

Treatment Outcome Analysis of Multi Drug Resistant Tuberculosis [MDR-TB] Patients at a District TB Centre: A Retrospective Cohort Study

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Received: 05-02-2023 / Revised: 14-03-2023 / Accepted: 20-04-2023

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Conflict of interest: Nil

Abstract

Introduction: MDR-TB is one of the most difficult challenges today the country is facing to achieve TB free status by 2025. For a better understanding of the local causal relationship, periodic assessment of various risk factors is needed to track public health responses. Accurate diagnosis with appropriate drug regimen as per the resistance pattern is the key to success in managing DR-TB.

Aim: In this context this study was conducted to assess the treatment outcomes and evaluate the treatment adherence among the MDR-TB cases.

Materials and Method: The study cohort was presumptive MDR-TB cases registered in the District TB Centre. Relevant clinical and laboratory data was extracted from PMDT records documented in the Nikshay Portal from January 2019 to December 2021. Approval from Institutional Ethics Committee and Office of the District TB Officer was obtained before the study procedures. The association between adherence to treatment as risk factor and treatment outcome were compared using Chi-square test / Fisher's exact test.

Results: Among the presumptive MDR-TB patients, 281 cases were pulmonary TB, 45.73% were on MDR Short Course TB Regimen. Among Pulmonary TB cases 42.70% had completed the given treatment regimen of which 16.37% were cured, 18.51% died & 13.17% were lost to follow up. 58% patients adhered to the given regimen but 42% were non adherent.

Conclusion: To conclude treatment outcome in terms of completion of the given course regimen or cure was favorable in our study cohort with no significant association between treatment adherence and outcome.

Keywords: MDR-TB, Short Course TB Regimen, treatment outcomes.

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Introduction

Drug resistant TB remains an important public health concern worldwide. World Health Organisation (WHO, 2019) published new consolidated guidelines on the drugs to be used for drug resistant TB which has substantially changed the approach to the treatment of MDR/XDR-TB. [1,2] The recently released National Health Profile (NHP) 2018 indicated that Odisha has notified 71,131 cases in 2017 posting a growth of over 62 % from previous year [3]. Moreover, the State has recorded 515 MDR and 20 XDR TB cases with the district Ganjam where the present study was conducted topping the list with 103 MDR cases. Programmatic Management of Drug Resistant TB Cases (PMDT) has been rolled out in the entire state since the year 2009. Also state government has initiated process to open Drug Resistant Tuberculosis (DRTB) centres at all District Headquarters Hospitals (DHHs) and step-up measures in order to achieve the goal of TB-free State by 2025 [4]. Factors contributing to poor treatment outcome of TB depend on the local settings of populations as well as the resistance pattern. Adherence to the long course of TB treatment is a complex, dynamic phenomenon with a wide range of factors impacting on treatment taking behaviour. [5] However, there is inadequate information available on adherence as a risk factor for poor outcomes in patients with MDR-TB in this region which is an important parameter in assessing adherence and success of DOTS Program. Therefore, a constant monitoring of the ongoing PMDT Services with most recent and comprehensive evidence is need of the hour. The present study was an attempt to cater some evidence to the ongoing National Program.

In the above context, the present study aims to examine the characteristics, treatment outcomes and risk factors associated with

poor treatment outcome among the patients diagnosed with MDR-TB and on different regimens with the following objectives:

1. To assess the treatment outcomes among MDR- TB patients.
2. To evaluate the treatment adherence among MDR- TB patients.
3. To determine the association between adherence and treatment outcomes.

Materials and Methods

This was a retrospective cohort study that was conducted at the District Tuberculosis Centre. Clinical and laboratory data of all presumptive MDR-TB cases were extracted from Programmatic management of drug resistant tuberculosis [PMDT] records documented in the Nikshay Portal from January 2019 to December 2021. A pretested, structured and validated Case Record Form was used for data collection following due approval from Institutional Ethics Committee and Office of the District TB Officer.

Data on socio-demographic variables, clinical and laboratory variables, adherence to the prescribed regimen and final treatment outcomes of the study cohort was compiled for evaluation. “Adherence” refers to the completeness with which a patient follows medical instructions; “non-adherence” has been measured as any patient belonging to either intensive or continuation phase who missed one week [7days] of treatment in a month [either consecutive or sporadic doses totaling a week] [6]. For analysis purposes “treatment outcome” has been categorized as ‘Cured’, ‘Treatment completed’, ‘Died’, ‘Failed-culture non conversion’, ‘Failed – culture reversion’, ‘Failed – Additional Drug resistance’ ‘Failed – Adverse Drug Reaction’ ‘Lost to follow up’, ‘Regimen change’ and ‘Not evaluated’ as per the PMDT treatment card [7]. Patients who had completed treatment but had less than 12

months post treatment follow up were excluded from the analysis.

Information collected on socio-demographic profile (age, gender, weight, past history of disease or drugs), MDR-TB regimen details was represented as frequencies and percentages. [8-11] The association between adherence to treatment as risk factor and treatment outcome were compared using Chi-square test / Fisher's exact test. P-value <0.05 was taken as indicative of statistically significant.

Results

Demographic characteristics: During the 2-month study period, data of 293 Presumptive MDR TB cases was retrieved of which 281 cases were pulmonary TB and 12 were extra pulmonary. Presumptive TB refers to a patient who presents with symptoms or signs suggestive of TB (previously known as a TB suspect). There were 201 (68.60%) males and 92 (31.39%) females among the study population. Nearly 63.14% patients were young adults in the age group of 15–44 years with a median age of 35 years (Table-1)

Table 1: Demographic Characteristics of MDR-TB cohort

| Variable | n (%) |
|--------------------------|-------------|
| Gender [N=293] | - |
| Male | 201 (68.60) |
| Female | 92 (31.39) |
| Age group (years) | |
| <15 | 5 (5.11) |
| 15-44 | 185 (63.14) |
| 45-64 | 87 (29.69) |
| ≥ 65 | 16 (5.46) |
| Marital Status | |
| Married | 81 |
| Unmarried | 19 |

Clinical characteristics of the study population revealed 97.95% were newly diagnosed MDR-TB patients and they didn't had any contact of MDR/RR TB or Follow up Smear +ve at end of Intensive Phase or were of Private Referral. (Table -2)

Table 2: Clinical Characteristics of MDR-TB cohort

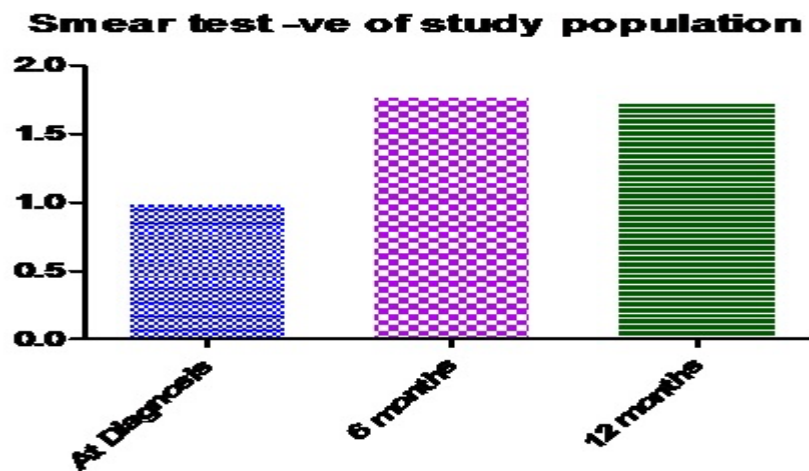
| Variable | n (%) |
|------------------------------|-------------|
| MDR-TB details | |
| New | 287 (97.95) |
| Previously Treated | 6 (2.04) |
| Presumptive MDR TB | |
| At Diagnosis | 293 (100) |
| Contact of MDR/RR TB | 0 |
| Follow up Sm+ve at end of IP | 0 |
| Private Referral | 0 |
| TB Site | |
| Pulmonary | 281 (95.90) |
| Extra pulmonary | 12 (4.09) |

Laboratory findings: At diagnosis, the rate of smear positivity and culture positivity in pulmonary cases was 54.09%, and 0.35% respectively whereas smear positivity in extra pulmonary cases was 66.66% with no culture positivity. Chest X-Ray revealed 32.38% Pulmonary TB cases had signs of lung involvement on first visit. (Table 3)

Table 3: Laboratory findings among patients with MDR-TB [N= 293] at Diagnosis

| Variable | Laboratory Test | +ve (%) | -ve (%) | Not Done/available (%) |
|----------------------------|-----------------|----------------|----------------|------------------------|
| Pulmonary [n= 281] | Smear | 152 (54.09) | 0 (0) | 129 (45.91) |
| | Culture | 1 (0.35) | 187 (66.54) | 93 (33.09) |
| | X-ray | 91 (32.38) | 181 (64.41) | 9(3.20) |
| Extra Pulmonary [n= 12] | Smear | 8 (66.66) | 0 (0) | 4 (33.33) |
| | Culture | 0 (0) | 9 (5) | 3 (25) |
| | X-ray | 4 (33.33) | 7 (58.33) | 1 (8.33) |

Significant number of patients had tested negative for smear test at 6 months and 12 months respectively compared to that at diagnosis. (Figure 2) but there was no such significant change in culture negativity among the study population at the end of 6months and 12 months. (Figure 1)



Kruskal-Wallis test"; P value <0.05

Figure: 1: Smear test-ve of study population

Treatment outcomes: 134 (45.73%) of the study population were on MDR short course TB regimen followed by 82 (27.99 %) were on MDR Conventional TB regimen. (Figure 4) Significant number (45.91%) of Pulmonary TB cases were on Short course MDR TB regimen compared to extra pulmonary cases. (Table-4) 42.70% and 25% of Pulmonary and extra pulmonary cases had completed the given treatment regimen. 16.37 % and 16.67 % of Pulmonary and extrapulmonary cases were found to be cured of MDR TB during the study period. But on analysis was no

significant difference between treatment outcomes of patients with pulmonary or extrapulmonary multidrug-resistant tuberculosis. 18.51% patients of pulmonary TB and 8.33% of extra pulmonary TB had died before completion of treatment. 13.17% patients of pulmonary TB and 25% of extra pulmonary TB had loss to follow up during the study period. (Table-5) Average duration for treatment outcome was 331 days for pulmonary TB cases and more 377 days for extra pulmonary cases.

Adherence: Patients who had completed treatment and cured were considered as adherent to treatment whereas patients with treatment failure, changed regimen or died were non-adherent to the prescribed

regimen. Though 42% patients were non-adherent to treatment, on analysis there was no significant association between Treatment outcome and Adherence to treatment from the present study. (Figure 2)

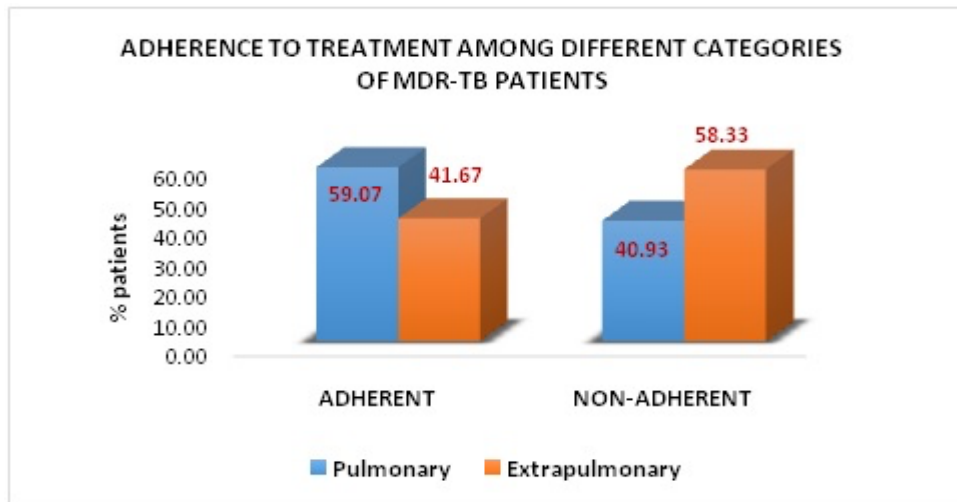


Figure 2: Adherence to treatment among different categories of MDR-TB patients
 Analysed by "Fisher's exact test"- 'p' value: 0.2473 [not significant]

Table 4: Treatment Regimen of patients with multidrug-resistant tuberculosis

| Variable | Pulmonary (%) N= 281 | Extra Pulmonary (%) N= 12 |
|------------------------|----------------------|---------------------------|
| Type of regimen | | |
| MDR CONVENTIONAL | 27.76 | 33.33 |
| MDR SHORT | 45.91* | 41.67 |
| XDR | 1.42 | 16.67 |
| MIXED H | 0.71 | 8.33 |
| MDR_FQ | 2.14 | - |
| MDR MOD KM | 0.71 | - |
| MDR_SLI_NEW | 1.07 | - |
| NEW | 0.36 | - |
| MIXED NEW | 0.36 | - |
| MDR_FQ_NEW | 3.91 | - |
| MDR MOD LFX | 0.36 | - |
| H MONO POLY | 14.23 | - |
| MDR SLI | 0.36 | - |
| MDR_XDR_FAIL_NEW | 0.71 | - |

* χ^2 test = P value = 0.0021 (<0.05)

Table 5: Treatment outcomes of patients with multidrug-resistant tuberculosis

| Variable | Pulmonary (%) N= 281 | Extra Pulmonary (%) N= 12 |
|---------------------------|----------------------|---------------------------|
| TREATMENT COMPLETE | 42.70 | 25.00 |
| CURED | 16.37 | 16.67 |
| TREATMENT REGIMEN CHANGED | 6.76 | 25.00 |
| DIED | 18.51 | 8.33 |
| TREATMENT FAILURE | 0.71 | 0.00 |
| LOST TO FOLLOW UP | 13.17 | 25.00 |
| NOT EVALUATED | 1.78 | 0.00 |

Analyzed by χ^2 test = P value = 0.2312 (>0.05) - not significant

Discussion

The present study which evaluated the Sociodemographic distribution showed that adult males and age group <15 years were the predominantly affected by MDR-TB. This finding was in assistance with studies done by Om Prakash Giri et.al, Dholakia YN, Java A, in other parts of the country. [12,13] Prevalence of MDR was 3.5% among new and 26.7 % among previously treated TB patients in India in a study conducted by Ayush Lohiya et, al [14]. However, our collected data reveals that most of the cases were newly diagnosed Presumptive TB cases corroborating with the findings of Kibriti Mehari et, al. [15] In our study though smear test was negative at 6 months and 12 months follow up, culture reports were not in accordance with the smear tests on follow up. A smear sample may test negative but still grow mycobacteria in culture media as low numbers of bacteria not visible in a microscopic examination may get multiplied and be detected. Pulmonary TB cases dominated in our study confirming the findings of studies by Sandgren A, Kruijshaar M E and Raveendran R, that MDR-TB was less frequent among extra pulmonary TB cases than among pulmonary TB cases [16].

The treatment of MDR/XDR-TB requires the use of bactericidal and bacteriostatic drugs for prolonged duration. Our study showed that 45.73% of the study population were on MDR short course TB regimen which has been the standard of care since

1993 and studies have interpreted that at times such short course treatment as a part of DOTS strategy can paradoxically exacerbate the problem [17]. Success of treatment depends not only on the choice of an effective regimen but also on the constant follow up, management of adverse events associated comorbidities, potential drug-drug interactions, and even the patient's adherence to the drug regimen. [18] As per study [19] conducted by Piparva KG et al, good cure rate (50.93%) was observed which was slightly higher (47.2%) and failure rate was reduced as compared to previous year reports among MDR-TB patients at a district TB Centre in Rajkot, India. Our study findings corroborate with the results observed by the above study. If a patient does not complete the full course of TB treatment, it may be because of the incorrect dose or duration of treatment, non-availability of the drugs for the ongoing regimen or poor quality of the drugs. In our study cohort, 42% showed completion of the given treatment regimen 16% cure rate and only 7% treatment failure which points towards favorable ongoing services at the District TB Centre. Several treatment outcome studies conducted in different parts of our country revealed variable results which might be variable demographic profile, co morbid conditions of the study population, laboratory settings, and strict supervision of the ongoing program at the district TB Centre. [20-21]

Conclusion

In the present study treatment outcome in terms of completion of the given course regimen or cure was favorable in our study cohort but no significant association between treatment adherence and outcome could be obtained. There was incomplete information on many of the enrolled patients as some of them died during the study period and many were loss to follow up. Death could have been due to other associated co- morbid conditions data on which was not collected. To ensure complete and accurate detection of drug-resistant TB an updated TB surveillance system at all levels of health care is the need of the hour. In resource poor settings like India there still exists a gap in patient education, identification of modes of recent transmission or in some settings an efficient laboratory facility to detect the emerging patterns of resistance. Maintaining systematic records of demographic profile including address, contact number is equally important. This helps the surveillance team to gather information about ongoing treatment regimen like, whether the patient is on the prescribed doses, follows the given duration, reports adverse events if any and adheres to treatment protocol. Further the health team will be able to carry out periodic treatment outcome analysis for all patients on MDR regimen in that particular centre and help in making policy decisions in long run.

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