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## A study of rifampicin resistance among new and retreatment cases of pulmonary tuberculosis using cartridge based nucleic acid amplification test (CBNAAT) in tertiary care hospital

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### Abstract

**Background:** Pulmonary tuberculosis is a common infection disease seen in India. Anti tubercular therapy is highly effective in treatment but prevalence of drug resistant cases is increasing, mostly due to inadequate doses and/or duration of treatment. Early detection of drug resistance case is vital for correct treatment.

**Materials and Methods:** An observational study was done in patients of new and recurrent cases of pulmonary tuberculosis coming to OPD/IPD in Geetanjali Medical College and Hospital, Udaipur. After taking written consent, the detailed clinical history was obtained. Sputum sample were sent for AFB smear examination and CBNAAT testing. Bronchoscopy was done in patients whose chest x ray shadows were suggestive of pulmonary tuberculosis but sputum for AFB smear was negative or sputum was not produced.

**Results:** A total of 200 patients were included in study out of which 107 were primary and 93 were recurrent cases of pulmonary tuberculosis. Most common symptom was fever (65%) followed by cough (55%) then weight loss (20%). Out of 200 cases, 65 patients underwent bronchoscopy. Rifampicin resistant was seen in 2.8% patients of primary tuberculosis and 16.1% of recurrent pulmonary tuberculosis. Presence of pallor, bronchial breathing and higher AFB smear grading were predictive of rifampicin resistance tuberculosis.

**Conclusion:** Rifampicin resistance was seen in 2.8% patients of primary tuberculosis and 16.1% of recurrent tuberculosis. Since the drug resistance in tuberculosis is increasing, hence early detection and timely addition of sensitive drugs should be done in every case to improve outcome.

**Keywords:** Bronchial, CBNAAT, fever, labourers, MDR-TB, pallor, rifampicin, resistance

### Introduction

Pulmonary tuberculosis is a common infectious disease seen in India. India is harboring 2.5 million tuberculosis cases ahead of the six leading nations in the world suffering from this disease. Multidrug-resistant tuberculosis has been known to be a major challenge in TB control programme. In recent years 3.5% of new cases and 20.5% of previously treated TB cases have MDR TB. The prevalence of MDR tuberculosis is 1-3% in new cases and in retreatment cases it is about 12-17% in India. Anti-tubercular therapy is highly effective in treatment but prevalence of drug resistant cases is increasing, mostly due to inadequate doses and/or duration of treatment. Early detection of drug resistance case is vital for correct treatment<sup>[1, 2]</sup>.

Drug-resistant tuberculosis having the microbiological, clinical and programme failure reasons. In microbiological view, the MDR TB is caused due to the mutation in the genes which makes drug inability and inefficacy against those mutant bacilli. MDR TB is a man-made problem because of the inadequate treatment, ineffective drugs, poor monitoring and very less drug adherence leads to the drug resistant tuberculosis.

When mycobacterium tuberculosis is resistant for at least Isoniazid (H) and Rifampicin (R) with or without resistance to other TB drugs used is called as Multi Drug Resistant tuberculosis (MDR TB). Poly Resistance tuberculosis is defined as resistant to more than one

first line drug other than rifampicin, isoniazid. Most of the rifampicin resistance mycobacterium tuberculosis bacilli are also resistant to isoniazid approximately 90% hence they are considered as suffering from MDR TB<sup>[3]</sup>.

The Lowenstein Jensen (LJ) medium is the commonly used solid media for culture of mycobacterium tuberculosis. But it is a slow test usually taking 4 - 8 weeks, not widely standardized, and not economical for screening purposes. This delays initiation of anti-tubercular treatment especially for drug-resistant forms of tuberculosis, increases risk of transmission of (drug-resistant) tuberculosis in the community and increases the risk of spread to extra pulmonary sites within the patient. CBNAAT is a Mycobacterium tuberculosis-specific automated, cartridge based nucleic acid amplification assay, having fully integrated and automated amplification and detection using real-time PCR, provides results within 100 minutes<sup>[4, 5]</sup>.

Some patients with pulmonary tuberculosis do not produce sputum or sputum sample is inadequate, in such cases sputum smear examination can be falsely negative. The use of fiberoptic bronchoscopy is recommended in such cases (if facility is available) and bronchoalveolar lavage should be sending for smear examination and CBNAAT testing<sup>[6]</sup>.

### Materials and Methods

This was an observational study conducted in the department of Respiratory Medicine at Geetanjali Medical College and Hospital, Udaipur, India. Patients suspected of suffering from pulmonary tuberculosis were included in this study. After taking written consent, the detailed clinical history was obtained through interview and physical examination was performed in every patient and documented on a predesigned and pretested Performa. Chest X-ray PA view and routine investigations were sent in every patient. Sputum sample were sent for AFB smear examination and CBNAAT. Bronchoscopy was done in patients whose chest x ray was suggestive of pulmonary tuberculosis but sputum for AFB smear was negative or sputum not produced.

### Results

We prospectively enrolled 200 patients out of whom 107 patients were having primary pulmonary tuberculosis and 93 patients having of retreatment pulmonary tuberculosis. Out of 200 cases 134 were males and 66 females (figure 1). Majority were labourers 37.5% (figure2). Most common symptom was fever (130 patients, 65%) followed by cough (110 patients, 55%) and weight loss (40 patients, 20%). On auscultation crepts were heard in 55 patients (27.5%), wheeze in 54 patients (27%) and bronchial breathing in 36 patients (18%). Pallor was seen in 75 patients (37.5%). Sputum for CBNAAT was sent in 135 patients (67.5%). Out of these 135 patients 40 (29.7%) patients were having 3+ sputum grading, 44 (32.5%) with 2+ sputum grading and 51 (37.7%) with 1+ sputum grading. Rifampicin resistance was seen in 13 patients in this group.

Bronchoscopy was done and BAL sample was sent in 65 patients (32.5%). Out of these 65 patients, rifampicin resistant was seen in 5 (7.3%) patients and all were retreatment cases of pulmonary tuberculosis.

In this study, out of 200, 18 patients were diagnosed as having rifampicin resistance (figure3). Out of these 18 patients 3 were suffering from primary tuberculosis and 15 from recurrent pulmonary tuberculosis. Bronchial breath

sound was heard in 15 (83.3%) out of 18 patients of rifampicin resistant tuberculosis. Prevalence of rifampicin resistance in primary tuberculosis is 2.8% and in recurrent tuberculosis patients is 16.1%.

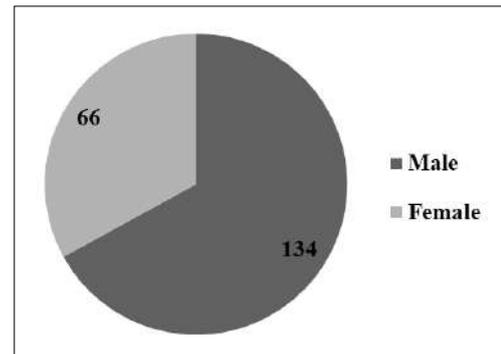


Fig 1: Sex distribution

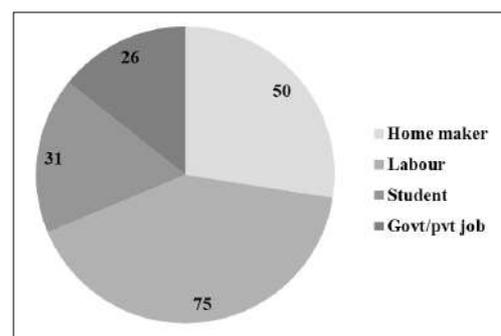


Fig 2: Occupation

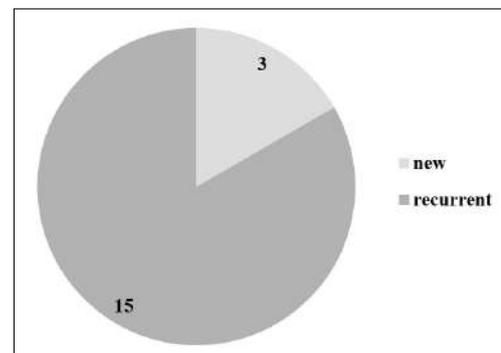


Fig 3: Rifampicin resistant

### Discussion

The study conducted in Geetanjali medical college, Udaipur to find out the prevalence of rifampicin resistance in patients of pulmonary tuberculosis in new and recurrent cases respectively. Out of 200 patients majority were labourers (37.5%). Out of 200 patient's majority were anaemic (36%) which indicates poor nutrition has a huge effect in such cases. Most of the patient were from low socioeconomic background and were nutritionally challenged.

In our study fever was most common symptom (65%) followed by cough/sputum (55%) and weight loss (20%). Study done by Datta *et al.* Showed fever 57% whereas weight loss was on higher side with 61%<sup>[7]</sup>. Out of 135 patients in whom sputum smear and CBNAAT examination was done higher sputum grading was seen in rifampicin resistant group (8 out of 13 patients, 61.5%) as compared to rifampicin sensitive group (32 out of 122 patients, 26.22%). In study done by Kumarnatrajan *et al.* Patients having 3+

sputum grading were 18% and with 2+ sputum grading 43%<sup>[8]</sup>. This seems reasonable as patients suffering from MDR tuberculosis have relatively higher bacillary load. Our study also showed significant difference sputum grading of rifampicin sensitive and rifampicin resistant patients. ( $p < .005$ ) Bronchoscopy was done in 65 patients as these patients were either having dry cough or there sputum for AFB was negative. Out of these 65 patients, 60 (92.3%) were suffering from rifampicin sensitive tuberculosis and 5 (7.3%) were having rifampicin resistant tuberculosis. All these 5 patients were having recurrent tuberculosis. Our studied showed higher prevalence of bronchial breathing in rifampicin resistant cases (15 out of 18 patients, 83.3%) as compared to rifampicin sensitive cases (21 out of 122 patients, 11.6%). In study done by Kumarnatrajan *et al.* 34% patients were having bronchial breath sound. This may be due to the fact that patients who are already treated with anti tubercular drugs are having more chances of residual cavities and/or fibrotic lesions which can result to bronchial breathing. Also, in present study all patients of primary rifampicin resistant were having bronchial breath indicating there association common in resistance pulmonary tuberculosis cases. In our study resistant in primary cases of tuberculosis were 2.8% and in recurrent cases were 16.1% respectively. This result is comparable to study done by Ramachandran *et al.* Found 2.4% in primary and 17.4% in recurrent cases of rifampicin resistant pulmonary tuberculosis. In study done by Bansal *et al.* Found 1.94% in primary and 10.3% in recurrent cases of rifampicin resistant pulmonary tuberculosis<sup>[9, 10]</sup>. In study done by Hamusee *et al.* In 2.4% of patients were primary resistant tuberculosis and 14.3% patients were recurrent resistant cases.

**Conclusion**

Our study of 200 patients of pulmonary tuberculosis showed prevalence of rifampicin resistance tuberculosis is 9% (18 patients out of 200). Prevalence of rifampicin resistance in primary tuberculosis is 2.8% (3 out of 107 patients) and recurrent tuberculosis patients is 16.1% (15 out of 93 patients). Presence of pallor, bronchial breathing and higher AFB smear grading are predictors of rifampicin resistance tuberculosis.

As drug resistant cases in tuberculosis are increasing globally hence early detection of drug resistance is essential. All patient of pulmonary tuberculosis must undergo CBNAAT testing to detect MDR TB. Bronchoscopy should be considered in cases of smear negative suspected tuberculosis or if sputum production is absent. There is need to expand MDR-TB diagnostic facilities in order to timely diagnose MDR –TB.

**Table 1: Risk factors**

Factors	Sensitive	Resistant
Sex distribution	Male-67%,female - 32.9%	Male-66.6%,female- 33.3%
Sputum grading	3+ in 26.2%	3+ in 61.5%
Pallor	Present in 34.6%	Present in 66.7%
Bronchial breath	In 11.6%	In 83.3%

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