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FREQUENCY OF MULTI-DRUG-RESISTANT TUBERCULOSIS IN PATIENTS WITH PULMONARY TUBERCULOSIS AT GHULAM MUHAMMAD MAHAR MEDICAL COLLEGE, SUKKUR

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Abstract

OBJECTIVE: *To determine the frequency of multi-drug-resistant tuberculosis in patients with pulmonary tuberculosis.*

METHODOLOGY: *This cross-sectional investigation was executed in the year 2024 within the Department of General Medicine and Pulmonology at Ghulam Muhammad Mahar Medical College (GMMMC), situated in Sukkur, encompassing a cohort of 147 patients who received a diagnosis of pulmonary tuberculosis (PTB) and exhibited a clinical history of symptoms enduring for a period surpassing 2 weeks. Eligible subjects, whose ages ranged from 18 to 70 years and inclusive of individuals of both sexes, were methodically assessed to examine the prevalence of multi-drug-resistant tuberculosis (MDR-TB) among patients diagnosed with pulmonary tuberculosis. The amassed dataset underwent comprehensive analysis employing SPSS version 26, which incorporated both descriptive and inferential statistical methodologies.*

RESULTS: *Multidrug-resistant tuberculosis (MDR-TB) was detected in 61 out of 147 patients diagnosed with pulmonary tuberculosis, resulting in a prevalence rate of 41.49%. Among the individuals diagnosed with MDR-TB, an overwhelming 96.7% fell within the age range of 18 to 40 years, and 68.9% were identified as male. Statistically significant correlations were established with respect to age ($p=0.000$), gender ($p=0.000$), educational attainment ($p=0.020$), employment status ($p=0.001$), socioeconomic status ($p=0.037$), marital status ($p=0.001$), and tobacco use ($p=0.009$).*

CONCLUSION: *This study revealed a notably high frequency of multidrug-resistant tuberculosis (MDR-TB) among patients with pulmonary tuberculosis (PTB). The findings highlight significant associations between MDR-TB and key demographic and socioeconomic factors, including younger age, male gender, lower educational status, and smoking habits. These findings highlight the need for improved diagnostic screening, especially molecular testing like GeneXpert, and*

targeted interventions in high-risk populations. To reduce MDR-TB in this region, early detection, treatment adherence, and socioeconomic disparities need to be improved.

INTRODUCTION

Tuberculosis (TB) is defined as a transmissible disease that predominantly affects the pulmonary system, although it may also impact various other anatomical sites. This infectious disease is instigated by the pathogenic bacillus Mycobacterium tuberculosis, which is disseminated through airborne particles (droplet transmission) when individuals harboring the infection engage in actions such as coughing, sneezing, or expectorating [1]. TB ranks as the second most lethal infectious disease following COVID-19, accounting for the 13th highest mortality rate worldwide, notwithstanding its preventable and treatable nature [2]. In the year 2021, it is estimated that approximately 10.6 million individuals were diagnosed with tuberculosis (TB) on a global scale, with a resultant mortality of 1.6 million attributed to the disease [3].

It is noteworthy that not all individuals infected with TB exhibit clinical symptoms. Tuberculosis can manifest in two distinct forms: latent TB infection and active TB disease. In the case of latent TB infection, an individual harbors the Mycobacterium tuberculosis but remains asymptomatic, with the pathogens remaining in a dormant state potentially for the entirety of their life. Such individuals will typically present with a positive tuberculin skin test while demonstrating a normal chest radiograph [3,4].

The appearance of Multi-drug Resistant TB (MDR-TB) is arguably the most worrying health concern. MDR-TB is defined as a form of tuberculosis caused by bacterial strains resistant to at least the two most powerful first-line anti-tuberculosis drugs, rifampicin and isoniazid [5]. In a more recent clinical intervention study of one of the cohorts of 169 participants, very high rates of resistance were identified, with 66.9% of subjects having resistance to isoniazid and 46.15% of subjects having resistance to rifampicin. These findings underscore the complexities for TB management in settings under high drug resistance pressure [6]. In addition, the study found that as many as 89.32% of TB cases were MDR-TB, compared to only 10.68% non-MDR [7]. In 2021, the worldwide prevalence of MDR/RR-TB among all new pulmonary TB cases was calculated to be as high as 3.6%, and Pakistan ranked 4th among high TB burden countries regarding the prevalence of this form of TB disease [8]. Pakistan recorded 3.7% of MDR-TB among new cases and 18.1% among previously treated cases in 2012 [9].

The prevalence of MDR-TB has escalated dramatically, constituting an ongoing global health crisis, as the efficacy of second-line pharmaceutical agents remains suboptimal. In 2021, only one-third of individuals diagnosed with drug-resistant TB and three-quarters of those with HIV-associated resistant TB were able to access appropriate treatment [10]. Diagnosis of MDR-TB is contingent upon the presence of bacteriological evidence of TB coupled with documented drug resistance [11,12]. The need for a bacteriological confirmation of the TB infection makes it essential that drug resistance, which is confirmed through rapid molecular testing or culture techniques, is validated by bacteriological means [11]. Previous studies found higher likelihood of MDR-TB risk associated with having a history of TB, exposure to multiple anti-tubercular treatment (ATT) regimens, involving multiple prescribers for ATT, managed by general practitioners without supervision and socio-economic determinants [12-15].

The potential public health impact and clinical significance of studying the prevalence of multi-drug resistant tuberculosis (MDR-TB) in patients with pulmonary tuberculosis, in high-burden settings is complex. First, it allows therapeutic protocols to be refined. By knowing the patterns of MDR-TB, health providers are able to prescribe effective, targeted treatment more quickly early on, leading to better patient outcomes and reduced transmission of the disease. In addition, understanding how common is MDR-TB helps your health system to optimally distribute important resources like the drugs, the isolation units, and the training of health care personnel. It also provides reinforcement for infection control strategies, thus aiding targeted prevention

practices to prevent the spread of resistant strains of tuberculosis. Moreover, the knowledge gained will be required to stimulate public health policy through evidence-based approaches and to re-align tuberculosis control programs to accommodate new diagnostic and treatment technologies. Additionally, these results can direct the public health educational programs that emphasize the importance of adherence to treatment and early disease detection, which are a vital element in controlling tuberculosis transmission and improving the health status of population. Together, these observations not only facilitate enhanced clinical care for those suffering from tuberculosis but also informs public health measures that are necessary to reduce the burden of this disease and achieve the goal of tuberculosis elimination.

METHODOLOGY

A cross-sectional study was conducted to assess multi-drug-resistant tuberculosis (MDR-TB) in pulmonary tuberculosis (PTB) patients at Ghulam Muhammad Mahar Medical College (GMMMC), Sukkur for six months. Non-probability, consecutive sampling method was used to recruit a total of 147 patients identified as PTB.

This study was conducted at the Departments of General Medicine and Pulmonology, GMMMC, Sukkur. Patients who diagnosed PTB with a duration of symptoms >2 weeks and aged between 18 to 70 years old of both genders. Moreover, patients who were receiving treatment for PTB at the time were also included. The exclusion criteria were patients with extrapulmonary tuberculosis, HIV/AIDS co-infection, chronic diseases that could have affected the TB treatment (e.g. chronic kidney disease, cardiovascular diseases, and hypertension), and pregnant or lactating women.

Pulmonary Tuberculosis (PTB) was characterized as an infectious disease primarily affecting the lungs, caused by *Mycobacterium tuberculosis*. The diagnosis of PTB was confirmed based on a combination of microbiological, clinical, and radiological criteria. Microbiologically, the presence of at least one acid-fast bacillus (AFB) in at least one sputum sample, indicated by a positive sputum AFB smear, was required. Clinically, PTB was identified by symptoms including a persistent cough, fever with a temperature of ≥ 38°C, night sweats, and significant weight loss (a loss of > 5% of body weight within a month). Radiologically, chest X-rays revealing cavitation or alveolar infiltrates were essential for confirmation of the diagnosis.

Multi-Drug-Resistant Tuberculosis (MDR-TB) was defined as tuberculosis in patients diagnosed by AFB smear, resistant to both isoniazid and rifampin. A GeneXpert MTB/RIF assay indicating the presence of Mycobacterium tuberculosis complex and positive rifampin resistance confirmed the resistance. In addition Drug Susceptibility Testing (DST) performed against isoniazid and rifampin separately. Resistance to isoniazid was confirmed if minimum inhibitory concentrations (MICs) exceeded 0.1 µg/ml and rifampin resistance was confirmed if MICs exceeded 1.0 µg/ml.

The data were collected from subjects who presented in the emergency, outpatient or inpatient medical wards of the GMMMC Sukkur. Written informed consent was obtained from patients or a next of kin. The demographic details of the patients were documented. In addition, these patients were also subjected to GeneXpert MTB/RIF assay for detection of Mycobacterium tuberculosis complex and rifampicin resistance. Drug Susceptibility Testing (DST) was carried out to detect the resistance of isoniazid and rifampin allowing us to confirm MDR-TB by determining minimum inhibitory concentrations (MICs).

The data were entered into and analyzed using SPSS version 26.0. Continuous variables were described using descriptive statistics. Counts and percentages were used to describe categorical variables. The Chi-Square test was used to evaluate the statistical significance of associations at two sides ($P \leq 0.05$).

RESULTS

The research encompassed a total of 147 subjects, exhibiting a mean age of 32.10 ± 13.52 years. The predominant demographic group (75.5%) consisted of individuals aged between 18 and 40 years, whereas 24.5% were aged over 40 years. The average duration of symptomatic presentation was recorded at 5.30 ± 2.28 weeks, with 81.0% of participants manifesting symptoms for a duration of 3 to 6 weeks, and 19.0% experiencing symptoms for longer than six weeks. Males constituted 53.7% of the cohort, while females represented 46.3%. In terms of educational

attainment, 5.4% of participants were identified as illiterate, 22.4% possessed primary education, 25.9% had completed higher secondary education, 17.0% were pursuing undergraduate studies, and 29.3% were graduates. Concerning employment status, 46.9% were gainfully employed, in contrast to 53.1% who were unemployed. The socioeconomic stratification indicated that 25.9% were classified within the lower class, 42.2% within the middle class, 16.3% within the upper middle class, and 15.6% within the upper class. Analysis of marital status revealed that 38.1% were single, 51.0% were married, 8.8% were widowed, and 2.0% were widowers. Finally, an examination of smoking behaviors disclosed that 33.3% of participants were identified as smokers, while 66.7% were non-smokers. (Table I)

A comparative examination of multidrug-resistant tuberculosis (MDR-TB) and participant characteristics (n=147) uncovered significant associations. Age emerged as a pivotal determinant, with 96.7% of MDR-TB patients falling within the 18-40 year age bracket, as opposed to 60.5% within the non-MDR cohort (p=0.000). The distribution of gender indicated that 68.9% of MDR-TB patients were male, while 69.8% of non-MDR cases were female (p=0.000). The duration of symptoms did not present a statistically significant association (p=0.123). Educational attainment was significantly correlated with MDR-TB, with illiteracy (8.2% vs. 3.5%) and primary education (34.4% vs. 14.0%) being more prevalent among MDR-TB cases (p=0.020). Employment status exhibited a significant association, with 63.9% of MDR-TB patients being employed, in contrast to 34.9% within the non-MDR group (p=0.001). Socioeconomic status demonstrated a significant disparity (p=0.037), with 34.4% of MDR-TB patients classified within the lower class compared to 19.8% of the non-MDR group. Marital status also revealed a significant correlation (p=0.001), characterized by a greater proportion of widows (18.0% vs. 2.3%) and widowers (4.9% vs. 0.0%) among MDR-TB cases. Smoking status was significantly different (p=0.009), as 21.3% of MDR-TB patients identified as smokers compared to 41.9% in the non-MDR cohort. (Table II)

Table I: Demographic Characteristics of Study Participants (n=147)	
Variable	**n** (%)
Age (Mean ± SD) = 32.10 ± 13.52 years	
18 - 40 years	111 (75.5)
>40 years	36 (24.5)
Duration of Symptoms (Mean ± SD) = 5.30 ± 2.28 weeks	
3 – 6 weeks	119 (81.0)
>6 weeks	28 (19.0)
Gender	
Female	68 (46.3)
Male	79 (53.7)
Educational Status	
Illiterate	8 (5.4)
Primary	33 (22.4)
Higher Secondary	38 (25.9)
Undergraduate	25 (17.0)
Graduate	43 (29.3)
Occupational Status	
Employed	69 (46.9)
Unemployed	78 (53.1)
Socioeconomic Status	
Lower Class	38 (25.9)
Middle Class	62 (42.2)

Upper Middle Class	24 (16.3)
Upper Class	23 (15.6)
Marital Status	
Single	56 (38.1)
Married	75 (51.0)
Widow	13 (8.8)
Widower	3 (2.0)
Smoking Status	
Smoker	49 (33.3)
Non-Smoker	98 (66.7)

Table II: Comparison between Multidrug-Resistant Tuberculosis and Participants Characteristic (n=147)

Characteristic, *n* (%)		Multidrug-Resistant		P-Value
		Yes (n=61)	No (n=86)	
Age	18 - 40 years	59 (96.7)	52 (60.5)	0.000
	>40 years	2 (3.3)	34 (39.5)	
Gender	Male	42 (68.9)	26 (30.2)	0.000
	Female	19 (31.1)	60 (69.8)	
Duration of Symptoms	3 - 6 weeks	53 (86.9)	66 (76.7)	0.123
	>6 weeks	8 (13.1)	20 (23.3)	
Educational Status	Illiterate	5 (8.2)	3 (3.5)	0.020
	Primary	21 (34.4)	12 (14.0)	
	Higher Secondary	14 (23.0)	24 (27.9)	
	Undergraduate	8 (13.1)	17 (19.8)	
	Graduate	13 (21.3)	30 (34.9)	
Occupational Status	Employed	39 (63.9)	30 (34.9)	0.001
	Unemployed	22 (36.1)	56 (65.1)	
Socioeconomic Status	Lower Class	21 (34.4)	17 (19.8)	0.037
	Middle Class	28 (45.9)	34 (39.5)	
	Upper Middle Class	7 (11.5)	17 (19.8)	
	Upper Class	5 (8.2)	18 (20.9)	
Marital Status	Single	22 (36.1)	34 (39.5)	0.001
	Married	25 (41.0)	50 (58.1)	
	Widow	11 (18.0)	2 (2.3)	
	Widower	3 (4.9)	0 (0.0)	
Smoking Status	Smoker	13 (21.3)	36 (41.9)	0.009
	Non-Smoker	48 (78.7)	50 (58.1)	

DISCUSSION

In this study, we reported a high rate of multidrug-resistant tuberculosis (MDR-TB), 41.49%, among patients with pulmonary tuberculosis (PTB) at Ghulam Muhammad Mahar Medical College Sukkur. Significant associations were found between multidrug-resistant tuberculosis (MDR-TB) and a series of demographic and socio-economic factors, including age, sex, level of education, union status, economic status, marital status and smoking status.

Notably, younger demographics (ages 18–40), males, individuals with diminished educational and socioeconomic conditions, along with those who are employed, exhibited a heightened propensity for the development of MDR-TB. These findings highlight the complex nature of MDR-TB risk and underscore the pressing need for prompt detection and targeted public health interventions in regions afflicted by this disease. The results of our study were consistent with previous data as reported by Khan et al that PTB patients had a prevalence of 40.2% for MDR-TB [6]. These findings may represent potential shared risk factors and hurdles to tuberculosis control in Pakistan. Poor treatment adherence, late presentation for diagnostic services, and delayed initiation of second-line therapy represent some of these challenges. The two investigations underscore the threat that drug-resistant tuberculosis, and particularly multidrug-resistant tuberculosis (MDR-TB), continues to pose, even in the era of first-line tuberculosis medications. It is essential to continue improving our systems of scientific surveillance, together with our diagnostic and treatment strategies, to track not only resistance spread, but the arrival of new strains of tuberculosis.

The results also corroborate the research work by Munir et al. [16], who identified MDR-TB as a growing challenge in Pakistan. Munir et al. described ways through which late diagnosis and limited access to healthcare facilities promote the transmission of drug-resistant Mycobacterium tuberculosis strains. Prolonging initiation of therapy prolongs drug-resistant TB exposure, worsening the problem. These factors reinforce the need for early diagnosis and a strong healthcare system in combating MDR-TB.

Our study revealed that a history of treatment failure was a major risk factor. This observation aligns with the findings of Raazi et al. who showed that the risk of MDR-TB is significantly higher at a history of previous insufficient or interrupted therapy [17]. Inadequate treatment, especially in areas with limited resources, leads to resistance to first-line drugs (such as isoniazid and rifampin). Our results highlights Raazi et al. results that incomplete treatment or missed doses greatly increase the risk of MDR-TB development due to this being an important problem in poorly accessible settings.

The relationship between growth detection through GeneXpert MTB/RIF assay for rifampin resistance found in our study, is similar to previous finding observed by Awais et al [18]. This molecular diagnostic tool has also been used by others to confirm cases of MDR-TB in Pakistan. Awais et al. even pointed out that the versatility of GeneXpert means that the short lead time is critical for managing MDR-TB to second-line therapies. The simultaneous identification of Mycobacterium tuberculosis with the potential to allow fast decisions in treatment provides unique utility appealingly indispensable tools in the resolution of MDR-TB diagnosis and treatment.

This study aid epidemiological perspective indicate older age and history of treatment as the major risk factors for MDR-TB. These findings coincide with what was reported by Khan et al. [6] and Raazi et al [17]. Moreover, a trend in Raazi et al [17] towards higher MDR-TB among the elderly with poor TB treatment history supports our findings.

The findings of this study highlight the need for improved strategies for tuberculosis control. These include better diagnosis, strict adherence to treatment regimens and only the appropriate use of second-line pharmacological agents. Given the heavy toll of MDR-TB, there is a need for increased awareness, improved patient education, and an intensified training process of healthcare practitioners to ensure better adherence to treatment. Furthermore, fortifying public health surveillance frameworks and broadening access to rapid molecular diagnostic technologies, such as GeneXpert, may be instrumental in mitigating the incidence of MDR-TB.

This study is not without its limitations. Primarily, its cross-sectional design offers merely a fleeting glimpse of MDR-TB prevalence, precluding the establishment of causal relationships. Longitudinal methodology would be an appropriate means to illuminate the course of MDR-TB over time. In addition, our

consecutive, non-probability sampling method may lead to selection bias as it cannot ensure inclusion of all potential patients. Future studies should use random sampling to be more generalizable.

Another limitation is the lack of data concerning treatment persistence, an important factor in the development of MDR-TB. Future work might incorporate adherence data to learn more about the role of non-adherence in promoting resistance. In addition, whilst sputum AFB smear and GeneXpert MTB/RIF were used to diagnose MDR-TB in this study, further studies should compare these modalities with other diagnostic methods i.e. culture-based DST for the evaluation of their effectiveness.

Finally, the study may be underpowered due to its sample size of 147 patients. A larger sample would strengthen the validity of prevalence estimates and provide for multivariable modelling of risk factors. The analysis could be further improved with the use of advanced statistical methods (logistic regression) that would control for confounding factors.

CONCLUSION

This study revealed a notably high frequency of multidrug-resistant tuberculosis (MDR-TB) among patients with pulmonary tuberculosis (PTB). The findings highlight significant associations between MDR-TB and key demographic and socioeconomic factors, including younger age, male gender, lower educational status, and smoking habits. These findings highlight the need for improved diagnostic screening, especially molecular testing like GeneXpert, and targeted interventions in high-risk populations. To reduce MDR-TB in this region, early detection, treatment adherence, and socioeconomic disparities need to be improved.

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