

Original Research

Pattern of drug resistance in sputum positive smear cases of pulmonary tuberculosis

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ABSTRACT:

Background: The present study was undertaken for assessing the pattern of drug resistance in sputum positive smear cases (new patients who are sputum positive during follow-up and previously treated) of pulmonary tuberculosis using Line probe assay. **Materials & methods:** A total of 200 patients were included in this study. 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 for Line Probe Assay. Pattern of drug resistance in sputum positive smear cases of pulmonary tuberculosis using Line probe assay was assessed. **Results:** Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 52 percent of the patients, while R: Sensitive, H: Resistant was found to be present in 32 percent of the patients. H: Sensitive, R: Resistant was found to be present in 4 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 12 percent of the patients. **Conclusion:** Our findings carry significant importance because there have been scarce data on the prevalence of MDRTB among pulmonary TB patients from the recent past. Since drug-resistance is a dynamic phenomenon, it is important to monitor the trend of drug-resistance periodically.

Key words: Sputum positive, Pulmonary tuberculosis

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INTRODUCTION

Mycobacterium tuberculosis (MTB) is the causative agent of tuberculosis (TB), an ancient human disease which mainly affects the lungs and hence pulmonary tuberculosis is the most common presentation. Evidence of TB has been found in human thousands of years ago and there have been references to this ancient scourge. For a human pathogen with no known environmental reservoir, Mycobacterium tuberculosis has refined the art of survival and has persisted in human communities from ancient time through modern time.¹⁻³

In healthy people, Mycobacterium Tuberculosis infection often does not cause disease, since the person's immune system acts to "wall off" the bacteria. People infected with tuberculosis bacilli have a 5–15% lifetime risk of falling ill with TB.⁴

In the past few decades, there has been a collaborative global effort to eradicate TB. Some positive returns had

been fetched with these efforts especially since 2000 when the World Health Organization (WHO, 2017) estimated that that global incidence rate for tuberculosis has fallen by 1.5% every year.⁵⁻⁷

Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB. Extrapulmonary tuberculosis (EPTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or WRD-WHO Approved Rapid Diagnostic tests (such as Xpert MTB/RIF). A patient is confirmed to have drug

resistant TB, only when the results are from a RNTCP quality-assured Culture & DST Laboratory and by a RNTCP-endorsed testing method.⁸⁻¹⁰ The present study was undertaken for assessing the pattern of drug resistance in sputum positive smear cases (new patients who are sputum positive during follow-up and previously treated) of pulmonary tuberculosis using Line probe assay.

MATERIALS & METHODS

The present study was conducted for assessing the pattern of drug resistance in sputum positive smear cases of pulmonary tuberculosis using Line probe assay. Patients with potential symptoms suggestive of pulmonary tuberculosis and history of treatment with antituberculosis drugs. The study was conducted on sputum smear positive previously treated pulmonary TB patients and follow up sputum smear positive new pulmonary TB patients. A total of 200 patients were included in this study. 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 for Line Probe Assay. Pattern of drug resistance in sputum positive smear cases of pulmonary tuberculosis using Line probe assay was assessed. All the data were compiled in Microsoft excel sheet and were analysed by SPSS software.

RESULTS

Mean age of the patients was 45.8 years. 68 percent of the patients were males while the remaining 32 percent were females. Fever and cough was found to be present in 88 and 96 percent of the patients. Shortness of breath and weight loss was found to be present in 48 percent and 72 percent of the patients. Night sweats, hemoptysis and chest pain was found to be present in 40 percent, 8 percent and 14 percent of the patients. Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 52 percent of the patients, while R: Sensitive, H: Resistant was found to be present in 32 percent of the patients. H: Sensitive, R: Resistant was found to be present in 4 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 12 percent of the patients. While correlation the H& R sensitivity pattern with age-wise and gender-wise distribution of patients, non-significant results were obtained.

DISCUSSION

Disseminated tuberculosis (TB) is defined as the presence of two or more noncontiguous sites resulting from hematogenous dissemination of *Mycobacterium tuberculosis*, occurring as a result of progressive primary infection, reactivation of a latent focus with subsequent spread, or rarely through iatrogenic origin. Nowadays, the term miliary TB also refers to

progressive and widely spread forms of TB. It entails a hematogenous spread of the disease to several organs, even if the classical pathologic or radiologic findings are absent.^{11,12} The present study was undertaken for assessing the pattern of drug resistance in sputum positive smear cases (new patients who are sputum positive during follow-up and previously treated) of pulmonary tuberculosis using Line probe assay.

Table 1: Pattern of H and R resistance

H and R pattern	Number	Percentage
H: Sensitive R: Sensitive	26	52
H: Resistant R: Sensitive	16	32
H: Sensitive R: Resistant	2	4
H: Resistant R: Resistant	6	12

Mean age of the patients was 45.8 years. 68 percent of the patients were males while the remaining 32 percent were females. Fever and cough was found to be present in 88 and 96 percent of the patients. Shortness of breath and weight loss was found to be present in 48 percent and 72 percent of the patients. Night sweats, hemoptysis and chest pain was found to be present in 40 percent, 8 percent and 14 percent of the patients. Chaudhary J et al evaluated the performance of Line Probe Assay (LPA) for rapid identification and detection of drug resistance in MTBC in respiratory and non-respiratory samples. Samples other than Cerebro Spinal Fluid (CSF) were digested and decontaminated by NALC-NaOH method. Microscopy by ZN (Ziehl-Neelsen) staining, liquid culture by MGIT (Mycobacterial Growth Indicator Tube, BD BBLTM), and LPA by the GenoType MTBDRplus assay, VER 2.0, HAIN Life Science) were performed on all the samples. Results: A total of 70 samples were considered which includes 34 respiratory samples and 36 non-respiratory samples. Out of the 70 samples, 13 (18.6%) were smear positive, 23 (32.8%) grown in culture and 29 (41.4%) were detected positive for MTBC by LPA. Considering culture as gold standard the sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of the LPA for diagnosis of TB in respiratory and non-respiratory samples were found as (83.33%, 72.73%), (72.73%, 80%), (62.5%, 61.54%) and (88.89%, 86.96%) respectively while sensitivity of LPA in smear positive and smear negative samples were found as 90% and 69.23% respectively. All the samples except two showed sensitivity to Isoniazid (INH) and Rifampicin (RIF). Two samples were found resistant to INH only. LPA performed directly on samples is a wonderful tool for fast detection of MTBC in the respiratory samples along with INH and RIF resistance.¹³

Isoniazid (H): Sensitive, Rifampicin (R): Sensitive was found to be present in 52 percent of the patients, while

R: Sensitive, H: Resistant was found to be present in 32 percent of the patients. H: Sensitive, R: Resistant was found to be present in 4 percent of the patients while H: Sensitive, R: Sensitive was found to be present in 12 percent of the patients. While correlation the H& R sensitivity pattern with age-wise and gender-wise distribution of patients, non-significant results were obtained. Prasad PG et al determined the levels and patterns of resistance of MTB isolates to two key anti-TB drugs (rifampicin, RIF and isoniazid, INH) and the type of mutations in drug resistance genes (rpoB, katG and inhA) of the isolates at the southern coastal region of Andhra Pradesh, India, using commercially available GenoType MTBDRplus assay under the Revised National TB Control Program. GenoType MTBDRplus assay was performed on 2859 sputum smear-positive samples and the mutations in the genes responsible for resistance (rpoB, katG and inhA) were analyzed. Among the line probe assay (LPA) valid isolates (2894), 1990 (68.76%) were drug susceptible, 437 (15.13%) were INH monoresistant, 104 (3.59%) were RIF monoresistant, and 363 (12.54%) were multidrug resistant. The frequency of mutations in MTB in the coastal region of Andhra Pradesh, India, was similar to that in retreatment cases from most settings, with close to 80% in rpoB codon 516, 526, and 531, and over 80% in codons katG 315 and/or inhA promoter.¹⁴

CONCLUSION

Our findings carry significant importance because there have been scarce data on the prevalence of MDRTB among pulmonary TB patients from the recent past. Since drug-resistance is a dynamic phenomenon, it is important to monitor the trend of drug-resistance periodically.

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