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Original Research Article

CLINICAL PROFILE, LPA-BASED RESISTANCE PATTERNS, AND TREATMENT OUTCOMES IN INH MONO-RESISTANT TUBERCULOSIS: AN EIGHT-YEAR RETROSPECTIVE STUDY FROM A TERTIARY CENTER IN INDIA

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ABSTRACT

Background: Isoniazid (INH) mono-resistant tuberculosis (TB) poses a major challenge to TB control due to its association with unfavorable outcomes and the risk of progression to multidrug-resistant TB. This study evaluated the clinical profile, Line Probe Assay (LPA)-based resistance patterns, and treatment outcomes of patients with INH mono-resistant TB at a tertiary care center in India.

Materials and Methods: This retrospective observational study included 622 microbiologically confirmed INH mono-resistant TB patients diagnosed by first-line LPA between January 2018 and June 2025 at GMC, Chhatrapati Sambhajinagar. Demographic, clinical, molecular resistance, and treatment outcome data were retrieved from NTEP records.

Results: The mean age of patients was 33.0 ± 12.8 years, with males comprising 67.8% of the cohort. Most patients were adults (95.0%), and HIV co-infection was present in 7.2%. Pulmonary TB accounted for 91.6% of cases, while 93.6% were newly diagnosed patients. Molecular analysis showed katG mutations in 64.1% of patients, inhA mutations in 24.0%, dual katG + inhA mutations in 5.1%, and unclassified mutations in 6.8%. The number of detected cases increased from 21 in 2018 to 113 in 2023. Overall, treatment outcomes were favorable, with 534 patients (85.9%) achieving cure. Mortality, treatment failure, and loss to follow-up occurred in 3.9%, 1.6%, and 1.9% of patients, respectively. Patients with isolated katG mutations had the highest cure rate (90.2%), followed by those with inhA mutations (87.2%). Dual katG + inhA mutations were associated with poorer outcomes, including lower cure rates (65.6%) and higher mortality (9.4%).

Conclusion: INH mono-resistant TB predominantly affected young adult males and was mainly pulmonary in presentation. katG mutations were the most common resistance mechanism. While treatment outcomes were generally favorable, dual katG + inhA mutations were associated with poorer outcomes, highlighting the importance of mutation-specific resistance profiling and universal molecular drug susceptibility testing.

Keywords: Isoniazid mono-resistant tuberculosis; Line Probe Assay; katG mutation; inhA mutation; treatment outcomes; India.

INTRODUCTION

Tuberculosis (TB), caused by Mycobacterium tuberculosis, continues to be a major global public health challenge despite sustained control efforts. In 2022, an estimated 10.6 million new TB cases and 1.6 million deaths were reported worldwide, underscoring its persistent burden. The emergence of drug-resistant TB has further complicated disease control due to longer, costlier, and less effective treatment regimens.[1] Among drug-resistant forms, mono-resistance to first-line anti-tubercular drugs is increasingly recognized as a significant clinical entity. Mono-resistant TB is defined as resistance to a single first-line drug while retaining susceptibility to others. Of particular concern is isoniazid (INH) mono-resistant TB, given the central role of INH in first-line treatment regimens. In India, which bears the highest global TB burden, there is growing evidence of increasing INH mono-resistance, particularly among newly diagnosed pulmonary TB cases.[2] This trend suggests a shift toward primary transmission of resistant strains rather than resistance acquired due to inadequate treatment.

INH has long been a cornerstone of TB therapy due to its potent early bactericidal activity and favorable pharmacokinetic profile. It is a prodrug activated by the mycobacterial enzyme catalase-peroxidase enzyme encoded by the katG gene, leading to inhibition of mycolic acid synthesis via the InhA enzyme.[3] Resistance to INH commonly arises due to mutations in the katG gene, resulting in high-level resistance, or in the inhA promoter region, leading to low-level resistance.[4] These mutations compromise treatment efficacy and are associated with increased risks of treatment failure, relapse, and progression to multidrug-resistant TB (MDR-TB).[5] Furthermore, INH-resistant strains may exhibit altered pathogenicity and host interactions, adding complexity to disease management.[6]

Estimates indicate that INH resistance occurs in approximately 7–11% of new TB cases and up to 25% of previously treated cases, posing a substantial programmatic challenge.[7] Under the National Tuberculosis Elimination Programme (NTEP), a significant proportion of drug-resistant TB cases includes INH mono- or poly-resistance, emphasizing its public health relevance.[8]

Despite its importance, INH mono-resistance often remains underdiagnosed in routine clinical practice. Many widely used rapid molecular tests, such as cartridge-based nucleic acid amplification tests, primarily detect rifampicin resistance and may miss INH resistance.[9] Consequently, patients are frequently initiated on standard first-line regimens without knowledge of underlying INH resistance, leading to suboptimal bactericidal activity and prolonged infectiousness.[7] Evidence suggests that treatment outcomes in INH mono-resistant TB are inferior compared to drug-sensitive TB when managed with conventional regimens.[10] These challenges highlight the need for universal drug susceptibility testing that includes detection of INH resistance.

The Line Probe Assay (LPA) has emerged as a valuable molecular diagnostic tool for rapid detection of INH resistance by identifying mutations in the katG and inhA genes.[11] LPA not only enables early diagnosis but also differentiates between high- and low-level resistance, which has important therapeutic implications. Early identification of resistance allows timely initiation of appropriate levofloxacin-based regimens as recommended under Programmatic Management of Drug-Resistant TB (PMDT) guidelines, thereby improving treatment outcomes and reducing the risk of further resistance development.[12] Additionally, mutation-specific patterns may influence prognosis, with some studies suggesting better outcomes in katG mutations compared to inhA or dual mutations.[13]

However, the implementation of LPA-based diagnostics faces several challenges in resource-limited settings. Delays in sample transportation, limited laboratory infrastructure, and occasional invalid results can hinder timely diagnosis and treatment initiation.[14] Moreover, the distribution of katG and inhA mutations varies geographically and may be influenced by local epidemiology and circulating M. tuberculosis strains.[4] This underscores the importance of region-specific data to guide clinical decision-making and programmatic strategies.

Despite the growing recognition of INH mono-resistant TB, there is a relative paucity of comprehensive studies from India evaluating its clinical profile, molecular resistance patterns, and treatment outcomes over extended periods.[15] Given the increasing burden of INH resistance and its implications for TB control, there is a critical need for real-world evidence from programmatic settings.

In this context, the present study aims to evaluate the clinical characteristics, LPA-based resistance patterns, and treatment outcomes of patients with INH mono-resistant TB at a tertiary care center in India. By providing detailed insights into demographic trends, mutation profiles, and therapeutic responses, this study seeks to bridge existing knowledge gaps and inform clinicians and policymakers on optimizing management strategies for INH mono-resistant TB within the framework of national TB control programs.

MATERIALS AND METHODS

Study design: This retrospective observational study was conducted in the Department of Pulmonary Medicine at Government Medical College (GMC), Chhatrapati Sambhajinagar, Maharashtra, India. The study spanned an eight-year period from January 2018 to June 2025. The institution is a designated nodal center under the National Tuberculosis Elimination Programme (NTEP) and caters to a large

population in Western India, providing comprehensive diagnostic and treatment services for tuberculosis, including drug-resistant TB. The study was reviewed and exempted by the Institutional Ethics Committee of Government Medical College, Chhatrapati Sambhajinagar, due to its retrospective design. The requirement for informed consent was waived. All patient data were anonymized prior to analysis to maintain confidentiality and ensure compliance with ethical standards.

Study Population: All microbiologically confirmed cases of isoniazid (INH) mono-resistant tuberculosis diagnosed using first-line Line Probe Assay (LPA) during the study period were included. INH mono-resistance was defined as resistance to isoniazid with susceptibility to rifampicin and other first-line anti-tubercular drugs. Patients with multidrug-resistant TB (MDR-TB), rifampicin-resistant TB, poly-drug resistant TB, or those with incomplete laboratory or treatment records were excluded from the study. Data were retrieved from multiple sources, including Programmatic Management of Drug-Resistant TB (PMDT) registers, microbiology laboratory records, and the Nikshay portal, which is the national digital TB surveillance system.

Data Collection: Data were collected using a pre-designed structured proforma. Variables included demographic details (age, sex, year of diagnosis), clinical characteristics (site of disease—pulmonary or extrapulmonary, HIV status, treatment history), and microbiological findings. Laboratory diagnosis was carried out as per standard NTEP and World Health Organization (WHO) guidelines. Sputum samples and other clinical specimens were subjected to Ziehl–Neelsen staining for acid-fast bacilli and culture using the Mycobacteria Growth Indicator Tube (MGIT 960) system. First-line LPA was used to detect mutations associated with INH resistance, specifically in the katG gene (high-level resistance) and the inhA promoter region (low-level resistance). In cases where LPA results were invalid or uninterpretable, repeat testing was performed whenever feasible; otherwise, such cases were recorded separately.

Treatment Regimen and Outcome Definitions: All patients were treated according to the Programmatic Management of Drug-Resistant TB (PMDT) 2021 guidelines under NTEP. The recommended regimen for INH mono-resistant TB consisted of a six- to nine-month course of rifampicin, ethambutol, pyrazinamide, and levofloxacin (REZ-Lfx).

Treatment outcomes were defined as per NTEP/PMDT guidelines: A patient was considered cured if they had bacteriologically confirmed pulmonary tuberculosis at baseline, completed the prescribed treatment, and demonstrated bacteriological conversion with no evidence of treatment failure. Treatment completed referred to patients who finished the treatment regimen as per protocol but did not fulfill the criteria for cure or failure. Treatment failure was defined as a situation where the treatment regimen had to be terminated or modified due to lack of clinical, radiological, or bacteriological response, or in cases of bacteriological reversion after initial conversion. The outcome was categorized as died if the patient expired for any reason before or during the course of treatment. Lost to follow-up included patients who either did not initiate treatment or had an interruption of treatment for one month or more. Patients were classified under treatment regimen changed if, after initiation of therapy, additional drug resistance was detected necessitating a shift to an alternative regimen; such cases were excluded from the outcome analysis of the initial regimen. Lastly, not evaluated referred to patients for whom treatment outcomes were unavailable, including those who were transferred out to another treatment unit and whose final outcomes could not be ascertained.

Data Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0. Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages.

RESULTS

A total of 622 patients with INH mono-resistant tuberculosis were identified between 2018 and 2025. The number of cases increased over the study period, rising from 21 cases in 2018 to a peak of 113 cases in 2023, followed by 102 cases in 2024 and 78 cases in 2025. Males constituted the majority of patients throughout the study period, accounting for 422 cases (67.8%), compared to 200 females (32.2%). The mean age of the study population was 33.0 ± 12.8 years, indicating that the disease predominantly affected young adults. Pediatric patients (<15 years) represented a small proportion of the cohort, with 31 cases (5.0%). HIV co-infection was observed in 45 patients (7.2%), with relatively higher proportions in 2018 (23.8%) and 2021 (15.6%) compared to other years. Overall, the findings indicate that INH mono-resistant TB was more common among adult males, with a low prevalence of pediatric disease and HIV co-infection in the study population [Table 1].

Table 1: Year-wise and Demographic Distribution of INH Mono-Resistant TB Cases (2018–2025).

Year	Total Cases	Male n (%)	Female n (%)	Mean Age (yrs) ± SD	Pediatric (<15 yrs) n (%)	HIV Positive n (%)
2018	21	16 (76.2)	5 (23.8)	35.8 ± 11.9	2 (9.5)	5 (23.8)
2019	79	58 (73.4)	21 (26.6)	34.2 ± 12.3	6 (7.6)	6 (7.6)
2020	65	45 (69.2)	20 (30.8)	31.8 ± 12.7	0 (0.0)	8 (12.3)
2021	64	39 (60.9)	25 (39.1)	32.6 ± 13.8	2 (3.1)	10 (15.6)

2022	100	64 (64.0)	36 (36.0)	31.4 ± 13.1	4 (4.0)	9 (9.0)
2023	113	74 (65.5)	39 (34.5)	29.6 ± 15.8	5 (4.4)	3 (2.7)
2024	102	69 (67.7)	33 (32.3)	34.5 ± 12.0	7 (6.9)	2 (2.0)
2025	78	57 (73.1)	21 (26.9)	30.6 ± 14.0	5 (6.4)	2 (2.6)
Total	622	422 (67.8)	200 (32.2)	33.0 ± 12.8	31 (5.0)	45 (7.2)

Among the 622 patients with INH mono-resistant tuberculosis, pulmonary TB was the predominant form of disease, accounting for 570 cases (91.6%), while extrapulmonary TB was observed in 52 patients (8.4%). Most patients were newly diagnosed cases (582; 93.6%), whereas only 40 patients (6.4%) had a history of previous treatment. Sputum was the most common sample type, being used in 570 cases (91.6%), while 52 patients (8.4%) were diagnosed using other clinical specimens. Molecular resistance profiling by Line Probe Assay (LPA) showed that katG mutations associated with high-level isoniazid resistance were the most frequent, occurring in 399 patients (64.1%). inhA mutations, indicating low-level resistance, were identified in 149 patients (24.0%), while dual katG and inhA mutations were detected in 32 patients (5.1%). Mutation-specific classification was unavailable or could not be retained in 42 patients (6.8%) whose treatment regimens were modified during the course of therapy [Table 2].

Table 2: Clinical and Resistance Characteristics of INH Mono-Resistant TB Patients (n = 622).

Characteristic	Domain	n (%)
Type of TB	Pulmonary	570 (91.6)
	Extrapulmonary	52 (8.4)
Treatment History	New cases	582 (93.6)
	Previously treated	40 (6.4)
Sample Type	Sputum	570 (91.6)
	Other samples	52 (8.4)
Resistance Pattern (LPA)	katG mutation (high-level resistance)	399 (64.1)
	inhA mutation (low-level resistance)	149 (24.0)
	Dual mutation (katG + inhA)	32 (5.1)
	Mutation pattern unavailable/modified treatment*	42 (6.8)

*Mutation-specific classification could not be retained among patients whose regimen was modified during treatment.

The study population comprised 622 patients with INH mono-resistant tuberculosis, of whom 422 (67.8%) were male and 200 (32.2%) were female. Adults aged 15 years or older constituted the majority of cases (591; 95.0%), while pediatric patients accounted for only 31 cases (5.0%). HIV co-infection was present in 45 patients (7.2%), whereas 554 patients (89.1%) were HIV-negative and HIV status was unknown in 23 patients (3.7%). Pulmonary tuberculosis was the predominant disease presentation, observed in 570 patients (91.6%), compared to 52 patients (8.4%) with extrapulmonary disease. Most patients were newly diagnosed cases (582; 93.6%), while only 40 patients (6.4%) had a history of previous treatment. Sputum was the most common specimen used for diagnosis, accounting for 570 cases (91.6%), whereas other clinical samples were utilized in 52 cases (8.4%). These findings indicate that INH mono-resistant TB primarily affected adult males and was predominantly diagnosed as pulmonary disease among newly detected cases [Table 3].

Table 3: Demographic and Clinical Profile of Patients (n = 622).

Parameter	Domain	n (%)
Sex	Male	422 (67.8)
	Female	200 (32.2)
Age Group	Pediatric (<15 years)	31 (5.0)
	Adult (≥15 years)	591 (95.0)
HIV Status	HIV positive	45 (7.2)
	HIV negative	554 (89.1)
	Unknown	23 (3.7)
Type of TB	Pulmonary	570 (91.6)
	Extrapulmonary	52 (8.4)
Treatment History	New	582 (93.6)
	Previously treated	40 (6.4)
Sample Type	Sputum	570 (91.6)
	Others	52 (8.4)

Among the 622 patients with INH mono-resistant tuberculosis, 534 patients (85.9%) were cured. Mortality was observed in 24 patients (3.9%), while treatment failure occurred in 10 patients (1.6%). A total of 12 patients (1.9%) were lost to follow-up during the treatment period. Treatment regimens were modified in 42 patients (6.8%) due to factors such as additional drug resistance, adverse drug reactions, or clinical considerations requiring a change in management. Overall, the findings

demonstrate a high treatment success rate and relatively low rates of failure, mortality, and loss to follow-up, indicating favorable outcomes with the programmatic management of INH mono-resistant TB [Table 4].

Table 4: Treatment Outcomes of INH Mono-Resistant TB Patients (n = 622).

Treatment Outcome	n (%)
Cured	534 (85.9)
Failure	10 (1.6)
Death	24 (3.9)
Lost to follow-up	12 (1.9)
Treatment changed	42 (6.8)
Total	622 (100.0)

Among the 580 patients with documented mutation profiles, treatment outcomes varied according to the resistance pattern. Patients with isolated katG mutations demonstrated the most favorable outcomes, with 360 of 399 patients (90.2%) achieving cure, along with low rates of death (2.5%), treatment failure (1.0%), and loss to follow-up (1.3%). Patients with inhA-only mutations also had a high cure rate of 87.2% (130/149), although slightly lower than that observed in the katG group. In contrast, patients with dual katG + inhA mutations experienced comparatively poorer outcomes, with a cure rate of 65.6% (21/32), higher mortality (9.4%), greater loss to follow-up (6.3%), and the highest proportion of treatment modifications (15.6%). Overall, among the 580 patients included in mutation-specific analysis, 511 (88.1%) were cured, while death, treatment failure, and loss to follow-up occurred in 2.9%, 1.2%, and 1.7% of patients, respectively. These findings suggest that treatment outcomes were generally favorable but tended to worsen in patients harboring dual resistance mutations, highlighting the prognostic importance of resistance-pattern profiling [Table 5].

Table 5: Association Between Resistance Pattern and Treatment Outcomes.

Resistance Type	Total Cases	Cured n (%)	Death n (%)	Failure n (%)	Lost to Follow-up n (%)	Treatment Changed n (%)
inhA only	149	130 (87.2)	4 (2.7)	2 (1.3)	3 (2.0)	10 (6.7)
katG only	399	360 (90.2)	10 (2.5)	4 (1.0)	5 (1.3)	20 (5.0)
katG + inhA	32	21 (65.6)	3 (9.4)	1 (3.1)	2 (6.3)	5 (15.6)
Total	580	511 (88.1)	17 (2.9)	7 (1.2)	10 (1.7)	35 (6.0)

Outcome analysis by resistance pattern was available for 580 patients with documented mutation profiles. Forty-two patients whose treatment regimen was modified were not included in resistance-pattern stratification.

DISCUSSION

This eight-year retrospective study evaluated the clinical profile, molecular resistance patterns, and treatment outcomes of 622 patients with INH mono-resistant tuberculosis. The overall cure rate was 85.9%, while mortality, treatment failure, and loss to follow-up rates were 3.9%, 1.6%, and 1.9%, respectively. Molecular analysis demonstrated that katG mutations were the predominant resistance pattern (64.1%), followed by inhA mutations (24.0%) and dual katG + inhA mutations (5.1%). These findings indicate that high-level INH resistance associated with katG mutations remains the most common mechanism of INH mono-resistance in our setting.

The annual number of detected INH mono-resistant TB cases increased from 21 in 2018 to a peak of 113 cases in 2023. This trend may reflect improved implementation of molecular diagnostic techniques such as Line Probe Assay (LPA) under the National Tuberculosis Elimination Programme (NTEP), along with enhanced surveillance and case detection. The mean age of patients was 33.0 ± 12.8 years, indicating that INH mono-resistant TB predominantly affects young and economically productive adults. Similar observations have been reported by Kwak et al., who found that INH mono-resistant TB was more common among younger adults, highlighting its public health and socioeconomic impact.[10] Male patients constituted 67.8% of the cohort, consistent with previous Indian and international studies that have reported a higher burden of tuberculosis among males, likely due to occupational exposure, behavioral risk factors, and delayed healthcare-seeking practices.[10]

The demographic and clinical profile observed in the present study is broadly comparable to that reported by Khan et al. from Mumbai, who evaluated 217 patients with INH mono-resistant TB treated under routine programmatic conditions. In both studies, pulmonary TB was the predominant disease presentation (91.6% in the present study versus 88% in the Mumbai cohort), and katG mutations represented the most common resistance pattern (64.1% versus 65%).[16] However, our cohort included a substantially higher proportion of newly diagnosed patients (93.6% versus 61%), suggesting that primary transmission may be a major contributor to the burden of INH mono-resistant TB in our region. Furthermore, male patients accounted for 67.8% of cases in our study compared with 46% in

the Mumbai cohort, indicating possible regional differences in disease epidemiology and healthcare access.

Pulmonary tuberculosis accounted for 91.6% of cases, highlighting the dominant role of pulmonary disease in the transmission of INH-resistant strains. Moreover, 93.6% of patients were newly diagnosed, suggesting that primary transmission rather than acquired resistance contributes substantially to the burden of INH mono-resistant TB. The high proportion of newly diagnosed patients in our cohort suggests that transmission of resistant strains may contribute substantially to the disease burden.[15] The relatively low proportion of pediatric cases (5.0%) and HIV co-infection (7.2%) suggests that INH mono-resistant TB in this cohort primarily affected immunocompetent adults, although continued surveillance among vulnerable populations remains essential.

The distribution of resistance mutations in our study is consistent with previous reports from India and other high-burden settings. KatG mutations were identified in 64.1% of patients, followed by inhA mutations in 24.0% and dual mutations in 5.1%. Similarly, Khan et al. reported katG mutations in 65% and inhA mutations in 29% of patients with INH mono-resistant TB.[16] Ranjan et al. also demonstrated a predominance of katG mutations among Indian patients with INH-resistant tuberculosis.[11] Furthermore, a systematic review by Seifert et al. identified katG mutations, particularly the S315T mutation, as the most common genetic mechanism underlying INH resistance worldwide.[17] The predominance of katG mutations has important therapeutic implications because these mutations are associated with high-level INH resistance while generally preserving susceptibility to rifampicin and fluoroquinolones, thereby supporting the effectiveness of levofloxacin-based treatment regimens.

The overall cure rate of 85.9% observed in our study compares favorably with previously published literature. Alemu et al., in a systematic review and meta-analysis of patients with INH mono-resistant tuberculosis, reported a pooled treatment success rate of 78%.[18] Likewise, the India TB Report 2023 documented a treatment success rate of approximately 82% among patients with INH mono/poly-resistant TB treated under the national program.[8] Khan et al. reported favorable treatment outcomes in 87% of patients receiving a levofloxacin-based regimen, which is comparable to the findings of the present study.[16] Collectively, these findings support the effectiveness of the currently recommended REZ-Lfx regimen for the management of INH mono-resistant tuberculosis under routine programmatic conditions.

Outcome analysis according to mutation profile demonstrated variation in treatment response across resistance patterns. Patients with katG-only mutations achieved the highest cure rate (90.2%), whereas those with dual katG + inhA mutations had substantially poorer outcomes, including a lower cure rate (65.6%), higher mortality (9.4%), and greater need for treatment modification (15.6%). Patients with inhA-only mutations showed intermediate outcomes, with a cure rate of 87.2%. Similar observations have been reported in previous studies, where dual mutations were associated with more complex resistance mechanisms and less favorable treatment outcomes.[11,17] These findings emphasize the clinical value of mutation-specific resistance profiling and support the need for closer monitoring of patients harboring dual resistance mutations.

Among the total study population, 42 patients (6.8%) underwent treatment modification because of additional drug resistance, adverse drug reactions, clinical considerations, or transfer to another treatment center. Such cases reflect the complexity of managing drug-resistant tuberculosis in real-world settings and highlight the importance of ongoing drug susceptibility testing and individualized patient care.

The low loss-to-follow-up rate observed in our study (1.9%) compared with the 9.2% reported by Khan et al. may indicate stronger treatment adherence and follow-up mechanisms within our programmatic setting.[16]

From a programmatic perspective, the findings reinforce the effectiveness of the PMDT 2021 recommendation of a levofloxacin-containing regimen for INH mono-resistant TB. The high cure rate and relatively low rates of mortality, treatment failure, and loss to follow-up demonstrate that favorable outcomes can be achieved when early molecular diagnosis and appropriate treatment are available. Expansion of LPA services, universal drug susceptibility testing, and timely initiation of individualized therapy remain critical for improving outcomes and preventing progression to more severe forms of drug-resistant tuberculosis. Particular attention should be given to patients with inhA and dual mutations, who may require closer follow-up and enhanced adherence support.

The strengths of this study include its large sample size, extended eight-year study period, and use of routine programmatic data from a tertiary care center. The study also provides detailed information on mutation-specific resistance patterns and treatment outcomes among patients with INH mono-resistant tuberculosis. However, the retrospective single-center design may limit generalizability. Information regarding socioeconomic status, nutritional status, smoking, alcohol use, and long-term post-treatment follow-up was unavailable. Additionally, mutation-specific outcome analysis could not be performed for all patients because treatment regimens were modified in a subset of cases.

CONCLUSION

This eight-year retrospective study demonstrated that INH mono-resistant tuberculosis predominantly affected young adult males and was mainly

associated with pulmonary disease with a high proportion of newly diagnosed cases, suggesting a possible contribution of primary transmission. Molecular resistance profiling revealed that katG mutations were the most common resistance mechanism, followed by inhA and dual katG + inhA mutations. Treatment outcomes were generally favorable, with an overall cure rate of 85.9% and low rates of treatment failure, mortality, and loss to follow-up, supporting the effectiveness of the levofloxacin-based REZ-Lfx regimen recommended under PMDT guidelines. Patients with dual mutations exhibited comparatively poorer outcomes, highlighting the importance of mutation-specific resistance profiling for risk stratification and clinical monitoring. Strengthening universal access to rapid molecular drug susceptibility testing, expanding LPA services, and ensuring timely initiation of appropriate therapy are essential for optimizing treatment outcomes and preventing the emergence of more extensive drug resistance. These findings provide valuable real-world evidence to support programmatic management strategies for INH mono-resistant tuberculosis in India.

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