

# Prevalance of MDR-Tuberculosis in A Tertiary Care Hospital in Haryana

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## ABSTRACT

**Introduction:** Drug resistant TB is on rise in world and India, and the most common risk factor for MDR TB is previous treatment history that is failure, relapse, default cases. This study was undertaken in our hospital to determine prevalence of MDR TB in retreatment cases.

**Material and Methods:** This prospective observational study was conducted in MMIMSR Haryana, which included 100 Category II pulmonary TB patients who satisfied the inclusion criteria. Sputum samples of these patients were tested for drug resistance using L.P.A. Results were analyzed and the prevalence of MDR calculated. Then MDR patients were compared with the Non MDR ones with reference to age, gender, habits, previous treatment history, clinical features, and drug susceptibility pattern.

**Results:** The prevalence of MDR in Cat II patients was found to be 20%, statistically significant association was seen between following failure cases and MDR TB, alcohol abuse and MDR TB, alcohol+smoking and MDR TB, Diabetes mellitus and MDR TB. Only a single case of Isoniazid mono resistance was found, no case of Rifampicin mono resistance was found.

**Conclusion:** The prevalence of MDR is high and fast increasing in retreatment cases and since these patients are at higher risk of morbidity, mortality and risk for infecting others with MDR strains, immediate measures for early diagnosis and proper treatment should be instituted and the patients should be counseled appropriately regarding compliance to treatment. We also stress on need of more studies which would establish risk factors of MDR TB in India.

**Keywords:** MDR-TB, Drug resistance, Drug susceptibility testing, MDR prevalence, line probe assay

parameters such age, gender, habits, previous treatment history, chest x ray findings and the drug resistance patterns. also in accordance with latest PMDT guidelines 2012 we are including sputum negative retreatment cases. Even though it is a hospital based study it is a step in direction of having more large scale studies including new molecular techniques, and that include even sputum negative retreatment cases as per new guidelines.<sup>4-6</sup> Aims and objectives of the study were to know the prevalence of MDR-TB in smear positive as well as smear negative retreatment cases, to study the pattern of drug resistant tuberculosis and to study clinical profile of these patients.

## MATERIAL AND METHODS

This study was conducted in MMIMSR Haryana, and included 100 Category II pulmonary TB patients who satisfied the inclusion and exclusion criteria. The project was approved by ethical committee MMIMSR Mullana ethical committee clearance number was – IEC/MMIMSR/16/178

### Inclusion criteria

1. All sputum positive failure, defaulter and relapse cases. i.e. all patients started on cat 2 ATT
2. All sputum negative cases which are put on retreatment with ATT based on radiological or clinical findings. i.e. All sputum negative patients put on cat 2 ATT

### Exclusion criteria

1. Presence of immunodeficiency conditions such as
  - a. HIV / AIDS.
  - b. Organ transplantation.
  - c. Malignancy
2. Extra-pulmonary TB and/or patients requiring surgical intervention.
3. Patients unwilling to take part in study.

The premise of study was that all patients on ATT retreatment i.e. Put on cat 2 ATT there sputum samples are to be sent to IRL Karnal for drug sensitivity testing to rule out MDR TB, since implementation of PMDT guidelines 2012 in Haryana makes it mandatory so 100 cat 2 patients were taken up for study who met inclusion criteria and taking into consideration exclusion criteria. These samples were sent to IRL Karnal in cold chain by RNTCP certified lab technicians at govt TB hospital Ambala,

## INTRODUCTION

Tuberculosis is one of the biggest killers among infectious diseases. Despite the emergence of anti tubercular drugs in 20<sup>th</sup> century, and emergence of live attenuated vaccine against tuberculosis.<sup>1</sup> In 2014, 9.6 million new cases of tuberculosis were reported worldwide, there were 1.5 million deaths reported because of tuberculosis. Nearly 43% cases were reported from India, China and Indonesia.<sup>2</sup> Multi drug resistance tuberculosis is an ever increasing menace MDR TB is defined as tuberculosis strain resistant to both Rifampicin and Isoniazid with or without resistance to other first line anti tuberculosis drugs that is Isoniazid, Rifampicin, Ethambutol, Pyrazinamide and streptomycin.<sup>3</sup> Globally according to WHO report there are 3.6% MDR TB in new cases and 20.2% in retreatment cases. According to this report there are about 450000 new cases of MDR TB worldwide. In 2008 rapid molecular test that is line probe assay was introduced on a global scale for detection of RR TB and MDR TB. This is the technology we are using in our study. In this study we attempt to find out the prevalence of MDR TB among the retreatment TB patients visiting our hospital and try to look at their clinical profile taking into account the various

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as our area falls under jurisdiction of district Ambala, so all samples were sent via district hospital Ambala samples were sent in cold chain to IRL Karnal which used L.P.A. method for drug sensitivity testing, prior to that patients clinical exam was thoroughly carried out with complete treatment history, personal history, past history. Patients were asked to follow up after they received Drug sensitivity reports, results of D.S.T. were analyzed and prevalence of MDR TB calculated, patients were then divided into two groups MDR group and Non MDR group and compared statistically with respect to following variables age, gender, habits (smoking, alcoholism), previous treatment history, clinical features, drug susceptibility pattern.

## STATISTICAL ANALYSIS

Chi-square test was used to find the significance of frequency distribution of study parameters between MDR and non MDR groups. Student t test was used to find the significance of mean values of study parameters between both the groups. Microsoft Excel and Word were used to prepare the tables and graphs.

## RESULTS

This study done was done in MMIMSR Hospital for a period of two years. It incorporated a sum of 100 (n=100) category II pulmonary TB patients. Sputum positive as well as negative. Patient populace was partitioned into two gatherings of MDR (n=20) and Non MDR (n=80) as indicated by the drug susceptibility results. After that the prevalence of MDR was determined which was 20% (n=20). These two gatherings were then examined to search for statistically significant association between groups.

### Gender

Out of 100 patients, 73 were male and 27 were female. Out of 20 MDR patients 13 (65%) were male and 7 (35%) were females. In Non MDR group of 80, 60 (75%) were male and 20 (25%) were females. Male: Female proportion in MDR group was 1.9:1

### Age

Total mean age in MDR group was 42.25±15.80. In Non MDR

group, over all mean age with S.D. was 43.93±16.21.

### Alcoholism Smoking and MDR TB (HABITS)

In habits statistically significant association was seen between alcohol abuse and MDR TB and smoking plus alcohol and MDR TB, however smoking and MDR TB did not show statistically significant association. P value for alcohol abuse = 0.021 and p value for smoking plus alcohol = 0.0051.

### Prior treatment history

In prior treatment history statistically significant association was seen between failure and MDR TB with p value = 0.009, failure was present 50% (n=10) in MDR group and 21% (n=17) in Non MDR group. Relapse was present 40% (n=8) in MDR group and 51% (n=41) in Non MDR group. Default was present 10% (n=2) in MDR group and 28% (n=22) in Non MDR group.

### Clinical features

Significant association was found between fever and MDR TB (p value -0.007), hemoptysis and MDR TB (p value-0.041), breathlessness MDR TB (p value 0.023).cough and expectoration was found in every patient in both groups where as fever was found in all patients in MDR group and 73% in Non MDR group.

### Diabetes mellitus and MDR TB

We observed significant association between diabetes mellitus and MDR group (p=.0017). In MDR group 45% (n=9) had diabetes mellitus where as in Non MDR group 14% (n=11) had diabetes mellitus.

Resistance pattern 20 patients out of 100 had resistance to Isoniazid and Rifampicin that is MDR TB and 2 patients had mono resistance to Isoniazid. None of the patients in our study showed mono resistance to Rifampicin.

## DISCUSSION

This study was undertaken to determine the prevalence of MDR TB patients visiting tertiary care hospital in Haryana and to study risk factors. The patients were analyzed on basis of their age, gender, clinical features, habits, treatment history,

Habits		MDR		Non MDR		$\chi^2$	P- Value
		n	%	n	%		
No Habit	Present	4	20%	43	54%		
	Absent	16	80%	37	46%		
Alcohol	Present	3	15%	2	3%	5.2632	.021781
	Absent	17	85%	78	97%		
Smoking	Present	8	40%	31	38%	0.0105	.918351
	Absent	12	60%	49	62%		
Smoking+Alcohol	Absent	5	25%	4	5%	7.8144	.005183
	Present	15	75%	76	95%		

Table-1: Habits and MDR TB

History of treatment		MDR		Non MDR		$\chi^2$	P- Value
		n	%	n	%		
Defaulters	Present	2	10%	22	28%	2.6864	.101208
	Absent	18	90%	58	72%		
Failures	Present	10	50%	17	21%	6.7098	.009588
	Absent	10	50%	63	79%		
Relapses	Present	8	40%	41	51%	0.8103	.368024
	Absent	12	60%	39	49%		

Table-2: History of treatment and MDR TB

	MDR		Non MDR		$\chi^2$	P - Value
	n	%	n	%		
Diabetes Mellitus						
Present	9	45%	11	14%	9.7656	.001778
Absent	11	55%	69	86%		
Total	20	100%	80	100%		

Table-3: Diabetes and MDR TB

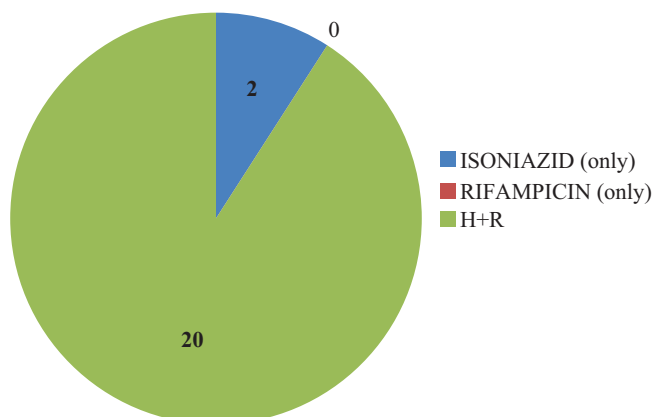


Figure-1: Drug susceptibility pattern

clinical signs and symptoms, drug susceptibility and chest x-ray findings.

#### Prevalence of MDR TB

Prevalence of MDR TB was found to be 20% which was comparable to studies done by Sharma et al<sup>7</sup> at Delhi and another study done by Jain et al<sup>8</sup> at Lucknow which showed prevalence around 20.4% and 19.8% in retreatment cases respectively. According to WHO report 2013 the incidence of MDR TB in new cases is 2.2% and in retreatment cases its 15% but there are some other studies like one done by Paramsivan et al<sup>9</sup> which was retrospective study of 2816 these patients were repeatedly treated and prevalence found was 53% so we can deduce safely from data above from all parts of India that MDR prevalence varies from place to place and study to study, hence a large nationwide study is the need of the hour.

#### Age

In a study conducted by Sharma et al<sup>7</sup> at Delhi the mean age of MDR TB patients was (33.25±12.04) (18-55) years in our study age was (42.25±15.80) (14-70) in MDR group. The mean age and maximum age in our study was found to be higher but the minimum age was lower than study by Sharma et al<sup>7</sup> similarly in another study by Dholakia et al<sup>10</sup> mean age was 31 (15-61) once again our study had higher mean age and maximum age though minimum age was lower than study by Dholakia et al<sup>10</sup>

#### Smoking and alcoholism

Smoking is a known risk factor for tuberculosis with studies showing two fold increase of risk of progression to active tuberculosis<sup>11</sup>, similarly alcohol consumption according to studies too increases the risk of development of tuberculosis up to three times with consumption of around 40 g or more alcohol per day.<sup>12</sup> In our study in MDR group 15% (n=3) had alcohol alone, 40% (n=8) were smokers and 25% were both alcoholic and smoker in MDR group and there was a statistically significant association between alcoholism and MDR TB. P value =0.02 and people who both smoked and had alcohol p value = 0.005, statically significant association between smoking alone and

MDR TB was not seen. Very few studies have been done on subject of MDR TB and alcoholism and MDR TB and smoking our study is a hospital based study with small sample size. So more national level studies are required on this subject. A few studies I would like to point out which show statically significant association between alcoholism and MDR TB are, a study by Garcia et al<sup>13</sup> in Madrid Spain titled "risk factors of Multi Drug Resistant Tuberculosis in a tuberculosis unit in Madrid Spain" showed statistically significant association between alcohol abuse and MDR TB. Similarly a study by Skraihna et al<sup>14</sup>, titled "Multi Drug Resistant Tuberculosis in Belarus: The size of problem and associated risk factors" showed statically significant association between alcohol abuse, and MDR TB, as well as smoking and MDR TB.

#### Previous treatment history

Prior treatment history, poor prescribing practices, poor adherence to drug regimen poor patient compliance all account for important risk factor for development of MDR TB. In our study in MDR group 10% (n=2) were defaulter, 50% (n=10) were failure cases, and 40% were relapses (n=8), In contrast the study done by Sharma et al<sup>7</sup> in Delhi showed 72.5% relapse, 20 percent defaulter, and 7.5 percent failure cases. In our study if we break up prior treatment history group into defaulter, failure, and relapse significant association was seen between failure and MDR TB with p value of 0.009, but our findings have to be interpreted in light of limitations firstly it is a hospital based study and there is a significant referral bias. But still since retreatment cases are so much more prone to develop MDR 20.4 percent in retreatment cases as compared to 3.6% in new cases. So adherence to DOTS and proper implementation of DOTS is of utmost importance

#### Diabetes Mellitus

Fisher Hoch et al<sup>15</sup> showed association of MDR TB and Diabetes Mellitus, according to their study 36.7% patients of MDR TB in Texas had Diabetes Mellitus. In our study 45% patients in MDR group had Diabetes Mellitus which is statistically significant with p value =0.001.

In another study by Gomez et al<sup>16</sup> titled "diabetes and other risk factors of multi drug resistant tuberculosis in Mexican population with pulmonary tuberculosis a case control study". They showed that there were 47.2% patient with MDR TB which was statically significant p value = 0.028. More nationwide studies on this topic would put more light, as our study has limitations.

#### Drug susceptibility pattern

In our study samples were sent to IRL KARNAL they used L.P.A. molecular assay so in our study resistance or sensitivity to only Isoniazid and Rifampicin was noted, and not other three first line drugs, by W.H.O. definition resistance to at least Isoniazid and Rifampicin with or without resistance to other drugs constitutes MDR TB. In our study 20% (n=20) were

MDR cases that is resistant to both drugs and there were two cases of mono resistance to Isoniazid alone (2%) and no case of mono resistance to Rifampicin were observed in our study. Now if compared to study done by Sharma et al<sup>7</sup> they used mycobacterial culture and drug susceptibility testing (DST) Isoniazid mono resistance was not noted, Rifampicin mono resistance was noted in 1.5% (n=3) cases, resistance to H+R+S was noted in 2.04% (n=4) cases and H+R resistance was noted in 18.4% cases (n=36). So in total 20.44% (n=40) cases were MDR cases which is very comparable to data we obtained by L.P.A., similarly Dholakia N et al<sup>10</sup> encountered 11% cases of mono resistance and 14% were MDR. Jain Aet al<sup>8</sup> found MDR prevalence to be 19.8%.

## CONCLUSION

The prevalence of MDR is high and fast increasing in pretreated cases and since these patients are at higher risk of morbidity, mortality and risk for infecting others with MDR strains, immediate measures for early diagnosis and proper treatment should be instituted and the patients should be counseled appropriately regarding compliance to treatment. We also stress on need of more studies which would establish risk factors of MDR TB in India.

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