



## PREVALENCE OF MULTIDRUG RESISTANT (MDR) TUBERCULOSIS IN MDR SUSPECT PATIENTS.

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### ABSTRACT

**Background:** Prevalence of multidrug-resistant tuberculosis (MDR-TB) is increasing all over the world. India has 2nd highest MDR-TB burden in the world after China. Most important risk factor is poor adherence to treatment. But in recent years chances of infection increases in newly diagnosed patients. We aimed to find prevalence of MDR TB in suspected patients.

**Methodology:** this retrospective study included 677 suspected patients from March 2016 to April 2017 from registered RNTCP patients. The samples of all suspected cases were processed for detection of rifampicin resistance by Cartridge based Nucleic Acid Amplification Testing (CBNAAT) technique. Data was tabulated and analyzed using spss 16.

**Results:** Out of total 677 suspected patients, 9 (1.33%), 444 (65.58%), and 224 (33.09%) were classified into Criteria A, B and C. 430 (63.52%) MDR suspect patients were detected to be having MTB. Out of total MDR TB patients, 39 (9.07%) were rifampicin resistant while remaining 391 (90.93%) were sensitive to rifampicin.

**Conclusion:** Multidrug resistant TB has been an area of growing concern and poses a threat to control of TB.

**KEYWORDS :** MDR-TB, CBNAAT, MDR suspect.

### INTRODUCTION

Multi Drug resistant-TB (MDR-TB) is defined as resistance to isoniazid and rifampicin with or without resistance to other drugs [1]. India is one of the countries with largest burden of MDR TB in the world. As per the WHO Global Report on Tuberculosis 2013, India accounts for 62,000 MDR TB cases out of 3,00,000 cases estimated globally [2]. Data from studies have found MDR- TB levels of 2.2% in new TB cases and 16% in re-treatment cases in the SEAR [3]. MDR-TB is a man-made phenomenon- poor treatment, poor drugs and poor adherence to therapy leads to the development of MDR TB [4]. Neivelle, et al. had described the emergence of drug-resistant TB as the third epidemic [5]

The World Health Organization (WHO) estimates that 3.9% of all new TB cases had MDR-TB or rifampicin-resistant TB (RR-TB) in 2015<sup>6</sup>; in comparison to 21% of TB patients with a history of prior treatment.

Various diagnostic methods are used to diagnose TB. Smear microscopy is one of the method to diagnose TB in limited resource area. Culture is the gold standard for final determination but it is largely inaccessible in resource limited setting. However in accessible setting, culture results are not available for 2-6 weeks. Gene Xpert® MTB/RIF, was recently endorsed by the World Health Organization (WHO), has the potential to lead a revolution in the diagnosis of active TB disease and multidrug-resistant (MDR) TB.

### METHODOLOGY:

This was a retrospective analysis of the RNTCP data maintained at a District TB hospital in the city of Chandrapur. We had included all suspected MDR- TB patients who were referred to the hospital between March 2016 to April 2017<sup>7</sup>.

The sputum samples of all suspected MDRTB cases were processed for detection of rifampicin resistance by Cartridge based Nucleic Acid Amplification Testing (CBNAAT) technique at RNTCP certified Culture and DST laboratory. Patients who were diagnosed to have MDR-TB were then started on Category-IV DOTS, which consists of Intensive Phase (Kanamycin, ethionamide, levofloxacin, cycloserine, pyrazinamide and ethambutol) for 6 months and Continuation Phase (levofloxacin, ethionamide, cycloserine and ethambutol) for 18 months as per RNTCP guidelines<sup>8</sup>.

Data was tabulated and analyzed by spss 16 version.

### RESULTS:

Table 1 shows that total 677 patients were suspected as MDR-TB during March 2016- April 2017. Patients were classified into 3 criteria<sup>9</sup> as per RNTCP strategy. Out of these, 9 (1.33%), 444 (65.58%), and 224 (33.09%) were classified into Criteria A, B and C. 3 (0.44%) were all

failures of new TB cases, 1 (0.15%) was Smear positive previously treated cases who remain positive at 4th month onwards and 5 (0.74%) were all pulmonary TB cases who are contacts of MDR-TB. Whereas, 126 (18.61%) were any smear positive follow up result in new or previously treated case and 318 (46.97%) were all smear positive previously treated pulmonary TB cases at Diagnosis. Similarly, 148 (21.86%), 48 (7.09%) and 28 (4.14%) were all smear negative previously treated pulmonary TB at diagnosis, HIV TB co-infected cases at diagnosis and Extra pulmonary cases (tissue sent for culture and sensitivity) respectively.

Table 2 depicts that 430 (63.52%) MDR suspect patients were detected to be having MTB whereas 247 (36.48%) were not having MTB. Out of total MTB detected patients, 253 (58.84%), 110 (25.58%) patients belong to criteria B (all smear positive previously treated pulmonary TB cases at Diagnosis, any smear positive follow up result in new or previously treated case) for MDR suspects suggesting higher prevalence in previously treated patients. This could be due to incomplete drug treatment previously, poor drug compliance etc.

Table 3 illustrates that out of total MDR TB patients, 39 (9.07%) were rifampicin resistant while remaining 391 (90.93%) were sensitive to rifampicin. Data shows that out of total rifampicin resistant strain, 24 (61.54%), 8 (20.51%) were belonged to criteria B (all smear positive previously treated pulmonary TB cases at Diagnosis, any smear positive follow up result in new or previously treated case respectively) indicating higher prevalence in previously treated patients. This could be due to default in treatment, failure cases etc. Similarly more cases was found in all pulmonary TB cases who are contacts of MDR-TB (2 (5.13%)).

### DISCUSSION:

Devesh Pratap Singh et al<sup>10</sup> in their study on Prevalence Of Multidrug Resistant (MDR) Tuberculosis. In MDR suspect Patients & Assessment of Various Reasons for Developing Drug Resistance shows that a total of 303 MDR suspect patients were identified between October 2010 to July 2012, however 89 patients were excluded from this study because of various reasons. Out of these 214 patients total 183 patients were belonging to CAT-II failure group, 27 patients were belonging to CAT-I failure group and 4 sputum smear positive pulmonary TB patients had prior history of contact with known MDR-TB cases. Overall prevalence of MDR-TB in MDR-suspect patients was found to be 61.68%.

Our study found that 430/677 (63.52%) subjects had MTB positive. Laura J. Martin et al<sup>11</sup> in their study on Rationing tests for drug-resistant tuberculosis – who are we prepared to miss? Shows that Overall, 147/1,545 (9.5 %) subjects had culture-positive TB, of which 32 (21.8 %) had DR-TB (MDR, 13.6 %; isoniazid mono-resistant, 7.5

%; rifampicin mono-resistant, 0.7%).

In our study, 39 (9.07%) patients had rifampicin resistance. Devesh Pratap Singh et al<sup>10</sup> in their study on Prevalence Of Multidrug Resistant (MDR) Tuberculosis In MDR Suspect Patients & Assessment Of Various Reasons For Developing Drug Resistance shows that Out of 183 CAT-II failure patients a total of 116 patients were found to be the cases of MDR-TB, out of 27 CAT-I failure patients a total of 12 patients were found to be the cases of MDRTB and out of 4 patients having history of contact with known MDR-TB patient, all of them were found to be the cases MDR-TB (table-1). Therefore, prevalence of MDR-TB in CAT-II failure patients, CAT-I failure patients and sputum smear positive patients having history of contact with known MDR-TB cases, came out to be 63.38% , 44.44% and 100% respectively Gneyya Bhatt et al<sup>12</sup> in their epidemiological study of multi drug resistant tuberculosis cases registered under RNTCP shows that 70% patients were resistant to all four drugs, 16.3% were to H, R and S, 6.5% were to H, R and E, 7.6% were to H and R. only 1 (1.2%) was found to be HIV positive.

Soma Chakraborty et al<sup>13</sup> in their study from May 2015 to January 2016 as a research project under Suraksha Genomics, found that out of the 331 clinical samples (both pulmonary and extra pulmonary), 51(15.4%) were positive for Mycobacterium tuberculosis and the prevalence of Rifampicin resistance to TB was 13.7% from all pulmonary samples and 8.69% from all extra-pulmonary samples.

Different studies from around India have reported a Rifampicin mono-resistance at around 9% [14] [15].

A study in 2011-2012 by Surajit Lahiri et al reported a Rifampicin mono-resistance of 4.69% [16] where as another study by M. Giridhar Kumar et al. shows 0% Rifampicin resistance among MTB positive cases in 2010-2012 mainly from South India<sup>[17]</sup>.

**CONCLUSION:**

Multidrug resistant TB has been an area of growing concern and poses a threat to control of TB. The MDR-TB is a human-made problem and its emergence can be prevented by prompt diagnosis and effective treatment of all TB cases. Sound infection control measures to avoid further transmission of MDR-TB and research towards the development of new diagnostics, drugs and vaccines should be promoted to control MDR-TB.

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Conflict of interest- None

**Table 1: Classification of MDR-TB suspects**

Criteria A	No. of suspects	%
<b>Criteria A</b>		
All failures of new TB cases	3	0.44
Smear +ve previously treated cases who remain +ve at 4th month onwards	1	0.15
All pulmonary TB cases who are contacts of MDR-TB	5	0.74
<b>Criteria B</b>		0.00
Any smear +ve FU result in new or previously treated case	126	18.61
All smear +ve previously treated pulmonary TB cases at Diagnosis	318	46.97
<b>Criteria C</b>		
All smear negative previously treated pulmonary TB at Diagnosis	148	21.86
HIV TB co-infected cases at diagnosis	48	7.09
Other Extra pulmonary cases (tissue sent for culture and sensitivity)	28	4.14
<b>Total</b>	<b>677</b>	<b>100</b>

**Table 2: Distribution of MDR suspect according to MTB detected or No**

MDR suspects	MTB detected	MTB Not detected
<b>Criteria A</b>		
All failures of new TB cases	2	1
Smear +ve previously treated cases who remain +ve at 4th month onwards	1	0
All pulmonary TB cases who are contacts of MDR-TB	5	0
<b>Criteria B</b>		
Any smear +ve FU result in new or previously treated case	110	16
All smear +ve previously treated pulmonary TB cases at diagnosis	253	65
<b>Criteria C</b>		
All smear negative previously treated pulmonary TB at Diagnosis	22	125
HIV TB co-infected cases at diagnosis	25	23
Other Extra pulmonary cases (tissue sent for culture and sensitivity)	12	16
<b>Total</b>	<b>430</b>	<b>247</b>

**Table 3: Prevalence of Rifampicin drug resistance**

MDR Suspect	RIF Resistant	RIF Sensitive
<b>Criteria A</b>		
All failures of new TB cases	0	2
Smear +ve previously treated cases who remain +ve at 4th month onwards	0	1
All pulmonary TB cases who are contacts of MDR-TB	2	3
<b>Criteria B</b>		
Any smear +ve FU result in new or previously treated case	8	102
All smear +ve previously treated pulmonary TB cases at Diagnosis	24	229
<b>Criteria C</b>		
All smear negative previously treated pulmonary TB at Diagnosis	3	19
HIV TB co-infected cases at diagnosis	1	24
Other Extra pulmonary cases (tissue sent for culture and sensitivity)	1	11
<b>Total</b>	<b>39</b>	<b>391</b>

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