

## DRUG RESISTANT TUBERCULOSIS: EXTENT OF PROBLEM AND TREATMENT RESULTS FROM A DISTRICT IN KERALA

Sebastian N M<sup>1,\*</sup>, Sheela P Haveri<sup>2</sup>, Sameera K K<sup>3</sup>, Jacob John<sup>4</sup>, Jesha M M<sup>5</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Professor, <sup>3</sup>Junior Resident, <sup>5</sup>Assistant Professor,  
Dept. of Community Medicine, MES Medical College, Perinthalmanna, Kerala

<sup>4</sup>Senior DRTB/TB HIV coordinator, District TB Centre, Manjeri, Kerala

**\*Corresponding Author:**

E-mail: nmsebastian@gmail.com

### ABSTRACT:

**Background:** MDRTB is a Public Health Problem in India also. DOTS plus is implemented in India to address this problem. This study attempts to reveal the extent of MDRTB problem and treatment results in a District in Kerala namely Malappuram.

**Methodology:** This study is a cross sectional study conducted by collecting and analyzing secondary data from RNTCP registers and reports from 2008 to 2013 available in District TB Centre.

**Objectives:** To study the proportion of MDRTB, outcome of its treatment, the pattern of drug resistance and the prevalence of diabetes among the cases in the District of Malappuram, Kerala.

**Results and Discussion:** Out of 13029 TB cases registered for treatment in the study period, 1099 (8.4%) turned out as MDRTB suspects. Among these suspects 79 were identified as MDRTB. Among these 72 were put on CAT IV treatment. Cases for which treatment results were available shows a cure rate of 46.5%, default rate of 16.3%, failure rate of 9.3% and death rate of 27.9%. Among MDRTB cases 44% were diabetics. HIV is positive for only 2.5 %.

**Conclusions:** Prevalence of MDRTB is low in the District. Cure rate is less than half and Death rate is currently high among MDRTB cases in the District. There is also high prevalence of diabetes among MDRTB cases.

**Keywords:** MDRTB, Drug Resistance, MDRTB Suspects, RNTCP, Cure Rate, Death Rate.

### INTRODUCTION

Resistance of Mycobacterium Tuberculosis to the first line drugs has become a major Public Health problem in many countries including India. Drug Resistance Surveillance Studies conducted under Revised National Tuberculosis Control Programme (RNTCP) in India shows that drug resistance is relatively low in most regions of India<sup>1</sup>. Tuberculosis Research Centre (TRC), Chennai and National Tuberculosis Institute (NTI) Bangalore, conducted studies and found MDR-TB levels are less than 1% to 3% among new TB cases and around 12% in re-treatment cases. A similar trend of low emergence of resistance is expected across the country as high cure rates are observed in DOTs Programme. Even with low rates, the total number of cases in India is high because of the large population and high incidence of TB cases.

There is an increase in number of drug resistant Tuberculosis including Multi drug resistant TB in India, which are difficult to treat and contribute to increasing mortality. In many developing countries particularly those in Asia, acquired drug resistance remains high. Human immunodeficiency virus (HIV) associated TB is a major global public health challenge in both diagnosis and treatment<sup>2</sup>. Drug resistance is suspected based on history of prior treatment. Drug resistance develops either due to infection with a resistant strain or as a result of inadequate treatment. In 2012, there were an estimated 371 million

cases of Diabetes mellitus globally<sup>3</sup>. There is a clear association between Diabetes Mellitus and Tuberculosis. Diabetes with its increasing prevalence in India and especially in Kerala poses another threat to TB control. Studies from Kerala a state in India has reported the dual burden of TB and Diabetes<sup>4</sup>.

State specific data on drug resistance is not available at present because of lack of quality assured culture and District level laboratory facilities<sup>1</sup>. RNTCP in India is incorporating identification and treatment of MDR cases. The present study is conducted in the District of Malappuram, Kerala where the CAT IV and CAT V regimes are included in RNTCP for management of MDR tuberculosis cases under DOTs plus. The results obtained can be valuable for implementation of DOTs plus in the District.

### OBJECTIVES

1. To study the proportion of MDR tuberculosis among all TB cases in the District of Malappuram, Kerala.
2. To study the outcome of treatment in these MDRTB cases.
3. To study the pattern of drug resistance and the proportion of MDRTB cases with diabetes.

### MATERIALS AND METHODS

The study is conducted collecting secondary data from registers and records maintained in the District TB Centre under RNTCP. Malappuram

district has 8 TB treatment units, and detect and treat on an average to 2500 cases of TB patients via RNTCP annually.

The District TB Centre implemented diagnosis of MDR TB cases by sputum solid culture and sensitivity testing till December 2011 and from January 2012, Line probe assay is being used. For this sputum samples are sent to intermediate laboratory attached to the state TB Centre in Trivandrum. The introduction of line probe assay reduced the time taken for results to 2 weeks from almost 4 months with solid culture. From January 2012 onwards criteria C is followed for selecting MDRTB suspects, where all retreatment cases, all follow up sputum positives, contacts of MDR cases and HIV positives with cough are identified as MDR suspects. Sputum samples are collected from these MDRTB suspects and sent to the Intermediate Referral Laboratory, Trivandrum. Those who are diagnosed to be MDR are put under CAT IV regime as DOTs. For this study, the Personal data on MDR suspects, such as age gender, and Previous treatment History, history of diabetes, culture results, details of CAT IV treatment and its outcome on all MDR cases diagnosed from 3<sup>rd</sup> quarter 2008 till 3<sup>rd</sup> quarter 2013 were collected from records and entered on a structured format. The data was entered in Epi-info programme and analysed. The proportion of MDR suspects, Proportion of MDR cases, Pattern of drug resistance, status of HIV positivity and diabetes, duration between receipt of results and initiation of treatment and outcome of treatment are analysed.

**Study Population:** All Tuberculosis patients registered and treated under RNTCP in District of Malappuram for the period of study

**Inclusion criteria:** All TB patients registered under RNTCP whose data is available

**Exclusion criteria:** Any case whose data is incomplete are excluded

**Study Period:** From July 2008 to December 2013

**Study Design:** Cross sectional study using secondary data

**Study setting:** District TB Centre, Manjeri, Kerala

**Sample Size:** All cases whose data is complete for the study period are included

**RESULTS**

During the study period 13029 cases of tuberculosis were registered and treated in the district. Of these 1099 cases (8.4%) were identified as MDR-suspects as per criteria laid down by RNTCP. Among those identified sputum samples were collected from 984 cases (89.5%) and sent to the state laboratory (IRL) for culture and sensitivity. This is 7.5 % of all TB cases for the period. Among those samples tested at IRL, 79 cases turned out to be

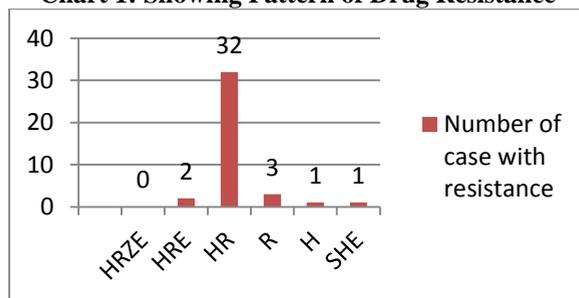
MDR-TB which is 8% of MDR suspects and 0.6% of all TB cases.

Among these MDR-TB cases 72 patients were started on CAT IV regime under DOTs. 7 patients died while awaiting results (10%). 29 cases are still under treatment when study was completed, 22 in continuation phase and 7 in intensive phase. Of the 43 cases whose results are available, 20 are cured (46.5%). 12 patients died while on treatment (27.9%), 7 patients defaulted (16.3%) and 4 patients were to be switched over to CAT V as failures of treatment (9.3%). Among those treated for MDR-TB, 32 cases were diabetic (44%). The drug resistance pattern shows that 82.1% are resistant to INH and Rifampicin, 7.7% are Rifampicin mono-resistant which are also treated like MDR as per RNTCP guidelines.

**Table.1. Shows Number and percentage of MDRTB suspects and cases.**

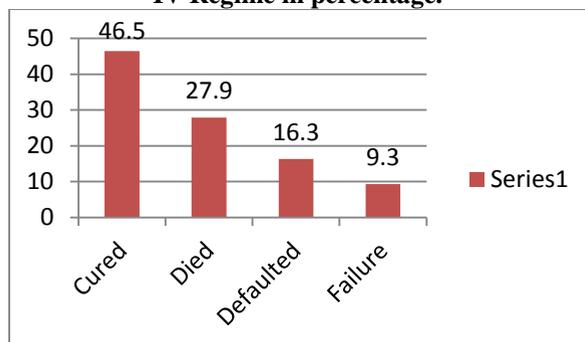
	Number	Percentage
1 Total Number of TB cases	13029	
2 MDR-TB suspects	1099	8.43
4 MDR-TB	79	0.61
5 Put on CAT IV treatment	72	0.55
6 Died while awaiting result	7	0.05
7 Diabetes among MDR cases	32	44

**Chart 1: Showing Pattern of Drug Resistance**



H= Isoniasid, R = Rifampicin, E= Ethambutol, Z= Pyrazinamide, S= Streptomycin

**Chart 2: Showing result of treatment with CAT IV Regime in percentage.**



## DISCUSSION

Global project on tuberculosis Drug Resistance surveillance by W H O/ International Union on Tuberculosis and Lung Diseases have shown the MDRTB prevalence in North Arcot, Wardha and Raichur districts in India ranging from 0.5 to 2.8%. The prevalence of 0.6% in our study is within this range towards the lower side. This finding also is similar to the observation of TRC Chennai and NTI Bangalore. WHO Global Tuberculosis Report 2014 gives a prevalence of 2.2% among new cases and 15% among retreatment cases.<sup>5</sup> A study from a tertiary care hospital in Hyderabad reports as high as one third of drug resistant case among specialty clinic patients in the hospital<sup>6</sup>. May be due to the fact that patients who are not cured by the first line drugs are attending specialty clinics.

The districts DOTs plus gives currently a cure rate of 46.5%, death rate of 27.9%, default rate 16.3% and failure rate 9.3%. The high death rate (27.9%) and low cure rate can be attributed to the fact that until recently treatment with CAT IV regime was not available to the common patient or if it was available diagnosis and initiation of treatment was unduly delayed. The cost of treatment was also high. These are likely to change with the introduction of new diagnostic tests and the new criteria for identifying MDRTB suspects under DOTs plus Programme. The high prevalence of diabetes is another observation which needs interventions for simultaneous control of diabetes among TB patients. 82% of Drug resistant cases were resistant to both INH and Rifampicin.

## CONCLUSIONS

The percentage of MDR cases among all cases is low in the District (0.6%) with available data till end of study period. The percentage of MDR-TB suspects among all TB cases in the study district is 8.4%. At present, less than half of the MDRTB cases treated are cured and there is high death rate among MDR cases treated.

## LIMITATIONS

The study is done with the limited number of 79 MDR patients available till December 2013 and is likely to affect the precision of proportions. The data is obtained from first 4.5 years from start of DOTs plus in the District. With increasing availability of diagnosis and early treatment initiation, better results may be reached in later years.

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