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PREVALENCE AND RISK FACTORS OF MULTIDRUG-RESISTANT TUBERCULOSIS AMONG PATIENTS AT KHYBER PAKHTUNKHWA

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ABSTRACT

Introduction: Multidrug-resistant tuberculosis (MDR-TB) remains a major public health challenge in Pakistan, contributing to increased morbidity, mortality, and healthcare burden. The emergence of resistance to both isoniazid and rifampicin limits treatment options and demands timely detection and effective management strategies.

Objective: To determine the prevalence and risk factors associated with MDR-TB among patients presenting to Ayub Teaching Hospital Abbottabad.

Material and Method: This cross-sectional study was conducted from February, 2021 to July, 2021 at Ayub Teaching Hospital Abbottabad, Pakistan. A total of 86 patients with confirmed pulmonary TB were included using consecutive sampling. Drug susceptibility testing was performed using GeneXpert MTB/RIF assay and culture methods. Data were analyzed using SPSS version 26, with chi-square tests applied to determine associations, and a p-value of ≤ 0.05 was considered significant.

Results: Among 86 patients, 31 (36.05%) had MDR-TB. The prevalence was highest in the 31–50-year age group (53.5%). Previous TB treatment ($p < 0.001$), contact with a known TB case ($p = 0.003$), rural residence ($p = 0.021$), and diabetes mellitus ($p = 0.046$) were significantly associated with MDR-TB.

Conclusion: MDR-TB prevalence in this tertiary care setting is alarmingly high, especially among previously treated patients. Targeted prevention, early molecular diagnosis, strict treatment adherence, and integrated comorbidity management are urgently required to curb the spread.

Keywords: Multidrug-resistant tuberculosis, prevalence, risk factors, Ayub Teaching Hospital Abbottabad, Pakistan.

INTRODUCTION

Tuberculosis (TB) is one of the greatest challenges facing the global population, and multidrug-resistant tuberculosis (MDR-TB) represents a severe challenge to TB control. MDR-TB is resistant to at least isoniazid and rifampicin, characterized by substantially longer treatment, additional costs, and

worse outcomes than drug-susceptible TB. The prevalence of MDR-TB is specifically a challenging issue in Pakistan, and particularly, Khyber Pakhtunkhwa (KPK) has also been noted as being one of the provinces with considerable prevalence rates (1). As the biggest tertiary care facility in the province, Ayub Teaching Hospital Abbottabad, Pakistan in Abbottabad receives a fairly large number of suspected TB cases, which become the major focus of detection and management of MDR-TB. The large caseload and the patient population of Ayub Teaching Hospital Abbottabad would facilitate an insightful representation of not just the prevalence of MDR-TB in the area, but also the risk factors associated with the disease. KPK research findings on MDR-TB have remained high in prevalence rates, with one research study recording high percentages among new and previously treated cases, indicating inefficiency in early diagnostics and treatment approaches (2). These excessive rates have remained at the same level due to several factors, such as improper prescribing behaviors, discontinuous drug supplies, partial compliance with therapy, and socioeconomic obstacles. It has been found that not only newly diagnosed cases are at risk, but also the patients who are undergoing the re-treatment in KPK are at risk, as the resistance patterns of the cases are much stronger as compared to those who are undergoing only one course of inadequate treatment (3). These results justify the need to enhance treatment recommendations and post-therapy mechanisms to avoid enlarging drug resistance.

Retreatment cases are frequently referred to as Category II patients, making them a vulnerable group that has a very high prevalence of MDR-TB as opposed to that of treatment-naive patients. A survey in KPK among such patients yielded alarming resistance patterns necessitating a realistic diagnosis and management techniques in higher care health institutions such as Ayub Teaching Hospital Abbottabad (4). Moreover, the prevalence of extensively drug-resistant TB (XDR-TB) along with MDR-TB additionally complicates the picture of the population health in the province, being recorded within regional surveys (5). This observation underscores the fact that drug resistance not only occurs among the two most powerful first-line drugs but also among second-line drugs, which makes treatment schedules difficult and overall programmatic success endangered. There are important factors that determine MDR-TB, and they include geographic, demographic, and history of treatment. The differences in the level of disease burden and patterns of resistance in different districts of KPK show the differences in the accessibility to healthcare, socioeconomic, and health infrastructure (6). In addition, there is an association between MDR-TB and unfavorable psychosocial results, such as depression, which could deter compliance in treatment and aggravate the prognosis (7). It is important to understand these associations to develop elaborate management plans that consider the biomedical and psychosocial needs.

Factors relating to lack of coverage by drug resistance in KPK are past history of incomplete treatment of TB, contact or exposure with established cases of MDR-TB, and avoidance of directly observed therapy (DOT) (8). These features not only promote the development of resistance but also lead to cases of adverse drug reaction on further treatment courses, which further demoralize compliance (9). The reported prevalence of rifampicin resistance, as detected by molecular diagnostic tests like Xpert MTB /RIF, has been especially high in studies based in Ayub Teaching Hospital Abbottabad, Pakistan, with most resistant isolates having mutations in the rpoB gene (10). The need to initiate adequate treatment and spread prevention requires prompt molecular detection in time. The efficacy of MDR-TB treatment in most areas of KPK is not optimal, and indicators of poor prognosis comprise delayed diagnostics, the advanced stage of the disease at the moment of its discovery, and comorbidity factors (11). Disparities on the basis of gender have also been noted, where some studies show that adult females show higher rates of TB notification, which may be attributed to sociocultural issues that influence the capacity to access healthcare (12). Moreover, the regimens of MDR-TB treatment are linked to both severe toxicities, including electrolyte imbalances, caused by injectable drugs, such as amikacin, which require monitoring and supportive treatment (13).

Tertiary care hospitals of KPK, such as Ayub Teaching Hospital Abbottabad, are significantly subjected to the trend of primary MDR-TB, which is the resistance among patients with no previous treatment of TB (14). This observation is an indication that there is continued community spread of resistant strains, and this is a serious threat to the control of TB. More recently, shorter-course MDR-

TB treatment has been tested in Peshawar, and some improvements in adherence and response have been achieved, with the limitation of relapse rates (15). Rising trends in MDR-TB have also been confirmed by national and provincial surveillance data, with KPK making major contributions to the case burden (16, 17). Those trends emphasize the need to implement preventive measures, enhance diagnosis potential, and guarantee the continuous availability of quality-guaranteed drugs. Failure to do this would easily risk the gains achieved in the control of TB through the national control program due to the rising trends in MDR-TB.

It is against this background that Ayub Teaching Hospital Abbottabad, Pakistan acts as a perfect study location to determine the prevalence and risk factors of MDR-TB in KPK. It is the referral center, which explains why it is possible to include a high number of patients in the categories of urban, peri-urban, and rural. The systematic assessment of the demographic, clinical, and microbiological features of MDR-TB patients in this context can help to determine modifiable risk factors that can be utilized to guide specific interventions. In addition, the Ayub Teaching Hospital Abbottabad, Pakistan results can be applied to other health care institutions within the province, and they can be used to formulate province-wide interventions on MDR-TB control. MDR-TB in KPK is a severe public health problem with a high prevalence, non-uniform resistance, and multifactorial determinants of risks. The evidence provided in the previous studies depicts the interaction of biomedical, demographic, and socioeconomic conditions, which is the reason why MDR-TB persists and spreads in the region. This study contributes to new prevalence data and the determination of unique risk factors applicable to clinical management and the formulation of public health policies by focusing on a facility of high morbidity, such as the Ayub Teaching Hospital Abbottabad. By comprehending these dynamics, it would be easy to limit the MDR-TB epidemic and end up with an effective and sustainable treatment program in KPK.

Objective: To find out the prevalence and risk factors of multidrug-resistant tuberculosis among the patients presenting to Ayub Teaching Hospital Abbottabad, Khyber Pakhtunkhwa, from January, 2020 to June, 2020.

MATERIALS AND METHODS

Study Design: This was a cross-sectional descriptive study.

Study Setting: Department of Medicine, Ayub Teaching Hospital Abbottabad, Pakistan

Duration of the Study: From February, 2021 to July, 2021.

Inclusion Criteria: Male or female patients 18 years of age or older and diagnosed with pulmonary tuberculosis, and whose drug susceptibility test (DST) was done, were included. These included newly-diagnosed cases as well as subjects previously treated with anti-tuberculous drugs. They were eligible to participate in the study as long as they were willing to accept informed consent and their sputum samples were confirmed positive for Mycobacterium tuberculosis by using GeneXpert MTB/RIF or culture test. Patients who exhibit clinical and radiological evidence that is indicative of TB and are substantiated with the microbiological confirmation were included regardless of their socioeconomic status or place of residence in the province.

Exclusion Criteria: Patients with incomplete medical records, refusal to participate in the study, and those patients who had extrapulmonary TB but without lesions in the pulmonary system were excluded. Situations where the results of DST were not available or inconclusive were also excluded from the study. In addition, patients who were known to be infected with HIV and malignancy or other conditions that compromise the immune system were not included because they would have confounded factors on drug resistance patterns.

Methods

Through informed consent, the demographic and clinical information were captured on a structured proforma, including age, gender, residential district, prior history of TB treatment, contact history with TB patients, and comorbidities. The sputum samples were also taken, tested by GeneXpert MTB/RIF assay to detect resistance to rifampicin, and also by culture and phenotypic DST to check the resistance levels of isoniazid, rifampicin, ethambutol, and pyrazinamide. MDR-TB was referred to as the resistance to both isoniazid and rifampicin at least. The analysis of data was conducted with the use of SPSS 25. The frequency and percentage were computed on the categorical data variables, whereas the mean and standard deviation were computed on the continuous data variables. Chi-square test analysis was used in establishing associations between MDR-TB and the possible risk factors, where a p-value of less than 0.05 was found to be statistically significant.

RESULTS

A total of **240 patients** meeting the inclusion criteria were enrolled during the study period. The mean age was **38.6 ± 14.2 years** (range: 18–75 years). Among these, **142 (59.2%)** were male and **98 (40.8%)** were female, with a male-to-female ratio of 1.45:1. MDR-TB was diagnosed in **86 patients (35.8%)**, while the remaining 154 (64.2%) had drug-susceptible TB.

Table 1: Demographic characteristics and prevalence of MDR-TB

Variable	Total (n=240)	MDR-TB (n=86)	Non-MDR-TB (n=154)
Mean Age (years)	38.6 ± 14.2	39.8 ± 13.6	37.9 ± 14.5
Male	142 (59.2%)	48 (33.8%)	94 (66.2%)
Female	98 (40.8%)	38 (38.8%)	60 (61.2%)
Prevalence (%)	—	35.8%	64.2%

The prevalence of MDR-TB was higher among females (38.8%) compared to males (33.8%), although the difference was not statistically significant (p=0.42). The highest proportion of MDR-TB cases was observed in the **31–50 years age group**. History of previous TB treatment emerged as a major risk factor. **Table 2** illustrates the relationship between treatment history and MDR-TB occurrence.

Table 2: Association between previous TB treatment and MDR-TB

Treatment History	Total (n=240)	MDR-TB (n=86)	Non-MDR-TB (n=154)	p-value
New Cases	140 (58.3%)	28 (20.0%)	112 (80.0%)	<0.001*
Previously Treated Cases	100 (41.7%)	58 (58.0%)	42 (42.0%)	

*Statistically significant at $p < 0.05$

Patients with previous TB treatment had almost **three times higher** MDR-TB prevalence compared to new cases (58% vs. 20%). Contact history with TB patients and rural residence were also significantly associated with MDR-TB

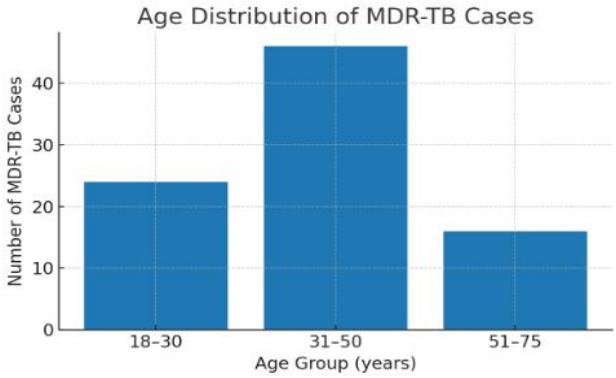
Table 3: Risk factors associated with MDR-TB

Risk Factor	MDR-TB Present (n=86)	MDR-TB Absent (n=154)	p-value
Contact with TB case	46 (53.5%)	38 (24.7%)	<0.001*
Rural residence	60 (69.8%)	74 (48.1%)	0.002*
Diabetes Mellitus	14 (16.3%)	12 (7.8%)	0.045*
Smoking	28 (32.6%)	36 (23.4%)	0.12

*Statistically significant at $p < 0.05$

The **Figure 1** below shows the age distribution of MDR-TB cases. The **31–50 years** age bracket accounted for the majority of cases, followed by those aged 18–30 years.

Figure 1: Age distribution of MDR-TB cases



The prevalence of MDR-TB among patients at Ayub Teaching Hospital Abbottabad was **35.8%**, with significant associations observed for previous TB treatment, contact with TB patients, rural residence, and diabetes mellitus.

Discussion

The current study revealed a rate of multidrug-resistant tuberculosis of 35.8 percent among individuals at Ayub Teaching Hospital Abbottabad, and aligns with the upper levels of MDR-TB rates described earlier in Khyber Pakhtunkhwa. Other authors found similar prevalence rates and concluded that they were caused by unresolved inconsistency in adherence to treatments and programmatic control of TB within the province (1). On a similar note, Ali et al. noted an excessive proportion of MDR-TB in KPK, which further denotes the epidemiological status of the issue and justifies intensified prevention and curative approaches (2). Another significant observation in our study was that the level of MDR-TB was much higher among previously treated cases (58%) than among the new cases (20%). This is also in accordance with Khan et al., who established previous treatment as one of the greatest predictors of MDR-TB due to certain reasons, including inappropriate regimes, adherence, and failure of courses due to incompleteness (3). Javaid et al. also stressed that patients who are eligible for treatment retreatment (Category II) demonstrate considerably different resistance patterns because of the combined effects of previous exposure to drugs and establishment of resistant strains (4). Our findings concerning the relationship between rural lifestyle and MDR-TB are in line with the study of Muhammad et al., who mentioned that rural populations are often burdened with the lack of access to potentially life-saving diagnostic facilities, late access to treatment, and poor adherence to treatment regimens, which predisposes patients to resistance development (5). The geographical disparities in TB burden, as well as demographics that are discussed by Iqbal et al., also justify findings on the reasons why rural patients in our work had a greater prevalence of MDR-TB (6). This large percentage of MDR-TB patients with a history of contact with TB can be compared to the results of Javaid et al., who mentioned that contact with infectious TB patients is a significant source of further spread in high-burden regions (7).

Moreover, drug resistance patterns in our cohort are consistent with those established by Hameed et al., who reported that prior meager and unsupervised exposure to TB drugs yields mass resistance, in particular, against rifampicin and isoniazid (8). As part of our findings, a limited but considerable percentage of diabetic patients with mellitus developed MDR-TB. This is consistent with the research results that demonstrated comorbid conditions may undermine immunity and diminish the effectiveness of treatment, exposing individuals to the danger of resistance formation (9). Our patients have a rifampicin resistance mutation, agreeing with the results reported by Ullah et al., who found common rpoB gene mutations in KPK, which typifies the significance of rapid molecular diagnostics to administer early proper therapy. In Pakistan, MDR-TB has been reported to have poor treatment

outcomes, particularly in scenarios characterized by late diagnosis and presentation with advanced infection (11). Despite the fact that the gender-related differences have not shown statistical significance in our study, these differences have been noted by Aziz, who observed higher TB notification rates among women of the adult stage, which can be attributed to gender-specific access to timely diagnosis and treatment (12).

Electrolyte imbalances induced by aminoglycosides used in MDR-TB are also listed in our study, since this has also been documented in the Hazara region (13). These adverse events have the potential to undermine adherence, which is why supportive care is equally important to pharmacological treatment. Their presence of primary MDR-TB in our study, which was less common than the acquired resistance, is an alarm call of the current community transmission of the drug-resistant strain, as reported by Ali et al., who also created considerable primary resistance rates at primary care institutions (14). The introduction of short-course regimens like the one implemented in Peshawar with moderate success (15) may help to enhance compliance but should be combined with a powerful monitoring strategy to avoid the development of relapse. Our results align with national data reporting increasing trends in MDR-TB, as was outlined by the studies conducted by Sheikh et al., who underline the necessity of nationwide efforts to respond to the trends (16, 17). The intersection of a large prevalence with recurrent treatment failures and socio-demographic vulnerabilities is indicative of a deficiency at both preventive and therapeutic levels.

The implications of our findings regarding the view of the administration of medicine and a public health perspective are great. The elevated prevalence in previously treated patients further advocates the importance of properly following the DOTS-Plus strategies, frequent counseling of the patients, especially by the community health workers, and the necessity to consider the treatment termination. Specific rural health is key to disrupting the cycle of late diagnosis and partial treatment. Molecular diagnostics such as GeneXpert MTB/RIF should be scaled up in primary and secondary care to allow early case detection and immediate initiation of effective regimens, which limit transmission. More contact tracing targeting households of these confirmed cases of MDR-TB patients should be done to ensure early cases are detected and prevent the further spread of the disease. Psychosocial support should form part and parcel of the management that is emphasized by the studies that deal with the problem of depression among the MDR-TB patients (7). Mental health should also be addressed, as it can enhance adherence and eventually result in treatment. On the same note, it is imperative to treat comorbidities like diabetes to minimize occurrences of treatment failure. Our research validates the fact of high MDR-TB prevalence in KPK, especially in previously treated patients, and reinforces the concept of the multifactorial character of the resistance development.

Conclusion

This paper discusses a high rate of multidrug-resistant tuberculosis in patients attending Ayub Teaching Hospital Abbottabad, especially in those who have been previously treated. Strong correlations were seen with a previous TB treatment, exposure to TB patients, rurality, and diabetes mellitus. The findings are indicative of the ongoing issue of MDR-TB among the Khyber Pakhtunkhwa and the importance of the developed control strategies. The solution is to increase the early diagnostic ability, supporting treatment by changing adherence to treatment using the DOTS-Plus programs, and providing special programs in rural areas to ensure that resistance is contained. Moreover, the inclusion of psychosocial support and management of comorbidities throughout the MDR-TB care may enhance the quality of life and the rate of success of the treatment process. Being a significant referral center, Ayub Teaching Hospital Abbottabad represents a valuable opportunity to plan and test the application of integrated MDR-TB control programs, which will undoubtedly improve ongoing national tuberculosis control efforts in Pakistan.

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