International Journal of Contemporary Research and Review
Received 22-12-2024 | Revised 23-12-2024 | Accepted 01-05-2025 | Published Online 01-02-2025

DOI: https://doi.org/10.52845/rrijcrr/2025/16-2-1

IJCRR 16 (02), 20272-20275 (2025)

ISSN (O) 0976-4852

Medical Sciences

Identification of the Genetic Mutations Associated With INH Mono Resistance in Mycobacterium Tuberculosis Isolates From Patients in a Tertiary Care Centre

Dr.Varnana Suresh A T[1] | Dr. Akshada M. Vernekar[2] | Dr. Uday C. Kakodkar[3] | Dr. Sanjivani Keny[4]

[1,2]Senior Resident,
[3]Professor and Head of the Department,
[4]Associate Professor
Department of Respiratory Medicine, Goa Medical College, Taleigao – Goa
Corresponding Author: Dr. Akshada M. Vernekar

Abstract:

Tuberculosis remains a significant public health issue worldwide, with India having one of the highest burden of disease. Isoniazid (INH) is a cornerstone drug in the treatment of TB. However, INH mono resistance poses a considerable challenge to effective TB control. Understanding genetic mutations responsible for INH resistance is crucial for the development of diagnostic tools and treatment strategies. Our study aims to identify and characterize the genetic mutations associated with INH mono resistance in Mycobacterium tuberculosis isolates from patients in Goa. Also, our study aims to evaluate whether patients developing isoniazid mono resistant tuberculosis occurs more in patients with anti-TB treatment in the past.

Introduction:

According to the World Health Organization's Global Tuberculosis Report 2024, India accounted for the highest number of TB cases worldwide in 2023, with 2.6 million cases, representing 26% of the global burden. In 2023, India also contributed to nearly a third of the world's multidrug-resistant (MDR) and rifampicin-resistant (RR) TB burden, reporting 400,000 new cases, which represented 28% of the global burden. Although the exact percentage of isoniazid resistance in India is not specified, the WHO reported a global prevalence of 7.2% among new TB patients and 11.5% among previously treated TB patients. (1).

Isoniazid is one of the most potent first line anti tuberculosis drug because of its both bactericidal and sterilizing actions. However, it has been noted that resistance to isoniazid is most common among all first-line anti TB drugs accounting for 7.2% [(2)]. Mutations in several genes, including *Kat*G, *Inh*A, *Ahp*C and *Kas*A have been associated with INH resistance. However, the two most common mutations which are responsible for resistance are *Kat*G and *Inh*A.

INH monoresistant tuberculosis complicates treatment protocols and necessitates alternative drug regimens. Understanding genetic mutations responsible for INH monoresistance can help in better diagnostic, treatment and prevention strategies.

Method:

- Study design: a cross sectional study
- Study population: patients diagnosed with INH monoresistant TB at various health care centres in Goa
- Sample size and duration of study: The study includes the patients diagnosed as a case of INH monoresistant tuberculosis from April 2022 to April 2024.
- Patient selection:
  - Inclusion criteria:

1. Patients diagnosed with INH monoresistant TB through Drug susceptibility testing

2. TB involving any system of the body

- Exclusion criteria:

1. Patients with multi drug resistant TB

- Data collection:
  - Collection of clinical data: patient demographics, past history of tuberculosis or anti TB treatment, treatment details
  - Collection of sputum samples and subsequent testing with CBNAAT, culture, Line probe assays and drug sensitivity testing, gene sequencing.
- Data analysis:

Statistical analysis of mutation patterns and their correlation with clinical data. Frequency and distribution of specific genetic mutation Comparative analysis with national and global data on INH resistance

Results:

Our study included a total of 84 INH monoresistant tuberculosis patients out of which 56 (66.6%) patients were males and 28 (33.3%) patients were females (Table 1). The age of patients ranged from 15 years to 78 years with mean age being 41.4 years. Kat G mutation was found to be most common mutation in these patients accounting to 54 patients (64.28%) of the study population while remaining 29 patients (34.52%) had Inh A mutation with exception of one patient (1.19%) who had mutations in both Kat G and Inh A genes (Table 2). Out of the 84 patients studied, only 11 patients (13.09%) had a history of tuberculosis in the past (Figure 1).

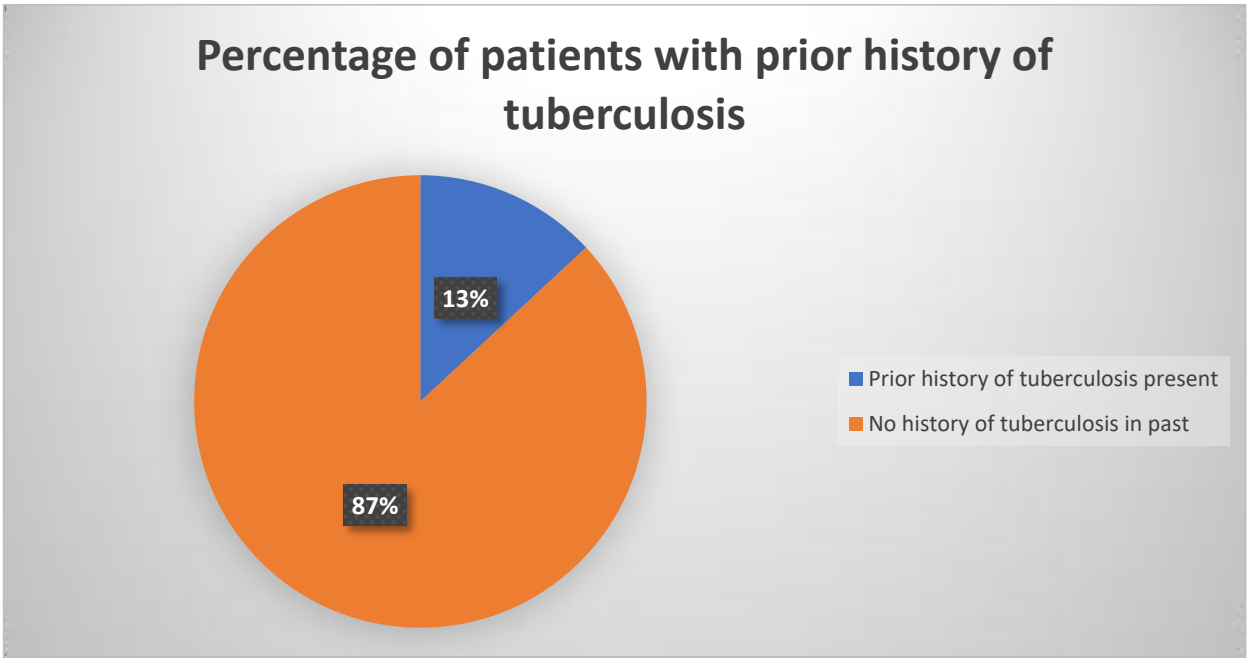
Table 1: The distribution of study participants according to sex

Sex of the patient	Number of patients	Percentage (%)
Male	56	66.6
Female	28	33.3
Total	84	

Table 2: The distribution of Kat G and Inh A mutations among study population

Type of mutation	Number of patients	Percentage(%)
Kat G mutation	54	64.28
Inh A mutation	29	34.52
Both Kat G and Inh A mutation	1	1.19
Total	84	

Figure 1: Figure showing the percentage of patients with INH monoresistant tuberculosis with a previous history of tuberculosis.



Discussion:

The findings of present study provide crucial insight into the demographic and genetic characteristics of INH monoresistant tuberculosis patients. The higher prevalence of INH monoresistant TB among males (66.6%) align with global data from the World Health Organization (WHO), which reports higher incidence of tuberculosis in males compared to females [(1)]. This gender disparity could be attributed to various socio-economic and biological factors that influence disease exposure and progression.

Our mutation analysis reveals a predominance of KatG mutations in 54 patients (64.28%), corroborating findings from previous studies [(3,4,5)]. The KatG gene is critical for the activation of isoniazid, and mutations in this gene impede the efficacy of the drug, leading to resistance. The InhA mutations, found in 29 patients (34.52%), also play a significant role in INH resistance by altering the target enzyme involved in mycolic acid synthesis, essential for the bacterial cell wall [(6)].

Interestingly, only one patient (1.19%) exhibited mutations in both KatG and InhA genes, suggesting that while dual mutations are rare, their presence can complicate treatment strategies. The WHO 2023 report emphasizes the need for comprehensive molecular diagnostics to detect such mutations accurately, facilitating appropriate treatment regimens.

The high percentage of patients with inh mono resistant tuberculosis without a prior history of taking anti-TB treatment (86. 91%) suggests that primary transmission of INH resistant strain is a significant concern. This aligns with the WHO's observations that primary drug resistant TB is increasing in many regions, driven by ongoing transmission rather than treatment failure or relapse (WHO, 2024). This finding underscores the importance of strengthening TB control programs, enhancing diagnostic capabilities, and ensuring prompt and effective treatment of TB cases to curb the spread of resistant strains.

Our demographic analysis, particularly the higher proportion of cases among middle aged adults, underscores the need for targeted public health interventions. Workplace health programs and community outreach initiatives could be pivotal in addressing TB in this age group. Additionally, the gender disparity in TB incidence calls for gender

sensitive approaches to TB prevention and treatment.

The WHO's 2024 report also highlights the critical role of social determinants in TB incidence and outcomes. Factors such as poverty, malnutrition, and access to healthcare significantly influence TB dynamics. The findings in present study reinforce the need for holistic strategies that address these underlying social determinants to effectively combat INH resistant TB.

References:

1. World Health Organization. Global tuberculosis report 2024. Geneva: WHO; 2024 https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2024
2. World Health Organization. WHO treatment guidelines for isoniazid resistant tuberculosis: Supplement to the WHO treatment guidelines for drug resistant tuberculosis. Geneva: World Health Organization;2018. https://www.who.int/publications/i/item/9789241550079
3. Zhang Y, Heym B, Allen B, Young D, Cole S. The catalase-peroxidase gene and isoniazid resistance of Mycobacterium tuberculosis. Nature. 2013;358(6387):591-3.
4. Seifert M, Catanzaro D, Catanzaro A, Rodwell TC. Genetic mutations associated with isoniazid resistance in Mycobacterium tuberculosis: a systematic review. PLoS One. 2015;10(3): e0119628.
5. Charan AS, Gupta N, Dixit R, Arora P, Patni T, Antony K, Singh M. Pattern of InhA and KatG mutations in isoniazid monoresistant Mycobacterium tuberculosis isolates. Lung India. 2020 May-Jun;(3):227-231. Doi: 10.4103/lungindia.lungindia_204_19.
6. Huang WL, Chi TL, Wu MH, Jou R. Performance assessment of the GenoType MTBDRsI test and DNA sequencing for detection of second-line and ethambutol drug resistance among patients with multidrug-resistant tuberculosis. J Clin Microbiol. 2014;52(6):1987-92.