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Research Article

A study on outcome of standardized treatment in multi-drug resistance tuberculosis patients

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ABSTRACT

Background: Programmatic management of Multi-drug resistance Tuberculosis (MDR-TB) using a standardized treatment regimen (STR) is being implemented under the Revised National Tuberculosis Control Programme (RNTCP) in India. Our study was undertaken to analyze the outcomes of MDR-TB patients treated at the Drug resistance centre (also known as Dots Plus Centre, DR-TB) Bellary, with the RNTCP recommended 24-27months STR, under programmatic conditions.
Methods: Patients confirmed to have MDR-TB by Line Probe Assay (LPA) method, from Intermediate reference laboratory (IRL) Bangalore, were treated with the RNTCP's STR in a prospective field trial on a predominantly ambulatory basis. Forty three patients were enrolled to the trial from December 2012 to April 2013.
Results: At the end of treatment, 19 (44.2%) were cured, 12 defaulted, 9 died, 1 failure and 2 were under XDR TB evaluation. Thirty two (74.2%) patients reported adverse drug reactions (ADRs) which required dose reduction or termination of the offending drug. No patient had XDR-TB initially, but 3 cases emerged for XDR-TB evaluation during treatment. Before start of treatment mean body mass index (BMI) was 17.67±3.627 kg/mt^2. 34 patients had far advanced lesions on chest x-ray. Outcome was better in those patients, whose tubercular bacilli resistant both to rifampicin and isoniazid and who had good adherence in the past tubercular treatment.
Conclusions: Outcomes of this small group of MDR-TB patients treated with the RNTCP's STR is encouraging in this setting. Close attention needs to be paid to ensure adherence, and to the timely recognition and treatment of ADRs.

Keywords: Multi-drug resistance tuberculosis, Line Probe Assay method, RNTCP

INTRODUCTION

After successfully establishing the DOTS services across the country in 2006, RNTCP introduced the "Programmatic Management of Drug Resistant TB" (PMDT) (erstwhile Dots Plus) services since 2007 to address the needs of this group of patients and is now rapidly scaling up services across the country while also expanding services towards universal access.[1]

The emergence of resistance to drugs used to treat tuberculosis (TB), and particularly multidrug-resistant TB (MDR-TB), has become a significant public health problem in a number of countries and an obstacle to effective TB control.

The term PMDT, refers to programme based MDR-TB diagnosis, management and treatment. These guidelines promote full integration of basic TB control and PMDT activities under the RNTCP, so that patients with TB are evaluated for drug-resistance and placed on the

appropriate treatment regimen and properly managed from the outset of treatment, or as early as possible.[1] These guidelines also integrate the identification and treatment of more severe forms of drug resistance, such as extensively drug resistant TB (XDR-TB).[1]

Confirmed MDR-TB case is defined as, A TB patient whose sputum is culture positive for Mycobacterium tuberculosis and is resistant in-vitro to isoniazid and rifampicin or rifampicin only, with or without other anti-tubercular drugs based on DST results from an RNTCP-certified Culture & DST Laboratory.[1,2]

Globally, 3.5% of new and 20.5% of previously treated TB cases was estimated to have had MDR-TB in 2013. This translates into an estimated 480 000 people having developed MDR-TB in 2013.[3]

Knowledge of the feasibility and effectiveness of a standardized treatment regimen (STR) given on an ambulatory basis for MDR-TB is very limited in India. [4] It is more than 7 years since the pilot project was launched in India. Moreover, there are reports of threats of extensively resistant TB. Thus the present study was undertaken to assess the treatment outcome in real life situations.

METHODS

This prospective, observational study was approved by the Institutional Ethics Committee of TB Hospital. Prior permission to conduct the study was obtained from the Head of TB and Chest disease department as well as District tuberculosis officer.

All Patients confirmed to have MDR-TB by Line Probe Assay (LPA) method, from Intermediate reference laboratory (IRL) Bangalore were included from January 2013 to July 2013. A total of 43 patients were enrolled in the study.

The baseline data of the patients were recorded in pretested case record form. Patients enrolled in the study were treated with daily supervised regimen. Following initial hospitalization for 1-2 weeks, ambulatory treatment was arranged at the nearest peripheral health centre according to the patient's residential address. The medicines were delivered to the patients by a DOT provider at the health centre. The standardized regimen consisted of an intensive phase (IP) of 6-9 months with six drugs, namely kanamycin (Km), levofloxacin (Lvx), ethionamide (Eto), pyrazinamide (Z), ethambutol (E), and cycloserine (Cs) given daily. This was followed by a continuation phase (CP) of 18 months of four drugs, such as Lvx, Eto, E and Cs. Pyridoxine was administered to all patients as a supplement.

Each patient was followed up every month for clinical assessment (body weight), sputum examination, and ADRs till completion of IP 6 months. Sputum cultures were done at the end of 3, 4, 5, 6, 7 months and once in every 3month in the continuation phase at IRL Bangalore. Chest X-ray was done at the end of intensive phase (6 months) and at the end of the study. For the first 6 months, haematological and biochemical tests (liver and renal function tests) were done every month and thereafter as and when required.

Treatment outcome was categorized as cured, defaulted, failure and death as per the RNTCP guidelines. A patient was declared cured after complete treatment for at least 24 months with last three cultures negative. However, patient having one or more of last three cultures positive was considered as failure. While completed treatment patients did not meet the criteria for cure or failure due to lack of bacteriological results. A patient who interrupted treatment for two or more consecutive months was labelled as default. And patients who did not respond to MDR TB treatment were considered for XDR TB evaluation.

Chest radiographs were obtained for every patient and classified according to the National Tuberculosis Association of USA (1961): (1) Minimal – Non-cavitatory lesions involving one or both lungs but the volume of involvement regardless of distribution less than or equal to one zone. (2) Moderately advanced – more advanced lesions than minimal but the total involvement not more than the volume of one lung. Cavities, if present, not to exceed a total diameter (of all cavities) of 4 cm. (3) Far advanced – any lesion more advanced than moderate.[5] The data was recorded in Microsoft Excel Worksheet and analysed by chi square and with the help of SPSS version 16.0 and Epi info software. $P < 0.05$ was considered statistically significant.

RESULTS

Table 1: Evolution and status of standardized treatment for MDR TB patients.

Status at end of Intensive Phase (6 months) n= 43	n (%)
Culture Positive	2(4.65)
Culture Negative	20(45.51)
Culture contamination/unavailable	8(18.6)
Died	6(13.95)
Default	7(16.28)
Status at end of Intensive Phase (12 months) n= 43	
Culture Positive	3(6.98)
Culture Negative	15(34.9)
Culture contamination/unavailable	4(9.3)
Died	9(20.9)
Default	11(25.6)
XDR TB evaluation	1(2.32)

Forty three patients were put on Cat IV regimen after MDR TB diagnosis. Mean age was 36.21±11.89 years (range: 20 to 71). Twenty-nine (67.4%) were male and 14 (32.6%) were female. Mean body mass index (BMI) was 17.67 ± 3.63 (range: 12 to 29.5). None of the patient was immune-compromised with HIV and not any female was pregnant before or after initiation of therapy. 67.4% of patients were employed during the survey. All patients had received ATT before enrolling into the study.

Table 2: Socio-demographic variables influencing MDR TB outcome.

Variables (n)	Cured (%)	Others (%)	p value	OR (95%CI)
Age group				
<30 years (13)	6(46.2)	7(53.8)	0.435	1.12(0.303-4.14)
30 - 45 years (23)	8(34.8)	15(65.2)	0.154	0.44(0.127-1.49)
> 45 years (7)	5(71.4)	2(28.6)	0.121	3.93(0.668-23.1)
Sex				
Female (14)	9(64.3)	5(35.7)	0.065	3.42(0.9003, 12.99)
Male (29)	10(34.5)	19(65.5)		1
Religion				
Hindu (35)	18(51.4)	17(48.6)	0.045	7.4(0.8233, 66.72)
Muslim (8)	1(25)	7(75)		1
Occupation				
Employed (29)	13 (44.8)	16 (55.2)	0.902	1.08 (0.2992, 3.923)
Unemployed (14)	6 (42.9)	8 (57.1)		1
Marital status				
Unmarried (6)	4 (66.7)	2 (33.3)	0.231	2.9 (0.4754, 18.1)
Married (37)	15 (40.6)	22 (59.4)		1
SES				
Class 3 &4 (26)	12(46.15)	14(53.85)	0.747	1.2(0.3558, 4.214)
Class 5 (17)	7(41.2)	10(58.8)		1
Smoking				
No(28)	16(57.2)	12(42.8)	0.019	5.3(1.226, 23.19)
Yes(15)	3(20.0)	12(80.0)		1
Alcohol				
No(25)	14(56)	11(44)	0.065	3.3(0.9028, 12.13)
Yes(18)	5(27.8)	13(72.2)		1

A past history of ATT for a period of 3-40 months was elicited from the patients. Eleven patients had taken more than 24 months of ATT and 23 patients outcome of last episode ATT was failure. At presentation, all had radiographic evidence of tuberculosis; 34 (79.1%) patients showed extensive disease, 6 had moderate disease and 3 showed minimal changes radiologically.

Thirty-three (76.7%) patients had M. tuberculosis strains resistant to both isoniazid and rifampicin, whereas ten (23.3%) had only rifampicin resistance.

By 6 months (i.e. end of intensive phase), 20 (45.5%) patients had culture converted, 2 had persistent culture positivity, 7 patients had defaulted, six had died (range, 12 days to 9 months after the treatment) and 8 patient's sputum culture was unavailable or contaminated. During the interim analysis after 12 months of completing treatment, adding to intensive phase end results, three more patients die and four more defaulted. One patient's culture remained positive throughout after end of intensive phase and sputum was sent for XDR TB evaluation. Two patients whose culture was negative and contaminated converted to positive now. Fifteen patients culture remained showed negative results (Table 1). At the end of treatment, out of 43 patients, 19 were cured, 12 defaulted, 9 died, one failure case and two were under XDR TB evaluation (Figure 1).

Of the socio demographic variables, that might be associated with the adverse treatment outcome is presence of Muslim religion and smoking. Patients from Hindu religion have higher odds [OR 7.412, CI 0.8233-66.72] of being cured when compared to Muslim religion patients and this difference was found to be statistically significant (p = 0.045). The cure rates were higher among non-smoking MDR TB patients [OR 5.333, CI 1.226, 23.19] than the smokers (Table 2).

An attempt was made to find out the relationship between different clinical variables and treatment outcome in MDR-TB patients. It was observed that variables like source of past ATT, resistance pattern to anti TB drugs, MDR suspect criteria and adverse drug reactions (ADR) may affect the treatment outcome. Patients who has taken past ATT from RNTCP source ($P < 0.05$), patients who suspected MDR TB with "Criteria B" ($P < 0.05$), whose M.TB bacilli resistance to rifampicin as well as isoniazid ($P < 0.05$) and those patients who reported for ADR ($P < 0.001$) were found to be positively associated with successful treatment outcome in MDR TB.[1] However, BMI, BCG scar, past type of TB, duration of the TB treatment in the past and the extent of chest X-ray lesions at initiation of treatment did not influence the treatment outcome (Table 3).

Table 3: Clinical variables influencing MDR TB outcome.

Variables (n)	Cured (%)	Others (%)	p value	OR (95%CI)
Past TB type				
others*(20)	11(55)	9(45)	0.183	2.29(0.67-7.84)
failure(23)	8(34.8)	15(65.2)		1
Past TB duration				
<1year(10)	7(70)	3(30)	0.065	4.08(0.89-18.8)
1 - 2 years(22)	9(40.9)	13(59.1)	0.446	0.76(0.23-2.55)
>2 years(11)	3(27.3)	8(72.7)	0.169	0.38(0.08-1.67)
Source of ATT				
RNTCP(31)	15(48.4)	16(51.6)	0.034	3.31(0.91-12.13)
RNTCP & non RNTCP(12)	4(33.4)	8(66.6)		1
MDR suspect criteria				
Retreatment case S+@4th month(6)	3(50)	3(50)	0.12	0.18(0.02-1.4)
S+ @diagnosis, retreatment case (6)	5(83.3)	1(16.7)	0.47	0.47(0.16-19.24
Any F/U S+ve(5)	4(80)	1(20)	0.363	1.33(0.11-14.9)
Any category failure(26)	7(26.9)	19(73.1)	0.006	6.5(1.67-25.28)
Resistance pattern				
Both R & H (33)	18(54.5)	15(45.5)	0.017	10.8(1.2, 95.2)
R only(10)	1(10)	9(90)		1
Chest X-ray lesions				
Minimal(3)	1(33.3)	2(66.7)	0.42	0.61(0.05-7.3)
Moderate(6)	5(83.3)	1(16.7)	0.05	8.2(0.87-77.7)
Extensive(34)	13(38.2)	21(61.8)	0.13	0.31(0.06-1.4)
BCG scar				
Present(16)	9(56.3)	7(43.7)	0.22	2.2(0.62, 7.7)
Absent(27)	10(37.1)	17(62.9)		1
BMI				
≥18.5(17)	9(52.9)	8(47.1)	0.27	1.8(0.5, 6.2)
<18.5(26)	10(38.5)	16(61.5)		1
ADR				
Yes(32)	19(59.4)	13(40.6)	0.0006	33.22
No(11)	0(0)	11(100)		1

Adverse drug reactions

Of 43 patients, 32 (74.42%) had adverse drug reactions of varying severity. The most common ones were related to gastrointestinal and skeletal system. Modification of drug regimen required in 9 patients. One patient had hypothyroidism after commencement of therapy and ethionamide was discontinued. Hypersensitivity was observed in one patient who required stopping ofloxacin. Various adverse drug reactions observed during therapy are depicted in Table 4.

DISCUSSION

Treatment of MDR-TB often poses serious challenge to patients and majority of such patients are usually referred to tertiary care. MDR-TB patients received standardized regimen of DOTS-Plus, which includes six drugs for first 6-9 months of intensive phase and four drugs for 18 months of continuation phase. This standardized regimen has shown 61-66% successful treatment outcome in pilot study.[4,6] However, our study observed low treatment outcome (44%) and low cure rate as similar with other studies [2]. While the cure rate seems to be high from 61% to 77% in few studies and 44% to 53% in South Korea, Taiwan and China.[7,12]

Table 4: Adverse drug reactions observed.

System	Manifestations	No. of patients (%)	Actions taken for ADR
Gastro intestinal	Nausea, vomiting, epigastric discomfort	28(65.1)	Symptomatic treatment, divided doses
Central nervous	Insomnia, depression, seizure, suicidal attempt, headache	9(20.1)	Counselling done, Cycloserine stopped if not responded and PAS added.
Skeletal	Joint pain, arthritis	14(32.6)	Symptomatic treatment, analgesics
Otovestibular	Impaired hearing, giddiness, tinnitus	5(11.6)	Stopped Kanamycin and added PAS
Endocrinal	Hypothyroidism	1(2.3)	Replaced Ethambutol with PAS
Renal	Renal function impairment	1(2.3)	Dose calculated according to GFR
Dermatologic	Hypersensitivity, rashes	2(4.6)	Temporarily stopped all drugs, Symptomatic treatment, divided doses given
Hepatobiliary	Jaundice, Impaired LFT	5(11.6)	Temporarily stopped all drugs, Symptomatic treatment, divided doses given
Cardio-vascular system	cor-pulmonale with LVH	4(9.3)	Temporarily stopped all drugs, referred to cardiac physician, Symptomatic treatment.

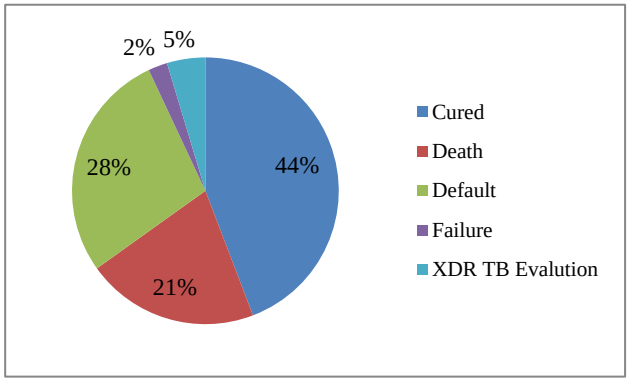

Figure 1: Treatment outcome among the participants.

Our study observed that 2% of patients were declared as failure, 28% defaulter, 21% died and 5% under XDR TB evaluation. Although DOTS care provider ensures compliance to drug treatment, the defaulter rate was also high. MDR-TB treatment defaulter are potentially harmful to community as these cases can relapse and spread the infection in the community, develop resistance to second line anti-TB drugs, and may result into extensive drug resistant TB (XDR-TB).

The results of this study demonstrate high default and death rates may be due to the vulnerable religion and socio-economic status and high rate of smoking in our cohort. The long duration of treatment, pill count per day, frequency of ADRs, and lack of education and awareness among patients could be possible reasons for default and are major challenges for a successful treatment outcome. Another important finding was that two treatment failure cases had extended their initial resistance patterns to XDR-TB during treatment. Whether this was because of amplification of the initial resistance pattern or external re-infection could not be confirmed.

Culture conversion rates were 45.5% and 34.9% at the end of 6 months and 12 months of treatment respectively. Similar findings in other studies.[2,4,9] The sputum culture conversion rate varies from 74% to 92% in different studies reported across globally.[6,7,13] Surprisingly, our study observed that out of 20 sputum culture converted patients initially (first 6 months treatment phase), one patient died, one turned back to sputum positive at the 12th month and became defaulter.

Sputum culture conversions of up to 74% per cent at 6 months have been reported from other studies in India on treatment of MDR-TB cases.[3,4]

The demographic profile of MDR-TB patients in our study was similar to other series, with a majority of male patients in the economically productive age group (25-54 years) with male patient predominance.[2,13]

One of our study limitations is that, as Dots Plus centre was newly started and the cohort we studied was the first cohort enrolled in the program and there was no much facility for the patients. According to PMDT guidelines, our centre has to enroll patients fulfilling criteria A and so majority of patients belong to failure group in the past TB treatment, more duration of exposure to ATT, and extensive chest lesions. The past history of ATT intake, both in terms of number of drugs used and duration of ATT, did not have any association with outcome.[1]

A Turkish study also failed to find any association between duration of previous treatment and outcome.[15] As observed earlier the radiological extent also did not affect the outcome, probably because majority of the patients had radiological extensive disease at presentation.[14,16]

Cure rates were high with patient's bacilli showing resistance to both drugs rifampicin and isoniazid, patients who received ATT form RNTCP source. Treatment compliance was good with patients experiencing adverse drug reactions, as patients visit DOTS PLUS centre frequently and treatment could be monitored. However, the high incidence of adverse drug reactions observed in the study highlights the need for adequate clinical back up for managing ADRs while decentralizing treatment for MDR-TB.

Furthermore, the population treated in this cohort may not reflect the overall MDR-TB population in Karnataka; these patients represent the earliest cohort to be enrolled in this program and may have different clinical and social characteristics compared with patients who were enrolled later.

Though severe adverse reactions were frequent, treatment could be continued in most cases with modification of the treatment regimen. Other studies have reported major adverse reaction ranging from 19-72 per cent.[6,17-19] Thus close monitoring, prompt and timely administrative actions are essential for treatment adherence. Most common adverse event (65.1%) was related to gastro intestinal which is also seen in other studies.[2]

From this study, it appears feasible to treat MDR-TB patients effectively in India on the predominantly ambulatory RNTCP standardized regimen, with certain additional inputs into the existing health care system. Close attention needs to be paid to ensure adherence, and to the timely recognition and treatment of adverse drug reactions.

To conclude, the long duration of treatment (24 months), pill count per day and lack of education, awareness among patients are major obstacles for successful outcome. Hence prevention of MDR TB is more important rather than treatment. Strengthening the program by intensely evaluating treatment regimens, assuring treatment adherence, supporting true DOTS, aggressive and proactive management of adverse events and infection control are very essential.

CONCLUSION

The study concludes that gaps exist in the doctor patient communication. Nearly half of the patients are not satisfied after their consultation with doctors. Present doctors fail to provide sufficient information to patients in many a time. Proper behavior from the patients and also adequate information provided to them by consulting doctors increases the patient satisfaction and may affect treatment outcome. Doctors need to be trained in Communication and this has to be included as an important topic in Medical Education.

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REFERENCES

1. Central TB Division (CTD), Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. DOTS-plus guidelines. New Delhi: CTD; May 2012.
2. Kapadia VK, Tripathi SB. Analysis of 63 patients of MDR TB on DOTS plus regimen: An LG hospital, TB Unit, Ahmedabad experience. GMJ. 2013;68(2):52-7.
3. WHO. Global Tuberculosis Control: Report, 2011. Last accessed on 2012 Apr 21. Available from: http://www.whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf.
4. Pouline J, Vijaya BRD, Nalini SM, Jemima SF, Rajeswari R, Balambal R, et al. Outcome of standardized treatment for with MDR-TB from Tamil Nadu, India. Indian J Med Res. 2011;133:529-34.
5. Jonna IDH, Anna W, Daniel E, Feleke M, Assefa G, Aschalew G, et al. Nitric oxide production in the exhaled air of patients with pulmonary tuberculosis in relation to HIV co-infection. BMC Infectious Diseases. 2008;8:146.
6. Singla R, Sarin R, Khalid UK, Mathuria K, Singla N, Jaiswal A, et al. Seven-year DOTS-Plus pilot experience in India: Results, constraints and issues. Int J Tuberc Lung Dis. 2009;13:976-81.

7. Van DA, Salim MA, Das AP, Bastian I, Portaels F. Results of a standardised regimen for multidrug-resistant tuberculosis in Bangladesh. Int J Tuberc Lung Dis. 2004;8:560-7.
8. Shin SS, Pasechnikov AD, Gelmanova IY, Peremitin GG, Strelis AK, Mishustin S, et al. Treatment outcomes in an integrated civilian and prison MDR-TB treatment program in Russia. Int J Tuberc Lung Dis. 2006;10:402-8.
9. Kalpesh J, Mira D, Rajesh S, and Ram Kumar D. Treatment outcome of standardized regimen in patients with multidrug resistant tuberculosis. J Pharmacol Pharmacother. 2014;5(2):145-9.
10. Chiang CY, Enarson DA, Yu MC, Bai KJ, Huang RM, Hsu CJ, et al. Outcome of pulmonary multidrug-resistant tuberculosis: A 6-yr follow-up study. Eur Respir J. 2006;28:980-5.
11. Park SK, Lee WC, Lee DH, Mitnick CD, Han L, Seung KJ. Self-administered, standardized regimens for multidrug-resistant tuberculosis in South Korea. Int J Tuberc Lung Dis. 2004;8:361-8.
12. Liu CH, Li L, Chen Z, Wang Q, Hu YL, Zhu B, et al. Characteristics and treatment outcomes of patients with MDR and XDR tuberculosis in a TB Referral Hospital in Beijing: A 13-year experience. PLoS One. 2011;6:e19399.
13. Prasad R, Verma SK, Sahai S, Kumar S, Jain A. Efficacy and safety of kanamycin, ethionamide, PAS, and cycloserine in multidrug-resistant pulmonary tuberculosis patients. Indian J Chest Dis Allied Sci. 2006;48:183-6.
14. Yew WW, Chan CK, Chau CH, Tam CM, Leung CC, Wong PC, et al. Outcomes of patients with multidrug- resistant pulmonary tuberculosis treated with ofloxacin/levofloxacin- containing regimens. Chest. 2000;117:744-51.
15. Tahaoglu K, Törün T, Sevim T, Atac G, Kir A, Karasulu L, et al. The treatment of multi-drug resistant tuberculosis in Turkey. N Engl J Med. 2001;345:170-4.
16. Mitnick C, Bayona J, Palacios E, Shin S, Furin J, Felix Alcántara F, et al. Community-based therapy for multi-drug resistant tuberculosis in Lima, Peru. N Engl J Med. 2003;348:119-28.
17. Malla P, Kanitz EE, Akhtar M, Falzon D, Feldmann K, Gunneberg C, et al. Ambulatory-based standardized therapy for multidrug resistant tuberculosis: experience from Nepal, 2005-2006. PLoS One. 2009;4:08313.
18. Torun T, Gungor G, Ozmen I, Maden E, Bicakci B, Atac G, et al. Side effects associated with the treatment of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis. 2005;9(12):1373-7.
19. Thomas A, Ramchandra R, Rehaman F, Jaggarajamma K, Santha T, Selvakumar N, et al. Management of multi-drug resistant tuberculosis in the field- Tuberculosis Research Centre experience. Indian J Tuberc. 2007:54:117-24.

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