Original Research Article

Clinico-Epidemiological Profile and Treatment Outcome of Multi-Drug Resistant Tuberculosis Patients of a South Indian District: An Observational Study

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Abstract

Background: Multi Drug Resistant Tuberculosis (MDR-TB) is a major public health problem that threatens progress made in TB treatment and control. India is the largest share of the global MDR TB burden (27%). Among 30 high burden countries India accounts for 26% of the global TB incidence. The Global Stop TB Strategy outlines and defines the Programmatic Management of Drug Resistant TB (PMDT). Prompt identification of presumptive MDR-TB patients, diagnosis and initiation of treatment is crucial to prevent the transmission of MDR-TB and reduce high morbidity and mortality.

Aim: The study aims to assess the clinico-epidemiological profile and treatment outcome of MDR TB patients in Madurai district, South India.

Methods: 67 microbiologically confirmed multidrug resistant tuberculosis patients diagnosed between July 2020 and March 2021 were enrolled. Clinical and demographic data of all eligible patients was collected. Patients were evaluated with physical examination, CXR, sputum AFB, CBNAAT, LPA and treated and followed up as per PMDT guidelines. Data was entered in Microsoft Excel and analysed using SPSS version 21.

Results: The study consisted of 43 (64.2%) males and 24 (35.8%) females. The mean age was 46 years. But most were 51-70 years 29 (43.3%) followed by 31-50 years 27 (40.3%) and 15-30 years 11 (16.4%). Of the 67 patients, 35 (52.2%) were previously treated, 32 (47.8%) were newly diagnosed patients, 36 (53.7%) were non diabetics and 31 (46.3%) were diabetics. HIV positivity rate was 3 (4.5%). Of all the patients, 22 (42.8%) and 18 (26.9%) were found to be smokers and alcoholics respectively. Treatment outcome is better in 31-50 years age group, males, non-smokers, non-alcoholics, non-diabetics, non-HIV patients and newly diagnosed pulmonary MDR TB patients.

Conclusion: Decentralized management of DR-TB under NTEP PMDT guidelines ensures early diagnosis, prompt treatment initiation, counselling to patients and family members, follow-up monitoring of nutrition, adherence and adverse events which predisposes to effective management of DR-TB patients.

Keywords: Tuberculosis, MDR-TB, Drug Resistant TB.

Introduction

Drug Resistant Tuberculosis (DR-TB) refers to TB patient's biological specimen being resistant to any anti-TB treatment drugs during in-vitro testing. Multidrug-resistant Tuberculosis (MDR-TB) is defined as TB patient's biological specimen being resistant to both Isoniazid and Rifampicin with or without resistance to other first line anti-TB drugs [1]. MDR-TB patients may have additional resistance to any other anti-TB drugs or Fluoroquinolones. Common causes for drug resistance are genetic mutation of Mycobacterium bacilli, inadequate doses, close contact with MDR-TB patients, poor treatment regimen and poor TB diagnostic and treatment services [1-7].

MDR-TB is a major public health problem that threatens the progress made in TB treatment and control. India has the largest share of the global MDR-TB burden (27%). Among 30 high burden countries, India accounts for 26% of the global TB incidence [2]. The Global Stop TB Strategy outlines and defines the Programmatic Management of Drug Resistant TB (PMDT). Prompt identification of presumptive MDR-TB patients, diagnosis and initiation of treatment is crucial to prevent the transmission of MDR-TB and reduce morbidity and mortality [1].

In India, MDR-TB patients are estimated to be 124000 (9.1/lakh population). As per the recent anti-Tuberculosis drug resistance survey (NDRS) 28% of TB patients were resistant to any anti-TB drugs (22% among new and 36.82% among previously treated TB patients) and 6.19% had MDR-TB (2.84% among new and 11.62% in previously treated TB patients) [2]. In India PMDT services were launched in 2007 for early diagnosis and management of Drug resistant TB. PMDT services expanded in terms of Diagnostic network of Culture & Drug Sensitivity Testing (C&DST), Cartridge based Nucleic Acid Amplification Test (CBNAAT), TrueNAT and Line Probe Assay (LPA) laboratories, availability of newer anti-TB drugs (Bedaquiline, Delamanid) and decentralised DR-TB treatment services [1,7].

Aims and Objectives

1. To assess the clinical and epidemiological profile of MDR-TB patients in Madurai district, South India.

2. To study the association between clinical and epidemiological variables and also the treatment outcomes of MDR-TB patients in Madurai district, South India.

Materials and Methods

This study was an observational study performed in Drug Resistant Tuberculosis Treatment (DR-TB) centre at a tertiary care teaching hospital in Madurai over a period of 2 years (July 2020 to June 2022). Biological samples were collected from all the presumptive DR-TB patients and tested for Rifampicin & Isoniazid resistance with CBNAAT and LPA molecular testing methods. Those patients who have tested positive for both Rifampicin & Isoniazid resistance (MDR-TB) were included in the study. Those patients who had either Rifampicin or Isoniazid resistance, resistance

to any other drug and drug sensitive TB patients were excluded. MDR-TB patients were either started on shorter MDR-TB regimen or longer oral MDR-TB regimen as per the diagnostic and treatment algorithm of PMDT. Clinical, demographic and microbiological data were collected from 67 microbiologically confirmed MDR-TB patients and initiated on MDR-TB treatment regimen. Data entry was done in Microsoft Excel and analyzed using SPSS version 21.0.

Results

The study consisted of 43 male (64.2%) and 24 female (35.8%) MDR-TB patients. The mean age was 46 years; most patients being in the age group of 51-70 years (29 patients-43.3%). The second highest was in the age group of 31-50 years (27 patients, 40.3%) followed by 15-30 years (11 patients, 16.4%). In our study, many patients hailed from rural area (33 patients, 49.3%), followed by urban area (18 patients-26.9%).

Table 1: Geographical data

		No (%) (n=67)
Age Group	15-30 Years	11 (16.4)
	31-50 Years	27 (40.6)
	51-70 Years	29 (43.3)
Sex	Male	43 (64.2)
	Female	24 (35.8)
Residence	Rural	33 (49.3)
	Urban slum	16 (23.9)
	Urban	18 (26.9)

Out of the 67 patients in our study, 65 patients had Pulmonary MDR-TB and 2 patients had Extra-Pulmonary MDR-TB. 32 patients (47.8%) newly detected with MDR-TB and they never had a history of TB infection or treatment in the past, 35 patients (52.2%) had a previous history of TB treatment completed, cured or lost to follow up as per the NTEP Definitions[1]. Based on the PMDT regimen, 20 patients (29.9%) were initiated on shorter MDR-TB regimen and 47 patients (70.1%) on longer MDR-TB regimen.

While assessing co-morbid conditions of MDR-TB patients, 36 (53.7%) were non diabetics and 31 (46.3%) were diabetics; 3 (4.5%) patients were HIV positive undergoing ART treatment. Of all the patients, 22 (42.8%) and 18 (26.9%) were found to be smokers and alcoholics respectively.

Table 2: Co-morbid conditions

		No (%) (n=67)
Smoking status	Non-smoker	45 (67.2)
	Smoker	22 (32.8)
Alcoholic status	Non-alcoholic	49 (73.1)
	Alcoholic	18 (26.9)
Diabetic status	Non-diabetic	36 (53.7)
	Diabetic	31 (46.3)
HIV status	Non-HIV	64 (95.5)
	HIV-positive	3 (4.5)

In our study group 36 patients (53.8%) had favourable outcomes and 18 patients (26.9%) had unfavourable outcomes and 13 patients (19.4%) are yet to be designated an outcome. Time to sputum smear/culture conversion was 3 months or less for 57.1% of the patients.

Table 3: Outcome of MDR-TB treatment

	No (%) (n=67)
Completed	4 (6)
Cured	32 (47.8)
Died	12 (17.9)
Lost to Follow-up	6 (9)
On Treatment	13 (19.4)

Treatment outcomes were better in 31-50 years age group, males, non-smokers, non-alcoholics, non-diabetics, non-HIV patients and newly diagnosed pulmonary MDR TB patients. Significant p-value was seen with non alcoholic, newly diagnosed and pulmonary MDR TB patients resulting in favourable treatment outcome.

Table 4: Factors with favourable treatment outcomes

	No (%) (N=36)	p-value
Age 31-50 years	15 (46.9)	0.524
Male sex	20 (62.5)	0.841
Lower socioeconomic class	17 (53.1)	0.976
Non-smoker	20 (62.5)	0.940
Non-alcoholic	23 (71.9)	0.429
Non-diabetic	19 (59.4)	0.029
Non-HIV	30 (93.8)	0.785
Pulmonary TB	31 (96.9)	0.012
Newly diagnosed patient	20 (62.5)	0.041

Discussion

All the TB patients should be screened for DR-TB. Early detection of TB and DR-TB is possible with the recent availability of newer rapid molecular testing methods (CBNAAT, True NAT, LPA) [3]. Our study had a predominantly male population (64), which correlates with study done by Smitha shivekar *et al*, Pushpinder verma *et al* and Chaudhary A *et al* [8-10]. In this study the MDR-TB is common among the age group >50 years which correlates with the study done by Pushpinder verma *et al* [9]. Our study had many MDR-TB patients from rural areas as malnutrition is a major concern in these areas along with poor control of co-morbid diseases [4,5]. In our study, majority of MDR-TB patients had pulmonary disease as MDR-TB was less common in Extra Pulmonary sites. In this study many MDR-TB patients from non-alcoholic, non-smoker and non-diabetic groups. Since it's a study with a smaller population the results of these associated co-morbidities cannot be extrapolated to the general population [5].

In this study MDR-TB in HIV seropositive patients is (3) 4.5%, which correlates with Indian studies done by Smitha shivekar *et al* [9]. While considering significant factors with unfavourable outcomes, 8 diabetics and 5 alcoholic patients died in the course of the study. In this study, 66.66 % patients had a

favourable outcome which is closely similar to other Indian studies done by Kiran B *et al* and Kumari SL *et al* [6,7]. Patients in the middle-aged male group with Pulmonary MDR-TB without any substance abuse or any co-morbid diseases had better treatment outcomes.

Strengths of the study: This is the first study to analyse the association of various clinical and demographic variables with treatment outcome of MDR-TB patients in a South Indian District after introduction of newer drugs in MDR-TB regimens. Our study highlights one of the major modifiable risk factors in unfavourable treatment outcomes – Diabetes Mellitus and 2 non-modifiable factors in favourable treatment outcomes – newly diagnosed and pulmonary MDR-TB.

Limitations of the study: Since it is a single centre study with smaller study population, the results cannot be extrapolated to the general population. The study population was not grouped and analysed as per the different available MDR-TB treatment regimen i.e., injectable and oral Bedaquiline containing regimen. Adverse drug reactions were not analysed as it is an important factor affecting treatment compliance and outcomes of MDR-TB treatment.

Conclusion

Comprehensive interventions should focus on the management of the existing co-morbidities. The most commonly reported co-morbidities in our study were smoking, alcohol abuse and diabetes. Strengthening of mechanisms like newer drugs and shorter regimen have contributed to the enormous treatment success rates. Improvement in patient centric care, early diagnosis, elimination of the prevailing discrimination and stigma and, protection of the confidentiality and dignity of the patient are important goals for effective execution of PMDT guidelines[1]. Regular follow-up every 6 months till 2 years of all successfully treated TB patients is also recommended.

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