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PREVALENCE OF RIFAMPICIN AND ISONIAZID RESISTANCE AMONG NEWLY DIAGNOSED SPUTUM SMEAR-POSITIVE PULMONARY TUBERCULOSIS PATIENTS: A STEP TOWARD EARLY PROGRAMMATIC MANAGEMENT OF DRUG-RESISTANT TB

General Medicine

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ABSTRACT

Introduction: Tuberculosis (TB) remains a leading cause of morbidity and mortality worldwide, with India bearing the highest burden. The emergence of drug-resistant TB, particularly resistance to rifampicin and isoniazid, threatens TB elimination strategies. This study aims to assess the prevalence of drug resistance in newly diagnosed sputum smear-positive pulmonary TB cases to facilitate early programmatic management. **Materials And Methods:** A cross-sectional study was conducted at Basaveshwara Teaching and General Hospital, Kalaburagi, over one year (May 2023–April 2024). A total of 120 newly diagnosed sputum smear-positive pulmonary TB patients were enrolled. Drug resistance was assessed using Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) and Line Probe Assay (LPA). Sociodemographic, clinical, radiological, and laboratory data were collected. Statistical analysis was performed using SPSS version 26. **Results:** Of 120 participants, 62.5% were male and 71.66% were aged 21–60 years. Most belonged to lower socioeconomic classes and had a mean BMI of 17.1 kg/m². Common symptoms included cough (95%) and expectoration (90.8%). Radiologically, infiltration (66.7%) and cavitation (45.8%) were predominant. Drug resistance was observed in 6.66% of cases—isoniazid monoresistance (5%), rifampicin monoresistance (2.5%), and MDR-TB (0.83%). **Conclusion:** The presence of drug resistance in new TB cases highlights ongoing community transmission of resistant strains. Routine drug susceptibility testing at diagnosis, combined with nutritional and socioeconomic support, is crucial for timely initiation of effective treatment and curbing the spread of drug-resistant TB.

KEYWORDS

Drug-resistant tuberculosis, Isoniazid resistance, Rifampicin resistance.

INTRODUCTION

Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB), remains one of the most persistent global health challenges. [1] Despite the availability of effective anti-tubercular chemotherapy and large-scale public health interventions, TB continues to be the second leading cause of death due to a single infectious agent, surpassed only recently by COVID-19. [2] In 2023, the global burden of TB was immense, with approximately 10.8 million people developing the disease and 1.25 million succumbing to it, including 161,000 individuals co-infected with HIV. [3] A particularly alarming development in recent decades has been the emergence and increasing prevalence of drug-resistant TB strains, especially multidrug-resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampicin, the two cornerstone drugs of the first-line TB treatment regimen. [4]

The global threat posed by MDR-TB is substantial. The Global Burden of Disease Study (GBD 2021) indicated only a marginal decline in TB incidence over the past 30 years, with 8.4 million new cases reported in 2021, heavily concentrated in low- and lower-middle-income countries. [5] Of particular concern, however, is the fact that less than 50% of the estimated MDR-TB cases in 2023 received appropriate treatment, due in part to diagnostic delays, limited access to drugs, and programmatic inefficiencies. [3] In 2022, around 450,000 people globally were estimated to have MDR or rifampicin-resistant TB (RR-TB), and the treatment success rate for MDR-TB remained below 60%, largely because of the toxicity, complexity, and duration of second-line treatment regimens. [6,7]

India bears the highest TB burden in the world and faces critical challenges in managing the growing threat of MDR-TB. The National TB Prevalence Survey (2019–2021) reported a pulmonary TB prevalence of 316 per 100,000 individuals aged ≥15 years. [8] India alone accounted for approximately 27% of the global TB burden in 2023 and reported nearly 140,000 cases of drug-resistant TB, a considerable proportion of which were found in new TB patients with no prior history of anti-TB therapy. [3,9] This disturbing trend indicates active community transmission of drug-resistant strains. Research from India has shown that MDR-TB prevalence among newly diagnosed, sputum smear-positive pulmonary TB patients ranges from 1.1% to 5.3%, reinforcing the urgent need for universal drug susceptibility testing (DST) at the time of diagnosis. [10]

The detection of MDR-TB in newly diagnosed cases—those presumed to have drug-susceptible TB—raises critical concerns about the primary transmission of resistant strains. Contributing factors include exposure to infectious drug-resistant TB patients, inadequate infection control measures, high mobility of populations, and the biological adaptability of resistant strains. [7,11] Various studies and meta-analyses have consistently identified additional risk factors such as low socioeconomic status, rural habitation, smoking, prior TB contact, and the presence of pulmonary cavities. [7,11,12] These insights highlight the importance of identifying resistance patterns early in the disease course to prevent further spread and improve treatment outcomes.

In addition to biomedical and behavioral factors, social determinants like poverty, undernutrition, and poor access to healthcare exacerbate the TB crisis in India and similar high-burden settings. Despite the ambitious targets set by the WHO End TB Strategy and India's National Strategic Plan for TB Elimination—to eradicate TB as a public health threat by 2030—the increasing incidence of MDR-TB among new patients threatens to undermine these goals. [3,5] The present study is undertaken to assess the prevalence of resistance to Rifampicin and Isoniazid in newly diagnosed sputum smear-positive pulmonary TB patients using CBNAAT and line probe assay. By evaluating resistance patterns in this population, the study aims to inform the early initiation of Programmatic Management of Drug-Resistant TB (PMDT) regimens, thereby strengthening national TB control efforts.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of General Medicine at Basaveshwara Teaching and General Hospital, affiliated with Mahadevappa Rampure Medical College, Kalaburagi. The study was carried out over a period of 12 months, from May 1, 2023, to April 1, 2024. Data were obtained from patients attending both outpatient and inpatient services during the study period.

A total of 120 patients were enrolled in the study. All participants underwent a detailed clinical evaluation using a structured proforma, followed by a comprehensive physical examination and relevant diagnostic investigations. The inclusion criteria comprised newly diagnosed sputum smear-positive pulmonary tuberculosis (TB) patients aged 18 years and above, irrespective of gender. Patients were

excluded if they had secondary immunodeficiency (such as HIV), diabetes mellitus, malignancy, were receiving immunosuppressive therapy (e.g., corticosteroids or cytotoxic drugs), were diagnosed with extrapulmonary TB, or were pregnant or lactating.

All enrolled patients underwent a set of investigations. Baseline laboratory tests included complete blood count (CBC), erythrocyte sedimentation rate (ESR), random blood sugar (RBS), liver function tests (LFT), renal function tests (RFT), and urine routine examination. A chest X-ray was performed in all patients for radiographic evaluation. Tuberculosis-specific diagnostic tests included sputum examination for acid-fast bacilli (AFB), culture and sensitivity, Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), and Line Probe Assay (LPA) for detecting resistance to rifampicin and isoniazid.

Ethical clearance for the study was obtained from the Institutional Ethics Committee of Mahadevappa Rampure Medical College, Kalaburagi. Written informed consent was obtained from all participants prior to inclusion in the study, with the consent form provided in the local language to ensure clarity and comprehension.

All collected data were entered and analyzed using SPSS Version 26. Continuous variables were analyzed using independent t-tests and one-way ANOVA, while categorical variables were evaluated using the Chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

This cross-sectional study included 120 participants. Most were in the 21–40 and 41–60-year age groups (35.83% each). A male predominance was observed (62.5%). The most common occupation was labourer (40.83%), and the majority belonged to lower (40.83%) and upper lower (38.33%) socioeconomic classes. The mean BMI was 17.1 ± 3.44, indicating undernutrition (Table 1).

Table 1: Sociodemographic Profile Of Study Participants (N = 120)

Variable	Category	Frequency (n)	Percentage (%)
Age Group (years)	**< 20**	10	8.33
	21–40	43	35.83
	41–60	43	35.83
	> 60	24	20.00
Gender	**Male**	75	62.50
	Female	45	37.50
Occupation	**Labourer**	49	40.83
	Student	20	16.67
	Business	18	15.00
	Job	18	15.00
	Homemaker	15	12.50
Socioeconomic Status	**Lower**	49	40.83
	Upper Lower	46	38.33
	Lower Middle	25	20.83
Body Mass Index (BMI)	**Mean (± SD)**	17.1 ± 3.44	

Cough (95%) and expectoration (90.83%) were the most common presenting symptoms. Weight loss was noted in over half the participants (61.67%), while fever and haemoptysis were reported in fewer cases. On examination, pallor (68.33%) and crepitations (66.67%) were frequent findings (Table 2).

Table 2: Clinical Presentation Of Participants

Symptom / Finding	Frequency (n)	Percentage (%)
Symptoms		
Cough	114	95.00
Expectoration	109	90.83
Weight Loss	74	61.67
Fever	47	39.17
Haemoptysis	40	33.33
Physical Findings		
Pallor	82	68.33
Crepitations	80	66.67
Wheeze	41	34.17

Laboratory investigations showed a mean haemoglobin of 10.35 ± 1.65 g/dL. Total leucocyte count and liver function tests remained within normal limits (Table 3).

Table 3: Laboratory Parameters Of The Study Population

Parameter	Mean	Standard Deviation (SD)
Haemoglobin (g/dL)	10.35	1.65
Total Leucocyte Count (/mm³)	7162.67	2544.24
Total Bilirubin (mg/dL)	0.95	0.17
SGOT (U/L)	36.83	16.98
SGPT (U/L)	37.80	19.91

Sputum AFB was positive in all cases, with 1+ grading being most common (44.17%). Radiologically, infiltration (66.67%) and cavitation (45.83%) were the predominant findings, while pleural effusion was rare (1.67%) (Table 4).

Table 4: Radiological And Microbiological Findings

Investigation	Category	Frequency (n)	Percentage (%)
Sputum AFB Grading	**1+**	53	44.17
	2+	40	33.33
	3+	27	22.50
Chest X-ray Findings	**Infiltration**	80	66.67
	Cavitation	55	45.83
	Pleural Effusion	2	1.67

Drug resistance was observed in 6.66% of participants. Isoniazid resistance was most frequent (5%), followed by rifampicin resistance (2.5%) and multidrug resistance in one case (0.83%) (Table 5).

Table 5: Drug Resistance Patterns (N = 120)

Resistance Type	Frequency (n)	Percentage (%)
Isoniazid Only	6	5.00
Rifampicin Only	3	2.50
Isoniazid + Rifampicin (MDR)	1	0.83
Total Resistant Cases	**8**	**6.66**

DISCUSSION

This cross-sectional study evaluated the clinicodemographic profile and laboratory characteristics of 100 newly diagnosed sputum smear-positive pulmonary tuberculosis (PTB) patients. The majority of cases were found in the 21–60 year age range, consistent with findings by Agarwal et al. and Gamachu et al., who noted high TB prevalence among young and middle-aged adults in endemic regions [13,14]. Interestingly, 20% of our patients were aged over 60 years, aligning with trends reported by Kumarnatarajan et al., indicating increasing TB incidence among the elderly due to age-related immunosenescence and possible reactivation of latent infections [15]. These age trends emphasize the need for broader screening strategies and TB awareness campaigns, particularly targeting both economically productive age groups and the aging population.

A male predominance was observed in our cohort (62.5%), comparable to findings from studies by Agarwal et al., Sobhy et al., and Kumarnatarajan et al. [13,15,16]. This gender disparity may be attributed to higher exposure to risk factors such as smoking and occupational hazards among men, as well as differential health-seeking behavior. The predominance of labourers (40.83%) and individuals from lower socioeconomic strata (79.16% falling into lower and upper-lower categories) is consistent with observations by Kumarnatarajan et al. and Gamachu et al., who underscored the role of poverty, malnutrition, and overcrowded living conditions in TB transmission and outcomes [14,15]. These findings highlight the importance of integrating TB control efforts with socioeconomic upliftment and occupational health measures.

Low BMI (mean 17.1 kg/m²) was a notable finding, indicating prevalent undernutrition among patients. This aligns with Gamachu et al. and Sobhy et al., who reported that malnutrition is both a risk factor for TB progression and a predictor of poor treatment outcomes [14,16]. Cough (95%) and expectoration (90.83%) were the most common presenting symptoms, in agreement with classic TB symptomatology as described by Agarwal et al. and Kumarnatarajan et al. [13,15]. Additionally, pallor (68.33%) and chest crepitations (66.67%) were frequent physical findings, reflecting systemic involvement and pulmonary pathology, respectively. These clinical features remain critical for early suspicion and diagnosis, especially in resource-limited settings where access to advanced diagnostics may be restricted.

Laboratory results revealed mild anemia and mildly elevated transaminases, in line with earlier reports by Kumarnatarajan et al.

[15]. Sputum grading showed a predominance of 1+ and 2+ positivity, suggesting moderate bacillary load in most patients; however, 22.5% had 3+ positivity, which, as reported by Agarwal et al., is associated with higher transmission risk and slower sputum conversion [13]. Chest X-ray findings predominantly included infiltrates (66.67%) and cavities (45.83%), which reflect active disease and are known indicators of higher bacillary burden and worse prognosis, as also noted by Gamachu et al. [14]. These findings underscore the role of radiological assessment in stratifying disease severity. Drug resistance was detected in a small fraction of patients, with isoniazid resistance being more common than rifampicin resistance, underscoring the need for routine molecular testing like CBNAAT and LPA for early detection and effective treatment planning.

CONCLUSION

This study highlights the continued burden of pulmonary tuberculosis among individuals from lower socioeconomic backgrounds, particularly in the economically productive age group. The clinical presentation was dominated by classical symptoms such as cough, expectoration, and weight loss, accompanied by frequent findings of anemia and pulmonary infiltrates or cavitations on radiographic imaging. The high prevalence of undernutrition and the presence of drug resistance, especially isoniazid monoresistance, underscore the importance of integrating nutritional rehabilitation and routine drug susceptibility testing into TB control programs. Early diagnosis, tailored therapy based on resistance patterns, and a multidisciplinary approach addressing both clinical and social determinants are essential for improving treatment outcomes and reducing transmission in vulnerable populations.

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