

Prevalence of multidrug resistance among retreatment pulmonary tuberculosis cases in a tertiary care hospital, Hyderabad, India

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ABSTRACT

Background: India is one of the high tuberculosis (TB) burden countries in the world. India ranks second in harboring multi drug resistant (MDR)-TB cases. About 50,000 of MDR cases are recorded in retreatment pulmonary TB cases. This study was conducted in a tertiary care facility (Government General and Chest Hospital) in Hyderabad, India. **Objectives:** To assess: Proportion of the TB patients having MDR-TB at the initiation of retreatment regimen; the prevalence of isoniazid (INH) resistance in this geographical area. **Materials and Methods:** An analytical, observational, prospective cohort study of patients attending the out-patient department from December 2010 to March 2011. **Results:** Sputum samples from 100 patients were subjected to acid fast bacilli (AFB) culture and drug sensitivity testing. Of these, 28 (28%) were MDR-TB, 42 (42%) were non-MDR-TB and 39% being INH resistance. **Conclusions:** In conclusion, one third of the retreatment pulmonary TB cases attending a tertiary care institute for TB will be MDR-TB at the initiation of treatment and there is a need to include ethambutol in the continuation phase of new TB case treatment in view of high INH resistance.

KEY WORDS: Category IV (category four), directly observed treatment, short-course plus (DOTS plus), India, multidrug resistant tuberculosis, retreatment cases.

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INTRODUCTION

India is one of the high tuberculosis (TB) burden countries in the world accounting for nearly 20% of the global incidence constituting 9.4 million TB cases.^[1] India ranks second in harboring multi drug resistant (MDR)-TB cases, i.e., about 99,000 cases. Among these, 50,000 cases are recorded in retreatment pulmonary TB cases.^[2]

To control the TB burden in the country, the Government of India started Revised National Tuberculosis Control Program (RNTCP) in 1997.^[3] The RNTCP is implementing directly observed treatment, short-course (DOTS) plus facility in the country, to control the MDR-TB burden, since October 2007.^[4]

The Government General and Chest Hospital (GG and CH) is a tertiary care institute, implementing the RNTCP for the management of drug sensitive and drug resistant TB.

There are anecdotal publications in the literature about the prevalence of MDR, among TB patients who are started on retreatment category. In this study, we assessed (a) Proportion of the patients harboring MDR-TB strains, who are considered for retreatment regimen. (b) The prevalence of isoniazid (INH) resistance in this geographical area.

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MATERIALS AND METHODS

Design

A prospective, analytical, observational, cohort study.

Study period

From December 2010 to March 2011.

Study setting and population

When our study was initiated, the DOTS plus programme considered a patient whose sputum Acid Fast Bacilli (AFB) smear was positive at the end of 4th month of the retreatment regimen as an MDR-TB suspect and eligible for culture and drug susceptibility testing (DST) [Table 1]. Patients, who were found to be resistant to Rifampicin (R) and INH or resistant to R, were initiated on category IV (category four).

In this study, all TB patients attending the out-patient department of the GG and CH, were registered and categorized, those who are fulfilling the criteria of relapse, treatment after default [Table 2] and who have taken the anti-TB treatment irregularly outside the RNTCP, were admitted.

Patients were instructed to collect two sputum samples in the falcon tubes, under the supervision of ward nurse or in-charge doctor. The collected samples are immediately transported to the state accredited intermediate reference laboratory (IRL), which was sharing a common wall with GG and CH. In this laboratory, the samples were subjected to the culture in Lowenstein Jensen media followed by the DST to the four first line anti-TB drugs, i.e., R, INH, ethambutol and streptomycin (SM). The information regarding those patients who are found to be resistant to the R and INH or only R was intimated at the earliest possible time either by telephonic or electronic message and they were initiated on DOTS plus category IV (category four) regimens after

pre-treatment evaluation as per the program guidelines.

Data collection and analysis

Data was entered in case records, culture forms and later into a pre-structured Microsoft Excel sheet. The data was analyzed using Epi-Info (version 6.0 CDC, Atlanta, USA).

Ethical approval

The study was approved by Institutional Ethical Committee of GG and CH. As this study was a prospective study, the individual written patient consent was taken. Electronic databases created for analysis were stripped off personal health identifiers and maintained securely.

RESULTS

Study population

A total of 100 patients samples were subjected to the culture and DST, of whom 69 were males. Of the 100 patients, 36 were relapse cases and 64 were defaulters, including patients with irregular treatment outside RNTCP.

Prevalence of drug resistance

Of the 100 patients, 16(16%) showed no growth, 3(3%) patient's samples was contaminated, which are recollected within 1 week of the result and 84(84%) were culture positive.

Nearly, 42(42%) were sensitive to all the four drugs. 28(28%) samples were declared as MDR positive. 14(14%) were declared as drug resistant TB other than MDR. The pattern of drug resistance is shown in Figure 1. About 39 (39%) cases were resistant to INH.

Among the samples showed drug resistance, nine patients were resistant to R, INH, SM and pyrazinamide (Z), seven

Table 1: Treatment categories and regimens for TB patients in India

Treatment category	Type of patients	Treatment regimens***	
		Intensive phase	Continuation phase
Category 1 (new case)	New sputum smear-positive PTB New sputum smear-negative PTB New EPTB	2 (H ₃ R ₃ Z ₃ E ₃)	4 (H ₃ R ₃)
Category 2 (retreatment)	Sputum smear-positive relapse Sputum smear-positive treatment failure Sputum smear-positive treatment after default	2 (H ₃ R ₃ Z ₃ E ₃ S ₃)+1 (H ₃ R ₃ Z ₃ E ₃)	5 (H ₃ R ₃ E ₃)
Category 4	All patients with diagnosed Multidrug resistant TB	6 (9) Km levo Eto Cs Z E	18 levoEto Cs E

PTB: Pulmonary tuberculosis, EPTB: Extra pulmonary tuberculosis, H: IsoniazidR: Rifampicin, Z: Pyrazinamide, E: Ethambutol, S: Streptomycin, Km: Kanamycin, Levo: Levofloxacin, Eto: Ethionamide, Cs: Cycloserine, TB: Tuberculosis. ***Prefix indicates month and subscript indicates thrice weekly

Table 2: World Health Organization recommended case definitions

Category	Definitions
Relapse	A patient previously treated for TB for whom treatment has been successful (i.e., who has been declared cured or who has completed treatment but does not meet the criteria to be classified as cured or as having treatment failure), and is diagnosed with bacteriologically positive (smear or culture) TB
Treatment after default	A patient who returns to treatment, positive bacteriologically. Following interruption of treatment for 2 months or more
Multidrug resistant TB	An MDR suspect whose sputum is positive for Mtb culture and resistant <i>in vitro</i> to at least Rifampicin and isoniazid, based on the results from an RNTCP certified culture and DST laboratory
Drug resistance other than MDR	A patient who has active TB with bacilli resistant to other than Rifampicin and isoniazid

TB: Tuberculosis, MDR: Multidrug resistant, RNTCP: Revised National Tuberculosis Control Program, DST: Drug susceptibility testing

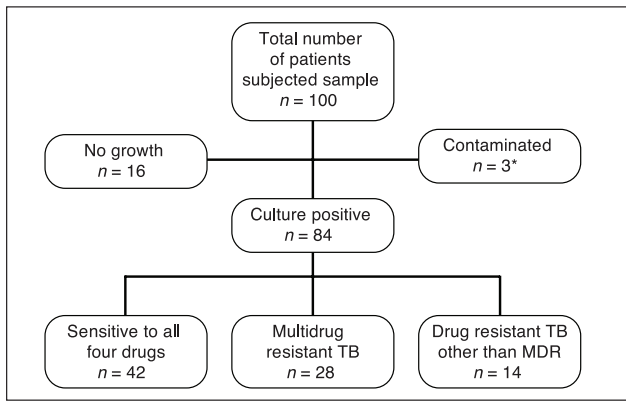


Figure 1: Prevalence drug resistance among retreatment pulmonary tuberculosis patients, in Government General and Chest Hospital, Hyderabad, India. *Contaminated samples are recollected within 1 week of the result

patients were R, INH and SM resistant, 12 patients were R and INH resistant, 1 patient was resistant to only SM, 2 patients were resistant to only R and 11 patients were resistant to INH only.

The individual resistance to various anti-tubercular drugs is depicted in Figure 2.

DISCUSSION

This study showed that every three patients among 10 retreatment cases are being declared as having MDR-TB bacilli, who need treatment with second line anti-TB drugs. According to the DOTS plus guidelines during the study period, these patients are delayed for 4 months in the initiation of the category IV (category four). As there is a chance of positive case to infect 10 or more persons in a year,^[5] this study can indicate that this delay of 4 months for a patient, might infect 3 or more persons with MDR bacilli in this delayed period.

This study also revealed that INH resistance is seen in 39% cases in this geographical area. According to Burugina Nagaraja *et al.*,^[6] treatment outcomes of patients who fail a first-line anti-TB therapy and who are not placed on an MDR-TB regimen are unacceptably poor.^[6] Hence, there is a need to start MDR-TB regimen in cases of drug resistant TB other than MDR.

Hence, our study suggests following recommendations to the RNTCP:

- First, subjecting every retreatment category patient to sputum AFB culture and DST at the initiation of the treatment, which will have a good impact on controlling the TB burden and preventing the MDR-TB in the community.
- Second, as there was high prevalence of INH resistance, the program should give a serious thought to include ethambutol in the continuation phase of the treatment regimen of the new cases.

The strengths of this study are proper selection of the cases,

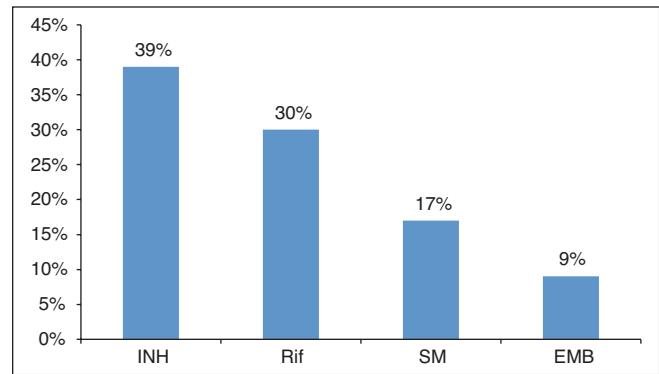


Figure 2: Individual drug resistance patterns includes individual and combined resistance in retreatment pulmonary tuberculosis patients

proper collection and immediate transport of sputum samples to the RNTCP accredited IRL.

The limitation of our study includes the inability to report the treatment outcomes of these patients, because of the long duration of the treatment.

In conclusion, one-third of the retreatment pulmonary TB cases in a tertiary care institute will be MDR-TB at the initiation of the treatment and there is a need to include ethambutol in the continuation phase of the new TB case treatment in view of high prevalence INH resistance.

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