

ORIGINAL ARTICLE

Socio-economical and Clinico-Radiological Profile of 474 MDR TB Cases of a Rural Medical College

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Abstract

Objective: To study the socio economical and clinico radiological profile of 474 diagnosed MDR TB cases who came for the initiation of MDR TB regimen in DRTB center of R.D.Gardi Medical college, Ujjain

Methodology: This is a retrospective and prospective observational study for a total period of three years from October 2013 to September 2016. The patients were evaluated clinically, radiologically and were investigated thoroughly according to PMDT guidelines and then were started on MDRTB treatment. The study was conducted at drug resistance tuberculosis center (DR-TB) managed by Department of Pulmonary Medicine.

Results: 474 cases were included in the study and we found that patients were in the age range of 10-84 years, maximum patients were in age group of 30 to 39 years, and mean age was 38 yrs. Male to female ratio was 2.73 to 1, most of the patients in the study were from rural area i.e. 61.6%. Illiteracy was found in 339 (71.5%) cases and out of these 339, 165 patients (48.6%) were defaulter, 101(29.8%) are cases of relapse, 39(11.5%) were failure, 34(10.02%) of new cases. Maximum numbers of patient were in lower class accounting 63.7% and upper lower class 31.6%, lower middle class only 4.5%. Study also showed mean BMI was 14.9 kg/m² (range 5.7-25.4 kg/m²), 88.6% of patients were undernourished with BMI less than 18.5kg/m². The most common symptoms was cough seen in 96%, followed by fever 67.5%, Dyspnea 52.7%, Anorexia 26.2%, chest pain in 19.8% and least common was haemoptysis seen in 7.6% of patient. Common co-morbidities with MDR-TB found was anemia in 176 out of 474 (i.e.37.1%), 123(25.9%) COPD. Radiological severity showed 219(46.2%) moderate lesion, 139 (29.3%) mild, 107(22.6%) extensive lesion and 9(1.9%) normal, 312(65.8%) of patient are non-cavitary and 162 (34.2%) are cavitary in which 99 (20.9%) were unilateral and 63(13.3%) are bilateral cavitary lesion. Defaulter are most common accounting of 218(46.0%), relapse 139 (29.3%) and failure 68 (14.3%), new 48 (10.2%), most of them had taken more than one episode of ATT (72.8%). Most common source of ATT taken by patient is RNTCP it accounts 424 (89.5%) and 46 (9.7%) from private. 181 out of 474 (38.2%) cases delayed the treatment for 1-7 days, 82 out of 474 (17.3%) cases delayed treatment for 8-10 days, 96 out of 474 (20.3%) cases delayed treatment for 11-19 days and 115 out of 474 delayed the treatment for more than 19 days. 95 out of 474 cases i.e. 20.1% cases come from more than 150 km away from their residing area for the initiation of treatment.

Conclusion: The epidemiological picture of TB showed that males were predominant in our study however female were more affected in younger age group compared to male. More than 51% of the cases were in productive age group which affects the socioeconomic condition of family and society. More than 2/3 of patients were from lower socioeconomic group with low BMI. Therefore improving nutrition and immunity can play an important role. 2.3% of the cases were HIV reactive and were on ART. Co-morbidities like COPD and Diabetes were seen in our study which were statistically significant and had impact on the treatment outcome of results. Significant delay in initiation of MDR-TB regimen from date of DST was seen in 24.3% cases which is matter of concern. Most of the patients had taken ATT from RNTCP in which Defaulter and relapse was major contributor of MDR-TB suspect in our study and patient taking ATT privately were less. Large number of cases which resides more than 150 kilometers from DRTB center initiated the drug after a gap of more than 19 days from the date of DST.

Introduction

Tuberculosis now ranks alongside Human Immunodeficiency Virus (HIV) as a leading cause of death worldwide.¹ Tuberculosis (TB) kills more adults in India than any other infectious disease. In India every day

- More than 6000 develop tubercular disease.
- More than 600 people die of tuberculosis (i.e. 2 death every 5 min).¹

India has the highest burden of both tuberculosis and multi drug resistance tuberculosis and second highest of Human Immunodeficiency Virus (HIV) associated tuberculosis based on estimates reported in global tuberculosis report 2015. An estimated 71000 cases of multi drug resistance

tuberculosis emerge annually from the notified cases of pulmonary tuberculosis in India, based on sub-national drug resistance survey carried out in three states of India 3% among the new tuberculosis cases and 12%-17% among previously treated tuberculosis in the world. An estimated 1.1 lac HIV

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Table 1: Co-morbidities and associated conditions with MDR-TB

Co-morbidities	Frequency (n=474)	Percent (%)
Anemia	176	37.1
COPD	123	25.9
Bronchiectasis	78	16.5
Heart disease	50	10.5
Diabetes	39	8.2
Resp failure	27	5.7
Renal impairment	26	5.5
Hepatic impairment	28	5.9
Hypo thyroid	27	5.7
Pleural Effusion	21	4.4
Hyper thyroid	6	1.3
Pyothorax	5	1.1
DVT	2	0.4
Pregnancy	2	0.4
Pneumothorax	1	0.2

associated tuberculosis occurred in 2014 and 31000 estimated number of patients died among them.¹ A major obstacle to tuberculosis control is the emergence of *mycobacterium* resistance to antitubercular chemotherapy.² Multi drug resistant tuberculosis is caused by strains of *Mycobacterium tuberculosis* that are resistant *in-vitro* to isoniazid and rifampicin with or without other anti-tubercular drugs based on drug sensitivity test results from a Revised National Tuberculosis Control Program certified culture and drugs sensitivity tests laboratory. The outcome results of multi drug resistant tuberculosis patients remain suboptimal.

Material and Methods

This is a retrospective and prospective observational study for a total period of three years from October 2013 to September 2016. The study was conducted at drug resistance tuberculosis center (DR-TB) managed by Department of Pulmonary Medicine. Our study was conducted in six districts (Neemuch, Mandsaur, Dewas, Ratlam, Shajapur, Ujjain) of western Madhya Pradesh linked to DR-TB center of Ujjain with population of 86,84,807 people (census 2011).

Inclusion criteria: All patient of multi drug resistance tuberculosis (MDR-TB) registered in DOTs plus site.

Exclusion criteria: Those cases were not included who were started on MDR TB regimen at the periphery and did not reported to DRTB center.

Procedure planned: All the multi-drug resistance tuberculosis (MDR-TB) cases which were diagnosed at drug

resistance tuberculosis (DR-TB) center of R.D. Gardi Medical College or referred from other places for initiation of second line drugs underwent an initial evaluation of the patient was done which includes:

Step 1

- Demographic variables of patient which includes age, sex, education level.
- Detailed history of patient which include history of presenting illness, past history, personal history and family history
- General examination of the patient including vitals, height and weight Oxygen saturation of patient (SpO₂) by pulse oximetry.
- Systemic examination of the patient including respiratory, cardiovascular, central nervous system, gastro intestinal system.

Step 2

Basic investigations like:

- Pathology- Complete Blood Count, blood grouping,
- Biochemistry- random blood sugar, liver function test, renal function test, serum electrolytes, serum calcium.
- Radiological test-chest x-ray
- Cardiac evaluation-Electrocardiogram, echocardiography if required.
- Special tests - HIV testing, HBsAg and thyroid profile.

Step 3

Collection of data and analysis

- Descriptive data was collected and studied accordingly.
- Significant statistical test were applied.

Observations and Results

A total of 474 MDR-TB patients were included in the study. The mean, mode, and median age are 38, 40, 36 year respectively and range is 10-84 year. Standard Deviation (SD) is 13.4 year. The total of more than 51% cases was in the age group between 20-49 years i.e. in the productive age group with Male: Female ratio equals to 2.73: 1 showing male were predominant. Female were more in younger age group compared to male with chi-square value 44.38 and p value is 0.00. study shows that most of patient belongs to rural area i.e. 61.6%

with illiteracy seen in 71.5% of cases followed by primary school education in 19.4% cases, higher secondary education in 7% cases and graduate 2.10% cases. Maximum numbers of patient were in lower class accounting 63.7% and upper lower class 31.6%, lower middle class only 4.5%.

Mean body mass index (BMI) was 14.9 kg/m², (range 5.7 – 25.4 kg/m²), maximum cases were undernourished with BMI less than 18.5 kg/m² in which 72.2% were severely undernourished had BMI less than 16 kg/m² followed by (8.6%) with moderate thinness and (7.8%) were mild thinness, a total of (11.2%) of patients had normal BMI and only one patient was overweight.

Smoking history was found to be in 168 (35.4%) of total patients with 91 patients (19.2%) with alcohol history while 81 patient consumed both alcohol and smoking. Most common symptoms was cough seen in 96%, followed by fever 67.5%, Shortness of breath 52.7%, anorexia 26.2%, chest pain in 19.8% and least common was haemoptysis seen in only 7.6% of patients.

The occupational profile of patients revealed that a majority of them were from labour class (36.3%) and farmer (31.2%) followed by housewife (15.2%), students (9.1%) and rest (8.2%) are driver, salesman, watchman, constable, electrician, LIC agent, shopkeeper etc. In our study we found that 11(2.3%) cases out of 474 were HIV positive and were on ART.

Table 1 shows most common co-morbidities and associated condition with MDR-TB is anemia in 176 out of 474 (i.e.37.1%), 123 (25.9%) COPD, 78 (16.5) Bronchiectasis, 50 (10.5%) heart disease, 39 (8.2) DM, 28 (5.9%) hepatic disease, 27 (5.7%) respiratory failure, 27 (5.7%) hypothyroid, 26 (5.5%) renal impairment, 21(4.4%) Effusion, 6(1.35) hyper thyroid, 5(1.1%) pyothorax, 2(0.4%) DVT, 2(0.4%) pregnancies, 1 (0.2%) pneumothorax. Study also show out of 27 patients having hypothyroidism 15 are male and 12 of them are female. Proportion of hypothyroidism is significantly higher in both and females as compared to hyperthyroidism, chi-square value 6.37 and p-value 0 .04, statistically significant.

Most common site is lung parenchyma seen in 464 (97.9%) cases, and only 10 (2.1%) extra-pulmonary

Table 2: Mean Body Mass Index (BMI) of MDR-TB cases in different studies

Different studies	Mean BMI (kg/m ²)	Range
Kapadia <i>et al</i> ⁵	18.67 ± 3.45	14-23.5
Mukherjee <i>et al</i> ¹⁰	18.5 ± 4.025	12-31
Present study	14.9 ± 2.96	5.7-25.4

cases were found. A total of 6.8% (32 out of 474) cases had history of contact with patients of tuberculosis

Radiological severity showed 219 (46.2%) cases with moderate, 139 (29.3%) with mild, 107 (22.6%) extensive lesion and 9 (1.9%) normal with 312 (65.8%) cases with non-cavitary lesion and 162 (34.2%) cases with cavitary lesion in which 99 (20.9%) were unilateral and 63 (13.3%) are bilateral cavitary lesion. Most of the cases 345 i.e. 72.8% took ATT for more than one episode and only 86 i.e. 16.9% took single episode of ATT while 49 i.e. 10.3% cases had no history of ATT prior to initiation of MDR-TB drugs. Regarding ATT taken by the patient prior to MDR-TB they were categorized as defaulter are most common accounting of 218 (46.0%), relapse 139 (29.3%) and failure 68 (14.3%), new 48 (10.2%). Cross tabulation was done which showed most of the patient are illiterate that is 339 (71.5%) and out of these 339, 165 patients (48.6%) were defaulter, 101 (29.8%) are cases of relapse, 39 (11.5%) were failure, 34 (10.02%) of new cases. Cases belonging to lower socioeconomic defaulted on treatment more often (Chi-square= 16.06 and p value 0.01). In our study, most common source of ATT taken by patient is from RNTCP and it accounts 424 (89.5%) cases and 46 (9.7%) cases took treatment from private sources.

181 out of 474 (38.2%) cases delayed the treatment for 1-7 days, 82 out of 474 (17.3%) cases delayed treatment for 8-10 days, 96 out of 474 (20.3%) cases delayed treatment for 11-19 days and 115 out of 474 delayed the treatment for more than 19 days. 95 out of 474 cases i.e. 20.1% cases come from more than 150 km away from their residing area for the initiation of treatment.

Cross tabulation was done between delay in treatment start and distance of patient from DRTB center (Chi-square= 11.557 and p value = 0.009) Concluding that person residing far from DRTB center initiated the drug after a gap of more than 19 days (26.3%). Logistic regression were applied and we found that chances of mortality in MDR-TB

patients having COPD is 0.486 times higher as compare to non-COPD patients and chances of mortality in MDR-TB patients having diabetes is 0.325 times higher as compare to non diabetic patients.

Discussion

Our study at Drug Resistance (DR-TB) centre mostly covered a rural population. Most of the patient in our study were from a low socioeconomic, background with low education level and were nutritionally challenged.

The study gave special attention to spatiotemporal pattern of the MDR-TB patients so that the spread of the cases can be analyzed along with the co morbidities associated with cases so that any factor could be found out that may prevent spread of the disease, resolving of these factor may also help in better compliance of treatment.

In the present study majority of the MDR-TB, cases (more than 51%) were in the productive age group (20-49 years); mean age was 38 years. In a retrospective study done in a TB unit in Mumbai, by Dholakia and Shah³ noted, that majority of the cases (67.6%) were in the age group 15-35 years with a mean age of 31 years. Udwardia and Moharil, Sharma *et al*^{4,5} reported that prevalence of younger age group among MDR-TB patients with the mean age of their study groups being 29.7 years and 33.25 years respectively. As most of our patients are from economically productive age group and some are the sole source of income for the family, the illness will impose an economic burden at all level in society and for the nation. Financial and nutritional support of these patients now being planned by government and NGO is a useful step in the direction.

Males constitute 73.2% (347 cases) of patients included in this study while females were 26.8% (127 cases) with male to female ratio is 2.73 to 1. However, studies by Udwardia *et al*⁴ reported female were predominant Our study almost coincide with Singh *et al*,⁶ Ibrahim *et al*,⁷ Songhua *et al*⁸ but did not coincide with Udwardia *et al*⁴ which is based on urban area and well educated class of society. Majority of our cases were male (73.2%) male predominance among MDR-TB cases has been also reported by other authors.⁹ Mean age of females (31.66 ± 12.63) was less than

that of males (40.33 ± 13.03), which is statistically significant (t=6.46, p=.000). Poulomi *et al*¹⁰ also reported that mean age of female (28.59 ± 12.50) was less than male (34.97 ± 12.84).

Ibrahim *et al*⁷ Males were significantly older than females [38.99 ± 12.01 versus 34.52 ± 14.36 years, (P < 0.05)]. The T-test is 6.46. The p-value is 0.000. The result is significant at p < 0.05. Conclude that young age group female more affected than male.

Most of patient belongs to rural area i.e. 61% of total and rest 31% resides in the urban area. Results were statistically significant (Z-score is 6.755 and p value is < 0.05). Study, coincide with Ibrahim *et al*⁷ which showed that 81.5% patients were lived in rural area and 18.5% of patients were in urban. K.Aid *et al*¹¹ also reported that most of the patients were from rural area.

Most of the patients were illiterate 71.5% followed by primary school 19.4%, higher secondary 7% and graduate 2.1%. Khurram *et al*¹² reported that 18 (60%) patients were illiterate in his study, Dholakia *et al*³ only 14.17% of patients are illiterate did not coincide with our study, because this is urban based study. Songhua, *et al*⁸ the education levels of the cases were as follows: 57 (58.2%) had finished elementary school or graduated from middle school and 17 (17.3%) had never been to school or did not finish elementary school.

Based on Kuppusswami scale¹³ most of the patients in our study 302 (63.7%), belongs to lower class followed by upper lower class 150 (31.6%) and lower middle 22 (4.5%) class respectively. Study coincide with Atre *et al*¹⁴ study shows most of patient come under unemployed and unskilled worker. The long duration of debilitation further pushes the family to economic hardship.

420 patients (88.6%) were undernourished with BMI less than 18.5 kg/m² in which 72.2% were severely undernourished had BMI less than 16 kg/m² followed by 8.6% with moderate thinness and 7.8% were mild thinness. A total of 11.2% of patients had normal BMI and only one patient was overweight with Mean Body Mass Index (BMI) of 14.9 kg/m², (range 5.7-25.4).

The mean BMI of present study was less than other studies because

Table 3: Frequency of MDR-TB cases with Diabetes in different study

Different study	Frequency	Percent
Dholakia <i>et al</i> ³	2/34	5.88
Singh <i>et al</i> ⁶	7/56	12.5
Kapadia <i>et al</i> ¹⁷	4/63	6.34
Poulomi <i>et al</i> ¹⁰	27/172	15.69
Ibrahim <i>et al</i> ⁷	30/200	15
K. Aid <i>et al</i> ¹¹	3/29	10.3
Marina <i>et al</i> ¹⁸	104/1970	5.8
Present study	39/474	8.2

this is rural based study and majority of our patients belonged to lower socioeconomic class with poor nutritional status (Chi-square =86.96 and p value =0.000).

Regarding the associated addiction, it was seen that 35.4% of the included patients were smokers. Ibrahim *et al*⁷ shows 42.5% of the studied patients were tobacco smokers with significantly higher prevalence among males [56.8% of males verses 1.9% of females were tobacco smokers (p< 0.001)]. Khurram *et al*¹² reported Eighteen (60%) patients were smokers, K.Aid *et al*¹¹ who reported 74% were smokers which might be because of small sample size i.e.29 in which males were predominant. In present study cough was most common symptoms seen in 455 (i.e. 96%) of patient. Other studies in India to be shows that most common symptoms was cough by Udhwadia *et al*,⁴ Mukherjee *et al*[10]etc.

The occupational profile of our patients revealed that a majority of them were labour 36.3% followed by farmer 31.2% and housewife 15.2%. Mukherjee *et al*¹⁰ reveals most common group was household worker. Wei-bin *et al* shows unskilled worker was most commonly affected followed by farmer

Study, by Atre *et al*¹⁴ also coincides with our study. Gupta *et al*¹⁶ observed a significantly higher prevalence of pulmonary TB in blue-collar then white-collar workers.

Our study showed that 39 out of 474 cases suffered from Diabetes and study coincides with studies done by Singh *et al*⁶ and K. Aid *et al*.¹¹ Patients were managed with insulin and in some cases oral hypoglycemic agent for the control of blood sugar. Suitable advices on diet and disease control were given. Kapadia *et al*¹⁷ did not reported any patient with thyroid abnormality, in our study out of 27 cases of hypothyroidism 15 were male and 12 were female (chi-square 6.37 and

p value 0.04 i.e. <0.05).

In our study 123 of 474 (25.9%) are suffering from COPD, Kapadia *et al*¹⁷ study shows COPD is common co-morbidities, Poulomi *et al* [10] reported most common co-morbidities amongst study group (17.44%).

Assessment based on radiological severity was done and we found that 219(46.2%) had moderate lesion, 139 (29.3%) mild, 107(22.6%) extensive lesion and 9(1.9%) normal which were cases of extra pulmonary tuberculosis, endobronchial TB, laryngeal TB. Our study showed that 312 (65.8%) of patient had non-cavitary lesion and 162 (34.2%) cases had cavitary lesion out of which 99 (20.9%) were unilateral and 63 (13.3%) are bilateral cavitary lesion. K.Aid *et al*¹¹ study do not coincide with our study shows 62 patients (52.1%) as minimal lesions, 53 patients (44.5%) as moderately advanced and 4 patients as far advanced lesions (3.4%). Ebru *et al*¹⁹ shows 51 (79.7%) patients had cavity and 34 (53.1%) patients had extensive disease whereas, 30 (46.9%) patients had limited disease. This study did not coincide with our study. Udhwadia *et al*⁴ shows, 33 (42.3%) patients had unilateral disease while 42 (53.8%) had bilateral and advanced disease. Findings of our study do not coincide with Fawzy *et al*,²⁰ where minimal lesions were the most common presentation among his patients whereas in our study moderate presentation was dominant and Abdelazim *et al* who revealed that 58% of patients had far advanced lesion in chest X-ray followed by minimal lesion in chest X-ray 26%. Dholakia *et al*³ shows a total of 20 of the 25 PTB cases had cavitary lesions, 13 single and 7 more than one cavity; 14 cavities were unilateral and 6 bilateral. A total of 20 of the 25 PTB cases had moderate to extensive lesions on x-rays.

Majority of cases belongs to defaulter that is 218(46%), 139(29.3%) were relapse followed by failure 68(14.3%) of previous anti-tuberculosis treatment. A study by ICMR shows most of patient belongs to failure followed by defaulter then relapse.

Study by Santha *et al*²¹ and Johnson *et al*²² coincide with our study reporting defaulter as most common group affected on basis of previous ATT taken by patient. We already know that our study is rural based so that

lack of education, low income and lack of knowledge about the disease are contributing factors to default. However, studies by Poulomi *et al*,¹⁰ Ebru *et al*,¹⁹ which shows a high relapse rate as predominant group.

Conclusion

MDR-TB is an important public health problem in India. The epidemiological picture of TB showed that males were predominant in our study however female were more affected in younger age group compared to male. More than 51% of the cases were in productive age group which affects the socioeconomic condition of family and society. More than 2/3 of patients were from lower socioeconomic group with low BMI. Therefore improving nutrition and immunity can play an important role. Majority of our patients were from rural area i.e. 61%. 19.2% cases were addicted to alcohol and 35.4% cases were addicted to smoking. Co-morbidities like COPD and Diabetes were seen in our study which were statistically significant and had impact on the treatment outcome of results. 6.8% of the cases had history of contact to cases of tuberculosis so all the contact must be screened up. Significant delay in initiation of MDR-TB regimen from date of DST was seen in 24.3% cases which is matter of concern Most of the patients had taken ATT from RNTCP in which Defaulter and relapse was major contributor of MDR-TB suspect in our study and patient taking ATT privately were less. Large number of cases which resides more than 150 kilometers from DRTB center initiated the drug after a gap of more than 19 days from the date of DST.

Recommendations

Maximum cases of MDR-TB were in productive age group and the disease affects the socio economic status of family, so financial support can play an important support in the management of these cases i.e. some provision for providing them household jobs. Maximum number of cases had Anemia and lower BMI so nutrition may be added as integral part of the programme. Provision of long term oxygen therapy (LTOT) be considered in cases with poor lung reserve and respiratory failure. Cases with unilateral cavity can be considered for thoracic surgeries. Delay in initiation of DRTB regimen was seen in large no

of cases (24.3%) which leads to spread of disease and affect the outcome of disease so active surveillance of cases is essential. All the close contact of the patient should be screened for TB as significant cases (6.8%) had contact history of TB in family. De-addiction programme should be introduced in national programme as large no of cases in study were addicted to smoking and alcohol. Identification, effective management of co-morbidities and regular monitoring is very important in the cases which may help in better outcome of the result.

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