

Prevalence of Pre-Extensively Drug Resistant Tuberculosis, Extensively Drug Resistant Tuberculosis among the Multi Drug Resistant Tuberculosis Patients

Salman Khan¹, Naseeb-Ur-Rehman^{2*}, Mohammad Zubair³, Nisar Khan^{4*}

¹ Associate Professor, Department of Medicine, DHQ Teaching Hospital, Gomal Medical College, Dera Ismail Khan

² Associate Professor, Department of Medicine, Khalifa Gulnawaz Hospital, Bannu Medical College, Bannu

³ Assistant Professor, Department of Medicine, DHQ Teaching Hospital, Gomal Medical College, Dera Ismail Khan

⁴ Professors, Department of Medicine, MMMTH, Gomal Medical College Dera Ismail Khan

Corresponding Author:

Naseeb-Ur-Rehman

dmaseeb82@gmail.com

Abstract

Background: Multidrug-resistant tuberculosis (MDRTB) is a growing global health concern that is a chronic danger to world health due to tuberculosis (TB).

Objective: The aim of this study was to examine the frequency of both pre extensively drug-resistant tuberculosis (PXDRTB) and extensively drug-resistant tuberculosis (EXDRTB) in patients with multidrug-resistant tuberculosis (MDRTB).

Material and Method: A prospective study was performed at DHQ Teaching Hospital, Gomal Medical College, Dera Ismail Khan from March 2023 to February 2024. A cohort of 220 eligible patients with drug-resistant TB, aged 20 to 70, participated. Inclusion and exclusion criteria were applied, and patient profiles and drug susceptibility testing were obtained. Data analysis was conducted using SPSS 27.

Results: Of the total patients, 32.72% (n=72) had PXDRTB, and 8.18% (n=18) had EXDRTB. All PXDRTB cases showed resistant to fluoroquinolone (FQ).

Conclusion: In order to lessen the effect of drug-resistant tuberculosis on public health, tailored treatments and ethical antibiotic usage are important. This is highlighted by the high incidence of FQ resistance. These results have consequences for the early detection, management, and avoidance of tuberculosis that is resistant to drugs.

Keywords: Tuberculosis, Prevalence, Drug-resistant, fluoroquinolone

Cite this article: Khan S, Reham ur N., Zubair M, Khan N Prevalence Of Pre-Extensively Drug Resistant Tuberculosis, Extensively Drug Resistant Tuberculosis Among The Multi Drug Resistant Tuberculosis Patients. BMC J Med Sci. 2024. 5(1): 69-71

Introduction:

Millions of people get tuberculosis (TB) every year, making it a major worldwide health concern.¹⁻² One of the biggest obstacles in the fight against tuberculosis is multidrug-resistant tuberculosis (MDRTB), which is defined by an inability to tolerate a minimum of two of the foremost effective first-line anti-TB medications³⁻⁵. Treatment and management of tuberculosis are becoming more challenging due to the emergence of progressively resistant forms of the disease, such as extensively drug-resistant TB (EXDRTB) and pre-extensively drug-resistant tuberculosis (PXDRTB)⁶.

PXDRTB and EXDRTB point to a dire scenario where there is a significant lack of drugs that can be used to treat tuberculosis (TB), resulting in more difficult, time-consuming, and unsuccessful treatments⁷. Since these strains have the potential to spread drug-resistant tuberculosis and jeopardize not just the health of individual patients but also that of the greater population, they pose a severe concern to public health. Understanding the incidence of PXDRTB and EXDRTB among MDRTB patients is crucial for developing techniques for early identification, treatment, and prevention of the illness⁸.

In order to shed light on the traits and consequences of these more severe strains of the illness, the aim of this study was to

examine the prevalence of PXDRTB and EXDRTB in MDRTB patients. We may more successfully influence clinical therapies and public health initiatives meant to reduce the incidence and effects of drug-resistant TB by gaining more knowledge on the prevalence of these resistant strains.

Material and Method:

A prospective research was performed at DHQ Teaching Hospital, Gomal Medical College, Dera Ismail Khan from Feb 1, 2023, to March 31, 2024, a period of one year. A cohort of 220 patients who could provide informed permission the patients were of all genders and ages, ranging from 20 to 70.

Inclusion and Exclusion Criteria

At the time of presentation, these research patients had drug-resistant tuberculosis. Participants who were less than eighteen years of age or who had extrapulmonary involvement in addition to pulmonary involvement were deemed ineligible. Additionally, those who had renal failure, were receiving other ototoxic medications concurrently, were hesitant to participate, or had taken aminoglycosides for longer than one month in the six months before to the trial were not allowed to participate in the research.

Authorship Contribution: ¹⁻⁴Substantial contributions to the conception or design of the work; or the acquisition, data analysis, drafting the work or revising it critically for important intellectual content, Final approval of the version to be published & supervision

Funding Source: none

Conflict of Interest: none

Received: March 25, 2024

Accepted: June 16, 2024

Published: July 2, 2024

Data Collection and Patient Profiling in the Tuberculosis Diagnosis Process:

The patient's complete medical history was obtained, including information on any underlying medical conditions, antituberculosis treatment (ATT) history, and history of tuberculosis. After receiving signed permission, the study documented every data about the patient, including age, gender, place of residence, and body mass index. The GeneXpert MTB/RIF assay for drug resistance testing and genotypic and phenotypic drug susceptibility testing were used in the diagnosis of tuberculosis. Additionally, the whole medical history of the patients was reviewed in regard to anti-TB medications, and drug sensitivity testing for first- and second-line medications was carried out on all sample types by gene specialists. Analysis of the data was done using SPSS 26.

Results:

Out of the total patients, 94 (42.72%) were women and 120 (57.28%) were males. The age range of the patients was 10.57 years on standard deviation and 36.37 years on average. Their average body mass index, or BMI, was 24.17 kg/m², with a standard deviation of 2.14. Furthermore, table 1 shows that thirty-one individuals (14.09%) had a previous diagnosis of hypertension and 46 of them (20.90%) had been recognized with diabetes mellitus.

According to Figure 1, PXDRTB was present in 32.72% (n=72) and EXDRTB was present in 8.18% (n=18) of the individuals diagnosed with MDRTB. Nine patients with EXDRTB were resistant to amikacin, four patients were resistant to both fluoroquinolone and kanamycin, three patients were resistant to both amikacin and kanamycin, and two patients were resistant to capreomycin. Of the patients with PXDRTB, seventy-two (100%) were resistant to fluoroquinolone (Figure 2).

Table 1: Study Participants' Health and Demographic Details		
Variables	Numbers of Patients (n)	Percentage (%)
Mean BMI (Kg/m)	24.17 ± 2.14	
Mean age (years)	36.37 ± 10.57	
Gender Distribution		
Female	94	42.72
Male	126	57.28
Co-morbidity		
Hypertension	31	14.09
Diabetes	46	20.90

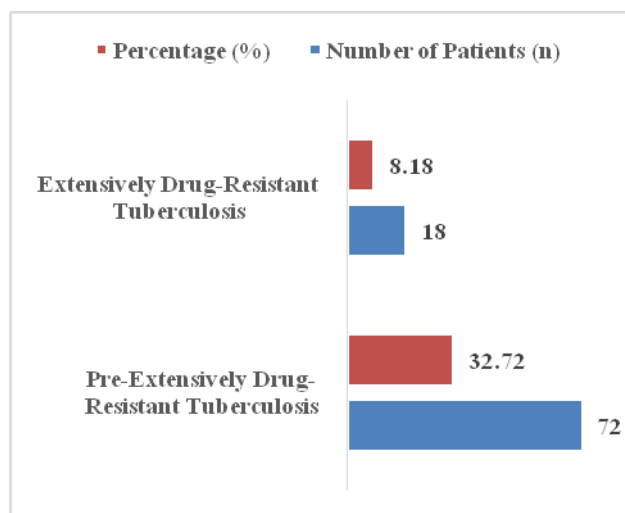


Figure 1: Frequency of PXDRTB and EXDRTB Cases

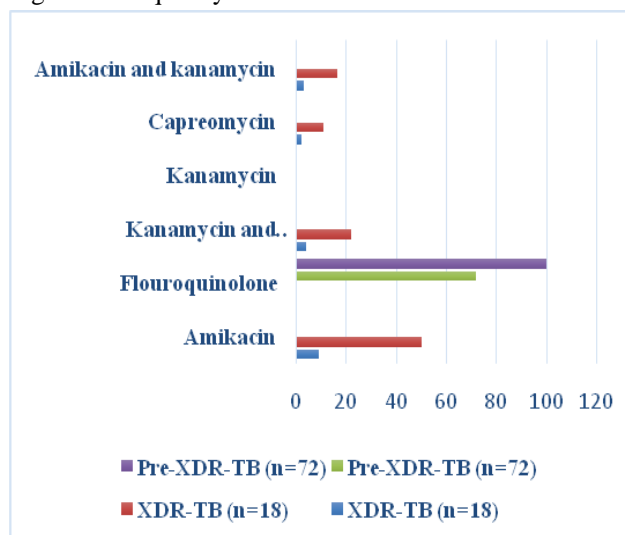


Figure 2: Patterns of Drug Resistance In PXDRTB AND EXDRTB

Discussion:

We discovered the drug resistance pattern of MDRTB patients in this research. Drug sensitivity tests were performed on amikacin (AM), kanamycin (KM), capreomycin (CM), and fluoroquinolone (FQ). In the current research, 8.18% (n=18) of MDR TB patients had EXDRTB, while 72 (32.72%) had PXDRTB TB. Fluoroquinolone (FQ) resistance was seen in all PXDRTB patients, in line with the findings of a research by Manan et al., (2018) reported results of 31.3% and 3.6% in MDR TB patients, respectively. Comparing these comparable findings to those reported by Rao et al., (2015), it was discovered that the frequency of PXDRTB and EXDRTB was 2.2% as well as 38.4% respective^{9,10}.

The majority of research findings have shown higher incidence rates of extensively drug-resistant tuberculosis (XDR-TB) in South Africa (13%), Nigeria (16%), China (33%), India (54%), Pakistan (23%), and Bangladesh (15%) when contrasted with our own study results (11–15). Our study's FQ resistance, which was 32.72% (n=72), was comparable to that of previous

research, which found that it was 12%, 16%, 23%, 32%, and 55%^{16–19}.

In addition to being used indiscriminately for MTB infections in Bangladesh, FQs are also often utilized for pneumonia and pyrexia of unknown origin, which may account for the greater incidence of FQ resistant PXDRTB patients identified in our investigation. FQs have two negative consequences when used as antibiotics. Firstly, their antimycobacterial activity might cause a delay in the diagnosis of tuberculosis. Second, treatment with these antibiotics in the past may have selected for FQ-resistant MTB mutations. Exposure to FQ medicines is more common since they are oral drugs that may be readily purchased in Pakistani drugstore without a doctor's prescription²⁰.

Conclusion:

Our findings revealed that 32.72% of MDRTB patients had PXDRTB, and 8.18% had EXDRTB. Notably, all PXDRTB cases were resistant to fluoroquinolone (FQ). The extraordinary frequency of FQ resistance suggests the indiscriminate use of these antibiotics in various infections, contributing to drug-resistant TB. These results underscore the worldwide challenge of drug-resistant TB, highlighting the importance of targeted interventions and responsible antibiotic use to mitigate its impact on public health.

References:

1. Chakaya J, Khan M, Ntumi F, Akillu E, Fatima R, Mwaba P, Kapata N, Mfinanga S, Hasnain SE, Katoto PD, Bulabula AN. Global Tuberculosis Report 2020—Reflections on the Global TB burden, treatment and prevention efforts. *International journal of infectious diseases*. 2021 Dec 1;113:S7-12.
2. Floyd K, Glaziou P, Zumla A, Raviglione M. The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. *The Lancet Respiratory Medicine*. 2018 Apr 1;6(4):299-314.
3. Sandhu GK. Tuberculosis: current situation, challenges and overview of its control programs in India. *Journal of global infectious diseases*. 2011 Apr;3(2):143.
4. Singh V, Chibale K. Strategies to combat multi-drug resistance in tuberculosis. *Accounts of chemical research*. 2021 Apr 22;54(10):2361-76.
5. Kirimuhuzya C. Multi-drug/extensively drug resistant tuberculosis (Mdr/Xdr-Tb): renewed global battle against tuberculosis. *Understanding Tuberculosis-New Approaches to Fighting Against Drug Resistance*. 2012 Feb 15:376.
6. Sloan DJ, Lewis JM. Management of multidrug-resistant TB: novel treatments and their expansion to low resource settings. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2016 Mar 1;110(3):163-72.
7. Law S. Exploring TB patient journeys and the emergence of MDRTB in India and South Africa: A multi-methods study. McGill University (Canada); 2019.
8. Adwani S, Desai UD, Joshi JM. Prevalence of pre-extensively drug-resistant tuberculosis (Pre XDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) among pulmonary multidrug resistant tuberculosis (MDRTB) at a tertiary care center in Mumbai. *Journal of Krishna Institute of Medical Sciences University*. 2016 Jul 1;5(3).
9. ul Manan MA, Naqvi S, Mushtaq A, Shafqat M. Prevalence of PXDRTB and XDR-TB among MDRTB patients. *Pakistan Journal of Chest Medicine*. 2018;24(4):208-11.
10. Rao N, Baig S, Hussain N, Ahmed N, Rao D. Prevalence of PXDRTB, XDR-TB among MDRTB patients registered at Ojha Institute of Chest Diseases, Karachi.
11. Adwani S, Desai UD, Joshi JM. Prevalence of pre-extensively drug-resistant tuberculosis (Pre XDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) among pulmonary multidrug resistant tuberculosis (MDRTB) at a tertiary care center in Mumbai. *Journal of Krishna Institute of Medical Sciences University*. 2016 Jul 1;5(3).
12. Daniel O, Osman E, Oladimeji O, Dairo OG. Pre-extensive drug resistant tuberculosis (PXDRTB) among MDRTB patents in Nigeria. *Global Advanced Research Journal of Microbiology*. 2013 Feb;2(2).
13. Mlambo CK, Warren RM, Poswa X, Victor TC, Duse AG, Marais E. Genotypic diversity of extensively drug-resistant tuberculosis (XDR-TB) in South Africa. *The international journal of tuberculosis and lung disease*. 2008 Jan 1;12(1):99-104.
14. Tasnim T, Tarafder S, Alam FM, Sattar H, Kamal SM. Pre-extensively drug resistant tuberculosis (PXDRTB) among pulmonary multidrug resistant tuberculosis (MDRTB) patients in Bangladesh. *Journal of Tuberculosis Research*. 2018 Jul 23;6(3):199-206.
15. Yuan X, Zhang T, Kawakami K, Zhu J, Li H, Lei J, Tu S. Molecular characterization of multidrug-and extensively drug-resistant Mycobacterium tuberculosis strains in Jiangxi, China. *Journal of clinical microbiology*. 2012 Jul;50(7):2404-13.
16. Agrawal D, Udwadia ZF, Rodriguez C, Mehta A. Increasing incidence of fluoroquinolone-resistant Mycobacterium tuberculosis in Mumbai, India. *The International journal of tuberculosis and lung disease*. 2009 Jan 1;13(1):79-83.
17. Ramachandran R, Nalini S, Chandrasekar V, Dave PV, Sanghvi AS, Wares F, Paramasivan CN, Narayanan PR, Sahu S, Parmar M, Chadha S. Surveillance of drug-resistant tuberculosis in the state of Gujarat, India. *The International journal of tuberculosis and lung disease*. 2009 Sep 1;13(9):1154-60.
18. Sharma SK, George N, Kadiravan T, Saha PK, Mishra HK, Hanif M. Prevalence of extensively drug-resistant tuberculosis among patients with multidrug-resistant tuberculosis: a retrospective hospital-based study. *Indian Journal of Medical Research*. 2009 Oct 1;130(4):392-5.
19. Dalal A, Pawaskar A, Das M, Desai R, Prabhudesai P, Chhajed P, Rajan S, Reddy D, Babu S, Jayalakshmi TK, Saranchuk P. Resistance patterns among multidrug-resistant tuberculosis patients in greater metropolitan Mumbai: trends over time. *PLoS one*. 2015 Jan 21;10(1):e0116798.
20. Mirza IA, Khan FA, Khan KA, Satti L, Ghafoor T, Fayyaz M. Extensively and pre-extensively drug resistant tuberculosis in clinical isolates of multi-drug resistant tuberculosis using classical second line drugs (levofloxacin and amikacin). *J Coll Physicians Surg Pak*. 2015 May 1;25(5):337-41.