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Evaluating Multidrug-Resistant Tuberculosis Prevalence in Smear-Positive Pulmonary Tuberculosis Patients: Insights from Balochistan, Pakistan

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ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a critical public health issue, especially in high-burden regions such as Pakistan. We aimed to evaluate the prevalence and resistance patterns of MDR-TB among smear-positive pulmonary tuberculosis patients in Balochistan, along with associated demographic and clinical characteristics.

Methods: A retrospective cross-sectional study was conducted at Fatima Jinnah Hospital, Quetta (Capital city of Balochistan), involving 673 confirmed smear-positive pulmonary TB patients from Jan 2021 to Dec 2024. Demographic data, treatment history, and drug susceptibility results were collected. Rifampicin resistance was initially detected using the Gene Xpert MTB/RIF assay, followed by confirmatory testing with Line Probe Assay (LPA) and culture. Statistical analysis included chi-square tests to assess associations between treatment outcomes and resistance patterns.

Results: Of the total participants, 60.3% were female, with the largest age group being 15–34 yr. Smoking (15.6%) and type 2 diabetes (4.6%) were the most prevalent comorbid conditions. Rifampicin resistance was present in all participants, while 84.7% showed resistance to both rifampicin and isoniazid. Fluoroquinolone resistance was observed in 17.2% of cases, and ofloxacin resistance in 8.5%. A significant relationship was identified between gender and treatment outcomes (χ^2 = 14.1846, P=0.0067), although no significant gender-based differences in specific drug resistance were noted.

Conclusion: The high rate of MDR-TB and second-line drug resistance in this cohort highlights the urgent need for enhanced diagnostic tools, public health surveillance, and patient-centered treatment strategies. Tailored interventions are essential to curbing MDR-TB transmission and improving treatment success rates in high-burden settings.

Keywords: Multidrug-resistant tuberculosis, Smear-positive pulmonary TB, Drug resistance patterns, Balochistan, Pakistan, Treatment outcomes.

Introduction

Multidrug-resistant tuberculosis (MDR-TB) presents a formidable challenge to global health, especially in areas with high tuberculosis (TB) infection rates. The rise of

MDR-TB complicates treatment protocols, resulting in increased morbidity, mortality, and healthcare expenditures. It is crucial to understand the prevalence of MDR-TB among smear-positive pulmonary TB patients to develop effective public health strategies and treatment guidelines. Recent research has underscored the concerning increase in MDR-TB cases globally, highlighting the necessity for localized studies to guide targeted interventions (1, 2).
The WHO has classified Pakistan as a high-burden nation for both TB and MDR-TB, ranking it fifth worldwide in terms of TB incidence. The growing prevalence of MDR-TB significantly hampers treatment efforts (3, 4). Annually, Pakistan reports over 413,450 TB cases, which includes a substantial proportion of MDR-TB cases (5). Notably, the prevalence of MDR-TB is markedly higher among previously treated patients compared to those with new TB cases; studies reveal that approximately 16% of previously treated individuals are affected by MDR-TB, whereas the prevalence among new cases is around 4% (4, 6). Several factors contribute to the high incidence of TB and MDR-TB in Pakistan, including poverty, overcrowding, malnutrition, and a deficient healthcare system. Recent reports indicate alarmingly high rates of MDR-TB, with significant resistance to first-line anti-TB medications (4, 7). This situation calls for immediate public health interventions and enhanced healthcare responses to curb the spread of TB and MDR-TB within the country (3). Recent reports indicate alarmingly high rates of MDR-TB, with significant resistance to first-line anti-TB medications (4, 7). This situation calls for immediate public health interventions and enhanced healthcare responses to curb the spread of TB and MDR-TB within the country (3). Data from local healthcare facilities reveal a troubling trend in drug resistance that requires urgent attention (8). In Balochistan, there has been limited research on the prevalence of MDR-TB among smear-positive patients, resulting in gaps in understanding the local epidemiology (9).
We aimed to assess the prevalence of MDR-TB among smear-positive pulmonary TB patients in Balochistan, offering valuable insights into the local epidemiological landscape and contributing to broader TB control efforts in Pakistan.

Materials and Methods

This retrospective study took place at Fatima Jinnah Hospital in Quetta, capital city of Balochistan, Pakistan, focusing on patients diagnosed with tuberculosis (TB) between Jan 2021 and Dec 2024. The hospital is a primary center for TB treatment in the area. The study involved 673 smear-positive pulmonary TB patients registered at Fatima Jinnah Hospital during the study period. Participants eligible for inclusion had confirmed positive sputum tests. Those excluded were patients with extra-pulmonary TB, negative sputum tests, or incomplete medical records.
Data were collected retrospectively from patient treatment records and electronic health files. The information gathered included demographic details (age, sex, and residence), clinical data (HIV status and previous TB treatments), and results of drug susceptibility tests. The Gene Xpert MTB/RIF assay was used for initial diagnosis and to evaluate rifampicin resistance. Patients identified as rifampicin-resistant through the Gene Xpert test were referred to the Drug-Resistant TB Center for further assessment. Confirmatory tests, such as the Line Probe Assay (LPA) and culture, were conducted to determine the presence of multidrug-resistant TB (MDR-TB) and to assess resistance to other first-line and second-line anti-TB drugs.

Data Analysis

Data analysis was performed using the SPSS software ver. 26, (IBM Corp., Armonk, NY, USA). The prevalence of MDR-TB was expressed as a percentage of the total smear-positive cases. Chi-square tests were utilized to explore relationships between drug resistance and various demographic and clinical factors. A *P*-value of less than 0.05 was regarded as statistically significant.

Ethical Considerations

Ethical approval was granted by the Medical Ethics Committee of Fatima Jinnah Hospital. Informed consent from patients was waived due to the retrospective design of the study, and all data were anonymized to maintain confidentiality.

Results

Demographic Characteristics

Overall, 673 participants were enrolled, with a gender distribution of 39.7% male (n=267) and 60.3% female (n=406). The age distribution indicated that the majority of participants were aged 15-24 yr (20.1%, n=135) and 25-34 yr (21.0%, n=141). The population was predominantly from Balochistan (95.8%, n=645), with minimal representation from Punjab (1.0%, n=7) and Sindh (3.1%, n=21) (Table 1).

Associated Factors

The analysis of associated factors revealed that smoking was the most prevalent factor, affecting 15.6% (n=105) of participants. Other associated conditions included diabetes mellitus type 2 (4.6%, n=31), and a small number of participants reported conditions such as HIV (1.2%, n=8) and hepatitis C (1.9%, n=13) (Table 2).

Table 1: Demographic characteristics of participants

Variable	***n= (total 673)***	***%***
Male	267	39.7
Female	406	60.3
Age		
0-4	5	0.7
5-14	13	1.9
15-24	135	20.1
25-34	141	21.0
35-44	99	14.7
45-54	87	12.9
55-64	96	14.3
+65	97	14.4
Province		
Balochistan	645	95.8
Punjab	7	1.0
Sindh	21	3.1

Table 2: Associated Factors in the Study Population

Variable	*n= (total 673)*	*%*
Cancer	1	0.1
Depression	1	0.1
DMT 1	3	0.4
DMT 2	31	4.6
HIV	8	1.2
HBV	3	0.4
HCV	13	1.9
HTN	2	0.3
IHD	2	0.3
Smoking	105	15.6

Treatment History

Among participants, 21.5% (n=145) were newly diagnosed, while 40.6% (n=273) had experienced treatment failure. Previous treatment history showed that 13.5% (n=91) were previously treated, and 2.4% (n=16) had lost follow-up (Table 3).

Table 3: Treatment History of Participants

Variable	*n= (total 673)*	*%*
New	145	21.5
Previously treated	91	13.5
Previously treated (loss to follow up)	16	2.4
Relapse	53	7.9
Treatment failed	273	40.6
Unknown	95	14.1

Drug Resistance

All participants exhibited rifampicin resistance (100%), while multi-drug resistance was noted in 84.7% (n=570) of cases. Isoniazid resistance was present in 56.6% (n=381), with other resistances noted for fluoroquinolone (17.2%, n=116) and ofloxacin (8.5%, n=57). Resistance to other drugs such as ethambutol (1.5%, n=10) and streptomycin (0.9%, n=6) was also documented (Table 4).

Table 4: Drug Resistance Profiles among Participants

Variable	*n= (total 673) c*	*%*
Rifampicin resistance	673	100
Multi drug resistance	570	84.7
Isoniazid resistance	381	56.6
Fluorogqinolone resistance	116	17.2
Ofloxacin	57	8.5
Ethambutol resistance	10	1.5
Kanamycin resistance	7	1.0
Streptomycin resistance	6	0.9
Capreomycin resistance	4	0.6
Pyrazinamide resistance	3	0.4

Statistical Comparisons

Chi-square tests were conducted to assess the relationship between gender and treatment outcomes. A significant association was found between gender and TB treatment outcomes (χ^2 = 14.1846, P=0.0067). However, no significant associations were detected between gender and various drug resistances, including isoniazid, streptomycin, and pyrazinamide (P>0.05 for all) (Table 5).

Table 5: Chi-Square Test Results for Gender and Treatment Outcomes

Comparison	*Chi-square (χ^2)*	*P-value*	*df*
Gender vs TB Treatment Outcome	14.1846	0.0067**	4
Gender vs Drug Resistance Type	3.3987	0.4934	4
Gender vs Isoniazid Resistance	1.2891	0.2562	1
Gender vs Streptomycin Resistance	0.0400	0.8414	1
Gender vs Pyrazinamide Resistance	0.5708	0.4499	1
Gender vs Ethambutol Resistance	0.0000	1.0000	1
Gender vs Fluoroquinolone Resistance	3.8326	0.0503	1
Gender vs Capreomycin Resistance	0.8877	0.3461	1
Gender vs Ethionamide Resistance	1.0323	0.3096	1
Gender vs Kanamycin Resistance	0.0480	0.8266	1
Gender vs Ofloxacin Resistance	1.5594	0.2117	1

Discussion

This study presents a thorough examination of MDR-TB among smear-positive pulmonary TB patients in Balochistan, Pakistan. The results underscore significant public health issues and provide valuable insights into demographic trends, associated risk factors, and drug resistance profiles. Notably, the study found a higher prevalence of MDR-TB among females (60.3%) compared to males (39.7%), which contrasts with some regional studies that reported a male predominance. For example, research conducted in Khyber Pakhtunkhwa indicated a higher incidence among males (4). However, other studies have also shown a similar female predominance, suggesting that the distribution of gender may vary due to local sociocultural contexts and differences in healthcare access (10).

The age distribution of TB patients typically reveals a notable prevalence among young adults, particularly those aged 15 to 34 yr. This observation is consistent with national data indicating that young adults constitute a high-risk group for TB. For example, in Brazil, while the highest TB incidence was observed among adult males, young males demonstrated the most significant increase in case rates, emphasizing the necessity for targeted prevention strategies within this

demographic (11). Furthermore, in countries with low TB incidence, the disease is increasingly concentrated among high-risk populations, including young adults, migrants, and individuals facing social vulnerabilities (12). Additionally, smoking emerged as the most common associated risk factor (15.6%), supporting existing literature that identifies smoking as a significant contributor to TB infection and disease progression (13).

Additional comorbidities, such as type 2 diabetes mellitus (4.6%), HIV (1.2%), and hepatitis C (1.9%), were also identified among patients. These conditions are known to impair immune function, increasing susceptibility to TB and complicating treatment outcomes. Specifically, diabetes is linked to a higher risk of developing TB and adverse treatment results. One study found that diabetes significantly increases the risk of mortality in TB patients, with an adjusted odds ratio of 5.16 for unfavorable outcomes (14). Co-infection with HIV also heightens the risk of TB and complicates treatment, as individuals with HIV are more likely to experience poor treatment outcomes, reflected in an adjusted hazard ratio of 3.74 for post-TB mortality (15). Furthermore, hepatitis C co-infection complicates TB treatment, leading to increased morbidity and mortality; the presence of hepatitis C has been identified as an independent risk factor for unfavorable TB treatment outcomes (14). Collectively, these conditions weaken immune responses, rendering individuals more vulnerable to TB and complicating their treatment regimens.

All participants in this study exhibited resistance to rifampicin, thereby confirming their classification as cases of MDR-TB. Moreover, 84.7% of participants demonstrated resistance to both rifampicin and isoniazid. These rates are notably higher than the national averages reported in earlier studies, which indicated MDR-TB prevalence rates ranging from 4.9% to 10.4% among various populations in Pakistan (16). The increased resistance rates observed in this study may be linked to several factors, including inadequate adherence to treatment, prior exposure to anti-TB medications, and limited access to quality healthcare services (17).

Resistance to second-line drugs, including fluoroquinolones (17.2%) and ofloxacin (8.5%), was also noted in this study. These findings align with other regional research that has reported substantial resistance to second-line medications, which presents significant challenges for effective MDR-TB management (18).

Conclusion

A notable association was identified between gender and TB treatment outcomes, indicating potential gender-specific factors that may influence treatment efficacy. However, no significant correlations were found between gender and resistance to specific drugs, such as isoniazid, streptomycin, and pyrazinamide. While gender may affect overall treatment outcomes, it does not seem to impact the development of resistance to individual drugs. The high prevalence of MDR-TB and the observed resistance patterns highlight the urgent need for improved diagnostic, treatment, and prevention strategies in Balochistan and similar contexts. Strengthening laboratory capabilities for rapid and accurate drug susceptibility testing is essential for the timely initiation of appropriate therapy. Additionally, implementing comprehensive patient education and support programs can enhance adherence to treatment regimens, thereby reducing the risk of treatment failure and the emergence of further resistance.

Recommendations for Future Research

Future research should prioritize longitudinal studies that monitor treatment outcomes over time and identify factors contributing to the emergence and transmission of drug-resistant TB strains. Exploring the influence of socioeconomic determinants, healthcare access, and patient behaviors will offer a more comprehensive understanding of the MDR-TB epidemic. This knowledge can inform the development of targeted interventions aimed at mitigating the impact of drug-resistant TB.

Conflict of interest

The authors declare that there is no conflict of interests.

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