

ORIGINAL RESEARCH

An Observational study on Risk factors among H mono Resistant Tuberculosis patients Registered under NTEP, Jamnagar District, Gujarat

¹Dr Keyur Patel, ²Dr Iva.S. Chatterjees, ³Dr Yogesh M

¹Assistant Professor in Respiratory Medicine Department at Zydus Medical College & Hospital, Dahod, India

²HOD & Professor, Department of Pulmonary Medicine, Shri MP Shah Medical College, Jamnagar India

³Junior Resident, Department of Community Medicine, Shri MP Shah Medical College, Jamnagar India.

Corresponding Author

Dr. Iva.S. Chatterjees

HOD & Professor, Department of Pulmonary Medicine, Shri MP Shah Medical College, Jamnagar India

Email: ivachatterjee73@gmail.com

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ABSTRACT

Background: India has the highest burden of TB in the world, accounting for about a quarter of all TB cases worldwide. The Indian government has taken steps to address the problem of drug-resistant TB, including expanding the availability of drug susceptibility testing and increasing access to second-line TB drugs. However, there is still much work to be done to control the spread of drug-resistant TB in India. Improved TB diagnosis and treatment, as well as efforts to prevent the spread of TB in communities, are critical in reducing the prevalence of isoniazid-resistant TB and other forms of drug-resistant TB in India. So, this study aims to assess the risk factors for poor treatment outcomes of H mono Resistant Tuberculosis patients Registered under NTEP, Jamnagar District, Gujarat. **Objectives:** To assess the risk factors for poor treatment outcome H mono Resistant Tuberculosis patients. To determine the association between poor treatment outcome and various risk factors of H Mono Resistant tuberculosis. **Methods:** It's a Hospital-based prospective observational Cross-sectional study conducted from February 2020 – August 2021 With a calculated sample size is 100 in Tertiary Care Center .100 patients diagnosed with isoniazid mono resistance tuberculosis and treated with an H mono regimen are enrolled in this study. All patient's sputum samples were collected and studied initially by smear AFB followed by First line and second-line probe assay. Under treatment, all patients were evaluated clinically and radiologically monthly till end of treatment. Sputum smear microscopy was carried out monthly till the end of treatment. sputum culture for MTB was carried out at the end of 3rd month and the end of treatment (6th month). **Conclusion:** The male (62%) has more incidence of isoniazid mono-resistant tuberculosis and inferior treatment outcome. underweight (OR=1.432, CI=1.2-1.7), previous TB treatment (OR=1.667, CI=1.294-2.147), substance addiction (OR=1.457, CI=1.2-1.7), cavity, and/or extensive radio lesion (OR=0.754, CI=0.656-0.866) (OR=13.6, CI=1.7-20) are Associated with H mono regimen failure. **Public health Implication:** Our findings have important clinical implications for the management of patients with TB. Physicians should consider the presence of cavitory or extensive lesions on chest X-rays and the presence of inhA or katG gene mutations when deciding on the appropriate treatment regimen. Patients with these risk factors may require more intensive treatment approaches, such as longer treatment duration, higher doses of drugs, or the addition of second-line drugs

Key words: H-mono-resistant tuberculosis, Risk factors, poor treatment outcome, underweight, cavity, and/or extensive radio lesion

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INTRODUCTION

Pulmonary TB remains one of the significant public health problems not only in India but all over the world. Globally, there were an estimated 10.4 million new TB cases with 1.4 million deaths in 2015.^[1] There is an estimated about 12,000 crores of rupees of economic loss to the Government of India every year.^[3]

The vision of the Government of India is for a “TB-free India” with a reduction in the burden of the disease until it ceases to be a major public health problem. To achieve this vision, the program has now adopted the new objective of achieving “universal access” to quality diagnosis and treatment for all TB patients in the community.^[4]

As per the Global TB Report 2021, the estimated incidence of all forms of TB in India for the year 2020 was 188 per 100,000 population (129-257 per 100,000 population). The total number of incident TB patients (new & relapse) notified during 2021 was 19,33,381 which was 19% higher than that of 2020 (16,28,161).^[2]

There are five categories of drug-resistant TB used by the national health programs at present: isoniazid (INH)-resistant TB, RRTB, and MDR-TB (RR and INH resistant), plus pre-extensively drug-resistant TB (pre-XDR-TB) and XDR-TB. Pre-XDR-TB is TB that is resistant to rifampicin (MDR/RR-TB) and any fluoroquinolone (a class of second-line anti-TB drugs XDR-TB is TB that is resistant to rifampicin (MDR/RR-TB), plus any fluoroquinolone, plus at least one of the drugs, bedaquiline, and linezolid. The estimated number of MDR and XDR-TB cases to have been put on treatment as per the global TB report 2021 was 4 per 100,000 and 1 per 100,000 population, respectively. During the pandemic, a significant reduction was observed in the total number of DR-TB patients started on treatment as compared to 2019. In 2020 and 2021, there was a reduction of 14% and 9% in the number of MDR patients put on treatment as compared to the estimated numbers.^[2]

The prevalence of isoniazid-resistant tuberculosis (TB) in India is significant, with estimates suggesting that around 25% of TB cases in India are resistant to isoniazid.^[3] This is due to a combination of factors, including the widespread use of isoniazid as a first-line treatment for TB, poor adherence to treatment regimens, and the emergence of drug-resistant strains of the TB bacteria.

India has the highest burden of TB in the world, accounting for about a quarter of all TB cases worldwide. The Indian government has taken steps to address the problem of drug-resistant TB, including expanding the availability of drug susceptibility testing and increasing access to second-line TB drugs.

However, there is still much work to be done to control the spread of drug-resistant TB in India. Improved TB diagnosis and treatment, as well as efforts to prevent the spread of TB in communities, are critical in reducing the prevalence of isoniazid-resistant TB and other forms of drug-resistant TB in India. So, this study aims to assess the risk factors for poor treatment outcome H mono Resistant Tuberculosis patients Registered under NTEP, Jamnagar District, Gujarat.

Aim and Objectives

The study aims to assess the risk factors for poor treatment outcome H mono Resistant Tuberculosis patients Registered under NTEP, Jamnagar District, Gujarat.

Objectives

- To assess the risk factors for poor treatment outcome H mono Resistant Tuberculosis patients
- To determine the association between poor treatment outcome and various risk factors of H Mono Resistant tuberculosis

MATERIALS AND METHODS

Study Design

Hospital-based prospective observational Cross-sectional study.

Study Period

18 months: February 2020 – August 2021

Sample Size

Considering the prevalence of isoniazid-resistant tuberculosis (TB) in India is significant, with estimates suggesting that around 25% of TB cases in India are resistant to isoniazid (3) has been calculated with the help of the formula $n = 4pq/L^2$. Here allowable error L has been taken as 8. The calculated sample size is 100.

100 patient diagnosed with isoniazid mono resistance tuberculosis and treated with an H mono regimen are enrolled in this study

Study Design

Tertiary care Hospital.

Methods

All diagnosed cases of Isoniazid mono-resistant tuberculosis and treated with an H mono regimen were enrolled in this study after a prior informed consent of patients who were willing enough to give their node of approval for collecting and publishing personal data including detailed clinical history, radiological, microbiological and biochemical investigations. All patient's sputum samples were collected and studied initially by smear AFB followed by First line and second-line probe assay. Under treatment, all patients were evaluated clinically and radiologically monthly till end of treatment. Sputum smear microscopy was carried out monthly till the end of treatment. sputum culture for MTB was carried out at the end of 3rd month and the end of treatment (6th month). Liquid culture DST was advised in patients with smear/culture positive at 3rd month, end of treatment.

This study was prior approved by the institutional ethical review board of our hospital.

Inclusion criteria

All isoniazid mono-resistant pulmonary and extrapulmonary tuberculosis cases including new and previously treated.

Exclusion criteria

- Drug-sensitive TB patients.
- Multidrug resistant TB and rifampicin resistant TB.
- Terminally ill patients.
- Unwilling patients

RESULTS

Socio-demographic characteristics

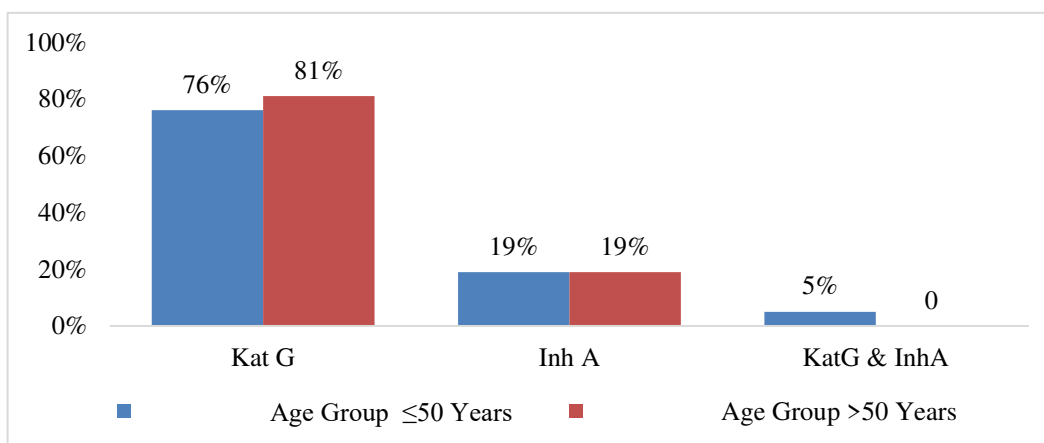
Variables	Categories	Frequency-with % (n=100)
Age	Greater than 45	40(40%)
	Less than 45	60(60%)
Gender	Male	62 (62%)
	Female	38(38%)
BMI	<18.5	48(48%)
	>18.5	52(52%)
Residence	Rural	59(59%)
	Urban	41(41%)
Substance Addiction	Present	42(42%)
	Absent	58(58%)
Co-morbidity history	Present	32(32%)
	Absent	68(68%)
Socio-economic class	Lower	73(73%)
	Middle	25(25%)
	High	2(2%)

Clinical profile (including Radiological and microbiological parameters)

Variables	Categories	Frequency with %
Treatment history	Newly diagnosed	70(70%)
	Previously treated	30(30%)
Clinical symptoms	Cough	99(99%)
	Cough-with expectoration	79(79%)
	Haemoptysis	26(26%)
	Dyspnoea	66(66%)
	Chest pain	26(26%)
	Fever	90(90%)
	Weight loss	80(80%)
Type of lesion in Chest Xray	Cavitary lesion	62(62%)
	Non-Cavitary	38(38%)
The extent of the lesion	Limited (<1 lobe)	45(45%)
	Extensive(>1 lobe)	55(55%)

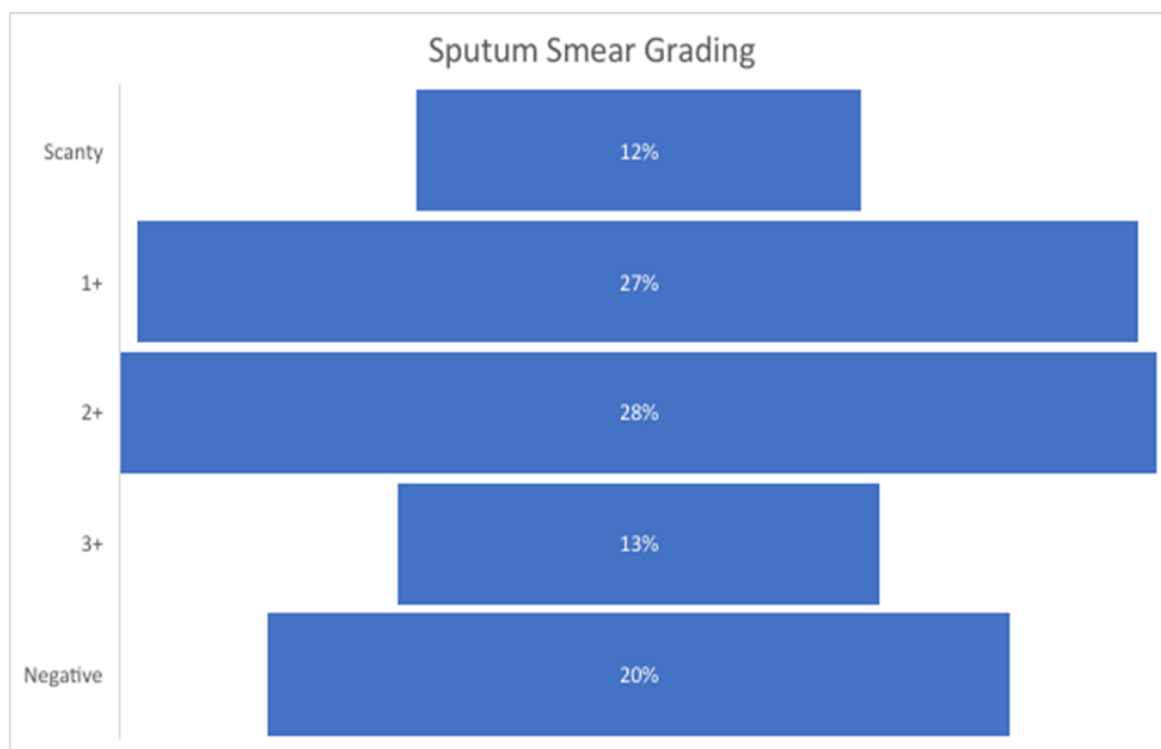
Resistance Mutation and Age Group Correlation

Mutation	Age Group		Total Patients
	≤50 Years	>50 Years	
Kat G	60	17	77 (77%)
Inh A	15	04	19(19%)
KatG and InhA	04	00	04(4%)
Total	79	21	100



Distribution According to Sputum Smear Grading

Grade	Scanty	1+	2+	3+	Negative	Total
No. of patients	12	27	28	13	20	100
% of patients	12%	27%	28%	13%	20%	100%

**Association between socio-demographic and clinical profile with treatment outcome at 6th month**

Variables	Treatment outcome		Total (%)	p-value
	Treatment cure	Treatment failure		
BMI	45	2	47(47%)	<0.005
>18.5	37	16	52(52%)	
<18.5				
Substance addiction	35	16	51(51%)	<0.005
Present	45	4	49(49%)	
Absent				
Types of lesions on chest -x-ray	49	16	65(65%)	<0.005
Cavitary	33	2	35(35%)	
Non-cavitary				
The extent of the lesion in chest X-ray	40	1	41(41%)	<0.005
Limited (<1 lobe)	44	15	66(66%)	
Extensive (>1 lobe)				
Gene mutation	83	13	96(96%)	<0.001
Inh A and kat G individually	1	3	4(4%)	
Inh A and Kat G together				
Previous history of TB	58	2	60(60%)	<0.005
Yes	24	16	40(40%)	
No				

Association of risk factors and sputum conversion at 3rd month

Variables	Treatment outcome		Total (%)	p-value
	Treatment cure	Treatment failure		
Previous history of TB				
Yes	58	2	60(60%)	<0.005
No	25	15	40(40%)	
Substance addiction				
Present	36	15	51(51%)	<0.05
Absent	47	2	49(49%)	

DISCUSSION

In the Present Study, out of a total of 100 cases, 62% of cases were male and 38% were female, out of a total of 100 cases, 40% of cases were from the <45 years of age group and 60% were from ≥ 45 years of age group, out of total 100 cases, 30% cases were previously treated for tuberculosis and 70% cases were newly diagnosed with H mono resistant. In the present study out of a total of 100 cases, 77% of cases had KatG mutation and 19% of cases had InhA mutation. out of a total of 100 cases, 84% cases were cured with the H mono regimen and 9% cases had regimen failure, 62% cases had cavitory lesions on CXR, 80% cases had sputum smear positive for AFB

The results of our study suggest that several risk factors are associated with H mono regimen failure in patients with tuberculosis (TB). In particular, we found that patients who are underweight, have undergone previous TB treatment, have a history of substance addiction, and have cavity and/or extensive radio lesions are at increased risk for treatment failure with the H mono regimen.

Our findings are consistent with previous studies that have identified these risk factors as predictors of poor TB treatment outcomes (Chen et al., 2019; Tessema et al., 2019).^[5] Underweight patients may have compromised immune function and may be more susceptible to adverse drug reactions, which can affect treatment adherence and efficacy (Chen et al., 2019)(OR=1.432, CI=1.2-1.7). Patients with previous TB treatment may have developed resistance to one or more anti-TB drugs, which can complicate subsequent treatment regimens (Tessema et al., 2019)^[6](OR=1.667, CI=1.294-2.147). Substance addiction can lead to poor treatment adherence and an increased risk of relapse (Kurbatova et al., 2015)^[7](OR=1.457, CI=1.2-1.7)

Our findings suggest that the presence of cavitory or extensive lesions on chest X-rays (OR=0.754, CI=0.656-0.866) (OR=13.6, CI=1.7-20) and the presence of inhA and katG gene mutations together are important risk factors for poor treatment outcomes in patients with TB (OR=19.154, CI=1.850-120). These findings are consistent with previous studies that have reported similar associations (Dheda et al., 2017; Lee et al., 2018).^[8-9]

Our findings suggest that substance abuse (OR=17.4, CI=3.7-81.8) and previous TB treatment (OR=9.7, CI=2.1-45) are important risk factors for a lower likelihood of sputum conversion at the 3rd month of H-mono resistance in patients with TB. These findings are consistent with previous studies that have reported similar associations (Chang et al., 2017; Wu et al., 2019).^[10-11]

The presence of cavitory or extensive lesions on chest X-ray may indicate more advanced disease, and therefore, a greater bacterial load, which can make treatment more challenging. Furthermore, the presence of inhA or katG gene mutations may result in resistance to isoniazid, one of the most commonly used drugs for TB treatment, which can make treatment less effective.

Our findings have important clinical implications for the management of patients with TB. Physicians should consider the presence of cavitory or extensive lesions on chest X-rays and the presence of inhA or katG gene mutations when deciding on the appropriate treatment regimen. Patients with these risk factors may require more intensive treatment approaches, such as longer treatment duration, higher doses of drugs, or the addition of second-line drugs.

Limitations of the study

were study was carried out at one center only, No control group, Small sample size, Patients from limited geographical areas, and a Correlative mycobacterial culture study were not done.

Further multicentric study evaluating the causal relationship of identified risk factors of treatment failure and resistance augmentation would help validate the findings and help evolve adversity reversal strategy in pursuit of a better outcome

CONCLUSION

Male has more incidence of isoniazid mono-resistant tuberculosis and inferior treatment outcome. underweight, previous TB treatment, substance addiction, cavity, and/or extensive radio lesion are Associated with H mono regimen failure.

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