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# A STUDY ON TREATMENT OUTCOME OF MULTI DRUG RESISTANT TUBERCULOSIS (MDR-TB) PATIENTS IN A DISTRICT IN SOUTH INDIA.

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**ABSTRACT**

**Background:** Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from HIV/AIDS. To control and eliminate TB, drug resistance is a public threat. Hence to assess the treatment outcome and adverse events this study was planned. **Objective:** To assess the knowledge, perception, level of satisfaction and the quality of life of beneficiaries utilising services of PMNDP.

**Materials and Methods:** A retrospective Cohort study was done on 658 Multidrug resistant TB cases registered in District TB centre, Kurnool and who have completed their treatment by July 2021 after consent. A semi structured questionnaire containing sociodemographic information, treatment outcome and history of adverse drug events was used to collect data by telephonic interview. Descriptive statistics and Chi square, correlation and regression was done in SPSS version 23.

**Results:** Out of 658 patients, 73.86% were male, 68.7% from rural areas, 50.3% on Shorter MDR, 60.2% have Rifampicin resistance. 66.4% were cured and 12.16% death rate was observed. Male, FLQ resistance and Rifampicin resistance are the statistically significant factors determining the unsuccessful treatment outcome in the study participants. Out of the 102 patients interviewed 83(81.37%) reported to have experienced one or more of the adverse events throughout their course of treatment.

**Conclusion:** To tackle high death rate and default rate and increase cure rate periodic counselling needed to motivate resistant cases to adhere and ensure compliance to the longer regimens.

**Keywords:** Multi drug, Outcome, Resistance, Tuberculosis, Treatment.

## INTRODUCTION

Tuberculosis is a curable and preventable communicable disease of public health importance. TB is a disease of poverty, and economic distress, vulnerability, marginalization, stigma and discrimination. Globally, an estimated 10.0 million (range, 8.9–11.0 million) people fell ill with TB in 2019, a number that has been declining very slowly in recent years. Drug-resistant TB continues to be a public health threat and an obstacle for effective TB control. Worldwide in 2019, close to half a million people developed Rifampicin-Resistant TB (RR-TB), of which 78% had multidrug-resistant TB (MDR-TB). The three countries with the largest share of the global burden were India (27%), China (14%) and the Russian Federation (8%). Globally in 2019, 3.3% of new TB cases and 17.7% of previously treated cases had MDR/RR-TB.[1]

India is the highest TB burden country in the world having an estimated incidence of 26.9 lakh cases in 2019 (WHO). In India, which constitutes one fourth of the global burden, a total of 66,359 Multi Drug Resistant/ Rifampicin Resistant (MDR/ RR) TB cases were notified and 56,500 (85%) of them were put on treatment, and an improvement of 7.6% seen over last year. Additionally, an injection free all-oral regimen was launched for all MDR/ RR TB patients who are not eligible for Shorter MDR TB regimen. Efforts to end TB in India through implementation of

the National Strategic Plan (2017-2025) has completed the first three years of implementation. During this period, the programme has seen tremendous success and is better poised today, to meet the ambitious goal pronounced by our Honourable Prime Minister at the Delhi End TB Summit in March 2018 of ending the TB epidemic by 2025 from the country, five years ahead of SDG goals for 2030. To accelerate momentum towards the ultimate goal, an appropriate and representative change in the name of the programme was imperative, and it was decided to rename the programme as "National Tuberculosis Elimination Program (NTEP)" from Revised National Tuberculosis Control Program (RNTCP).[2-4]

In light of the ambitious target of eliminating TB by 2025, the only hindrance is the enormous burden of Drug resistant TB. Treatment of MDR-TB requires the use of expensive and toxic second-line anti-tubercular drugs which are given for a longer duration. Adverse drug reactions (ADRs) of second-line antitubercular drugs affect compliance and thereby treatment outcome.[5]

In a retrospective record-based study (2009-2014) conducted in three major drug resistance TB treatment centers of Delhi by Sharma N etal (2020) on 2958 MDR-TB patients, showed that 1749(59.12%) were males, mean age was 30.56±13.5 years. Favourable treatment outcomes were reported in 1371 (53.28%) patients, showing a declining trend during the period of observation. On binomial logistic regression analysis, patients with age ≥35 yr, male sex and undernourishment (body mass index <18.5) at the time of treatment initiation had a significantly increased likelihood of unfavourable MDR-TB treatment outcome (P <0.001).[6]

The present study was planned to assess the treatment outcome and factors affecting it along with the adverse events occurring during the treatment. Thus will help us to understand the trends of treatment outcomes in MDR tuberculosis. The reasons behind the defaults will give us the area of focus and help us to observe the adverse events occurring. Hence we can evaluate whether our efforts are successfully leading us to the elimination of TB in India.

**Aims and Objectives**

1. To estimate the treatment outcome of multidrug resistant tuberculosis patients.
2. To assess the adverse events observed during treatment.
3. To compare between treatment success of different regimens.

## MATERIAL AND METHODS

This was an Observational, Retrospective Cohort study done on Multi Drug Resistant Tuberculosis patients registered in District Tuberculosis Centre (DTC), Kurnool during February 2021 – October 2021. All MDR TB patients registered in June 2018 and completed treatment by July, 2021 were included and those who died of natural causes other than disease were excluded. Out of 736 number of cases registered at DTC, Kurnool from June 2018, 658 number of cases have completed their treatment by July 2021. A semi-structured questionnaire containing socio-demographic information, treatment outcome in terms of Treatment success, death, default, failure, still on treatment, sputum conversion, culture conversion and adverse events.

**Definitions and Terminologies**

**Cured:** Treatment completed as recommended by the national policy without evidence of failure and three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

**Treatment completed:** Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

**Treatment failed:** Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of:

- Lack of conversion by the end of the intensive phase, or Bacteriological reversion in the continuation phase after conversion to negative, Evidence of additional acquired resistance to fluoroquinolones orsecond-line injectable drugs, or Adverse drug reactions (ADRs).

**Died:** A patient who dies for any reason during the course of treatment.

**Lost to follow-up:** A patient whose treatment was interrupted for 2 consecutive months or more.

**Not evaluated:** A patient for whom no treatment outcome is assigned. (This includes cases "transferred out" to another treatment unit and whose treatment outcome is unknown)

**Treatment success:** The sum of cured and treatment completed.

**Treatment unsuccessful:** Cases whose outcome was died, default, loss to follow up, transferred out are included.

**Cohort:** A group of patients where RR-TB has been diagnosed (including MDR-TB and XDR-TB), and who were started on a full course of a second-line MDR-TB drug regimen during a specified time period (e.g. the cohort of MDR-TB cases registered in the calendar year 2010). This group forms the denominator for calculating treatment outcomes. With the revised definitions, any patient found to have drug-resistant TB and placed on second-line treatment is removed from the drug-susceptible TB outcome cohort. This means that management of the basic management unit TB register and of the second-line TB treatment register needs to be coordinated to ensure proper accounting of the outcomes of treatment.

After the approval of Ethics Committee, and consent from District Tuberculosis Officer, data of the cases registered during 2018 - 2021 was obtained. Then

consent from the patients regarding participation in the study obtained over telephonic interview. All the data regarding socio-demographic information, treatment outcome and adverse events of all the MDR TB patients enrolled and treated with standard regimen for MDR-TB, as per RNTCP guidelines during the included period will be collected retrospectively. Data entered in Microsoft Excel 2007 and analysed using SPSS 23. Descriptive data is presented in percentages while inferential data with appropriate statistical tests like Chisquare, Correlation and Regression.

## RESULTS

Our study was started with the primary aim to find the treatment outcome in cohort of Multi-drug resistant tuberculosis patients registered in 2018 - 2020 at District Tuberculosis Centre, Kurnool. Out of 658 cases, cases registered in 2018, 2019, 2020 are 166(25.2%), 333(50.6%) and 159(24.2%) respectively.

The mean age of the patients registered was 42.01 ± 14.64 years. The majority of patients are in the age group of 30-45(n= 220, 33.49%), and male (n=486, 73.86 %), were from rural area (n=452, 68.7%) and only 6.84% are HIV positive.

Figure 1 shows the treatment regimen followed by the study participants. Majority of the participants (50.3%) were on Shorter MDR regimen among whom 73 cases were given Shorter with Amikacin/Kanamycin followed by H mono regimen for 36.32% cases.

Figure 2 shows the distribution of study participants according to the resistance to the MDR drugs. Majority of the cases were resistant to Rifampicin (396, 60.2%) followed by INH (294, 44.7%), FLQ (69, 10.5%) and SLI (7, 1.1%) respectively.

Figure 3 shows the treatment outcome trends in the study participants. Majority of our participants were cured (437, 66.41%) and 5.62%(n=37) have completed the treatment. Cured and treatment completed are regarded as Successful outcomes (n=474,72.03 %) and died, treatment failure, default/ lost to follow up, transferred out and switched to another treatment regimen are considered as unsuccessful outcomes (n=184,27.97 %).

Out of 27.97% of cases with unsuccessful outcome majority of participants died during the treatment (80, 12.16%) followed by 7%(n=46) cases switched to other regimens.

Table 1shows the association between age and treatment outcome. Pediatric age has maximum (83.3%) Cure rate followed by 15 - 30 yrs age group (71.2%). Least cure rate was observed in Senile (>60 yrs) age group and majority died (29.2%) too in them. Loss to follow up observed in 45 - 60 yrs (7.1%) and failure in <15 yrs (8.3%). In our cohort study, successful outcome of 72.03% is noted with the age group <15 years having highest frequency of 83.33% (n= 10 out of 12) followed by 15-30 (n=123 out of 163, 75.46 %); 45-60 (n=139 out of 197, 70.55 %); 30-45(n=154 out of 220, 70 %) and the least is noted in the age group of 60-80(n=38 out of 65, 58.46 %).A higher favourable outcome of 78.84% (n=135 out of 172) is noted in female patients than in male patients (n=339 out of 486, 69.75 %) and in Patients residing in rural areas (72.56 %) than in urban areas(70.87%), 71.11% among HIV positive patients(n=32out of 45) ,87.86 % (n= 210 out of 239) in patients put on H mono regimen. Statistically significant successful outcome was seen in younger age groups, female, newer regimens, INH resistance where as statistically significant unsuccessful outcome was observed in older age groups, male, RR, FLQ, Conventional treatment regimens. (Table 2) By Multivariate regression analysis, Male, FLQ resistance and Rifampicin resistance are the statistically significant factors determining the unsuccessful treatment outcome in the study participants. (Table 3)

Out of the 102 patients we have interviewed through telephone, 83(81.37%) reported to have experienced one or more of the adverse events through their course of treatment. Most of them reported to have experienced Nausea/Vomiting (n=64, 62.47 %) in the initial days of Intensive phase; Anorexia (n=33, 32.35%), gastritis (n=32, 31.37 %), abdominal pain (n=27, 26.47 %). The frequency of other adverse events experienced by patients were: Peripheral neuropathy (n=19, 18.62 %); arthralgia (n=18, 17.64 %); vertigo (n=14, 13.72 %); tinnitus (n=10, 9.8 %); deafness (n=8, 7.84 %); headache (n=10, 9.8%); visual disturbance (n=8, 7.84%) rash (n=6, 5.88%); constipation (n=3, 2.94%); hepatitis (n=2, 1.90%); diarrhoea (n=2, 1.96%); dizziness (n=1, 0.98%); skin pigmentation (n=2, 1.96%).

In our study, majority of the adverse events reported to have experienced by the patients during the period of treatment course are Gastro-intestinal (mainly Nausea/Vomiting, gastritis, abdominal pain, anorexia) followed by ototoxicity effects due to injectables. (Table 4) Table 5 shows the treatment outcomes in different drug regimens followed. Majority of the cases were cured in patients following H mono regimen (83.7%) followed by AOL H mono / Poly regimen (65.4%) whereas very few (39%) were cured by Conventional MDR regimen.

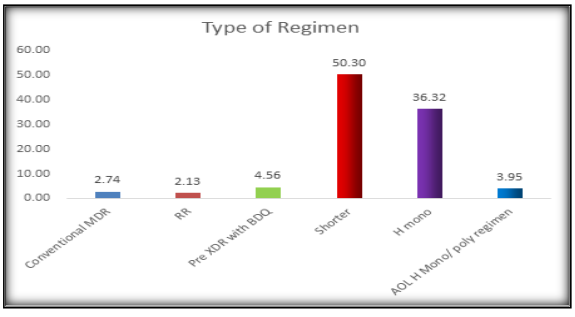


**Figure 1: Distribution of participants according to Treatment regimen**

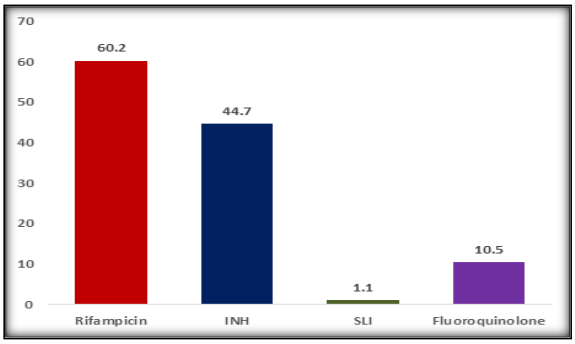


**Figure 2: Distribution of participants according to Drug resistance**

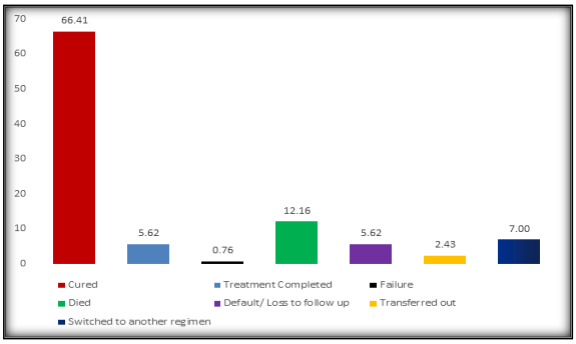


**Figure 3: Distribution of study participants according to Treatment outcome**

**Table 1: Association between Age and Treatment Outcome**

| Age | Outcome | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | Cured | Treatment completed | Loss to Follow up | Died | Treatment failure | Transferred out | Switched regimen | |
| <15 yrs | 10(83.3) | 0 | 0 | 0 | 1(8.3) | 0 | 1(8.3) | 12 |
| 15 - 30 yrs | 116(71.2) | 10(6.1) | 5(3.1) | 6(3.7) | 2(1.2) | 8(5) | 16(9.7) | 163 |
| 30 - 45 yrs | 143(64.7) | 14(6.3) | 14(6.3) | 28(12.7) | 0 | 5(2.3) | 17(7.7) | 221 |
| 45 - 60 yrs | 134(68) | 9(4.6) | 14(7.1) | 27(13.7) | 2(1) | 2(1) | 9(4.6) | 197 |
| > 60 yrs | 34(52.3) | 4(6.15) | 4(6.15) | 19(29.2) | 0 | 1(1.5) | 3(4.7) | 65 |
| Total | 437(66.4) | 37(5.6) | 37(5.6) | 80(12.2) | 5(0.75) | 16(2.4) | 46(7) | 658 |
| **Chi square test 57.6, *P 0.00013* Statistically significant*** | | | | | | | | |

**Table 2: Association between Socio-demography, drug resistance, regimen with Treatment Outcome**

| Factor | | No | Ssuccessful outcome (474, 72.03%) | | Unsuccessful outcome (184,27.97%) | | R | *P* |
|---|---|---|---|---|---|---|---|---|
| | | | no. | % | no. | % | | |
| Age group | <15 | 12 | 10 | 83.33 | 2 | 16.67 | 0.096 | 0.014* |
| | 15-30 | 163 | 126 | 77.3 | 37 | 22.7 | | |
| | 30-45 | 221 | 157 | 71 | 64 | 29 | | |
| | 45-60 | 197 | 143 | 72.6 | 54 | 27.4 | | |
| | 60-80 | 65 | 38 | 58.46 | 27 | 41.54 | | |
| Gender | Male | 486 | 339 | 69.75 | 147 | 30.25 | -0.086 | 0.028* |
| | Female | 172 | 135 | 78.48 | 37 | 21.55 | | |
| Residence | Rural | 452 | 328 | 72.56 | 124 | 27.44 | 0.017 | 0.654 |
| | Urban | 206 | 146 | 70.87 | 60 | 29.13 | | |
| HIV status | Positive | 45 | 33 | 71.11 | 12 | 28.89 | -0.008 | 0.841 |
| | Negative | 613 | 441 | 70.52 | 172 | 29.48 | | |
| Type of regimen | Conventional MDR | 18 | 8 | 44.44 | 10 | 55.56 | -0.202 | <0.001* |
| | RR | 14 | 9 | 64.28 | 5 | 35.72 | | |
| | Pre XDR with BDQ | 30 | 19 | 63.33 | 11 | 36.67 | | |
| | Shorter | 331 | 211 | 63.74 | 120 | 36.26 | | |
| | H mono | 239 | 210 | 87.86 | 29 | 12.14 | | |
| | AOL H Mono/ poly regimen | 26 | 17 | 65.38 | 9 | 34.62 | | |
| Type of resistance | RR | 396 | 249 | 62.87 | 147 | 37.13 | 0.251 | <0.001* |
| | INH | 294 | 241 | 82.00 | 53 | 18.00 | -0.199 | <0.001* |
| | SLI | 7 | 3 | 42.86 | 4 | 57.14 | 0.067 | 0.084 |
| | FLQ | 69 | 35 | 50.72 | 34 | 49.28 | 0.163 | <0.001* |

*Statistically significant on Pearson Correlation R

**Table 3: Multivariate Regression analysis for factors affecting Unsuccessful outcome**

| Parameters | B | Std. Error | Wald | df | Sig. | Exp(B) | 95% Confidence Interval for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower Bound | Upper Bound |
| Male | 0.652 | 0.225 | 8.402 | 1 | .004* | 1.92 | 1.235 | 2.985 |
| HIV status | 0.213 | 0.367 | 0.337 | 1 | 0.562 | 1.237 | 0.603 | 2.539 |
| FLQ resistance | -1.114 | 0.291 | 14.661 | 1 | .000* | 0.328 | 0.186 | 0.581 |
| Rifampicin resistance | -1.92 | 0.436 | 19.391 | 1 | .000* | 0.147 | 0.062 | 0.345 |
| INH resistance | -0.501 | 0.41 | 1.495 | 1 | 0.221 | 0.606 | 0.271 | 1.353 |
| SLIresistant | -0.204 | 0.853 | 0.057 | 1 | 0.811 | 0.816 | 0.153 | 4.336 |
| Residence | -0.159 | 0.2 | 0.627 | 1 | 0.428 | 0.853 | 0.576 | 1.264 |

**Table 4: Side effects reported in MDR Cases**

| ADVERSE EVENTS | NO. | % | ADVERSE EVENTS | NO. | % |
|---|---|---|---|---|---|
| **GASTROINTESTINAL** | | | **NEUROLOGICAL** | | |
| Nausea/Vomiting | 64 | 62.47 | Dizziness | 1 | 0.98 |
| Anorexia | 33 | 32.35 | Headache | 10 | 9.8 |
| Gastritis | 32 | 31.37 | Peripheral Neuropathy | 19 | 18.62 |
| Abdominal Pain | 27 | 26.47 | **PSYCHIATRIAC** | | |
| Diarrhoea | 2 | 1.96 | Psychosis | 4 | 3.92 |
| Constipation | 3 | 2.94 | Depression | 4 | 3.92 |
| Hepatitis | 2 | 1.96 | **OTHERS** | | |
| **OTOTOXICITY** | | | Arthralgia | 18 | 17.64 |
| Deafness | 8 | 7.84 | Visual Disturbance | 8 | 7.84 |
| Vertigo | 14 | 13.72 | Rash | 6 | 5.88 |
| Tinnitus | 10 | 9.8 | Skin Pigmentation | 2 | 1.96 |

**Table 5: Different regimens and the treatment outcomes**

| Treatment regimens | Outcome | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | Cured | Treatment completed | Loss to Follow up | Died | Treatment failure | Transfer out | Switched regimen | |
| Conventional MDR | 7(39) | 1(5.5) | 2(11.1) | 3(16.7) | 0 | 1(5.5) | 4(22.2) | 18 |
| RR | 8(57.2) | 1(7.1) | 2(14.3) | 2(14.3) | 0 | 0 | 1(7.1) | 14 |
| Pre XDR with BDQ | 17(56.6) | 2(6.7) | 1(3.3) | 8(26.7) | 2(6.7) | 0 | 0 | 30 |
| Shorter | 188(56.8) | 23(7) | 24(7.2) | 50(15.1) | 3(0.9) | 10(3) | 33(10) | 331 |
| H mono | 200(83.7) | 10(4.2) | 6(2.5) | 11(4.6) | 0 | 4(1.7) | 8(3.3) | 239 |
| AOL H Mono/ poly regimen | 17(65.4) | 0 | 2(7.7) | 6(23.1) | 0 | 1(3.9) | 0 | 26 |
| Total | 437 | 37 | 37 | 80 | 5 | 16 | 46 | 658 |
| Chi square test 89.97, *P <0.0001* Statistically significant* | | | | | | | | |
| *Correlation R -0.2, P <0.0001* Statistically significant* | | | | | | | | |

## DISCUSSION

In our retrospective cohort study done in the study setting of District Tuberculosis Centre, Kurnool, we have observed that mean age of our cohort is 42.01±14.64 years and majority of them belong to 30- 45 yrs age group. Similar studies done by Singh et.al, and others show the mean ages as 29.37±9.3, 34.83±12.19 and 30.56±13.5 years respectively. This may have occurred due to the heterogenicity in the chosen cohort in different regions.[3,6-8] In our study there is high incidence of MDR TB in male population which is about 73.86% . This finding is similar to the finding observed in the studies by Patel SV et.al (71.83%),[8] Alene et,al(71%),[9] and Singh A et.al(69.4%),[3] indicating that male population are at greater risk of getting MDR TB. 59.8% were only Male in the study done by Gupta N which is far less comparatively to our study.[7] In the present study 6.84% were HIV positive while only 3.8 % and 2.2% in study done by U Venkatesh in Uttar pradesh and N Gupta.[7,10]

Majority of the cases in our study were resistant to Rifampicin (396, 60.2%) followed by INH (294, 44.7%), FLQ (69, 10.5%) and SLI (7, 1.1%) respectively. In contrast to our study 78.9% resistance to FLQ and 21.7% to SLI which is far higher than our study findings.[7] In a study done by Ming etal in Taiwan, resistance to FLQ was 17.8%, SLI was 7.9% which was similar to our study findings, while 100% for Rifampicin, INH.[11]

Our study showed that at the end of the treatment, 66.4% were cured, 5.62% completed the treatment, 12.16% died before completing the treatment,5.62% were lost to follow up, 2.43% were transferred out to other districts/states, 7 % were switched to another regimen and 0.76% had treatment failure.

**A) Cure rate**

Similar findings were observed by Singh A et.al, whose treatment success rate is 74.5%,[3] Datta et al.[12] While lower treatment cure rate around 30 35% was observed in studies done by Patel SV et. Al, Alene et.al,[8,9] and studies in other countries.[13-14] Gupta. N et.al, Sharman et.al, and Nair et.al, cure

rates were 39%, 52%, and 50.95% respectively,[6,7,15] with highest success rate observed in study done by Ming et.al, whose success rate was 82.4%.[11]

Several studies including systematic reviews and meta-analysis revealed variable results, with treatment success rate for MDR-TB patients worldwide ranging from 21%- 83% with considerable unsuccessful treatment outcomes ranging from 29%- 39% (failure of relapse: 6%- 7.6%; treatment default: 12%- 15% and death rate: 11%- 13%).The variations in the treatment outcome may be due to heterogeneity in the socio-demographic profile of the cohort, frequency of associated co-morbid illnesses, cohort size, methodology, regimens used in that study period, definitions of treatment outcomes and regions.

The success rate was high in our cohort when compared with similar studies done in various settings and worldwide which is estimated to be about 56%. This may be attributable to the effective monitoring and regular counselling of patients by health care providers and patient co-operation and compliance in our district.

**B) Default rate**

The default rate in our study is observed to be 5.6% which is much less than that observed in the studies done by Patel SV et.al (21%), Alene et.al, (27%) Gupta.N.et.al (24%) and Nair et.al (13%).[7-9,15]

**C) Death rate**

The unfavourable outcome in our study is mainly due to death rate which contributed about 12.16% of the total outcome. Death rate in our study is similar to that in the study done by Ming et.al.in Taiwan and Nair et.al, where it is observed to be 12.1% and 11% respectively.[11,15] Higher death rates were observed in studies done Patel SV et.al, (30%); and Gupta et.al,(16%).[7,8] This high frequency of death rate in our study is may be due to high association of co-morbid conditions like Diabetes, Hypertension, HIV etc.,

**Loss to follow up**

Our study showed that 5.62% had loss to follow up which is a unsuccessful outcome and similar finding seen in other studies too.[11] In contrast to our finding other study showed high loss to follow up.[6]

**Age and treatment success**

Pediatric age has maximum (83.3%) Cure rate followed by 15 - 30 yrs age group (71.2%). Least cure rate was observed in Senile (>60 yrs) age group and majority died (29.2%) too in them. Study in Taiwan also showed that Patients who were aged ≥65 years were significantly less likely to have treatment success and more likely to die compared with patients who were <45 years old which was similar to our study.[11]

**Predictor of unsuccessful outcome**

Male, FLQ resistance and Rifampicin resistance are the statistically significant factors determining the unsuccessful treatment outcome in the study participants. Statistically significant successful outcome was seen in younger age groups, female, newer regimens, INH resistance whereas statistically significant unsuccessful outcome was observed in older age groups, male, RR, FLQ, Conventional treatment regimens. Other studies also predicted FLQ resistance as an independent predictor of unsuccessful/unfavourable outcome.[9] Similar to our study in a study by Ming etal too has shown that Age, FLQ , SLI resistance has shown statistically significant association with treatment success.[11]

**Adverse events**

In our study it was observed that 81.37% of the patients we have interviewed had any of the adverse events during their course of treatment of which gastro-intestinal (mainly Nausea/Vomiting, Gastritis, Anorexia and Abdominal pain) are experienced by majority of patients followed by Ototoxicity and Neurological adverse events. In studies of Sharma N et.al, psychological adverse events are reported more followed by gastro-intestinal and ototoxicity events.[6] In studies of Singh A et.al, and Nair et.al, similar findings of more gastro-intestinal followed by ototoxicity and Psychological were observed as major adverse events experienced by patients during the course of treatment.[3,15]

Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. Only about one in three people with drug resistant TB accessed treatment in 2020. But India is top in the number of retreatment cases that became MDR cases. So we need to carefully monitor and analyze the treatment outcome of the cases which involves intensive dedication, motivation and cost to do, so as to achieve our goal of eliminating TB in India.[16]

Strengths and Weaknesses:

The strength of our study was the large sample size, thus enabling to generalize the results and is highly representative. As we covered three years outcome, pre and post COVID along with Conventional and newer regimens this study has given wide scope to evaluate the programme effectively.

As our study is a retrospective Cohort study, recall bias was faced. Few patients expired too by the time of our study though successfully completed the treatment thus few sociodemographic and adverse events information were unable to gather, Being a retrospective study and with very stipulated study period journey of the patient was not extensively recorded.

**Future implications**

A prospective cohort study focusing on the risks factors for the unfavourable outcomes in the MDR cases and especially deaths and defaults would be more promising. A detailed study on co- morbidities including COVID, affecting treatment outcome, utilisation of heath benefits and adverse events is needed.

## CONCLUSION

In this retrospective cohort study we observed that the majority of patients who are registered in our DTC are adult population (30-45yrs), male, rural area indicating that they are at higher risk of developing MDR-TB. Majority of patients in our study are kept on Shorter regimen for treatment and were resistant to Rifampicin followed by INH, FLQ and SLI. Majority of the patients were cured and have completed the treatment. So the successful outcome is more but Death rate is also more. Pediatric agehad maximum cure rate while the senile age group had more death rate and less cure rate. Younger age, Female, INH resistance and patients on H mono regimen (newer regimens) are favourable treatment predictors as they had higher statistically significant successful treatment outcome. Majority of the adverse events experienced by the patients were due to Gastro-intestinal disturbances followed by Ototoxicity and psychological adverse events.

**Recommendations**

High death rate and default are major hindrance in achieving a good cure rate. To tackle it and increase cure rate periodic counselling needed to motivate resistant cases to adhere and ensure compliance to the longer regimens. Early diagnosis of MDR-TB and adequate clinical monitoring during treatment is essential to prevent undesired outcomes. Encourage community based projects to gather extensive information on the risk factors of multi drug resistance and factors affecting unfavourable outcome to take further action. Identifying adverse drug reactions, other co-morbidities and their optimal management can successfully contribute to eliminate Tuberculosis and achieve SDG by 2025, five years ahead of 2030 goal.

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**Conflict of interest:**

None declared**.**

## REFERENCES

1. Global tuberculosis report 2020. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. Available at http://apps.who.int/iris Last accessed on 25.2.2021.
2. India TB report 2020. National Tuberculosis Elimination Programme. Annual report. Central TB Division, Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi. March 2020. Available at http://www.tbcindia.gov.in. Last accessed on 25.2.2021.
3. Singh A, Prasad R, Kushwaha RA, Srivastava R, Giridhar BH, Balasubramanian V, et al. Treatment outcome of multidrug-resistant tuberculosis with modified DOTS-plus strategy: A 2 years' experience. Lung India 2019;36(5):384-92.
4. Chatterjee S, Poonawala H, Jain Y. Drug resistant tuberculosis: Is India ready for the challenge? BMJ Glob Health 2018;3: e000971.
5. Dela AI, Tank NKD, Singh AP, Piparva KG. Adverse drug reactions and treatment outcome analysis of DOTS-plus therapy of MDR-TB patients at district tuberculosis centre: A four-year retrospective study. Lung India. 2017;34(6):522-526. doi:10.4103/0970-2113.217569.
6. Sharma N, Khanna A, Chandra S, Basu S, Chopra KK, Singla N, Babbar N, Kohli C. Trends & treatment outcomes of multidrug-resistant tuberculosis in Delhi, India (2009-2014): A retrospective record-based study. Indian J Med Res. 2020 Jun;151(6):598-603. doi: 10.4103/ijmr.IJMR_1048_18. PMID: 32719234; PMCID: PMC7602924.
7. Gupta N, Jorwal P. Treatment outcomes associated with multidrug resistant tuberculosis. J Global Infect Dis 2018; 10:125-8.
8. Patel SV, Nimavat KB, Alpesh PB, Shukla LK, Shringarpure KS, Mehta KG, Joshi CC. Treatment outcome among cases of multidrug-resistant tuberculosis (MDR TB) in Western India: A prospective study. J Infect Public Health. 2016 Jul-Aug;9(4):478-84. doi: 10.1016/j.jiph.2015.11.011. Epub 2015 Dec 24. PMID: 26724262.
9. Alene KA, Yi H, Viney K, McBryde ES, Yang K, Bai L, Gray DJ, Clements ACA, Xu Z. Treatment outcomes of patients with multidrug-resistant and extensively drug resistant tuberculosis in Hunan Province, China. BMC Infect Dis. 2017 Aug 16;17(1):573. doi: 10.1186/s12879-017-2662-8. PMID: 28814276; PMCID: PMC5559784.
10. Venkatesh U, Srivastava DK, Srivastava AK, Tiwari HC. Epidemiological profile of multidrug-resistant tuberculosis patients in Gorakhpur Division, Uttar Pradesh, India. J Family Med Prim Care. 2018;7(3):589-595.
11. Yu MC, Chiang CY, Lee JJ, Chien ST, Lin CJ, Lee SW, Lin CB, Yang WT, Wu YH, Huang YW. Treatment Outcomes of Multidrug-Resistant Tuberculosis in Taiwan: Tackling Loss to Follow-up. Clin Infect Dis. 2018 Jul 2;67(2):202-210. doi: 10.1093/cid/ciy066. PMID: 29394358; PMCID: PMC6030934.
12. Datta BS, Hassan G, Kadri SM, Qureshi W, Kamili MA, Singh H, et al. Multidrug-resistant and extensively drug resistant tuberculosis in Kashmir, India. J Infect Dev Ctries 2010;4(1):19—23.
13. Calver AD, Falmer AA, Murray M, Strauss OJ, Streicher EM, Hanekom M, et al. Emergence of increased resistance and extensively drug-resistant tuberculosis despite treatment adherence, South Africa. Emerg Infect Dis 2010;16(2):264—71.
14. Jeon DS, Shin DO, Park SK, Seo JE, Seo HS, Cho YS, et al. Treatment outcome and mortality among patients with multidrug-resistant tuberculosis in tuberculosis hospitals of the public sector. J Korean Med Sci 2011;26(1):33—41.
15. D. Nair, B. Velayutham, T. Kannan, J. P. Tripathy, A. D. Harries, M. Natrajan, S. Swaminathan. Predictors of unfavourable treatment outcome in patients with multidrug-resistant tuberculosis in India.PHA 2017; 7(1): 32–38.
16. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO. Available at www.who.int /tb / data. Last accessed on 28.10.2021.