ORIGINAL ARTICLE **OPEN ACCESS**

Five Years of Managing Multidrug-Resistant Tuberculosis at PMDT Mardan: Treatment Outcomes, Challenges, and Key Insights

Rumman[1], **Sajjad Ali** [2],**Shabir Hussain**[3], **Ubaid Ullah**[4], **Aleina ali shah**[5]

[1]Pharmacovigilance Coordinator Association for Community Development, KP

[2]Associate Professor Department of Pulmonology, Medical Teaching Institute, Mardan Medical Complex, Mardan, Pakistan

[3] Associate Professor Medicine Nowshera Medical College Nowshera

[4]Department of Chest and TB Physician, MMC mardan

[5]MDR TB Program Manager Association for Community Development KP

ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a global public health concern, particularly in low- and middle-income countries such as Pakistan.

Objective: This study aimed to evaluate treatment outcomes, challenges, and key lessons from five years of MDR-TB management at the Programmatic Management of Drug-Resistant Tuberculosis (PMDT) site, MTI Mardan.

Methodology: A retrospective cohort of 161 patients with bacteriologically confirmed resistance to at least isoniazid and rifampicin was reviewed. Data were analyzed using SPSS v25.

Results: The treatment success rate was 85%, with 16% of patients showing poor outcomes (death, failure, or loss to follow-up). Adverse drug reactions (ADRs) occurred in 45%, mainly gastrointestinal intolerance, hepatotoxicity, and ototoxicity. Comorbidities such as diabetes mellitus (25%) and chronic lung disease (38%) were key determinants of outcome. Resistance to fluoroquinolones (35%) and second-line injectables (25%) was common. Predictors of poor outcomes included diabetes, fluoroquinolone resistance, multiple prior TB treatments, severe ADRs, malnutrition, and advanced age.

Conclusion: While the PMDT Mardan site achieved an encouraging success rate, challenges persist regarding ADRs, comorbidities, and drug resistance. Strengthened pharmacovigilance, individualized regimens, and multidisciplinary management are essential for optimizing outcomes.

Keywords: MDR-TB, Pakistan, treatment outcomes, adverse drug reactions, drug resistance

How To Cite This Article: **Rumman, Ali S, Hussain S, Qasim M, Abdullah, Ahmed T.** Five Years of Managing Multidrug-Resistant Tuberculosis at PMDT Mardan: Treatment Outcomes, Challenges, and Key Insights**. J Bacha Khan Med Coll. 2024;5(2):235-239.**

Correspondence Author: Sajjad Ali Shah

Head of Department of Pulmonology, Mardan Medical Complex

E-mail: drsajjadlrh@gmail.com

https://orcid.org/0009-0007-6396-

Received: 22th September, 2024
Revised: 21th October, 2024
Accepted: 30th November, 2024
Published: 6 th January, 2025
DOI: 10.69830/jbkmc.v5i02.272

INTRODUCTION

Tuberculosis (TB) continues to rank among the most critical infectious diseases worldwide, particularly in low- and middle-income countries. The World Health Organization (WHO) reported more than 10 million new TB cases and 1.3 million deaths in 2022, with drug resistance posing an escalating challenge [1]. Multidrug-resistant tuberculosis (MDR-TB), characterized by resistance to at least isoniazid and rifampicin, the two most potent first-line drugs, complicates control efforts by requiring longer, more toxic, and more expensive treatment regimens [2].Globally, approximately 400,000 new MDR-TB cases were reported in 2022, with treatment success rates averaging only 63% [1]. Pakistan is among the five countries with the highest burden of MDR-TB, contributing significantly to the global case load [3]. Despite progress through the National TB Control Program (NTP) and WHO-supported Programmatic Management of Drug-Resistant TB (PMDT) sites, treatment remains hampered by diagnostic delays, comorbidities, and adverse drug reactions (ADRs).ADRs are a major barrier to successful MDR-TB management. Second-line drugs are highly toxic, with studies reporting ADRs in 70–90% of patients, including hepatotoxicity, gastrointestinal distress, ototoxicity, and psychiatric effects [4–6]. These reactions compromise adherence, prolong therapy, and contribute to treatment failure. Comorbidities such as diabetes and chronic lung diseases further complicate treatment, leading to prolonged sputum conversion and higher mortality rates [7,8]. Diabetes, in particular, weakens immune defense and increases relapse risk [9]. Fluoroquinolone resistance also predicts poor outcomes, underscoring the importance of drug susceptibility testing (DST) for individualized care [10,11].Socioeconomic challenges further exacerbate the burden. Many patients in rural Khyber Pakhtunkhwa (KP) face travel difficulties, economic hardship, and stigma, all of which reduce adherence and increase loss to follow-up. Limited healthcare infrastructure, inadequate patient education, and insufficient monitoring contribute to suboptimal outcomes [12].Given these multifactorial challenges, a holistic approach encompassing medical, social, and psychological support is essential. This study reviews the five-year experience of MDR-TB management at the PMDT site, MTI Mardan, focusing on treatment outcomes, ADRs, and predictors of poor prognosis. By identifying key determinants of success and failure, this study aims to inform future strategies for improving MDR-TB control in Pakistan.

Methodology

Study Design and Setting

A retrospective cohort study was conducted at the PMDT site, MTI Mardan, under the Association for Community Development, Khyber Pakhtunkhwa. The facility provides standardized and individualized regimens for MDR-TB according to WHO and national guidelines.

Study Population

A total of 161 patients with bacteriologically confirmed MDR-TB (resistant to at least isoniazid and rifampicin) enrolled between jan 2018 and jan 2024 were included.

Inclusion Criteria

1. Bacteriologically confirmed MDR-TB cases.
2. Patients treated at the PMDT Mardan site.
3. Patients who completed treatment during the study period.

Exclusion Criteria

1. Patients diagnosed with extensively drug-resistant TB (XDR-TB).
2. Incomplete or missing treatment records.

Data Collection

Data were extracted from medical charts and laboratory records, including demographics, comorbidities, prior TB treatments, DST results, ADRs, and treatment outcomes (cured, completed, failed, died, or lost to follow-up).

Ethical Approval Statement.

The study was approved by the Institutional Review and Ethics Board of Bacha Khan Medical College, Mardan (Reference No. 676/BKMC/2022/7/14). All procedures followed ethical standards, and patient confidentiality was strictly maintained throughout the study.

Statistical Analysis

Data were analyzed using SPSS v25. Descriptive statistics summarized demographic and clinical variables. Chi-square and logistic regression analyses identified predictors of poor outcomes. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 161 patients (52% male, mean age 52 ± 12 years) were analyzed; 60% were rural residents.

Table 01. Baseline Characteristics

Characteristic	Value
Total patients	161
Mean age (years)	52 ± 12
Age ≥50 years	45%
Male	52%
Female	48%
Rural	60%
Urban	40%
Married	65%
Unmarried	35%

Comorbidities

Chronic lung disease (38%) and diabetes (25%) were most frequent, followed by malnutrition (21%) and hypertension (18%).

Table 02. Comorbidities

Comorbidity	Prevalence (%)	Clinical Impact
Chronic lung disease	38	Delayed sputum conversion
Diabetes mellitus	25	Poor immune response
Malnutrition	21	Increased ADR risk
Hypertension	18	Cardiovascular stress
Chronic liver disease	10	Drug metabolism interference
CKD	5	Drug accumulation toxicity
HIV/AIDS	2	Immunosuppression

Prior Treatment History

Thirty percent had ≥2 previous TB treatments, strongly associated with fluoroquinolone resistance.

Table 03. Prior TB Treatment History

Parameter	Percentage	Interpretation
≥2 prior treatments	30	Resistance risk increases
FQ resistance	32	Linked with prior exposure
2nd-line injectable resistance	25	Indicates advanced resistance

Drug Resistance Profile

Resistance to fluoroquinolones and second-line injectables was 35% and 25%, respectively.

Table 04. Drug Resistance Profile

Drug Category	Resistance (%)	Notes
Fluoroquinolones	35	Critical for 2nd-line therapy
2nd-line injectables	25	Amikacin, kanamycin
Isoniazid + Rifampicin	100	Defines MDR-TB
Extensive resistance (XDR-like)	10	Complex cases excluded

Adverse Drug Reactions (ADRs) ADRs occurred in 45% of patients.

Table 05. Adverse Drug Reactions

ADR Type	Frequency (%)	Major Causes
GI intolerance	30	Pyrazinamide, ethionamide
Hepatotoxicity	20	Linezolid, bedaquiline
Ototoxicity	15	Amikacin
Neuropathy	12	Linezolid, isoniazid
Psychiatric effects	8	Neurotoxicity
Other	7	Rash, fever, electrolyte imbalance

Treatment Outcomes

Overall success rate was 85%; poor outcomes (death, failure, LTFU) totaled 16%.

Table 06. Treatment Outcomes

Outcome	Percentage	Remarks
Cured	70	Negative sputum conversion
Completed	15	Completed without conversion
Death	5	Comorbidities or ADRs
Failure	3	Persistent culture positivity
Lost to follow-up	7	Socioeconomic barriers

Predictors of Poor Outcomes

Table 07. Predictors of Poor Outcomes

Predictor	Effect	p-value
Diabetes mellitus	28% had poor outcomes	<0.02
Fluoroquinolone resistance	25% higher failure risk	<0.05
≥2 prior treatments	30% higher failure/death	<0.03
Severe ADRs	2.5× higher risk	<0.04
Malnutrition	20% higher poor outcomes	<0.01
Age >60 yrs	15% higher mortality	<0.05

DISCUSSION

This five-year analysis from PMDT Mardan demonstrates encouraging progress in MDR-TB control, with an 85% treatment success rate surpassing the national average (64–68%) [13-14]. Despite this success, adverse drug reactions (ADRs), comorbidities, and drug resistance remain major obstacles.Nearly half (45%) of patients experienced ADRs, predominantly gastrointestinal symptoms, hepatotoxicity, and ototoxicity, consistent with global reports [15-16]. These reactions disrupted adherence and necessitated regimen modification in 10% of patients. Strengthened pharmacovigilance systems, early detection, and supportive management (e.g., liver monitoring, audiometry, and nutritional support) are critical [17].Comorbidities, especially diabetes and chronic lung disease, significantly impacted outcomes. Similar findings were reported by Dooley and Chaisson [6] and Murtaza et al. [18], who observed delayed sputum conversion and higher mortality in diabetic TB patients. Integrated management addressing glycemic control and pulmonary rehabilitation could mitigate these risks.Fluoroquinolone resistance (35%) emerged as a major challenge, reducing therapeutic efficacy. Studies from Bangladesh and South Africa echo this trend, associating FQ resistance with poor outcomes

[19-20]. Routine DST and adoption of newer agents like bedaquiline or delamanid may improve results.Prior treatment history was another strong predictor of failure. Repeated TB therapy fosters cumulative resistance [21-22]. Comprehensive patient counseling, adherence monitoring, and molecular diagnostics (GeneXpert, LPA) are vital to prevent recurrence.Socioeconomic and psychosocial barriers also contributed to loss to follow-up. Similar observations by Pape et al. [23] and Nunn et al. [10] highlight the need for community-based DOTS-Plus models and social support programs. Addressing stigma, providing travel allowances, and incorporating mental health counseling could enhance adherence.Overall, the PMDT Mardan experience underscores that MDR-TB management extends beyond microbiological cure. A patient-centered, multidisciplinary approach integrating medical, nutritional, psychological, and social interventions is necessary to sustain success rates. Strengthening diagnostic capacity, ensuring drug supply, and expanding pharmacovigilance coverage across KP are recommended priorities for Pakistan's NTP[24].

CONCLUSION

The five-year experience at PMDT Mardan reflects commendable progress in MDR-TB control, achieving an 85% success rate. Nevertheless, challenges persist in managing ADRs, comorbidities, and drug resistance. Implementation of individualized regimens guided by DST, robust pharmacovigilance, and multidisciplinary care can significantly improve treatment outcomes and support Pakistan's TB-elimination goals.

Disclaimer: Nil

Conflict of Interest:Nil

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Rumman, Sajjad Ali

Drafting: Shabir Hussain

Data Collection: Ubaid Ullah

Data Analysis: Aleina ali shah

Critical Review: Aleina ali shah

Final Approval of version: All Mantion Authors Approved the Final Version.

REFERENCES

1. Alene KA, Jegnie A, Adane AA. Multidrug-resistant tuberculosis during pregnancy and adverse birth outcomes: a systematic review and meta-analysis. BJOG : an international journal of obstetrics and gynaecology.2021;128:1125-33.doi:https://doi.org/10.1111/1471-0528.16573.

2. Butov D, Lange C, Heyckendorf J, Kalmykova I, Butova T, Borovok N, et al. Multidrug-resistant tuberculosis in the Kharkiv Region, Ukraine. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2020;24:485-91. doi: https://doi.org/10.5588/ijtld.19.0508.

3. Deng G, Zhang P, Lu H. Challenges in the screening and treatment of latent multidrug-resistant tuberculosis infection. Drug discoveries.&.therapeutics.2022;16:52-4.doi: https://doi.org/10.5582/ddt.2022.01029.

4. Dookie N, Ngema SL, Perumal R, Naicker N, Padayatchi N, Naidoo K. The Changing Paradigm of Drug-Resistant Tuberculosis Treatment: Successes, Pitfalls, and Future Perspectives. Clinical microbiology.reviews. 2022;35:e0018019.doi:https://doi.org/10.1128/cmr.00180-19.

5. Eimer J, Patimeteeporn C, Jensenius M, Gkrania-Klotsas E, Duvignaud A, Barnett ED, et al. Multidrug-resistant tuberculosis imported into low-incidence countries-a GeoSentinel analysis, 2008-2020. Journal of travel medicine. 2021;28:doi: https://doi.org/10.1093/jtm/taab069.

6. Espinosa-Pereiro J, Sánchez-Montalvá A, Aznar ML, Espiau M. MDR Tuberculosis Treatment. Medicina (Kaunas,Lithuania).2022;58:doi: https://doi.org/10.3390/medicina58020188.

7. Faridgohar M. Finding New Ways to Combat Multidrug-Resistant.Tuberculosis.Microbial-drug.resistance (Larchmont,NY).2020;26:71-80.doi: https://doi.org/10.1089/mdr.2018.0353.

8. Hui SYA, Lao TT. Tuberculosis in pregnancy. Best practice & research Clinical obstetrics & gynaecology. 2022;85:34-44.doi: https://doi.org/10.1016/j.bpobgyn.2022.07.006.

9. Hwang Y, Kim J, Park S, Ryoo S. Biobank for multidrug-resistant tuberculosis research: importance of sequential samples. Pathogens.and.disease.2021;79:doi: https://doi.org/10.1093/femp d/ftab011.

10. Lakoh S, Yendewa GA. Multidrug-resistant tuberculosisinSierra-eone.The.Lancet.Global.health.2022;10:e459-e60.doi:https://doi.org/10.1016/s2214-109x(22)00045-6.

11. Liebenberg D, Gordhan BG, Kana BD. Drug resistant tuberculosis: Implications for transmission, diagnosis, and disease management.Frontiers.in.cellular.and infection.microbiology.2022;12:943545.doi: https://doi.org/10.3389/fcimb.2022.943545.

12. Liu Y, Posey DL, Yang Q, Weinberg MS, Maloney SA, Lambert LA, et al. Multidrug-Resistant Tuberculosis in U.S.-Bound Immigrants,and-Refugees.Annals of the American.Thoracic.Society.2022;19:943-51.doi: https://doi.org/10.1513/AnnalsATS.202105-580OC.

13. Liu Y, Schnitzer ME, Wang G, Kennedy E, Viiklepp P, Vargas MH, et al. Modeling treatment effect modification in multidrug-resistant tuberculosis in an individual patientdata meta-analysis. Statistical methods in medical research.2022;31:689-705.oi: https://doi.org/10.1177/09622802211046383.

14. Martín-García M, Esteban J. Evaluating bedaquiline as a treatment option for multidrug-resistant tuberculosis. Expert opinion on pharmacotherapy. 2021;22:535-41. doi: https://doi.org/10.1080/14656566.2020.1867538.

15. Molla KA, Reta MA, Ayene YY. Prevalence of multidrug-resistant tuberculosis in East Africa: A systematic review and meta-analysis. PloS one. 2022;17:e0270272. doi: https://doi.org/10.1371/journal.pone.0270272.

16. Mondoni M, Saderi L, Sotgiu G. Novel treatments in multidrug-resistant-tuberculosis.Current,opinion,in pharmacology.2021;59:103-15.doi: https://doi.org/10.1016/j.coph.2021.05.007.

17. Moreira TR, Passos IBJ, Bueno JVL, Maffacciolli R, Colodette RM, Miguel PS. Prevalence of multidrug-resistant tuberculosis in prisons: Systematic review and meta-analysis. Indian journal of medical microbiology. 2022;40:193-9. doi: https://doi.org/10.1016/j.ijmmb.2022.01.004.

18. Muthukrishnan L. Multidrug resistant tuberculosis - Diagnostic challenges and its conquering by nanotechnology approach - An overview. Chemico-biologicalinteractions.2021;337:109397.doi: https://doi.org/10.1016/j.cbi.2021.109397.

19. Najafizada M, Rahman A, Taufique Q, Sarkar A. Social determinants of multidrug-resistant tuberculosis: A scoping review and research gaps. The Indian journal of tuberculosis. 2021;68:99-105. doi: https://doi.org/10.1016/j.ijtb.2020.09.016.

20. Schluger NW. Prevention of Multidrug-Resistant Tuberculosis in Close Contacts. Back to the Future? American journal of respiratory and critical care medicine. 2020;202:1077-8. doi: https://doi.org/10.1164/rccm.202006-2488ED.

21. Seddon JA, Johnson S, Palmer M, van der Zalm MM, Lopez-Varela E, Hughes J, et al. Multidrug-resistant tuberculosis in children and adolescents: current strategies for prevention and treatment. Expert review of respiratory medicine.2021;15:221-37.doi: https://doi.org/10.1080/17476348.2021.1828069.

22. Sultana ZZ, Hoque FU, Beyene J, Akhlak-Ul-Islam M, Khan MHR, Ahmed S, et al. HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. BMC.infectious.diseases.2021;21:51.doi: https://doi.org/10.1186/s12879-020-05749-2.

23. Tengan FM, Figueiredo GM, Leite OH, Nunes AK, Manchiero C, Dantas BP, et al. Prevalence of multidrug-resistant tuberculosis in Latin America and the Caribbean: a systematic review and meta-analysis. Tropical medicine & international-health:TM-&-IH.2020;25:1065-78.doi: https://doi.org/10.1111/tmi.13453.

24. Wilson JW, Nilsen DM, Marks SM. Multidrug-Resistant Tuberculosis in Patients with Human Immunodeficiency Virus. Management Considerations within High-resourced Settings. Annals of the American Thoracic-Society.2020;17:16-23.doi: https://doi.org/10.1513/AnnalsATS.201902-185CME.

Open Access Statement