

Original Article

Assessment of sensitivity pattern of isoniazid and rifampicin in tuberculosis patients

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ABSTRACT:

Background: Pulmonary tuberculosis (TB) refers to any bacteriologically-confirmed or clinically-diagnosed case of TB that involves the lung parenchyma or the tracheobronchial tree. A reliable preparation containing rifampicin, isoniazid, and pyrazinamide in combination is available, as is a combination tablet of all four of these first line drugs. Hence; the present study was conducted for assessing sensitivity pattern of isoniazid and rifampicin in tuberculosis patients. **Materials & methods:** Patients with potential symptoms suggestive of pulmonary tuberculosis and history of treatment with antituberculosis drugs reported to Chest and T.B department were enrolled. Two Sputum samples from each patient were collected in sterile containers and immediately sent for AFB smear microscopy. All sputum smear positive cases with previous history of treatment with first line antituberculosis drugs were instructed to collect sputum sample in a sterile, leak proof falcon tube. **Results:** A total of 100 patients of pulmonary tuberculosis were analyzed. Mean age of the patients of the present study was 38.47 years. Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 50 percent of the patients, while R: Sensitive, H: Resistant was found to be present in 28 percent of the patients. H: Sensitive, R: Resistant was found to be present in 6 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 16 percent of the patients. **Conclusion:** Line probe assay is a rapid and accurate tool for identification of drug resistance in pulmonary tuberculosis patients. Our findings carry significant importance because there have been scarce data on the prevalence of MDRTB among pulmonary TB patients from the recent past.

Key words: Isoniazid, Rifampicin

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INTRODUCTION

In the past few decades, there has been a concerted global effort to eradicate Tuberculosis (TB). According to the World Health Organization (WHO), about 8.6 million cases (8.3–9.0 million) were estimated to have occurred in 2012, approximately 2.9 of whom were in women. Most cases are estimated to be in Asia and Africa (58% and 27% respectively), with the highest incidence in India (range 2.0–2.4 million) and China (0.9 –1.1 million), together accounting for 38% of the total number of cases.¹⁻³ Pulmonary TB refers to any bacteriologically-confirmed or clinically-diagnosed case of TB that involves the lung parenchyma or the tracheobronchial tree based on the revised previous standard case definitions for TB by the World Health Organization

(WHO) in 2013.⁴ Pulmonary TB is an infectious disease caused by *Mycobacterium tuberculosis*. This microorganism not only infects the lung but also other organs such as brain, kidneys and lymph nodes.⁵ A reliable preparation containing rifampicin, isoniazid, and pyrazinamide in combination is available, as is a combination tablet of all four of these first line drugs. Fixed dose combinations of drugs in a single tablet have the great advantage of reducing the possibility of emergence of drug resistance. Pyridoxine is indicated only in malnourished patients or those with conditions predisposing to peripheral neuropathy. The results of susceptibility tests are nowadays usually available before the end of the two month period of intensive treatment: providing the organisms are sensitive to

rifampicin and isoniazid, the other two drugs can be discontinued at the end of the first two months and rifampicin and isoniazid continued for a further four months. Whenever possible, cure should be confirmed by smear and culture of sputum at the end of treatment. If the pleural cavities are involved, the chemotherapy regimen is the same, but pleural aspiration may be needed to reduce breathlessness. If the effusion recurs, glucocorticoids for three to six weeks help to prevent or reduce further reaccumulation.⁶

Drug-resistant tuberculosis (MDR-TB) has emerged as an important global health concern and is on the rise throughout the world. According to the 2012 World Health Organization (WHO) report, 3.7% of new TB cases (patients who have never had treatment for TB, or had been on anti-TB treatment for less than four weeks) and about 20% of retreatment patients (TB patients who had been cured for one month or more) had MDR-TB in 2012. Nine percent of these patients in 2012 had extensive drug-resistant tuberculosis (XDR-TB).⁷⁻¹⁰ Hence; the present study was conducted for assessing sensitivity pattern of isoniazid and rifampicin in tuberculosis patients

MATERIALS AND METHODS

Patients with potential symptoms suggestive of pulmonary tuberculosis and history of treatment with antituberculosis drugs reported to Chest and T.B department were enrolled.

INCLUSION CRITERIA

1. Patients of both sexes i.e. male and female and age >16years.
2. Patients who were willing and were able to give valid informed consent.

3. Cases of positive sputum smear for AFB with history of treatment with first line antituberculosis drugs were included in the study. All patients with potential symptoms of pulmonary Tuberculosis that reported were selected. Two Sputum samples from each patient were collected in sterile containers and immediately sent for AFB smear microscopy. All sputum smear positive cases with previous history of treatment with first line antituberculosis drugs were instructed to collect sputum sample in a sterile, leak proof falcon tube. The samples were immediately sent to Intermediate Reference Laboratory, for Line Probe Assay, as per guidelines. All the data were compiled in Microsoft excel sheet and were analysed by SPSS software. Fischer’s exact t test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

In the present study, a total of 100 patients of pulmonary tuberculosis were analyzed. Mean age of the patients of the present study was 38.47 years. 63 percent of the patients were males while the remaining 37 percent were females. Fever and cough was found to be present in 92 and 95 percent of the patients. Shortness of breath and weight loss was found to be present in 45 percent and 5 percent of the patients. Night sweats, hemoptysis and chest pain was found to be present in 40 percent, 10 percent and 66 percent of the patients. Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 50 percent of the patients, while R: Sensitive, H: Resistant was found to be present in 28 percent of the patients. H: Sensitive, R: Resistant was found to be present in 6 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 16 percent of the patients.

Table 1: Clinical symptoms

Clinical symptoms	Number of patients	Percentage of patients
Fever	92	90
Cough	95	97
Shortness of breath	45	49
Hemoptysis	5	6
Chest pain	10	12
Weight loss	66	76
Night sweats	40	42

Table 2: Pattern of H and R resistance

H and R pattern	Number of patients	Percentage	p- value
H: Sensitive R: Sensitive	50	50	0.0001*
H: Resistant R: Sensitive	28	28	
H: Sensitive R: Resistant	6	6	
H: Resistant R: Resistant	16	16	

Total	100	100	
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*: Significant

DISCUSSION

A nation-wide sample survey conducted during 1955–1958 estimated that India had a high prevalence of TB (400 microbiologically confirmed pulmonary TB cases, and 16,000 TB suspects with chest radiographic abnormalities, per 100,000 population). Extrapolation of these findings, immediately prior to initiation of the Revised National Tuberculosis Control Programme (RNTCP), in 1997 estimated the national burden to be around 3.5 million confirmed pulmonary TB cases and 14 million radiologically abnormal TB suspects. Subsequently, in 2005, an Expert Committee revised the estimated national burden to be around 8.5 million cases (inclusive of microbiologically proven, radiologically suspected, and extrapulmonary TB patients) based on a few studies in small geographic locations. The RNTCP has been quite successful in achieving high case detection and treatment rates in India, and data from isolated centers suggest a reduction of TB prevalence of upto 50% or more with successful implementation of this programme.³ Hence; the present study was conducted for assessing sensitivity pattern of isoniazid and rifampicin in tuberculosis patients

In the present study, a total of 100 patients of pulmonary tuberculosis were analyzed. Mean age of the patients of the present study was 38.47 years. 63 percent of the patients were males while the remaining 37 percent were females. Fever and cough was found to be present in 92 and 95 percent of the patients. Shortness of breath and weight loss was found to be present in 45 percent and 5 percent of the patients. Ninan MM et al compared the performance of line probe assay (GenoTypeMTBDRplus) with culture, as well as the Xpert MTB/Rif assay on sputum samples. Ninety-one consecutive suspects of multidrug-resistant pulmonary tuberculosis patients from January 2013 to June 2013 were enrolled in this study and the results of line probe assay compared to culture and Xpert MTB/Rif. Compared to culture, the assay demonstrated a sensitivity and specificity of 81.5% and 87.5% for the detection of tuberculosis, with sensitivity and specificity of 100% and 93.8%, respectively, for rifampicin resistance. For isoniazid resistance, sensitivity and specificity were 89.3% and 100%, respectively. Compared to Xpert MTB/Rif assay, the assay showed a sensitivity of 80% and specificity of 100% for the detection of tuberculosis a sensitivity of 94.3% (95%CI 80.8–99.3%) and specificity of 94.1% (95%CI 71.3–99.9%) for rifampicin resistance was attained.¹⁰

In the present study, night sweats, hemoptysis and chest pain was found to be present in 40 percent, 10 percent and 66 percent of the patients. Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 50 percent of the patients, while R: Sensitive, H: Resistant was found to be present in 28

percent of the patients. H: Sensitive, R: Resistant was found to be present in 6 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 16 percent of the patients. Arora J et al conducted a study to assess drug resistance detection and mutation patterns of multidrug resistant tuberculosis strains from children in Delhi. A total of 312 sputum samples from pediatric patients presumptive of multidrug resistant tuberculosis were tested for the detection of drug resistance using the GenoTypeMTBDRplus assay. A total of 193 (61.8%) patients were smear positive and 119 (38.1%) were smear negative by Ziehl–Neelsen staining. Line probe assay (LPA) was performed for 208 samples/cultures (193 smear positive samples and 15 cultures from smear negative samples). Valid results were obtained from 198 tests. Of these, 125/198 (63.1%) were sensitive to both rifampicin (RIF) and isoniazid (INH). 73/198 (36.9%) were resistant to at least INH/RIF, out of which 49 (24.7%) were resistant to both INH and RIF (multidrug resistant).¹¹ Muthaiah M et al analyzed prevalence of mutations in genes associated with rifampicin and isoniazid resistance in Mycobacterium tuberculosis clinical isolates from patients with possible MDR TB of Puducherry, South India and to explore the association of specific mutations conferring rifampicin (RIF) resistance. They performed a commercial GenoType MDRplus V.2.0 assay for the rapid detection of rifampicin and isoniazid resistance directly on sputum specimens of patients with possible MDR TB. Totally 558 multidrug resistant, 293 RIF mono resistant and 923 INH mono resistant tuberculosis were detected from the 12,786 patients with possible MDR TB samples. The 50.5% mutations were observed in the region of S531L in MDR TB patients and 55.6% in rifampicin monoresistant cases. In total isoniazid monoresistant, 68.0% mutations were detected in katG gene, which is more prevalent in comparison to inhA gene 32.0%. There were about 57.9% and 32.2% MDR TB cases diagnosed in the age group of > 15 to ≤ 45 years and > 45 to ≤ 60 years respectively. The rate of occurrences of mutations were found widely in the Rifampicin Resistant Determination Region (81 bp) of rpoB gene and the hypervariable region 530–533 codons of rpoB gene is alarming in the specification.¹²

CONCLUSION

Line probe assay is a rapid and accurate tool for identification of drug resistance in pulmonary tuberculosis patients. Our findings carry significant importance because there have been scarce data on the prevalence of MDRTB among pulmonary TB patients from the recent past.

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