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ORIGINAL ARTICLE

Management of multidrug resistant tuberculosis (MDR-TB) – Monitoring is the key to successful outcome

J.S. Akshata *, **Anushree Chakrabarthy**

Dept. of Pulmonary Medicine, SDS TB Research Centre and RGICD, Bangalore, India

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KEYWORDS

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Abstract *Context:* Treatment of multidrug resistant tuberculosis (MDR-TB) is challenging. In India, standard treatment regimen is established by Revised National Tuberculosis Control Programme (RNTCP). Adequate follow-up of patients during the treatment period is a challenging task under programmatic conditions. We did a retrospective analysis of patients enrolled and treated under the national programme to study the outcome.

Aims: To study the treatment outcome of MDR-TB and the factors affecting it.

Settings and design: Retrospective analysis of 69 patients treated with standard regimen for MDR-TB, as per RNTCP guidelines.

Methods and material: Retrospective analysis of 69 MDR-TB patients for the clinical and demographic profile. Treatment outcome is defined as cure rate, default rate, death rate and failure. The factors affecting this outcome are also studied.

Results: Sputum culture conversion rate was 33.9% and 62.5% at 3rd and 6th month of treatment respectively. Cure rate was 47.8%, death rate 27.5%, default rate 14.5% and failure 7.3%.

Conclusions: The major hindrance in achieving a good cure-rate was a high death rate and default. Early diagnosis of MDR-TB and adequate clinical monitoring during treatment is essential. Identifying adverse drug reactions, other co morbidities and their optimal management is the key to success.

Introduction

Multi drug resistant tuberculosis (defined as resistance to at least Rifampicin and Isoniazid) is a worldwide public health problem. As per recent global tuberculosis report of WHO, 5% of TB cases are estimated to have MDR-TB globally. 3.5% incidence of MDR-TB is reported among new cases. The proportion is higher among previously treated cases, about 20.5%. As per the data provided by national TB programs in 2013, an estimated 300,000 cases of MDR-TB are present. More than half of these cases were in India, China and the Russian federation [1].

* Corresponding author. Tel.: +91 9535971057.
E-mail address: drjsakshata@gmail.com (J.S. Akshata).
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WHO issued a guideline for the management of drug resistant TB in 1996. Programmised management for drug resistant tuberculosis (PMDT) services in India was initiated from August 2007. A standard category IV regimen for MDR-TB treatment has been approved in India. It is implemented under Revised National Tuberculosis Control Programme (RNTCP)-National DOTS plus committee [2]. Globally, only 48% of MDR-TB cases detected in 2011 were successfully treated. 16% died, 24% did not have their treatment documented or treatment interrupted and 12% were not cured despite proper treatment [1]. So, any effort made to determine the treatment outcome helps us to evaluate the programme, its efficacy and identifying the constraints.

Materials and methods

A retrospective cohort study of MDR-TB cases enrolled for treatment in 2011–2012 was done at SDSTRC and Rajiv Gandhi Institute of Chest Diseases (RGICD), a tertiary chest institute in Bangalore, India. Data were obtained from case sheets, registers and treatment cards of patients from August 2011 to August 2014.

Study population – All MDR-TB cases confirmed by RNTCP accredited laboratory and initiated with therapy from August 2011 to June 2012 as per PMDT guidelines. Patients belonged to various districts of Karnataka state.

All patients were hospitalised for pre-treatment investigations and treatment initiation. Patients were started on standardised Cat-IV regimen which includes Kanamycin, Levofloxacin, Ethionamide, Pyrazinamide, Ethambutol, Cycloseriene for 6–9 months and Levofloxacin, Ethionamide, Ethambutol and Cycloseriene for 18 months. PAS was used as a substitute drug in the case of major adverse effect or initial resistance to any of the second line drugs. Patients were monitored for tolerance and adverse drug reactions. After 10–30 days of hospitalisation, patients continued community based treatment at peripheral centres. Follow up sputum smears and culture were done as per guidelines. For follow up examination the sputum specimens were collected and examined by smear and culture at least 30 days apart from the 3rd to 7th month of treatment (i.e. at the end of the months 3, 4, 5, 6 and 7) and at 3-monthly intervals from the 9th month onward till the completion of treatment (i.e. at the end of the months 9, 12, 15, 18, 21 and 24). Patients will be considered culture converted after having two consecutive negative cultures taken at least one month apart. Time to culture conversion is calculated as the interval between the date of MDR-TB treatment initiation and the date of the first of these two negative consecutive cultures. Patients were referred to RGICD for management of any adverse drug reactions and for declaration of treatment outcome. Data were compiled and analysed for various demographic, clinico-radiological profile and treatment outcome.

Outcome definitions:

- *Cure*: A patient who has completed treatment and has been consistently culture negative (with at least 5 consecutive negative results in the last 12–15 months). If one follow-up positive culture is reported during the last three quarters, patient will still be considered cured provided this positive culture is followed by at least 3 consecutive negative cultures, taken at least 30 days apart, provided that there is clinical evidence of improvement.
- *Treatment completed*: A patient who has completed treatment according to guidelines but does not meet the definition for cure or treatment failure due to lack of bacteriological results.
- *Treatment failure*: Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12–15 months are positive, or if any of the final three cultures are positive.
- *Death*: A patient who dies for any reason during the course of MDR-TB treatment.
- *Treatment default*: A patient whose treatment was interrupted for two or more consecutive months for any reasons.
- *Transfer out*: A patient who has been transferred to another reporting unit (DR-TB Centre in this case) and for whom the treatment outcome is not known. Till the time the PMDT services are available across the country, the MDR-TB patients can be transferred out only to those districts, within or outside the state, where these services are available. If a patient moves from one district to another, both of which are covered by the same DR-TB Centre, transfer out will not be required.

Results

The study included 69 proved MDR-TB patients enrolled for treatment. Demographic, clinico-radiological and resistance profile of patients are described in Table 1.

Of the 69 patients 46 were male (66.7%) and 23 were females (33.3%). Mean age of the patients was 35.8 years (11–65 years) and mean body weight was 46.5 kg (19–72 kgs). Both urban and rural populations were affected almost equally. 12 patients (17.4%) were alcoholic. 55 patients were

Table 1 Demographic and clinical profile.

Patient characteristics			
Age, yrs	< 30	30	43.50%
	30–50	30	43.50%
	> 50	9	13.00%
Sex	Male	46	66.67%
	Female	23	33.33%
Body weight (kg)	< 30	2	2.90%
	> 30	67	97.10%
Residence	Urban	39	56.52%
	Rural	30	43.48%
Alcoholic		12	17.39%
Diabetes mellitus		8	11.59%
HIV positive		3	4.40%
Sputum bacterial load	3+	19	27.54%
	2+	13	18.84%
	1+	37	53.62%
Disease extent (chest X-ray)	Minimal	19	27.54%
	Extensive	16	72.46%
	B/L	44	63.77%
	Cavitary	34	49.28%
Resistance pattern	RH only	13	18.84%
	RHE	11	15.94%
	RHS	20	28.98%
	HRES	25	36.23%
Previous treatment	Cat I failure	14	20.29%
	Cat II failure	55	79.71%