



ORIGINAL RESEARCH PAPER

Pulmonary Medicine

CLINICO-RADIOLOGICAL PROFILE AND TREATMENT OUTCOME OF MDR TB PATIENTS IN WESTERN ODISHA

KEY WORDS: Multidrug-resistant tb, Treatment outcome, Clinico-radiological profile

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ABSTRACT

Introduction: India ranks second in harbouring MDR-TB cases next to china with incidence of 184 per lakh population is 1, 2. In India MDR-TB levels of 1% to 3% in new cases and around 12% in retreatment cases⁹. MDR-TB is emerging burden for health care system. Clinical profile, radiological status and treatment outcome important tools for management of MDR-TB. My study assessing the clinical & radiological profile and emphasizing outcome of patients on treatment.

Methodology: 115 Patients diagnosed as MDR TB at RNTCP accredited Culture & DST laboratory and admitted at DR-TB Centre, VSS MCH, Burla (Tertiary Care Hospital in Western Odisha) during November 2013 to October 2015 were included in the study. Evaluation of patients was done by direct interview, treatment card, DST report, investigation reports and clinical examination.

Results: In my study majority 74.78% patients were underweight. 73.9% patients did not have any addictions. Only 19% having co-morbidities among which DM (6.95%) was common. Majority of patients (67.82%) were from Cat-II failure group. Culture conversion by 3rd and 6th month occurred in 34(60.71%) and 51(91.07%) patients respectively. Most common presentation being cough. Pallor was the most common sign and anaemia being most common laboratory abnormalities. Cavitory lesion in chest X-ray was most common radiological pattern. Sputum culture conversion rate had no relation with radiological pattern of disease, initial sputum smears grading. 13 patients died 11 patients defaulted and 3 patients were declared as XDR.

Conclusion: MDR TB is more common in young males, patients with low BMI and belongs to low socioeconomic group. Addictions and co-morbid illness are not risk factor for MDR TB. Treatment failure is a major risk factor for MDR TB. Socio-economic up gradation, health education, strengthening the programme, assuring strict adherence, newer methods to diagnose MDR TB, early institution of treatment, will improve the treatment outcome.

BACKGROUND

Tuberculosis remains world's leading infectious cause of adult death.³ India is one of the high TB burden countries in the world accounting for nearly 20% of the global incidence constituting 9.4 million TB cases⁴.

The discovery of rifampicin in 1963 was measure break through in treatment of tuberculosis. Resistance to rifampicin was observed soon after it was first administered⁵. WHO declared TB a global emergency in 1993 due to increased in associated mortality and morbidity⁴ and in the same year formulated DOTS strategy. Following successful implementation of "DOTS-Plus" pilot projects for the management of drug resistant TB between 2000 and 2005, a new Stop TB Strategy was launched in 2006 which includes the diagnosis and the management of drug resistant TB.

The Global Tuberculosis Report 2014 estimated 3.5% of new cases and 20.5% of previously treated cases had MDR-TB. In 2013, there were an estimated 480,000 new cases of MDR-TB worldwide, and approximately 210,000 deaths from MDR-TB. Death rate due to TB in India is nearly 28 per lakh population which is highest death rate among other communicable diseases and accounts for 26% of all avoidable adult death⁶.

MDR-TB case defined as a TB patient whose sputum is culture positive for *Mycobacterium tuberculosis* and is resistant *in-vitro* to isoniazid and rifampicin with or without other anti-tubercular drugs based on DST results from an RNTCP-certified Culture & DST Laboratory⁷.

Drug resistance TB has microbial, clinical and programmatic causes. Potential causes of drug resistance include inadequate treatment provided by health services, poor case-holding, poor drug supply, poor quality of drugs, and non adherence of patients to the prescribed drug regimens and indiscriminate use of anti-tuberculosis drugs in the private sector.

Recent publication identified lung cavities as risk factor of drug resistance⁸. So radiological status of all MDR-TB patients should be emphasized. There are very few studies in clinical manifestation of MDR TB, which is equally important parameter for both patient and investigator point of view. For this my study emphasizing clinic-radiological profile of MDR-TB patients.

Management of MDR-TB is more difficult, complicated, challenging, and expensive and may pose a threat to the success of DOTS. Owing to the complex nature of second-line drug treatment in terms of cost, toxicity, and delivery of appropriate regimens, drug-resistant forms of tuberculosis present a real threat to TB control in some settings. Accurate diagnosis with proper supply of drug as per resistance pattern and under supervision is the key to success in treating DR-TB.

DOTS plus service was started in VSS Medical College Burla (Tertiary Care Hospital in Western Odisha) in the year 2013. Though it was started in odisha four years ago with establishment of IRL (Intermediate Reference Laboratory) at

SCB Medical College Cuttack. So data on MDR TB in western Odisha was lacking. There is dearth of study on clinic radiological profile of MDR TB patients which is an important parameter in treatment adherence and success of DOTS. This study was on clinical profile and radiological status of MDR TB admitted to the DR TB centre of VSS Medical College Burla and emphasized various risk factors, co morbid conditions related to emergence of MDR TB and drug resistance.

METHODOLOGY

Study Design and Population

Hospital based prospective observational study was conducted between November 2013-October 2015 at Drug resistant TB Centre, Department of Pulmonary Medicine, VSS Medical College & Hospital, Burla, Sambalpur, Odisha.

Patients of both the sexes with culture and sensitivity test of the sputa done at RNTCP-certified Culture & DST laboratory (IRL, Cuttack) showing growth of *Mycobacterium tuberculosis* and resistant to rifampicin, or rifampicin and isoniazid with or without other drugs referred and subsequently admitted at DR-TB Centre, VSS Medical college & Hospital, Burla during study period are included in the study. Extra pulmonary tuberculosis patients and patients with Culture and sensitivity test report from laboratory not accredited by RNTCP are not included in study.

Study Methods

Evaluation of patients were done after being referred from DTCs and got admitted at drug resistant TB centre based on direct interview, case card, treatment card, register book, DST report, investigation reports and clinical examination.

Patients-particulars like Name, Age, Sex, Address, Marital status, Literacy, Occupation, Socio-economic status, BMI etc. and presenting clinical features were recorded. Proper history of present illness, Personal history, History of Anti-TB Treatment, History of contacts, Family history, and associated co-morbidities were interviewed.

Patients were subjected to clinical examination and routine investigations including blood count, blood sugar, LFT, Thyroid profile, Blood urea, Serum creatinine, Sputum microscopy, Urine routine & microscopy, HIV, HbsAg, HCV test, Chest x-ray, Thyroid profile, Audiometry, pregnancy test (for all woman in child bearing age groups).

Then patients were treated as per PMDT guidelines. Any adverse drug events after initiation of MDR-TB regimen were documented and managed accordingly. Patients were advised to report any side effects experienced by them. When found clinically stable the patients were discharged at least after 7 days of the treatment initiation.

An informed consent was taken from each patient before participating in my study. I analyzed my study with proper statistical methods.

Monitoring progress during treatment

Clinical monitoring

Patients monitored by medical officer trained in RNTCP PMDT guidelines for clinical evaluation after discharge from the DR-TB Centre, at monthly intervals during the IP, and at 3-monthly intervals during the CP until the end of treatment. Medical officer assessed clinical, microbiologic, radiologic response to treatment, assessed possible adverse reactions. The results updated in treatment cards during follow-up visit.

Bacteriological monitoring

Done by sputum microscopy and sputum culture at monthly intervals during IP and at 3 monthly intervals during CP or as when indicated as per RNTCP guidelines. Sputum microscopy is done by LED fluorescent microscopy and culture is done by

liquid culture method during routine follow-up (except for special situations like HIV-TB co-infected cases and sputum negative re-treatment cases, where liquid culture media is used for easier detection).

Investigations during treatment

Chest radiograph was done during pre-treatment evaluation, at the end of IP, end of treatment and when clinically indicated. Serum creatinine was done every month for the first 3 months and every 3 months thereafter while the patient is receiving kanamycin. Other relevant investigations were done as and when clinically indicated.

Monitoring and management of adverse drug reactions

Close monitoring of patients to ensure that adverse effects of category IV anti-TB drugs are recognized early. Patients were not asked any leading questions to elicit any adverse reactions. However, if the patient makes any spontaneous complaint, he/she was interrogated in detail and necessary actions were taken.

Ethical Consideration

The study proposal was submitted to the ethical committee of Sambalpur University, Odisha for approval. All works were performed according to the international guidelines for human experimentation in clinical research.

Statistical Analysis

All data were analysed using Microsoft Excel and all data were analysed using SPSS version 20 statistical software. A p value of less than 0.05 was considered significant.

RESULTS

In my study majority of the patients are male, with male: female ratio of 1.5:1 (69:46). Majority of the patients were in the age group of 16-30 years (41.7%) followed by 31-45 years (28.7%). Mean age of the patients was 35.33±13.36. Out of 115 patients, 74.78% patients were underweight and 24.34% patients were having normal BMI. Only 0.86% patients were overweight. In this study majority of patients were from rural area (85.2%) and majority (66.95%) studied only up to primary level. Only 7.82% patients were graduate and 9.56% were illiterate. Most of the patients (84.34%) are below poverty line.

In present study 19 patients addicted to alcohol, 7 patients were smoker, 18 patients were addicted to tobacco. 85(73.91%) patients gave no history of addiction. Only 5.22% patients having known history of contact with MDR TB patients. In this study only 6.95% patients were diabetic, 3.48% patients were having hepatitis, 2.6% patients were having Chronic Kidney Disease and 0.87% patients were with HIV. In my study majority of patients (67.82%) are from treatment failure category. Sputum smear grading was negative in 11 patients (9.56%), scanty in 28 patients (24.34%), 1+ in 9 patients (7.82%), 2+ in 13 patients (11.3%) and 3+ in 54 patients (46.95%).

From 115 patients, culture conversion report is available in 56 patients. Among 56 patients, culture conversion by 3rd and 6th month occurred in 34(60.71%) and 51(91.07%) patients respectively. Only in 5(8.93%) patients culture conversion occurred after 6th month.

Majority of patients 98(85.21%) presented with cough followed by weakness, malaise in 76(66%) patients and anorexia in 70(60.87%) patients. About 36(31.3%) patients had dyspnoea, 31(26.95%) patients had haemoptysis, 28(24.34%) patients had fever and 28(24.34%) patients had chest pain at the time of presentation. On general examination 45.21% had pallor, 3.48% had icterus, 2.6% had clubbing, 1.74% had pedal oedema and only 0.87% had lymphadenopathy.

In present study 42 patients had anaemia, 22 patients had leucocytosis, 8 patients had hyperglycemia, 4 patients were with raised LFT, 3 patients had deranged renal function test, 8 patients had dyselectrolytemia, 3 patients had hypoalbuminemia and only two patients had hypothyroidism in pre treatment evaluation. In my study majority of patients had bilateral lesion i.e. 71(61.74%). In this study majority of patients i.e. 65(56.52%) had cavitory lesion. In this study it was found that majority of patients i.e. 59(51.3%) had extensive lesion, while 30(26%) patients had mild and 26(22.6%) patients had moderate radiological lesion.

In my study 81 patients were still on treatment, 2 patients were cured, 4 patients were completed the treatment, 11 patients were defaulted, 13 patients were died, 3 patients were declared XDR and one patient was transferred out from the state.

From 115 patients, culture conversion reports were available in 56 patients. Out of 56 patients culture conversion by 6th month occurred in 51 patients. Out of 26 patients with 3+ initial smear grade 22(84.61%) were culture converted by 6th month. Out of 14 patients with scanty initial smear grade 13(92.86%) were culture converted by 6th month and all patients with initial smear grade 2+, 1+, negative were culture converted by 6th month. Culture conversion by 6th month was 70% (7 out of 10) in Rifampicin monoresistant cases and 95.6% (44 Out of 46) in cases resistant to both drugs.

Culture conversion by 6th month seen in 13 patients (100%) with mild lesions, 11 patients (84.61%) with moderate lesions and 27 patients (90%) with extensive lesions. Culture conversion by 6th month among cavitory patients was 96.66% (29 out of 30), non-cavitory patients were 84.61% (22 out of 26), and unilateral patients were 90.9% (20 out of 22) and bilateral patients were 91.17% (31 out of 34 patients).

Variable	n	%
Age		
<16	4	3.47
16-30	48	41.73
31-45	33	28.69
>45	30	26.08
Mean Age	36.33	
Sex		
Male	69	60
Female	46	40
BMI		
<18.5	86	74.78
>18.5	29	25.21
Residence		
Rural	98	85.2
Non-rural	17	14.78
Literacy		
Literate	104	90.43
Illiterate	11	9.56
Addiction		
Smoking	7	6.08
Alcohol	19	16.52
Tobacco	18	15.65
Contact history		
Present	6	5.21
Co-morbid illness		
Diabetes mellitus	8	6.95
Hepatitis	4	3.45
CKD	3	2.6
Hypothyroidism	2	1.74
Hypertension	2	1.74
COPD	1	0.87
APD	1	0.87
Patient Category		
Failure	78	67.82

Relapse	26	22.6
TAD	8	6.95
Initial Sputum smear grading		
3+	54	46.95
2+	13	11.3
1+	9	7.82
Scanty	28	24.34
Negative	11	9.56
Culture conversion		

Clinico-radiological data

Variable	n	%
Cough	98	85.21
Fever	28	24.34
Haemoptysis	31	26.95
Chest pain	28	24.34
Dyspnoea	36	31.3
Weakness, malaise	76	66
Signs		
Pallor	52	45.21
Icterus	4	3.48
Clubbing	3	2.6
Lymphadenopathy	1	0.87
Pedal oedema	2	1.74
Laboratory abnormalities		
Anaemia	42	36.5
Leucocytosis	22	19.13
Hyperglycemia	8	6.95
Raised LFT	4	3.47
RFT abnormalities	3	2.6
Dyselectrolytemia	8	6.95
Hypothyroidism	2	1.74
Hypoalbuminemia	3	2.6
Chest X-ray		
Cavitory	65	56.52
Non-cavitory	50	43.48

Treatment Outcome

Variable	n	%
Still on treatment	82	71.3
Treatment completed	4	3.47
Cured	2	1.74
Default	12	10.43
Death	11	9.56
XDR	3	2.6
Transferred out	1	0.87

DISCUSSION

In my study population most of the patients were from younger age group (16-30 years) with mean age of 36.33±13.36. This age group represents the working force, thus the negative socio-economic impact of MDR-TB on our society. Majority of the patients were male with male: female ratio of 1.5:1. In my study male preponderance is due to social factor that in our society women tend to get neglected and are less likely to seek medical attention. Most of the patients were from rural areas having low socioeconomic status. More than sixty percent (60%) studied up to primary level. Majority of patients were labourer and farmer while majority of females were housewives.

74.78% patients were underweight. Under nutrition and low BMI is also an independent risk factor for emergence of MDR TB in my study. Majority of patients did not have any addictions. This contradictory finding due to the fact that 40% of my study population is female and addiction is relatively less common in female and they are hesitant to disclose their addiction publicly. Out of our 115 patients, 6 patients (5.2%)

had contact with MDR-TB patients in family which is comparable R. Singla et al 2006⁹ data that was 4%. So guidelines for contact tracing, screening procedure and prescription of preventing treatment is recommended. In my study co-morbid illness including HIV did not play as risk factor for development of MDR-TB.

Previous treatment for TB is the strongest risk factor development of MDR-TB as they have already been exposed to ATT. In my study majority of patients (67.82%) were from treatment failure category, 22.6% patients were from relapse category and 6.95% patients were from TAD category. So combining all those 97.37% MDR TB patients had previous treatment history for TB. This finding supported by Lomtadze N et al 2009¹⁰.

Majority of patients were having initial sputum smear grading 3+. In my study Sputum culture conversion is considered important interim indicator of the drug efficacy¹¹. Culture conversion by 3rd and 6th month occurred in 34(60.71%) and 51(91.07%) patients respectively. Only 5 patients acquired culture conversion after 6 months. So MDR-TB regimen is effective for sputum culture conversion.

Most common presentation being cough followed by weakness and malaise. Pallor is the most common sign and anaemia being most common laboratory abnormalities. Bilateral involvement, extensive lesions and presence of cavity in chest X-ray are most common radiological features in my study.

Of the 115 patients, 13 patients died during treatment, 11 patients defaulted, 3 patients declared as XDR cases, 1 patient transferred out to other TB centre, 4 patients had completed treatment and 2 patients declared cure. Rest 81 patients were still on treatment. Among 115 patients, 3 were put on XDR TB regimen. So total XDR cases were 2.6%. According to WHO 2010 update proportion of XDR cases among MDR was 5.4% and according to PMDT India update 2012 it was 4%¹². Defaulter rate in my study was 9.56%. Out of 11 defaulter all were below poverty line, 4 out of 11(36.336%) were having co morbidities, 1 addicted to alcohol, 7(63.63%) had extensive lesion and 2 faced drug related side effect. Majority of defaulter were from low socio-economic group and having radiological extensive lesion. Out of 13 patients died 9(69.23%) patients had radiologically extensive lesion, 3 patients were alcoholic and one was diabetic.

From 115 patients, culture conversion reports were available in 56 patients. Out of 56 patients culture conversion by 6th month occurred in 51 patients. Out of 26 patients with 3+ initial smear grade 22(84.61%) were culture converted by 6th month. Out of 14 patients with scanty initial smear grade 13(92.86%) were culture converted by 6th month and all patients with initial smear grade 2+, 1+, negative were culture converted by 6th month. Analysing the data with Chi-square test, the two tailed p value equal to 0.565. So there is no relation between initial sputum smear grading and 6th month culture conversion.

Culture conversion by 6th month was 70% (7 out of 10) in Rifampicin monoresistant cases and 95.6% (44 Out of 46) in cases resistant to both drugs. On comparing Rifampicin mono-resistant and both drug resistant by Chi-square test, the two tailed p value equals to 0.009 denoting it to be significant. From this it was evident that in rifampicin monoresistant patients rate of conversion delayed and more prone to failure.

Culture conversion by 6th month seen in 13 patients (100%)

with mild lesions, 11 patients (84.61%) with moderate lesions and 27 patients (90%) with extensive lesions. Culture conversion by 6th month among cavitary patients was 96.66% (29 out of 30), non-cavitary patients were 84.61% (22 out of 26), unilateral patients were 90.9% (20 out of 22) and bilateral patients were 91.17% (31 out of 34 patients).

On comparing mild and moderate group by Chi-square test, the two tailed p value equals to 0.141 denoting it to be insignificant and on comparing moderate to extensive lesions, the two tailed p value equals to 0.613 denoting it to be not significant. So extent of lesion has no relation with 6 month bacteriological conversion of patients.

On comparing cavitary and non-cavitary group by Chi-square test, the two tailed p value equals to 0.114 denoting it to be insignificant. So the rate of bacteriological conversion by 6 month has no relation with cavitary or non-cavitary lesion.

On comparing unilateral and bilateral lesion group by Chi-square test, the two tailed p value equals to 0.973 denoting it to be not insignificant. So rate of bacteriological conversion does not differ whether the patient has unilateral or bilateral lesion.

Limitation of My Study

Sample size is small. Resistance pattern other than Isoniazid and Rifampicin not studied due to lack of diagnostic facility in our set up. Out of 115 patients 11 patients died during treatment, 12 patients defaulted and one patient transferred out to other TB centre which affected my data and result interpretation. As treatment duration of MDR-TB patients are too long, so follow up of all patients were not done. Sputum culture conversion reports of all patients were not available.

CONCLUSION

MDR TB is more common in young males and patients with low BMI. The incidence of MDR TB is higher in rural area, low socioeconomic and low educational status population. Addictions and co-morbid illness are not risk factor for MDR TB. Treatment failure is a major risk factor for development of MDR TB. Sputum culture conversion rate has no relation with radiological pattern of disease, initial sputum smear grading, side and extent of lesion. Socio-economic upgradation, health education, strengthening the programme, assuring strict adherence, early institution of treatment will improve the treatment outcome.

Funding

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Conflict of Interest

None declared.

Ethical Approval

This study received ethical clearance from the Ethics Committee of Sambalpur University.

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