e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 57-61

Original Research Article

Study of Drug Susceptibility, Resistance Patterns and Mutations, in Patients Diagnosed with Drug Resistant Tuberculosis in a Tertiary Care Centre Aurangabad, Maharashtra

Akash Bhardwaj[1], Anupam Prakash[2], Sunil Jadhav[3], Ashish S. Deshmukh[4], Hafiz Deshmukh[5], Shivprasad Kasat[6]

[1]Senior Resident, Pulmonary Medicine, Kurma Sanskriti Medical College and Hospital, Jehanabad, Bihar, India

[2]Junior Resident, Department of Respiratory Medicine, MGM Medical College and Hospital, Chh. Sambhajinager, Maharashtra, India

[3]Professor, Department of Respiratory Medicine, MGM Medical College and Hospital, Chh. Sambhajinager, Maharashtra, India

[4]Professor and Head, Department of Respiratory Medicine, MGM Medical College and Hospital, Chh. Sambhajinager, Maharashtra, India

[5]Associate Professor, Department of Respiratory Medicine, MGM Medical College and Hospital, Chh. Sambhajinager, Maharashtra, India

[6]Assistant Professor, Department of Respiratory Medicine, MGM Medical College and Hospital, Chh. Sambhajinager, Maharashtra, India

Received: 01-01-2026 / Revised: 15-02-2026 / Accepted: 21-03-2026

Corresponding author: Dr. Anupam Prakash

Conflict of interest: Nil

Abstract

Background: Drug-resistant tuberculosis (DR-TB) remains a major public health challenge, particularly in high-burden countries like India. Resistance to first-line anti-tubercular drugs complicates treatment and contributes to increased morbidity and mortality. Understanding drug susceptibility patterns and associated genetic mutations is essential for effective management and control of DR-TB.

Methods: A prospective observational study was conducted over a period of two years at MGM Medical College and Hospital, Aurangabad, Maharashtra. A total of 82 patients diagnosed with drug-resistant tuberculosis were enrolled, of which 80 patients with complete data were included in the final analysis. Drug susceptibility testing and mutation analysis were performed for first- and second-line anti-tubercular drugs. Data were analyzed using R software (version 4.3.2). Demographic characteristics, clinical profile, resistance patterns, and associated mutations were assessed.

Results: Among the 80 patients studied, the majority belonged to the 10–30 years age group (51.25%), and males constituted 63.75% of cases. Most patients (93.75%) had no prior history of tuberculosis. Pulmonary tuberculosis was the predominant presentation (83.75%), while extrapulmonary disease accounted for 16.25%. Isoniazid resistance was observed in 96.25% of patients, with mutations in katG (79.22%) and inhA (28.57%). Rifampicin resistance associated with rpoB mutation was identified in 38.75% of patients. Fluoroquinolone resistance was seen in 23.75% of cases, predominantly involving gyrA mutation (100%) and gyrB mutation (63.16%). Resistance to second-line injectable drugs was identified in 5% of patients, associated with rrs and **eis** mutations. Pyrazinamide resistance was rare (1.25%).

Conclusion: The study demonstrates a high burden of drug-resistant tuberculosis among young adults, with significant resistance to first-line drugs and identifiable genetic mutations. Routine drug susceptibility testing and molecular diagnostics are essential for early detection and effective management of DR-TB.

Keywords: Drug-resistant tuberculosis, Drug susceptibility testing, Isoniazid resistance, Rifampicin resistance, Gene mutations, MDR-TB, Aurangabad, India.

DOI: 10.25258/ijcpr.18.4.9

Introduction

Multidrug-resistant tuberculosis (MDR-TB), characterized by resistance to at least rifampicin (RIF) and isoniazid (INH), remains a significant threat universally [1]. An estimated 10.6 million people developed TB, with approximately 410,000 cases of MDR/RR-TB reported. The prevalence of drug-resistant TB varies geographically, with countries like India, China and the Russian Federation bearing the highest burden. Worldwide, an estimated 3.3% of new TB cases and 20% of previously treated cases have MDR-TB, a level that has remained relatively stable in recent years. In 2014, an estimated 190,000 people died from MDR-TB, and only 50% of MDR-TB patients worldwide were successfully treated.In India, in 2015, MDR-TB was observed in 2.2% of newly notified pulmonary TB patients and 15% of retreatment cases [2,3]. In India in 2015, 339,478 drugresistant TB suspects were tested, and 28,876 MDR-TB patients were detected. In Maharashtra alone, 45,829 drug-resistant TB suspects were tested, and 5,302 MDR-TB patients were identified. In Western Maharashtra, 521 cases were registered for Category IV treatment. Though the incidence rate of Tuberculosis has been falling with a global cumulative reduction of 9%, we have failed to touch the 2020 milestone of WHO‘s End TB Strategy and are quiet far from the 2025 milestone of 50% reduction in TB incidence rate. Drug resistant TB remains one of the major road block in achieving these milestones [4].

India also has one of the largest burden of multi-drug resistant (MDR-) TB and extensively drug resistant (XDR-) TB, many of which are undetected and transmit the disease continuously. According to many studies, multi drug resistant TB cases in India is set to increase more than 12.4 percent by 2040, India already has the highest burden of the disease. Cases of XDR-TB is likely to rise by 9 percent in same period of duration. [5] With better management of TB programs, the emergence of resistance can be prevented and prevalance of MDR-TB can be reduced. These strains, such as multidrug resistant/ RIF resistant TB (MDR/RR-TB) and extensively drug-resistant TB (XDR-TB), have emerged and spread, complicating efforts to control and eliminate the disease worldwide [2]. MDR/RR-TB is resistant to two key anti-TB drugs, isoniazid (INH) and rifampicin (RIF), while XDR-TB, a subset of MDR/RR-TB, is also resistant to fluoroquinolones (FLQs) and at least one of bedaquiline or linezolid [2]. Rifampicin Resistance (RR) is a key indicator of multidrug-resistant tuberculosis, since >90 % resistance observed are also isoniazid resistant. Drug-resistant TB strains have a significant impact on both individuals and society, as they are associated with higher mortality rates compared to susceptible TB strains. The treatment outcomes for drug-resistant TB (DR-TB) are often poor due to limited access to and effectiveness of second-line anti-TB medications, long treatment durations, and higher drug toxicity [6]. Approximately 10% to 30% of MDR-TB cases result in treatment failure and death due to prolonged, limited, and expensive treatment options. Given the significant numbers mentioned earlier, it is crucial to perform drug susceptibility testing (DST) for the proper management of drug-resistant cases. Culture-based DST methods, which involve the inhibition of organisms in a culture medium containing anti-tubercular agents, can take weeks or even months to complete. During this time, undiagnosed drug-resistant cases can continue to spread the resistance [7]. Another ground breaking fully automated molecular assay is the Cepheid GeneXpert MTB/RIF, which utilizes real-time polymerase chain reaction technology to simultaneously detect Mycobacterium tuberculosis (MTB) and rifampicin-resistant mutations in the rpoB gene. In India, there is a focus on the rapid detection of multidrug-resistant tuberculosis (MDR-TB) in all suspected cases using line probe assays (LPAs) as part of the programmatic management of drug-resistant tuberculosis (PMDT) nationwide. Patients are referred to designated Reference Laboratories for MDR-TB diagnosis [8]. Primary health-care providers are essential in national and global TB control efforts. Primary care physicians, in particular, are key in early identification of MDR-TB suspects. Hence, raising awareness among them about the profile and characteristics of MDR-TB cases is crucial. This knowledge can help them recognize potential cases early, leading to prompt referral and prevention of further progression and spread within the community. Understanding the scope and associated comorbidities of drug-resistant TB is paramount [9]. Therefore, the primary objective of this study is to assess drug susceptibility, resistance patterns and mutations in patients diagnosed with drug-resistant tuberculosis at a tertiary care center in Aurangabad, Maharashtra.

Material and Methods:

Study Design: It is prospective and Observational study.

Study Duration: 2 years.

Study Area: This study was carried out at MGM Medical College & Hospital, Aurangabad.

Subjects: All patients diagnosed as Drug Resistant Tuberculosis (Pulmonary and Extrapulmonary) was investigated for their drug susceptibility and resistance pattern.

Sample size: 82.

Inclusion Criteria: All the diagnosed cases of microbiologically confirmed Drug Resistant Tuberculosis in the hospital.

Data cleaning: Whole data is checked for missing values, incorrect entries. Total 82 patients involve in the study. Amongst them 2 patient showing missing data for 5 to 6 places so we remove them from analysis, So total 80 data is used for statistical analysis. For Analysis R software version 4.3.2 is used.

Observation and Results:

Table 1: Demographic profile of patients diagnosed with drug resistant tuberculosis

Demographic profile		Number (Percentage)
Age-group [In years]	**10-30**	41 (51.25%)
	30-60	35 (43.75%)
	60-90	4 (5.00%)
Gender	**Male**	51 (63.75%)
	Female	29 (36.25%)

Out off 80 patients, majority of 41 (51.25%) patients are from age group 10-30 years, followed by 35 (43.75%) patients are from age group 30-60 years. Maximum 51 (63.75%) male patients and 29 (36.25%) female patients diagnosed with drug resistant tuberculosis are involved in the study.

Table 2: History of Tuberculosis in the past of patients diagnosed with drug resistant tuberculosis

History of Tuberculosis	Number (Percentage)
Yes	5 (6.25%)
No	75 (93.75%)
Total	**80(100%)**

75 (93.75%) patients have no history of tuberculosis in the past and 5 (6.25%) patients suffered from tuberculosis before.

Table 3: Site of disease (Pulmonary, Extrapulmonary) of patients diagnosed with drug resistant tuberculosis.

Site of disease	Number (Percentage)
Extrapulmonary(eptb)	13 (16.25%)
Pulmonary(ptb)	67 (83.75%)
Total	**80(100%)**

67 (83.75%) patients are from pulmonary tuberculosis, 13(16.25%) patients are from extra pulmonary tuberculosis.

Table 4: Final Diagnosis of patients diagnosed with drug resistant tuberculosis

Final Diagnosis	Number (Percentage)
DREPTB	10 (12.50%)
DREPTB(PL)	4 (5.00%
DRPTB	66 (82.50%)
Total	**80(100%)**

66 (82.50%) patients are from drug resistant pulmonary tuberculosis followed by 10 (12.50%) are from drug resistant extra pulmonary tuberculosis.

Table 5: Distribution of Resistant with frequency of its mutations

Resistant of its mutations		Number (Percentage)
Isoniazid resistant [n=]77	InhA	22 (28.57%)
	Kat G	61 (79.22%)
	INH resistance +InhA +Kat G	7 (9.09%)
Rifampicin resistance [n= 31]	rpoB	31 (100.00%)
	Isoniazid+Rifampicin	2 (6.45%)
Fluoroquinolones Resistance [n=19]	Gyr A	19 (100.00%)
	Gyr B	12 (63.16%)
	Q Resistance+ Gyr A+ Gyr B	12 (63.16%)
Second Line Injectable Drugs(SLID) resistance [n=4]	rrs mutation	4 (100.00%)
	eis mutation	4 (100.00%)
	SLID resistance + rrs mutation + eis mutation	4 (100.00%)
Pyrazinamide resistanc [n=1]		1(1.25%)

Patients with mutation Kat G (79.22%) and InhA (28.57%). 9.09% patients with INH resistance with both mutations InhA +kat G has present. 100% patients are showing rpoB resistance. 6.45%

patients were resistant to Isoniazid+Rifampicin. 23.75% patients are showing FQ resistance and 100% mutation gyrA present. Mutation gyrB is present in 63.16% patients. 63.16 % patients are FQ resistance with both the mutation present. 5 % patients are showing Second Line Injectable Drugs resistance present. Rss mutation and eis mutation is also showing same percentage 100%. Slid resistance with its both mutations together also showing same percentage 100%.

From total patient, 98.75% were showed Pyrazinamide resistance absent whereas only 1.25% shows Pyrazinamide resistance present

Discussion

The study includes 80 patients diagnosed with drug-resistant tuberculosis. The majority of patients fall within the 10-30 years age group, with only 5% in the 60-90 years age group. Of these patients, 63.75% are male and 36.25% are female. Regarding their medical history, 93.75% have no prior history of tuberculosis, while 6.25% have had tuberculosis before. In this study, among the patients, 83.75% have pulmonary tuberculosis and 16.25% have extrapulmonary tuberculosis. Specifically, 82.50% have drug-resistant pulmonary tuberculosis, and 12.50% have drug-resistant extrapulmonary tuberculosis. INH resistance is present in 96.25% of patients, with 79.22% having the Kat G mutation and 28.57% having the InhA mutation; 9.09% have both InhA and Kat G mutations. Similar outcomes have been shown in previous studies [10,11] : isoniazid resistance is primarily caused by genetic alterations in the katG gene (50–95%) and the inhA promoter region (20–35%), with variations depending on geographical distribution. Mutations in the katG gene prevent INH activation, while mutations in the inhA promoter region lead to over expression of the inhA gene, which encodes the target enzyme for INH [10,11].

In this study, prominent genetic changes associated with INH resistance include katG and inhA (44, 60). Similarly, in the study done by, Maurya, A et al.[12] reported amongst INHresistant isolates, mutations in the katG was most frequent (95%), while no inhA gene mutation was observed. In agreement with our findings, a recent multicenter study in Ethiopia reported a prevalence of 91.8% for katG mutation and a meta-analysis study that examined INH conferring gene mutations noted a prevalence of 95.8% for katG mutation [12]. Rifampin (RIF) is an important first-line anti-TB drug, and rifampin resistance (RIF-R) is a key factor in formulating treatment regimen and evaluating the prognosis of TB. Compared with other drugs resistance, the RIF-R mechanism of Mycobacterium tuberculosis (M. tuberculosis) is one of the clearest, which is mainly caused by RIF resistance-related mutations in the rpoB gene. This provides a convenient condition for developing rapid detection methods, and also an ideal object for studying the general drug resistance mechanisms of M. tuberculosis. previous review focuses on the mechanisms that influence the RIF resistance of M. tuberculosis and related detection methods. Besides the mutations in rpoB, M. tuberculosis can decrease the amount of drugs entering the cells, enhance the drugs efflux, and be heterogeneous RIF susceptibility to resist drug pressure. On the basis of outcomes of researches, many genes participate in influencing the susceptibility to RIF, which indicates the phenomenon of M. tuberculosis drug resistance is very complex. [10]

In this study, Rifampicin resistance is seen in 38.75% of patients, with 6.45% also showing isoniazid resistance. Additionally, 23.75% of patients have FQ resistance, with 100% having the gyrA mutation and 63.16% having the gyrB mutation; 63.16% show resistance with both mutations present. Slid resistance is found in 5% of patients, with RSS and EIS mutations both showing 100% prevalence. Slid resistance with both mutations together also shows a 100% prevalence. A study by Arora et al. [13] reported that among the isolates tested, 969 (19.7%) were sensitive to all four first-line drugs, while 3941 (80.3%) showed resistance to one or more drugs. Of these, 3041 (61.9%) isolates were resistant to both rifampicin (RIF) and isoniazid (INH), indicating multidrug resistance. Monodrug resistance was observed in 94 (1.9%) isolates to streptomycin (SM) and 8 (0.16%) to ethambutol (EMB). Specifically, 22 (0.44%) isolates exhibited RIF resistance without INH resistance, and 776 isolates were sensitive to RIF but resistant to INH. Among the latter group, 367 (7.47%) isolates showed INH resistance with resistance to EMB and/or SM, while 409 (8.3%) isolates were resistant to INH alone. The study also analyzed results from line probe assays conducted between 2012 and 2015, revealing an INH resistance rate of 9.32% (1462/15,676) among all isolates with valid results, with over 75% of these isolates carrying mutations in the katG gene associated with high-level resistance. These findings are relevant to our study.

In present study, 98.75% of the patients showed no resistance to pyrazinamide (PZA), while only 1.25% exhibited PZA resistance. These results align with the findings of Alehegn et al. [14], who reported that out of 308 patient samples from presumptive extra-pulmonary cases, 44 (14.3%) tested positive for MTBC. Among these, 25% of the 44 MTBC isolates displayed resistance to at least one of the five first-line drugs tested, with isoniazid (INH) and PZA resistance being the most common at 13.6% and 11.4%, respectively.

Additionally, two isolates (4.5%) were identified as MDR-TB. Using the Geno Type MTBDR plus assay, 5 out of 44 isolates (11.4%) showed mutations in the katG gene and 2 isolates (4.5%) showed mutations in the rpoB gene.

Conclusion

The study highlights a high prevalence of drug-resistant tuberculosis in younger adults, predominantly male, with no prior history of tuberculosis. Pulmonary tuberculosis is the most common form, with significant resistance to first-line drugs like Isoniazid and Rifampicin.

Resistance to fluoroquinolones and second-line injectable drugs, though less frequent, shows a high mutation rate. Based on my study all microbiologically diagnosed cases of tuberculosis should be investigated for resistance by DST irrespective of previous history of tuberculosis. .Pyrazinamide resistance is rare. These findings underscore the importance of targeted treatment strategies and ongoing surveillance to manage and control drug-resistant tuberculosis effectively.

Ethics Approval and Consent to Participate: Ethical approval for conducting the study was obtained from MGM Medical College and Hospital, Chh. Smabhajinagar, Maharashtra. Written informed consent was obtained from the patients for their participation in the study.

Consent: The participant's informed consent has been acquired for the publication of the case details, clinical images, and relevant medical information. All efforts have been made to ensure patients confidentiality, and any identifying information has been appropriately anonymized.

References:

1. World Health Organization. Global tuberculosis report: WHO Report 2016 WHO/HTM/ TB Geneva, Switzerland; 2016. Available at: http: www.who.int/ tb/publications/global report/11.
2. WHO. Global tuberculosis report. World Health Organization 2023. (2023). Available at: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/ global-tuberculosisreport-2023.
3. Government of India, TB INDIA 2015, RNTCP Annual Status Report, Ministry of Health and Family Welfare, New Delhi. 2015.
4. https://www.arogya.maharashtra.gov.in .
5. WHO. Global tuberculosis report 2020. Geneva: World Health Organization. License: CC BYNC-SA 3.0 IGO (2020).
6. Dookie N, Rambaran S, Padayatchi N, Mahomed S, Naidoo K. Evolution of drug resistance in Mycobacterium tuberculosis: a review on the molecular determinants of resistance and implications for personalized care. J Antimicrob Chemother. 2018; 73:1138–51.
7. World Health Organization. Policy statement; Molecular line probe assays for rapid screening of patients at risk of multi drug resistant tuberculosis (MDRTB): WHO Report 2008 WHO/ HTM/ TB Geneva, Switzerland; 2008. Available at: http:www.who.int/tb/features_archive/policy_statement.
8. Expert Group Meeting Report, World Health Organization. Using the Xpert MTB/RIF assay to detect pulmonary and extra-pulmonary tuberculosis and rifampicin resistance in adults and children, World Health Organization; 2013
9. More SW, Parande MA, Kamble SW, Kamble MS. Profile of drug-resistant tuberculosis in Western Maharashtra. J Family Med Prim Care. 2017 ;6(1):29-33
10. Conradie F., Bagdasaryan T.R., Borisov S., Howell P., Mikiashvili L., Ngubane N., Samoilova A., Skornykova S., Tudor E., Variava E., et al. Bedaquiline-Pretomanid-Linezolid Regimens for Drug-Resistant Tuberculosis. N. Engl. J. Med. 2022;387:810–823. 95.
11. Xu, G, Liu, H, Jia, X, Wang, X, and Xu, P. Mechanisms and detection methods of Mycobacterium tuberculosis rifampicin resistance: the phenomenon of drug resistance is complex. Tuberculosis. (2021) 128:102083.
12. Maurya, A, Singh, A, Kant, S, Umrao, J, Kumar, M, Kushwaha, R, et al. Use of GenoType® MTBDRplus assay to assess drug resistance and mutation patterns of multidrug-resistant tuberculosis isolates in northern India. Indian J Med Microbiol. (2013) 31:230–6.
13. Arora J, Singhal R, Verma AK, Kumar G, Bhalla M, Sarin R, Myneedu VP. Isoniazid resistance among rifampicin-susceptible Mycobacterium tuberculosis isolates from tuberculosis patients. Int J Mycobacteriol. 2016 Dec;5 Suppl 1:S127-S128.
14. Alehegn E, Gebreyohanns A, Berhane BW, Wright JA, Hundie GB, Geremew RA, Gorems K, Gebreyohannes Z, Amare M, Abebaw Y, Diriba G, Zerihun B, Gebremichael AW, Kassa M, Gize A. Phenotypic Drug Resistance Pattern and Mutation Characteristics of Mycobacterium tuberculosis from Different Body Fluids Among Extra Pulmonary Patients Presented in Selected Hospitals in Addis Ababa, Ethiopia. Infect Drug Resist. 2023 Aug 22;16:5511-5522.