

## DRUG SUSCEPTIBILITY PROFILE OF M.TUBERCULOSIS AMONG CATEGORY – II FAILURE PATIENTS UNDER RNTCP DRUG SUSCEPTIBILITY OF *M. TUBERCULOSIS*

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### ABSTRACT

**Introduction:** The aim of this study was to evaluate level of drug resistance in Directly Observed Treatment, short course (DOTS) CAT-II failure Pulmonary tuberculosis patients admitted for retreatment according to Indian Revised National Tuberculosis Control Programme (RNTCP).

**Methodology:** From January 2006 to December 2008 sputum samples were collected from all patients of DOTS CAT-II failure and transported to laboratory for *Mycobacterium tuberculosis* culture and drug susceptibility testing (DST). Category II failure pulmonary TB includes those patients who remained sputum positive after 5 months of CAT- II TB treatment. AFB culture was done on Lowan stein Jensen slopes (Solid culture), at Choithram hospital and research center which is RNTCP accredited laboratory.

**Results:** DST results were available for 148 sputum smear positive DOTS CAT-II failure patients. Mean age of the patients were 33.96 years (range 15-65 years), male to female ratio was 1.79:1. Of the 148 patients, 50(33.78%) had Multidrug-resistant tuberculosis (MDR-TB) and 11(7.43%) had extensively drug-resistant tuberculosis XDR-TB. Out of 148 patients, 80(54.05%) had treatment after default and 68(45.94%) had treatment failure. The prevalence of MDR-TB and XDR-TB among category-II failure pulmonary tuberculosis patients was 33.7 and 7.43 per cent.

**Conclusion:** The prevalence of MDR-TB strains was dramatically high among patients with pulmonary tuberculosis who failed category II therapy. Capacity of drug sensitivity testing is essential for continuous monitoring of drug resistance trends, in order to assess the efficacy of current programme and epidemiological surveillance for planning.

**Key words:** Pulmonary tuberculosis, Drug susceptibility testing, Central India

### INTRODUCTION

The Directly observed treatment, short course (DOTS) strategy is endorsed by the World Health

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Organization (WHO) as a current standard for tuberculosis treatment has been adopted for use by TB control programme in 148 countries.<sup>1</sup> The efficacy of DOTS in the treatment and control of TB is widely recognized.<sup>2-5</sup> However, treatment failures occur that are most often due to limited resources, inadequate re-treatment regimens and incomplete treatment and increasing the risk of multi-drug resistant tuberculosis (MDR-TB). Since 1998 there has been a rapid expansion of the DOTS – based Revised National Tuberculosis Control Programme (RNTCP) in India. With such a large DOTS based

programme in place, there is a need to assess the drug susceptibility profile among previously treated patients among programme condition. Drug resistance surveillance is considered useful tool to assess the effective functioning of tuberculosis (TB) control programmes.<sup>6</sup> Levels of drug resistance and its trends vary from place to place and serve as an epidemiological indicator to assess the extend of resistant bacterial transmission in the community.<sup>7</sup> Drug resistance levels among patients treated under TB control programmes are not available in many settings.

In poorer regions, DST is not routinely available. Empiric treatment regimens (ETRs) are generally customized to an individual's treatment and contact history but used in the absence of, or while awaiting, DST results.

We conducted this prospective analysis to evaluate level of drug resistance in DOTS CAT-II failure patients.

## METHODOLOGY

A total 148 randomly selected patients having clinical and or radiological features of tuberculosis attending out patients department of MGM Medical College & MY Hospital, Indore were enrolled in this study during January 2006 to December, 2008. Approval for the study was obtained from the institutional ethics committee. All patients gave informed consent to participate in the study.

MY Hospital, the tertiary referral hospital for Indore District covering about 5,000,000 population Choithram hospital was the only laboratory performing Mycobacterial cultures in that period.

Subjects attending to hospital with the history of received DOTS CAT- II and complaint of cough with expectoration were screened for sputum smear microscopy using the Ziehl- Neelsen method. All participants had active pulmonary TB disease, and had failed previous DOTS CAT-II treatment.

Sputum samples were collected from all patients of DOTS CAT-II failure. Patients were provided with

sterile bottles to collect sputum samples for culture and sensitivity test.

Sputum were collected and processed for culture by digestion, decontamination and concentration following modified Petroff's method and were inoculated on to two slopes of Lowenstein- Jensen (L-J) media for six weeks.

Sputum samples were process for culture of *M. tuberculosis* on Lowenstein - Jensen (LJ) slopes containing 0.5% pyruvate, glycerol and PNB (p-nitrobenzoic acid 500 mg/l) incubated at 37°C for upto 6 weeks at Choithram hospital and research center which is RNTCP accredited laboratory. Culture positive for *M. tuberculosis*, with more than 10 colonies grown after 6 weeks of incubation were subjected to sensitivity testing by the simplified proportion method for Isoniazid (H), Rifampicin (R), Pyrazinamide (PZA), Ethambutol (E), Streptomycin (S), Para amino salicylic acid (PAS), Ethionamide (Et), Ciprofloxacin (C), and Kanamycin (K).

Drug susceptibility testing for Pyrazinamide was performed after making media acidic. Data was handled and analyzed in MS Office, Excel.

### Inclusion criteria

DOTS CAT-II failure (Category II failure pulmonary TB includes those patients who remained sputum positive after 5 months of CAT - II TB treatment.)

### Exclusion criteria

The following patients were excluded from this study: (i) presence of secondary immunodeficiency states like HIV, organ transplantation, diabetes mellitus, malignancy, (ii) hepatitis B infection; (iii) seriously ill and moribund patients with very low lung reserve (iv) abnormal renal function.

Information on associated factors for Drug resistance, such as age, sex, history of alcoholism, smoking, occupation, family history of contact with PTB, personal history of contact with PTB and prior antitubercular treatment received (Table 1).

## RESULTS

**Table 1.** Showing associated factor for drug resistance (n=148)

Risk factor	No. of patients	Percentage
History of Smoking	15	10.13%
History of alcoholism	9	6.08%
Both smoking & alcoholism	40	27.02%
Family history of PTB	54	36.48%
History of contact with known PTB person	41	27.70%
Laborers	89	60.13%

A final total of 148 cases were included in the study, male 95 (64.18%) and female 53 (35.81%). Male to female ratio was 1.79:1. Mean age of the patients were 33.96 years (range 15-65 years).

Of 148 patients, 50 (33.78%) patients was resistant to at least Isoniazid and Rifampicin (MDR-TB) and 11 (7.43%) were resistant to Kanamycin and Ciprofloxacin along with Isoniazid and Rifampicin (XDR-TB).

The most common single drug resistance was of Isoniazid which was present in 11 (7.43%) patients followed by Streptomycin and Pyrazinamide. In 53 (35.81%) patients, resistance to more than 4 drugs were present (Table 2).

**Table 2.** Drug susceptibility profile among CAT-II failure patients (n=148)

Resistant to	No	Percentage
H	11	7.43%
R	3	2.02%
S	4	2.70%
Z	4	2.70%
SH	2	1.35%
SHE	1	0.67%
SHEZ	5	3.37%
RS	3	2.02%
RSE	1	0.67%
HR	50	33.78%
HRKC	11	7.43%
More than 4 Drugs	53	35.81%

When we analyzed associated factors in DOTS CAT-II failure patients, family history of contact with PTB was present in 54(36.48%), history of contact with PTB in 41(27.70%). Of the 148 patients, 64(43.24%) were addicted to either alcohol, smoking or both.

Out of 148 patients, 80 (54.05%) had treatment after default and 68 (45.94%) had treatment failure.

## DISCUSSION

The main finding of the above study among 148 patients of DOT CAT- II failure 50 (33.78%) patients were MDR, and 11 (7.43%) patients were XDR-TB. 22 (14.86%) were resistant to at least Isoniazid, Rifampicin, Pyrazinamide and Streptomycin and 53 (35.81%) were resistant to more than 4 drugs. Patients with resistant to first line drugs were 95 (64.18%). The prevalence of MDR-TB among patients of DOT CAT - II failure was dramatically higher overall than among the previously detected patients in the WHO (20% MDR-TB, 2% XDR-TB) study. The National Tuberculosis Institute (NTI) Bangalore, reported that 77% of 271 patients treated with Cat - I regimen and organism susceptible to SM, INH and Rifampicin and 2.2 % had HR resistance.<sup>8</sup> Among 226 patients treated with the Cat-II regimen, 59% had drug-susceptible organism, 27.4% had INH-resistant and 12.8% had HR-resistance.<sup>9</sup> Whereas study from South India reported resistant to both INH and RMP was 1.7% among newly diagnosed patient and 12% in previously treated patients. The remainder had single drug resistance.<sup>10</sup> Malhotra B, Gupta PR et al have reported higher prevalence of MDR-TB.<sup>11-12</sup>

A high prevalence of MDR – TB in CAT- II failure is not unique to India and has been documented in Vietnam<sup>13</sup>, Thailand<sup>14</sup>, Rwanda<sup>15</sup> in low to moderate risk groups.

Routine surveillance of drug resistant profiles found in specific populations of previously treated patients provides information that is useful for adapting strategies for effective treatment within National tuberculosis programmes (NTP's) and is

essential for the care of persons with chronic active tuberculosis disease.

In the present study there was a large proportion of MDR –TB patients. If this findings is correct, it would mean that a high degree of resistant strains is already circulating in the community. In recent years, the WHO launched DOTS Plus initiative to procure second-line drugs at a lower cost that will facilitate the treatment of the many patients who currently require it. Establishment of programmes for the treatment of MDR-TB patients, when back by secure source of funds and technical assistance could strengthen an NTP. Several studies have estimated the prevalence of patients with resistant bacilli in specific locations and in recent years the IUATLD and the WHO have conducted large surveys to ascertain the importance of resistant TB throughout the world, utilizing a systemic approach and common laboratory techniques.<sup>6-16</sup>

## CONCLUSION

The prevalence of MDR-TB strains was dramatically high among patients with pulmonary tuberculosis who failed category II therapy. Capacity of drug sensitivity testing is essential for continuous monitoring of drug resistance trends, in order to assess the efficacy of current programme and epidemiological surveillance for planning.

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