al in their study where anti-TB drug resistance surveillance data from 30 countries estimated to have more than 700 notified multidrug-resistant TB (MDR-TB) cases.11 Out of this new TB patients comprised a median of 54% of the total MDR-TB cases. They observed that new MDR TB cases number was in increasing trends, which was clear signal of escalated community spread of MDR TB infection. Ershova et al observed in their research that out of 60 MDR-TB patients 44 patients were newly diagnosed patients with no previous history of taking anti-TB drugs, which was near about 73 percent of the cohort.<sup>12</sup> This is a clear-cut sign of escalating trends of primary acquired MDR-TB in the community, which is alarming for policy makers.

Only 1 patient in our study defaulted from the treatment and the main factors in that case were the constant side effects, depressive state of mind and the long duration of the treatment.

#### Limitations

There are a lot of variables that we could not include in our study like the information about the tobacco and alcohol abuse, ease of approach to healthcare facility, XDR TB cases and polydrug resistance cases which are also important in understanding the true extent of the drug resistance TB and associated factors. Further research is also required to see the factors associated with increasing primary drug resistance cases.

#### **CONCLUSION**

We found in our study that male sex, lower literacy level, larger family size, poor socio-economic status were the factors associated with prevalence of MDR TB. Surprisingly, most of our patients did not have any previous TB history. We found that the factors associated with poor treatment outcome are the persistent side effects, longer duration of treatment and large pill burden along with carelessness of the patients.

In conclusion, in this study the prevalence is comparable to the National drug resistance survey conducted in India during 2014-2016. Early detection, timely treatment and contact tracing is vital in decreasing the MDR TB cases. Better supervision, constant monitoring, proper counselling and timely identification and management of adverse effects of the drugs will improve the treatment outcome among MDR TB patients and will reduce noncompliance in patients.

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