Multidrug-Resistant Tuberculosis (MDR-TB) Prevalence and Risk Factors Among TB-Patients at a Tertiary Care Hospital in Nawabshah, Sindh.

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ABSTRACT:

Objective: The purpose of this research was to ascertain the magnitude and determinants of multidrug resistant tuberculosis (MDR-TB) among TB patients in Nawabshah.

Methodology: This cross-sectional study was conducted at Biosafety level (BSL-2) TB laboratory at PMC hospital Nawabshah during August 2025 to October 2025. After getting informed consent sputum of 246 patients diagnosed as pulmonary tuberculosis (PTB) was tested using GeneXpert test (using real-time Polymerase Chain Reaction). This study includes new as well as recurrent cases. The laboratory performed the Xpert MTB/RIF Ultra and Xpert MTB/XDR tests to investigate rifampicin and isoniazid resistance respectively. Data collected on a structured questionnaire

Results: Among 246 PTB patients, the frequency of MDR-TB was 2.8%, with younger age groups accounting for nearly 70% of cases. The impact was disproportionately felt by urban residents, especially from densely populated areas. MDR -TB was significantly associated with low socioeconomic status (72%) and educational attainment, with 68% of patients having only primary or no formal education. Nearly two-thirds of cases were among low-skilled workers and unemployed individuals. Patients who were married (61%), underweight (54%), or had a family history of tuberculosis (43%) were at higher risk.

Conclusion: The study revealed a 2.8% prevalence of Multidrug-Resistant Tuberculosis (MDR-TB) across population of TB patients at Nawabshah, with high retreatment rates (3.84%). This finding underscores the need for effective control programs, especially for the most vulnerable populations, and the importance of improving DOTS monitoring, awareness initiatives, and access to remote areas to avoid travelling cost of patient and support for relapses.

Keywords: GeneXpert, Multidrug-Resistant Tuberculosis (MDR-TB), Frequency and determinants.

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Introduction:

Mycobacterium tuberculosis is the bacteria that causes pulmonary tuberculosis (TB). Not everyone infected with the TB bacteria develops the illness. Thus, two TB-associated disorders are latent TB infection and TB illness. Latent TB infection refers to presence of TB bacteria in the body of the patient but show no any signs of the illness. For most infected people, the TB stays dormant throughout their lives while the immune system of the individual with an active infection combat with the TB bacteria. The person with latent TB would have a positive tuberculin skin test but a normal chest X-ray. A person who has tuberculosis, on the other hand, is considered to display the symptoms and indicators of an active infection and ongoing clinical disease. Both the skin test and the chest X-ray would be positive for the person. Patients who have pulmonary tuberculosis can infect others by coughing, sneezing, or spitting because the disease is airborne. Tuberculosis remains highly significant global health problem, especially in low-income and underdeveloped nations. It is the 2nd leading determinant of mortality worldwide. Universally, tuberculosis continues to be a major cause of death despite recent advances in medicine. Every year, ten million people are afflicted with tuberculosis (TB). Even though TB is preventable and curable, still it remains a devastating illness accounting for 1.5 million lives annually. Although it is a worldwide illness, low and middle-income countries with high-burden and resource-limited settings account for major portion of TB cases. The median proportion of TB cases worldwide are found in eight countries: Bangladesh, China, India, Indonesia, Nigeria, Pakistan, the Philippines, and South Africa.[1-3] It is known as the "disease of the poor" because it is more common in people with malnutrition, treatment failure in the past, low socioeconomic status, and factors like job loss, overcrowding, and poor hygiene, immune-compromising illnesses (like HIV/AIDS), people taking immunosuppressive medications (like oncology patients, organ transplant recipients, and patients with immune-mediated diseases), young adults, the elderly and smokers.[4-6] Nearly 1.25 million people, including 161,000 HIV-positive individuals, died from tuberculosis in 2023. In 2023, there were an anticipated 10.8 million cases of tuberculosis universally, with 6.0 million, 3.6 million and 1.3 million cases occurring in men, women, and children respectively. When mycobacteria acquire resistance to the two most effective first-line TB drugs, isoniazid and rifampicin, multidrug-resistant tuberculosis (MDR-TB) results. Accord-

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ing to WHO standards, early and correct identification of tuberculosis (TB), particularly drug-resistant strains, is essential for effective management and control of disease. Mycobacterium tuberculosis (MTB) and rifampicin resistance (RR) can now be detected simultaneously thanks to GeneXpert. The MTB/RIF assay, a fully automated molecular diagnostic instrument, has revolutionized the field of tuberculosis diagnosis. Scrutinizing the real-time polymerase chain reaction (RT-PCR) technology, this assay directly amplifies and detects specific MTB gene sequences from clinical specimens, such as sputum. It also detected a mutation in the 81-base pair region of the *rpoB* gene, confirming resistance to rifampicin. GeneXpert has significantly improved the speed and accuracy of TB diagnosis, allowing for earlier treatment initiation and better tracking of drug -resistant TB strains. The use of GeneXpert MTB/RIF was authorized by the World Health Organization in December 2010. The screening was first recommended for high acuity populations, including children, individuals with HIV/TB co-infection, and those suspected of having multidrug-resistant TB (MDR-TB). In 2013, it was expanded to include all potential cases of tuberculosis. In over 90% of instances, rifampicin-resistant MTB (RR-MTB) is a trustworthy surrogate marker for MDR-TB. In 2014, Ethiopia strengthened its national TB control program by adopting the GeneXpert MTB/RIF assay as a diagnostic tool for TB and RR-MTB[7]. In both high and low-socioeconomic countries, multi-drug-resistant tuberculosis (MDR-TB) has been recognized as a serious public health issue. MDR-TB has been associated to a number of predisposing factors, including inadequate drug supply, inappropriate use of guidelines, non-adherence to treatment, deficient sanitary standards, hazardous medications deposits, inaccurate drug usage, inadequate surveillance by healthcare professionals, and direct contact with MDR-TB patients.[8] It was once thought that drug-resistant TB was difficult to spread and that resistance arises when patients do not take anti-TB medications as prescribed. According to recent reports, drug-resistant bacilli are just as contagious as drug-sensitive bacilli. Whether the bacilli are drug-resistant or drug-susceptible, the risk of transmission remains the same.[9] Studies have shown that the MDR-TB epidemic was predominantly caused by external infections, which mainly disseminated throughout the community, rather than endogenous recurrence of infection. This finding suggests that drug-resistant MTB strains from present MDR-TB patients are the primary driver of MDR-TB dissemination, not poor management of a previous treatment phase.[10] TB therapy is one of the most crucial strategies for TB control. Multidrug or Rifampicin-Resistant tuberculosis (MDR/RR-TB) was predicted to affect 410,000 people worldwide in 2022. The recovery proportion for individuals with MDR/RR-TB is statistically insignificant, despite a steady increase. As of 2020, 63% of those with MDR/RR-TB had successfully completed treatment worldwide, up from 60% in 2019 and 50% in 2012.[11] However, the extended course of treatment and associated side effects are the reason for non-adherence to treatment. Resistance of multidrug-resistant (MDR) strains in latent TB infection presents an additional challenge to current antitubercular treatment strategies.[12] Multidrug-resistant/Rifampicin-resistant tuberculosis (MDR/RR-TB) patients have 18% mortality rate, an 8% treatment failure rate, and more than half of patients who start medication are successful, according to the most recent treatment outcome data.[13] Drug-resistant TB remains a population health hazard. The bacteria undergo sequential resistance to one drug or set of drugs at a time.[14] Historically, treatment for multidrug resistant TB (MDRTB) required prolong regimens lasting 9 to 20 months often associated with high pill burden, increased adverse effects and poor adherence creating substantial clinical and economic burden. In contrast, drug resistant TB (DS-TB) is effectively cured with a standard 6-month course. The World Health Organization (WHO) current guidelines recommend shorter all-oral MDRTB regimens. This new regimen's high cure rate, shorter treatment time, and reduced pill load can mitigate the burden on the health system and free up precious resources to expand diagnostic and treatment coverage for everyone who needs it.[15, 16] With an annual incidence of 510,000 new TB cases and more than 15,000 drug-resistant TB cases , Pakistan ranks 5th among countries with a high TB burden universally and accounts for 61% of the WHO Eastern Mediterranean Region's TB burden. Furthermore, Pakistan is marked by its position in the top tier of nations, maintaining fourth-highest global prevalence of multidrug-resistant TB (MDR-TB). MDR-TB is thought to be present in 4.2% of new cases and 16% of patients who have already received treatment. Among the primary factors responsible for the development of drug-resistant diseases are delayed diagnosis, unsupervised, incorrect, and insufficient prescription regimens, instances that go unnoticed due to a lack of laboratory resources, inadequate follow-up, and the lack of a welfare provision program for high-risk groups.[17.18] According to a global TB study from 2019, there were about 0.5 million new cases of rifampicin-resistant TB (RR-TB) worldwide. Multidrug-resistant tuberculosis (MDR-TB) accounted for 78% of cases. Annually, there are around 500,000 new notifications of multidrug-resistant tuberculosis (MDR-TB). DR-TB is more likely to occur in patients who have previously undergone anti-TB medication. Compared to freshly treated TB cases (3.4%), the rate of MDR-TB/RR-TB in retreated cases was 18% higher. Coexisting diseases are becoming increasingly important in the control of tuberculosis. The questionnaire should contain the co-morbidities of the patients. It is strongly suggested that enhancing the health of the host, including early detection and effective comorbidity treatment, may stop the progression of TB and slow the transmission of DR-TB.[19,20] According to global statistics, 61% of people with TB that was bacteriologically proven in 2019 had rifampicin resistance, up from 51% in 2017 and 7% in 2012. The worldwide therapeutic efficacy rate for MDR/RR-TB was only 59%, according to a 2020 WHO report. As a cause of relapse and refractory treatment, MDR-TB is commonly seen in individuals who have experienced nonadherence to treatment with traditional short-course and relapse regimens. MDR-TB is a potential threat to healthy individuals and has a high mortality rate. Patients with this disease are almost incurable with first-line conventional TB medications. The widespread of MDR -TB will make TB an "incurable illness".[21, 22] Treatment for MDR-TB is difficult, intricate, and protracted; it typically lasts 18 to 24 months. The cornerstone of MDR-TB treatment plans is daily injectable aminoglycosides, whose long -term use has been linked with better therapeutic outcomes. According to current guidelines, aminoglycosides are prescribed for eight months during the intensive phase of treatment for MDRTB. However, aminoglycosides are linked with adverse consequences that include persistent hear loss and decrease health-related quality of life for individuals who can be cured of MDR-TB but have permanent disabilities. Renal failure and nerve damage are two more

adverse consequences of MDRTB therapy. Patients' compliance with treatment and, thus, treatment outcomes are greatly impacted by these side effects, lengthy treatment durations, and high costs.[23] The low adherence to treatment during anti-TB treatment such as failure to take TB drugs on a regular basis or failure to take a full dose of TB drugs lead to the development of DR-TB.[24] The international public health goal of eliminating TB by 2035 requires strategic response to address and effectively manage drug -resistant strains of Mycobacterium tuberculosis (MTB) .[25] Prevention of drug-resistant TB, especially MDR-TB, is integral part of the TB control effort. To decrease the burden of drug resistance, strategies for managing MDR-TB in the research domain should focus on optimizing public health education and reducing treatment interruptions for patients with TB and drug-resistant TB[26]. Tuberculosis is a major global health concern, and the increase of drug-resistant forms like MDR-TB threatens to undo decades of progress. Even though MDR-TB is treatable, it is more expensive, more difficult to treat, and has significant adverse effects. Inadequate diagnosis, treatment gaps, and community spread exacerbate the condition in high-burden countries like Pakistan. Understanding these drivers is essential in protecting vulnerable people and preventing more gearboxes.

Objective:

The purpose of this research is to ascertain the magnitude and determinants of multidrug resistant tuberculosis (MDR-TB) among TB patients in Nawabshah. The findings may assist better control techniques using evidence-based insights.

Methodology:

The study was conducted in the PMCH Biosafety Level (BSL-2) TB laboratory, which focused on patients referred for sputum genetic testing by chest specialists. The sample size was 246 PTB patients, and the study design was cross -sectional. This study encompassed patients diagnosed with pulmonary tuberculosis using GeneXpert, including all new and recurrent cases. The laboratory performed the Xpert MTB/RIF Ultra and Xpert MTB/XDR tests to investigate rifampicin and isoniazid resistance respectively.

Statistical data analysis:

The data were fully processed and encrypted in Microsoft Excel before being analyzed using SPSS version 26. For categorical variables, we calculated frequencies and percentages, while continuous variables were summarized using means and then categorized into discrete groups where appropriate. Pie charts were used to visualize the results. Additionally, the questionnaire was carefully reviewed to identify and correct errors, ensuring the accuracy of the analysis.

Results:

Among 246 patients of pulmonary tuberculosis, most patients were young to middle-aged (21-60 years), with an approximately equal gender distribution. A large proportion lived in rural areas (47.6%) and most (73.2%) belonged to the lowest economic class. More than half of the patients were illiterate (60.2%), and most lived in densely populated areas (77.2%). Notably, almost half (49.2%) of the patients reported a family history of TB. Detailed demographic is shown in table no 1.

Out of 246 total patients, the majority (236) were drug-susceptible cases. Among new cases, 189 were susceptible while only 5 had RIF + INH resistance (2.5%). In re-treatment cases, 47 were susceptible and 2 showed resistance (3.84%). Overall, 7 patients had RIF + INH resistance, giving a combined resistance rate of 2.8%. The immune response was slightly higher in re-treated patients compared to newly treated patients, indicating an increased risk in previously treated patients.

Table No 1: Socio-Demographic Characteristics of studied population.

Variable	Categories	Frequency	Percentage
Age	1-20	46	18.7
	21-40	86	35.0
	41-60	77	31.3
	61-80	33	13.4
	81-100	4	1.6
Sex	Male	122	49.6
	Female	124	50.4
Residence	Urban	100	40.7
	Urban slum	29	11.8
	Rural	117	47.6
Family income	lower class	180	73.2
	Lower middle	55	22.4
	Middle class	9	3.7
	Upper middle	2	.8
Education	Illiterate	148	60.2
	Primary	51	20.7
	Middle	19	7.7
	High	11	4.5
	Intermediate	11	4.5
	Graduate	5	2.0
	Professional degree	1	0.4
Living condition	Crowded	190	77.2
	Uncrowded	56	22.8
Family history of TB	Positive	121	49.2
	Negative	125	50.8

Asian Body Mass Index (BMI) was recorded for all patients with MDR-TB status. Most of the patients (46.75%) fall into the normal BMI of 17.50-22.99 category. 37.80% patients were <17.50, while only a small proportion (9.35%) were having BMI above normal (23.00-27.99) and very fewer (3.25%) were obese with BMI of ≥28.00. Positive MDRTB cases are rare across all BMI groups (approximately 1-3%), and do not show a clear pattern in any particular BMI category. Overall, most cases of MDR-TB were positive in the underweight category or in normal weight according to BMI. Results shown in fig 1.

Table No 2: MDR-TB cases.

Variable	New cases	Retreatment Cases	Sub-Total
Susceptible Patients	189	47	236
RIF + INH Resistance	5	2	7
Grand Total	194 (2.5%)	52 (3.84%)	246 (2.8%)

We found higher prevalence of MDR-TB in overweight category (4.16%) and underweight category (3.12%) among newly treated and re-admitted pulmonary tuberculosis pa-

tients, while it was 2.54% in patients with normal BMI as shown in table 3.

Fig No 1: BMI and MDR-TB

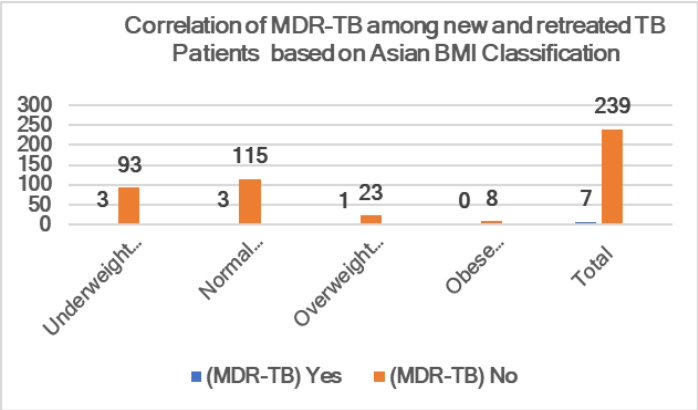


Table No 3: BMI and MDR–TB

BMI (Asian Classification)	(MDR-TB) Yes	(MDR-TB) No	Total
Underweight (<17.50)	3	93	96 (3.12%)
Normal (17.50-22.99)	3	115	118 (2.54%)
Overweight (23.00-27.99)	1	23	24 (4.16%)
Obese (28.00 & above)	0	8	8 (0%)
Total	7	239	246 (2.84%)

Patients were categorized into various socioeconomic stratum according to classification of Pakistan Bureau of Statistics. The results showed that all MDR-TB patients were from lower socioeconomic group as shown in fig 2 and 3

Fig No 2: MDR-TB and Socioeconomic status.

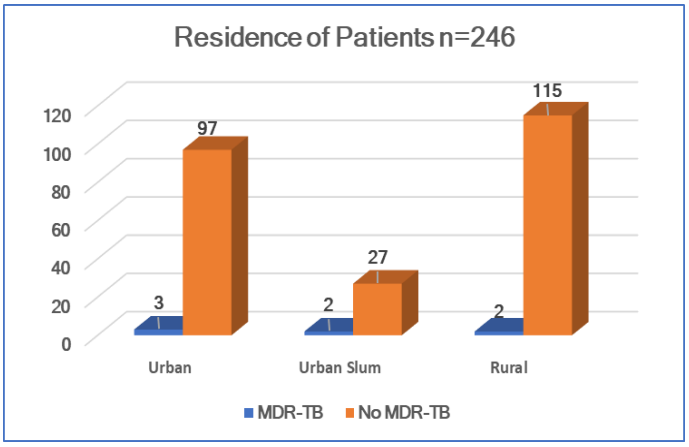
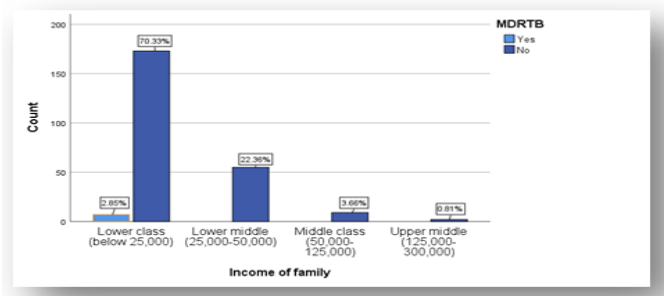


Fig No 3: socioeconomic stratum according to classification of Pakistan Bureau of Statistics and MDR-TB cases.



The residence of patients and distribution of MDR-TB was explored, and we found that among 7 patients of MDR-TB; 3 patients were resident of urban (1.21%), 2 (0.81%) were resident of urban slum areas of the city while 2 (0.81%) were belongs to rural area reflecting the fact that over-crowding predisposing factor for MDR-TB.

The family history of TB is a significant risk factor for the development of MDR-TB in TB patients. Among 7 cases of MDR-TB, family history of tuberculosis was found in 4 (57.14%) cases only.

Discussion:

This study looked into the prevalence of MDR-TB in the PMC hospital's Nawabshah among cohort of TB patients. The results show that a considerable proportion of TB cases have been converted to MDR-TB as a result of relapse, even though there are established treatment protocols for the disease. There is a significant burden on public health issues in Nawabshah due to the prevalence of MDR-TB, which is 2.5% among new cases and 3.8% among retreatment cases. The high reported prevalence of MDR-TB among retreatment cases could be explained by the substantial reservoir of initial transmission. The prevalence of MDR-TB in Pakistan is around 3.8% among newly diagnosed cases and 18% among TB cases that have already undergone treatment, according to the WHO global TB report.[27] We have very poor results in Nawabshah. Our study is comparable to other drug resistance studies carried out in Pakistan. For instance, a study carried out at the pulmonology outpatient clinic at Jinnah Hospital in Lahore discovered a high frequency of MDR in children, at 12.9%.[28] A very high frequency of MDRTB i.e. 64.1% was observed in another study carried out at a public hospital in Karachi. 4.8% of cases were mono-drug resistant, 27.9% were MTB with rifampicin resistance.[29] In contrast to our results, a study carried out in Punjab, Pakistan, revealed a greater prevalence of MDR-TB (9.3%). Their results showed that younger patients and those who had previously undergone TB therapy had a significantly increased probability of getting MDR-TB. However, even though our analysis identified MDR cases across a range of age groups, there was not enough data to demonstrate a meaningful association. The discrepancies between the two trials could be explained by their greater sample size and the inclusion of both new and retreatment cases, which offered stronger statistical power. Despite these differences, the two studies have one thing in common: they both imply that younger age and earlier therapy are important factors in the development of MDR-TB.[30] Based on our study, the prevalence rate of MDR-TB patients was 2.8%, whereas it is 51% in Punjab, 23% in Sindh, 15% in KPK, and 3.5% in Baluchistan[31], Hyderabad 28.7%[32], Karachi 5%[33], and Lahore 18.8%[34] whereas in India it is 6.7%[35] The prevalence of MDRTB in both newly diagnosed and previously treated cases is 2.5% and 3.84% in our study at Nawabshah, compared to 6.9% and 40% in Lahore[34] and 2.4% and 13.9% in Karachi[36]. In India, the rates for new and retreatment cases are 3.9% and 13.4%, respectively[35]. This significance reinforces the validity of our findings and shows how inadequate or incorrect therapy in cured cases might result in TB recurrence. Our analysis reveals that 57.14% of MDRTB patients are male and 42.86% are female, in contrast to Punjab, where 53% of MDRTB patients are male. Furthermore, compared to Punjab, which has 57% and 97% of MDR cases, we have higher in productive age groups such 21-40 years old (42.8%) and urban regions (42.8%).[37] Compared to 8.54% in India[38] and 1.4% in Ethopia[39], RIF mono-resistance is 1.22% in

our study, all of which are in retreatment cases. This study found that MDR-TB was mainly linked to preceding anti-tuberculosis medication in patients who had completed TB treatment, especially in those who required retreatment or relapsed. Inadequate institutional support and supervision at the start of treatment, such as the absence of direct monitoring during the first two months, further increased the risk. Social and economic problems were important. Patients with low incomes, those who had to pay for their transportation, and those who had to travel far to the DOTS facility were more likely to have MDR-TB. Treatment was further complicated by social stigma and displacement, and some patients reported social isolation and only partial compliance with cough hygiene. Our results are consistent with previous studies conducted in Pakistan. For example, a study conducted in Punjab found that individuals who had previously received therapy were almost five times more likely to have MDR-TB than those who had not. Additionally, age appeared to be important: young adults between the ages of 10 and 25 accounted for the bulk of MDR-TB cases in our analysis, indicating that younger populations may be particularly sensitive[30]. Evidence from a variety of settings shows the importance of programmatic and demographic factors in treatment adherence. Male patients were more likely than female patients to discontinue taking their anti-TB medicine, according to a Nigerian study. In a similar vein, a study conducted in Ethiopia revealed that patients who had a medical professional personally supervising their care were more likely to regularly take the recommended dosage and were less likely to miss doses. Frequent involvement in DOTS also makes it easier to communicate with medical specialists on a frequent basis, providing opportunities for counseling, support, and guidance—all of which can enhance adherence to treatment plans[40]. Patients who experienced social stigma related to prior or current tuberculosis were approximately nine times more likely to acquire multidrug resistant tuberculosis (MDR-TB), according to research from China, Ethiopia, and Serbia. This may be the case because stigma reduces social support and induces mental stress, which can lead to treatment pauses, relapse, treatment failure, and eventually drug resistance.[41] Cough hygiene is one of the five crucial stages in "Patient Management to Prevent Transmission of TB in Health Care Settings," according to the WHO. However, a study carried out in India found substantial gaps in knowledge and practice: over 90% of participants did not know how to properly dispose of sputum, and nearly two-thirds (64%) did not know how tuberculosis spreads. Overall, there was a low level of cough etiquette knowledge and practice[42]. Both patients were at risk for tuberculosis since they were ignorant of the illness due to their low socioeconomic level and lack of education. While global data highlight the importance of older age and lifestyle-related factors, all of these findings highlight the importance of younger age, poverty, hunger, low level education, and intra-household exposure as key determinants in our population. It is critical to raise awareness, ensure early screening, and improve treatment adherence in these high-risk individuals in order to reduce the burden of MDR-TB.[43]

Limitations:

Cross sectional design of the study has certain inherent limitations. First, socio-behavioral patient determinants, such as insurance services and health literacy, have not been studied. Second, being single center study, conclusions cannot be extended to the other rural areas. Thirdly, because there were few subgroups, the risk factor analysis was descriptive rather than inferential, which restricts the depth of the study.

Conclusion:

TB drug resistance and treatment failure is caused by the poor execution of DOTS, which lack of institutional support and direct monitoring. To lessen the incidence of MDR-TB in Nawabshah and similar areas, better DOTS monitoring, awareness, and focused support for relapse cases are crucial. Assistance is crucial during relapses.

Recommendations:

Based upon the finding of the current study, it is advisable that the DOTS method be reinformed with appropriate supervision if drug resistance is to be avoided. To prevent spread of TB, regular public awareness campaigns be carried out focusing to educate patients about the value of clean cough and adherence to prescribed medicines. Strategies should be develop to increase access to treatment that includes lowering travel expenses and offering financial support to patients from low socioeconomic stratum. High risk group, particularly young adults, those residing in urban area, needs retreatment, should be prioritize and screened as early as possible It is also wise to take community onboard and appropriate counselling of the patient if social stigma of tuberculosis is to be addressed.

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