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Original Research Article

Treatment outcomes of patients with isoniazid resistant tuberculosis under National Tuberculosis Elimination Programme in Ahmedabad city: a retrospective study

Jatin G. Nagar*, Kiran C. Rami, Meghna M. Patel, Kaushal M. Bhavsar

Department of Respiratory Medicine, GMERS Medical College and Hospital, Sola, Ahmedabad, Gujarat, India

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***Correspondence:**
Dr. Jatin G. Nagar,
E-mail: jtnagar19@gmail.com

ABSTRACT

Background: Drug resistance tuberculosis remains major public health problem worldwide. In India, the incidence of any isoniazid-resistant TB is 11.6% in new tuberculosis patients, while in previously treated patients, incidence is 25%. For isoniazid resistant cases management 6-9 months duration of H mono regimen containing rifampicin, pyrazinamide, ethambutol and levofloxacin is available under national tuberculosis elimination programme. We present a retrospective study on outcomes of patients of H mono regime in years 2019 and 2020 in Ahmedabad city.
Methods: Retrospectively we collected data about age, sex, co-morbid conditions, resistance level (high/low level isoniazid resistance) and treatment outcome of patients put on H Mono regimen under programme from January 2019 to December 2020 in Ahmedabad city from Ni-kshay, an online web-based portal.
Results: We have collected data of 251 patients (147 in 2019, 104 in 2020). Out of 251, 188 were males and 63 females. Out of 251, favourable outcome seen in 57.4% patients and unfavourable outcome seen in 42.6% patients. Favourable outcome was significantly higher among females compared to males.
Conclusions: Management of drug resistance tuberculosis according to drug sensitivity helps in better patient outcome. Early diagnosis of drug resistance and its treatment, timely diagnosis of treatment failure and management, better patient compliance and patient education about disease help in decrease in the unfavourable outcome.

Keywords: Tuberculosis, Isoniazid resistance, H mono regimen, Outcomes

INTRODUCTION

Tuberculosis (TB) is one of the major infectious disease pathogens contributing to the public health burden and causing deaths globally. The World health organization (WHO) global TB report 2021 shows an incidence of 9.9 million TB cases and 1.3 million deaths due to TB globally. India has the highest TB burden with around 26% of total TB cases globally. The total estimated TB incidence is 2.6 million cases for 2020 for India with 493,000 TB deaths.[1] Even though treatable, TB remains one of the major causes of death due to poor socioeconomic status, undernutrition, co-morbid conditions, tobacco addiction, development of drug resistance, and poor compliance in patients.[1,2]

Drug resistance tuberculosis (DR-TB) is one of the major public health issues adding to the TB burden in India and worldwide. Delay in the detection of DR-TB causes treatment failure, relapse, and the emergence of resistance to other drugs.[3] Globally, more than 150,000 cases were reported for DR-TB in 2020, out of which one-third of cases were reported in India. WHO has categorized DR-TB in five categories: Isoniazid resistant TB (Hr-TB),

rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB), pre-extensively drug resistance TB (pre-XDR TB), and extensively drug resistance TB (XDR TB).[1]

According to the first national antituberculosis drug resistance survey (NDRS) done in India, the incidence of any isoniazid-resistant TB is 11.6% in new TB patients, while in previously treated patients, the incidence is 25%. Any isoniazid resistance may lead to progression to RR-TB.[4]

Since 2017, under the National TB Elimination Programme (NTEP) in India, an H mono Regimen is available to manage cases of isoniazid resistance.[5] All patients with isoniazid resistance and rifampicin sensitive status are put on H mono regimen. Levofloxacin, rifampicin, ethambutol, and pyrazinamide are included in H- mono regimen. It is given for 6-9 months duration. There is no separate intensive or continuation phase in this regimen. The line probe assay (LPA) method is used under the programme for the detection of isoniazid resistance. First–line- line probe assay (FL LPA) detects mutation in Kat G gene and Inh A promoter region for isoniazid resistance. Mutation of Kat G gene leads to the development of high-level isoniazid resistance and mutation of Inh A results in weak isoniazid resistance.[6]

During the course of treatment with the H-mono regimen, the patient's evaluation is done by clinical examination, smear microscopy, and culture. Based on that assigned treatment outcomes as per programme guidelines are as follows: Cured- A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who completed treatment as recommended by the national policy with evidence of bacteriological response and no evidence of treatment failed. Treatment completed- A patient who completed treatment as recommended by the national policy whose outcome does not meet the definition for cure or treatment failed. Treatment failed- A patient whose treatment regimen needs to be terminated or permanently changed to a new regimen option or treatment strategy. Died- A patient who died before starting or during the course of treatment. Lost to follow-up- A patient who did not start treatment or whose treatment was interrupted for 1 consecutive month or more.[7]

The objective of our study was to evaluate the outcomes of treatment for patients on the H mono regimen under the programme from January 2019 to December 2020 in Ahmedabad city.

METHODS

This was a retrospective record review, based on programmatic data. The study was done by department of Respiratory medicine, GMERS medical college, Sola, Ahmedabad. All the patients aged 18 and above, who were put on H mono regimen from January 2019 to December 2020 and registered in Ni-kshay, a web-based, cased based monitoring software application were enlisted. Patients aged less than 18 years and transferred out patients were excluded from this study. Total 251 patients (147 patients in 2019 and 104 patients in 2020 were registered for H mono resistance treatment under the national programme.

Materials and methods

Data regarding age, sex, level of isoniazid resistance (high/low), HIV (Human immunodeficiency virus) status, presence of diabetes mellitus (DM), follow-up sputum, culture, and treatment outcome were downloaded.

This data was entered into the Microsoft office excel 2016 database. Based on their outcomes, cases were divided into two groups: 'Favourable outcomes and unfavourable outcomes'. Favourable outcomes included patients who were categorized as 'cured' and 'treatment completed'. Patients with the outcome of 'lost to follow-up', 'died', 'treatment failure', and 'treatment regimen changed' were included in unfavourable outcome group.

The study protocol was approved by the institutional ethics committee of GMERS medical college, Sola, Ahmedabad. Since this was a record review, a waiver of consent was sought.

Statistical analysis

After compiling the data in Microsoft excel 2016, the chi-square test was applied to compare the categorically variable data. Otherwise, the data was presented as a number (in %).

RESULTS

In the present study, a total of 251 patients (147 patients in 2019 and 104 patients in 2020) were enrolled under the H mono regimen under the programme. These included 63 females and 188 males with a male-to-female ratio being 2.98:1.

Most of the patients were in the age group 18-40 years followed by 41-64 years age group. In the age group of 18-40 years, there were 160 (63.7%) patients, while 76 patients (30.1%) were in the age group of 41-64 years. In females mean age was 38.8±13.1 (25.7-51.9) years, while in males mean age was 39.1±14 (25.1-53.1) years. So overall mean age was 38±14 (24-52) years. Of the study participants, 26 (10.4%) had diabetes and six patients (2.4%) had HIV co-infection (Table 1).

As per data retrieved, 183 (72.9%) patients had high-level isoniazid resistance, and 60 (23.9%) patients had low-level isoniazid resistance. In eight (3.2%) patients isoniazid resistance level was not mentioned on the Ni-kshay portal (Table 1).

Table 1: Patient characteristics based on treatment outcome.

Characteristics	Favourable outcome			Unfavourable outcomes					Total all patients	P value
	Cured	Treatment completed	Total	Treatment failure	Lost to follow up	Died	Regimen changed	Total		
Year										
2019	63 (42.9%)	17 (11.6%)	80 (54.5%)	21 (14.3%)	13 (8.8%)	33 (22.4%)	0 (0%)	67 (45.5%)	147 (58.6%)	
2020	50 (48.1%)	14 (13.5%)	64 (61.6%)	16 (15.3%)	5 (4.8%)	11 (10.6%)	8 (7.7%)	50 (38.4%)	104 (41.4%)	
Sex										
Female	34(53.9%)	9 (14.3%)	43 (68.2%)	7 (11.1%)	3 (4.8%)	9 (14.3%)	1 (1.6%)	20 (31.8%)	63 (25.1%)	0.043
Male	79 (42.0%)	22 (11.7%)	101 (53.7%)	30 (16.0%)	15 (8.0%)	35 (18.6%)	7 (3.7%)	87 (46.3%)	188 (74.9%)	
Age (in years)										
18-40	76 (47.5%)	20 (12.5%)	96 (60%)	25 (15.6%)	11 (6.9%)	23 (14.4%)	5 (3.1%)	64 (40%)	160 (63.8%)	0.467
41-64	32 (42.1%)	9 (11.8%)	41 (53.9%)	10 (13.2%)	4 (5.3%)	18 (23.7%)	3 (3.9%)	35 (46.1%)	76 (30.3%)	
>64	5 (33.4%)	2 (13.3%)	7 (46.7%)	2 (13.3%)	3 (20%)	3 (20%)	0 (0%)	8 (53.3%)	15 (5.9%)	
Co-morbid condition										
Diabetes										
No	102(45.3%)	24 (10.7%)	126 (56%)	36 (16%)	17 (7.6%)	39 (17.3%)	7 (3.1%)	99 (44%)	225 (89.7%)	0.196
Yes	11 (42.3%)	7 (26.8%)	18 (69.1%)	1 (3.9%)	1 (3.9%)	5 (19.2%)	1 (3.9%)	8 (30.9%)	26 (10.3%)	
HIV										
Non-reactive	111 (45.3%)	31 (12.7%)	142 (58%)	35 (14.3%)	18 (7.3%)	42(17.1%)	8(3.3%)	103 (42%)	245 (97.6%)	0.228
Reactive	2 (33.4%)	0 (0%)	2 (33.4%)	2 (33.3%)	0 (0%)	2 (33.3%)	0 (0%)	4 (66.6%)	6 (2.4%)	
Isoniazid resistance										
High level	78 (42.6%)	24 (13.1%)	102 (55.7%)	26 (14.2%)	14 (7.6%)	36 (19.7%)	5 (2.7%)	81 (44.3%)	183 (72.9%)	0.232
Low level	33 (55%)	6 (10%)	39 (65%)	8 (13.3%)	4 (6.7%)	6 (10%)	3 (5.0%)	21 (35%)	60 (24%)	
Not mentioned	2 (25%)	1 (12.5%)	3 (37.5%)	3 (37.5%)	0 (0%)	2 (25%)	0 (0%)	5 (62.5%)	8 (3.1%)	
All patients	113 (45.0%)	31(12.4%)	144 (57.4%)	37 (14.7%)	18 (7.2%)	44 (17.5%)	8 (3.2%)	107 (42.6%)	251 (100%)	

We divided 251 patients into two groups, favourable and unfavourable treatment outcomes. We included cured and treatment completed patients in favourable outcome groups. While we included treatment failure, lost to follow-up, died and regimen changed in unfavourable outcome.

Out of 251 patients, 113 (45%) patients were cured, 31 (12.4%) patients have treatment completed. 37 (14.7%) patients were diagnosed with treatment failure, 18 (7.2%) patients were lost to follow-up. Forty-four (17.5%) patients died during the course of treatment and in eight (3.2%) patients treatment regimen was changed. Out of 251 patients, 144 (57.4%) patients have favourable outcomes and 107 (42.6%) patients have unfavourable outcomes as shown in the table.

Favourable outcomes were significantly higher among females, as compared to males (p 0.043). (Table 1)

DISCUSSION

Tuberculosis is a major public health problem globally. As a part of Sustainable Development Goals (SDG), WHO has targeted to decrease in TB-related deaths by 90% and decrease the incidence of TB by 80% till 2030.[8] Drug-resistant tuberculosis is one of the major troublesome factors to achieve these targets. Early detection of drug resistance and early initiation of treatment of tuberculosis lead to a decrease in TB transmission in the community and decrease morbidity and mortality due to tuberculosis.

For years, the management of rifampicin-resistant/ MDR tuberculosis treatment regimen is available in India. Isoniazid is also the key first-line anti-tubercular agent along with rifampicin used in drug-sensitive tuberculosis. The first NDRS 2014-16 showed that any isoniazid resistance is seen in 16% in all with 11.6% in new cases and 25% in previously treated cases. While MDR TB was seen in 2.84% of new cases and 11.62% among previously treated cases. Resistant to isoniazid being a driving factor for resistance to other anti-tubercular agents.[7]

Among patients with isoniazid-resistant tuberculosis, this study demonstrated, that 45.02% of patients declared cured and 12.35% of patients declared treatment completed as per programmatic guidelines. Treatment success, a composite of cure and treatment completion, was recorded in 57.4% (144/251) patients for years of 2019 and 2020.

Other outcomes studies were done in South Africa, Peru, France, and Taiwan, but the treatment regimen for isoniazid-resistant tuberculosis was different in all countries.[9-12] A study was done in South Africa by Jacobson et al (n=155) from 2000 to 2009 had a treatment completion rate of 65%.[10] While in Peru by Cornejo et al, between 2012-2014, 77.2% (n= 947) patients had treatment success.[10] A study was done by Bachir et al (n=198) in 2021 showed the treatment success in 75.8% (75/99) cases, out of which 10.1% (10/99) were declared cured.[11] The treatment cure rate in the present study was 45.0%. While in Taiwan, a study done by Chien et al (n=395) showed that 328 (83.0%) patients were treated successfully.[12]

In India, the success rate of 78% is registered for H mono/poly DRTB regimen in 2019.[13] While in our study favourable outcome was seen in 57.37% of patients. The observed difference may be due to the small sample size of patients aged 18 years and more and we have taken data of patients with H mono regimen from Ahmedabad city only.

The study done by Chien et al showed treatment success rate was high-level and low-level isoniazid-resistant TB 82.2%, and 83.4%, respectively (p 0.785).[12] In our study treatment success was 65% in patients with low-level isoniazid resistance and 55.7% in patients with high-level isoniazid resistance, which is statistically not significant. (p 0.232).

In a study done by Cornejo et al 186 (19.6%) patients were lost to follow-up. In the present study, 18 (7.2%) patients were lost to follow-up.[10]

In our study, treatment failure was seen in 37 (14.7%) patients and 44 (17.5%) patients died during the course of treatment. So, in our study treatment failure and death were the major component of unfavourable outcomes. Out of 44 dead patients, 7 patients had co-morbid conditions, 5 were diabetic and 2 had reactive HIV status.

Limitation of our study

As we have taken data of patients on H mono regime from Ahmedabad city only. So we have small sample size. Large population study may help to confirm our findings.

CONCLUSION

Drug-resistant tuberculosis is one of the causes of tuberculosis-related morbidity and mortality in India. Early detection of drug resistance and drug sensitivity testing (DST) guided treatment of isoniazid-resistant tuberculosis helps in effective management of isoniazid-resistant tuberculosis which decreases morbidity and mortality of the disease. Treatment failure, lost to follow-up, and death during treatment are the factors for unfavourable outcomes. Better patient education about the disease and compliance of treatment helps in decreasing the number of lost to follow-up cases. Timely detection of treatment failure and effective management accordingly help in better treatment outcomes.

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REFERENCES

1. World Health Organization. Global Tuberculosis Report 2021. Geneva, Switzerland: WHO, 2021. Available at: https://apps.who.int/iris/handle/10665/346387. Accessed on 20 November 2021.
2. Chakaya J. Global Tuberculosis Report 2020 – Reflections on the Global TB burden, treatment and prevention efforts, International Journal of Infectious Diseases. 2021;1201-9712.
3. Dean AS, Zignol M, Cabibbe AM, Falzon D, Glaziou P, Cirillo DM, et al. Prevalence and genetic profiles of isoniazid resistance in tuberculosis patients: A multicountry analysis of cross-sectional data. PLoS Med. 2020;17(1):e1003008.
4. Ministry of health and family welfare, Government of India. Report of the first national anti-tuberculosis drug resistance survey: India 2014–16, New Delhi, India: Ministry of health and family welfare, Government of India, 2018. Available at: https://tbcindia.gov.in/showfile.php?lid=3315. Accessed on 20 November 2021.
5. Ministry of health and family welfare, Government of India. Guidelines on programmatic management of drug-resistant tuberculosis in India 2017. New Delhi, India: Ministry of health and family welfare, Government of India, 2017. Available at: https://tbcindia.gov.in/WriteReadData/Guideline%20for%20PMDT%20in%20India%202017.zip. Accessed on 21 November 2021.
6. Banerjee S, Siddiqi N, Hasnen S. Drug-resistant tuberculosis. In: Sharma S, ed. by. Tuberculosis. 2nd ed. New Delhi: Jaypee. 2009;388-90.
7. Ministry of health and family welfare, Government of India. Guidelines on programmatic management of drug-resistant tuberculosis in India 2019. New Delhi, India: Ministry of health and family welfare, Government of India. 2019.
8. World health Organization. The end TB strategy. World health Organization. Geneva, Switzerland: WHO, 2015. Available at: https://apps.who.int/iris/handle/10665/33126. Available at: 20 November 2021.
9. Jacobson KR, Theron D, Victor TC, Streicher EM, Warren RM, Murray MB. Treatment outcomes of isoniazid-resistant tuberculosis patients, Western Cape Province, South Africa. Clin Infect Dis. 2011;53(4):369-72.
10. Garcia CJG, Alarco´nGuizado VA, Ticona MA, Alarcon E, Heldal E, Moore DAJ. Treatment outcomes for isoniazid mono resistant tuberculosis in Peru, 2012-2014. PLoS ONE. 2018;13(12):e0206658.
11. Bachir M, Guglielmetti L, Tunesi S, Billard-Pomares T, Chiesi S, Jaffré J et al. Isoniazid Resistance Group. Isoniazid-monoresistant tuberculosis in France: Risk factors, treatment outcomes and adverse events. Int J Infect Dis. 2021;107:86-91.
12. Chien JY, Chen YT, Wu SG, Lee JJ, Wang JY, Yu CJ. Treatment outcome of patients with isoniazid mono-resistant tuberculosis. Clin Microbiol Infect. 2015;21(1):59-68.
13. Ministry of health and family welfare, Government of India. Guidelines for programmatic management of drug-resistant tuberculosis in India 2021. New Delhi, India: Ministry of health and family welfare, Government of India, 2021. Available at: https://tbcindia.gov.in/showfile.php?lid=3590. Accessed on 20 November 2021.

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