ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 04 | April - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

OUTCOME OF SHORTER ORAL BEDAQUILINE CONTAINING REGIMEN IN RIFAMPICIN RESISTANT PATIENTS –AT A TERTIARY CARE CENTER.

Respiratory Medicine

Dr. Akshat Mittal	3rd year Respiratory Medicine Resident.
Dr. Gunjan Mittal	3rd year Respiratory Medicine Resident.
Dr Vivek Yadav	Senior Resident Respiratory Medicine.
Dr Surinder Kumar Bansal	Professor in department of Respiratory Medicine.

ABSTRACT

The study aimed to evaluate the effectiveness, safety, and feasibility of this regimen in patients with rifampicin-resistant TB. This prospective observational study was conducted at K.D. Medical College, Hospital, and Research Center, Mathura, over two years. The study evaluated the effectiveness of all-oral shorter bedaquiline-containing regimen in rifampicin-resistant TB. **Results:** Sputum smear conversion was achieved in 63.33% of cases, while 10% remained positive. Treatment completion was observed in 46.66%, while 18.6% were classified as cured. Regimen change was required in 9.3%, and 4.65% experienced treatment failure. **Conclusion:** The shorter bedaquiline-based regimen was effective in achieving sputum smear conversion and treatment success in RR-TB patients.

KEYWORDS

rifampicin-resistant tuberculosis (RR-TB); CBNAAT; Bedaquiline; outcome

INTRODUCTION

Tuberculosis (TB) remains a critical global health challenge, causing millions of deaths and significant morbidity every year. Despite advancements in medical science, TB continues to be one of the leading causes of death from a single infectious agent, second only to COVID-19 in recent years.[1] In 2021, approximately 10.6 million people developed TB, with 1.3 million deaths attributed to the disease. Among those affected, rifampicin-resistant tuberculosis (RR-TB) and multidrug-resistant tuberculosis (MDR-TB) have emerged as major barriers to effective disease control. Together, these resistant forms of TB account for an estimated 410,000 cases annually.[2] Among TB patients, 28% were resistant to at least one anti-TB drug. Among newly diagnosed TB cases, 22% showed resistance to one or more drugs, while this figure increased to 38.62% among previously treated cases. [3]

Recognizing the need for more effective and less toxic treatment options, the World Health Organization (WHO) has consistently updated its guidelines for the management of MDR/RR-TB since 2000.[4] The inclusion of bedaquiline (Bdq), a diarylquinoline compound with a novel mechanism of action, marked a transformative shift in the treatment paradigm. Bedaquiline has demonstrated superior efficacy and safety in treating drug-resistant TB, leading to improved treatment outcomes and higher success rates, ranging from 70% to 90% in operational settings. These findings prompted the WHO to endorse all-oral shorter treatment regimens (STRs) that exclude SLIs and incorporate bedaquiline as a cornerstone drug.[5]

In 2018, the WHO recommended an all-oral STR for MDR/RR-TB patients, consisting of 4–6 months of treatment with bedaquiline, levofloxacin or moxifloxacin, ethionamide, clofazimine, pyrazinamide, ethambutol, and high 2 dose isoniazid, followed by 5 additional months of levofloxacin or moxifloxacin, clofazimine, pyrazinamide, and ethambutol.[6] This regimen aimed to enhance patient compliance, minimize treatment-related adverse effects, and reduce the overall duration of therapy. However, patients who were ineligible for the STR due to drug resistance, prior exposure to second-line drugs, extra-pulmonary TB, or other clinical contraindications were recommended to receive an all-oral longer treatment regimen (LTR) lasting 18–20 months.[7]

AIMS AND OBJECTIVES

1. To determine the outcomes of diagnosed cases of Rifampicin-resistant MDR TB put on an oral Bedaquiline-containing shorter regimen as per PMDT 2021 guidelines.
2. Patients with pulmonary tuberculosis were diagnosed as Rifampicin resistant based on CBNAAT/LPA reports.

Literature Review

Epidemiology Of Drug-sensitive And Drug-resistant Tuberculosis

Globally, the estimated proportion of new TB cases with multidrug resistant or rifampicin-resistant TB (MDR/RR-TB) was 3.9% in 2015 and 3.6% in 2021. Among previously treated cases, the proportion was higher, at 20% in 2015 and 18% in 2021. [8]

The global incidence of MDR/RR-TB has increased by 20% annually, reaching 650,000 cases, with the proportion of MDR and RR-TB higher in previously treated patients (17.7%) compared to new cases (3.3%) in 2019. In India, the burden of DR-TB is substantial. The first national anti-tuberculosis drug resistance survey (NDRS) revealed that 28% of TB patients were resistant to at least one anti-TB drug. Among new TB cases, 22% exhibited resistance to any drug, while this figure rose to 38.62% among previously treated cases. The prevalence of MDR-TB was 6.19% overall, with 2.84% of new cases and 11.62% of previously treated cases diagnosed with MDR-TB.

WHO-Recommended Shorter Treatment Regimen (STR):

o Duration: 9–12 months.
o Composition: Bedaquiline, levofloxacin/moxifloxacin, clofazimine, pyrazinamide, ethambutol, ethionamide, and high-dose isoniazid.
o Target Population: Patients without extensive resistance or prior second-line treatment.[9]

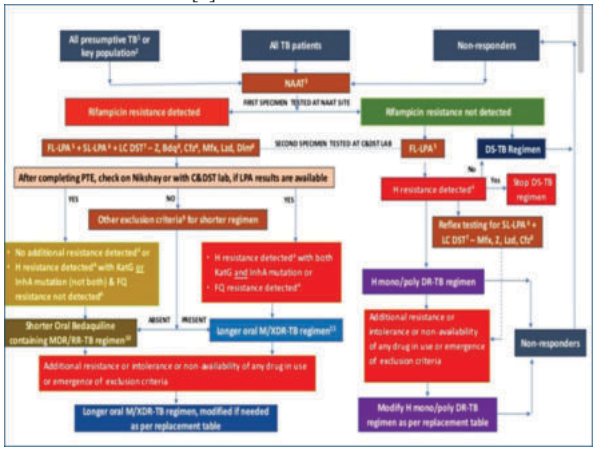

Figure 1: Integrated diagnostic and treatment algorithm for drug resistant tuberculosis:as per PMDT guideline 2021

Data Collection:

Data collection was performed using a standardized proforma to document patient demographics, clinical history, and examination findings comprehensively. Demographic details included name, age, sex, occupation, address, and NIKSHAY ID. Chief complaints and the progression of symptoms leading to the diagnosis of drug-resistant TB

were recorded, along with a detailed history of prior anti-tubercular therapy, including treatment episodes, regimens, and outcomes.

Investigations

All participants underwent diagnostic testing as per national TB management protocols:

1. **Chest X-ray**: Findings suggestive of TB were recorded.
2. **AFB Testing**: Sputum smear microscopy was performed.
3. **CBNAAT/TRUNAT**: Molecular testing was conducted to confirm rifampicin resistance.
4. **Line Probe Assays (LPA)**:

o First-line LPA (FL-LPA) was performed to detect isoniazid resistance, while second-line LPA (SL-LPA) was conducted to test for fluoroquinolone or injectable drug resistance.

5. **Culture**: Drug susceptibility testing through culture was performed if results were available.

Treatment Outcomes

At the end of the treatment, outcomes were classified based on PMDT Guidelines 2021:

1. **Cured**: Patients with bacteriological confirmation of TB at the start of treatment who completed the regimen with no evidence of treatment failure and achieved bacteriological response.
2. **Treatment Completed**: Patients who completed the regimen without meeting the criteria for either cure or failure.
3. **Treatment Failure**: Patients whose regimens were terminated or modified due to poor response or adverse events.
4. **Died**: Patients who passed away during the course of treatment.
5. **Loss to Follow-Up**: Patients who interrupted treatment for two consecutive months or more.

LIMITATIONS OF THE STUDY

Despite providing valuable insights into the demographic distribution, laboratory findings, resistance patterns, and treatment outcomes, this study has several limitations that must be acknowledged:

1. **Small Sample Size:** The study was conducted on a limited number of participants, which may not be fully representative of the broader population affected by tuberculosis (TB). A larger sample size would enhance the generalizability of the findings.
2. **Lack of Long-Term Follow-up:** The study focused on treatment outcomes within a defined period but did not include long-term follow-up data to assess relapse rates, post-treatment complications, or mortality beyond the study timeframe.
3. **Limited Assessment of Comorbidities and Risk Factors:** While some biochemical parameters were analyzed, the study did not comprehensively evaluate the impact of comorbid conditions such as diabetes, HIV, or malnutrition, which are known to influence TB treatment outcomes.
4. **Lack of Drug Adherence Monitoring:** The study did not assess patient adherence to treatment, which is a critical factor in determining treatment success, risk of relapse, and the emergence of drug resistance.
5. **Limited Data on Adverse Drug Reactions (ADRs):** Although treatment regimen changes were documented, specific details regarding the nature and severity of ADRs were not systematically recorded, making it difficult to evaluate the safety profile of the treatment regimens.
6. **Potential Underreporting of Treatment Failures:** Some patients were lost to follow-up (4.65%), which could underestimate the actual treatment failure rate if these individuals had poor treatment adherence or experienced complications.
7. **Single-Center Study:** Since the study was conducted at a specific healthcare facility, the findings may not reflect TB trends and treatment outcomes in different geographic regions with varying healthcare infrastructures, TB prevalence, and resistance patterns.

MATERIALS AND METHODS

Study Design

The study was a prospective observational study conducted on rifampicin- resistant tuberculosis (RR-TB) patients. These patients were either registered at or referred to K.D. Medical College, Hospital, and Research Center, Mathura, a tertiary care center for the management of drug-resistant tuberculosis. The study focused on the use of the shorter-term regimen containing bedaquiline, as outlined in the PMDT Guidelines 2021.

Study Duration

The study was conducted over a period of two years, concluding in April 2024.

Study Participants

The study included all cases of pulmonary MDR/RR-TB patients who met the eligibility criteria for the shorter bedaquiline-containing regimen.

Inclusion Criteria

The study included all diagnosed cases of rifampicin-resistant tuberculosis (RR-TB) and drug-resistant tuberculosis (DR-TB) with confirmed rifampicin resistance (RR) who were referred to K.D. Medical College, Mathura, for treatment as per the PMDT Guidelines 2021.

Exclusion Criteria

The following patients were excluded from the study:

1. Patients diagnosed with extrapulmonary tuberculosis.
2. Patients who were HIV-positive.
3. Patients below 18 years of age.
4. Pregnant and lactating patients.
5. MDR/RR-TB patients in whom fluoroquinolone (FQ) resistance was detected.
6. Patients with documented intolerance to any drug or an identified risk of significant toxicity from any component of the shorter oral bedaquiline- containing regimen.

RESULTS:

Age Distribution

The study population was predominantly young, with the highest proportion (46.67%) falling within the 18-29 years age group. The 30-39 and 40-49 age groups each accounted for 13.33% of the population. Individuals aged 50-59 represented only 3.33% of the total, while those aged 60 and above constituted 23.33%.

Sex Distribution

The study included more males (63.33%) than females (36.67%), demonstrating a higher prevalence of the condition or exposure under investigation in males.

Urban/Rural Distribution

A greater proportion of participants (56.67%) resided in rural areas compared to urban areas (43.33%).

Investigation Summary

Laboratory investigations revealed that the mean hemoglobin (Hb) level was **10.83 ± 2.03 g/dL,** with values ranging from 7.2 to 15.3 g/dL. The total leukocyte count (TLC) had a mean of **11.74 ± 4.0 ×10⁹/L,** indicating some cases of elevated white cell counts. Platelet counts varied widely, with a mean of **323.03 ± 140.83 ×10⁹/L.**

Previous History Distribution

The data indicates that a majority of the study population (73.33%) had a documented history of the condition under investigation, while 26.67% had no prior history.

Follow-up Smear Distribution

Among follow-up smear results, 63.33% tested negative, indicating successful treatment response or disease resolution. However, 10% had a positive follow- up smear, suggesting persistent infection or inadequate treatment response.

FL LPA Distribution

First-line Line Probe Assay (FL LPA) results showed that **30% of cases**had**M. tuberculosis detected with rifampicin resistance and high-level resistance to isoniazid**, while **10% had M. tuberculosis detected without further resistance information.**

SL LPA Distribution

Among the tested cases, **10% showed resistance to levofloxacin (LFX) and low-level moxifloxacin (MFX), but no resistance to second-line injectables (SLI) or kanamycin.**

Outcome Distribution

Regarding treatment outcomes,46.66% of cases completed their treatment, and 18.6% were classified as cured. However, 9.3% required a treatment regimen change. 4.65% of patients were lost to follow-up, 4.65% experienced treatment failure.

Culture Result Distribution

Culture testing results showed that 40% of cases were categorized as N/A, likely due to missing or unperformed tests. Among tested cases,

30% were culture-negative, while 20% tested positive for M. tuberculosis, confirming active infection.

CBNAAT result

Among new cases, 23.33% had M. tuberculosis detected with rifampicin resistance, while 3.33% had M. tuberculosis detected without rifampicin resistance. In previously treated cases, 73.33% had M. tuberculosis detected with rifampicin resistance.

DISCUSSION

This study provides an in-depth analysis of the demographic characteristics, laboratory findings, drug resistance patterns, and treatment outcomes among 30 patients diagnosed with tuberculosis. The findings highlight key epidemiological trends, resistance patterns, and treatment responses within the study population.

Our study population was predominantly young, with 46.67% falling in the 18- 29 years age group, followed by 13.33% each in the 30-39 and 40-49 years groups. The elderly population (≥60 years) comprised 23.33%.

In our study, males (63.33%) were more affected than females (36.67%). These findings suggest that men may have a higher risk of MDR-TB, possibly due to greater occupational exposure and differences in healthcare-seeking behavior.

We found that 56.67% of cases were from rural areas, suggesting that MDR- TB may be more prevalent in rural populations. This shows that the majority of cases came from socioeconomically disadvantaged regions, where limited healthcare access may contribute to late diagnosis and higher transmission rates.

Our study found that 73.33% of patients had a previous history of tuberculosis (TB), while 26.67% had no prior history, indicating a high prevalence of recurrent or previously treated cases. These results highlight the need for tailored treatment regimens for patients with prior TB history, as they may have a higher risk of drug resistance and treatment failure.

In our study, 46.66% of patients completed treatment, 18.6% were cured, 9.3% required a treatment regimen change, while 4.65% were lost to follow-up, and 4.65% experienced treatment failure. These findings suggest that shorter regimens improve adherence, increase treatment success, and reduce adverse outcomes.

CONCLUSION

This study provides valuable insights into the demographic characteristics, laboratory findings, drug resistance patterns, and treatment outcomes of the study population. The key findings suggest that the disease predominantly affects younger individuals (46.67% in the 18–29 age group) and males (63.33%), with a significant proportion residing in rural areas (56.67%). A majority (73.33%) had a prior history of the disease, emphasizing the challenge of recurrent cases and the importance of monitoring for drug resistance.

Treatment outcomes indicated that 46.66% completed treatment, and 18.6% were classified as cured. However, 9.3% required a treatment regimen change due to drug resistance or adverse effects, and 4.65% experienced treatment failure. Loss to follow-up (4.65%) remained a concern, emphasizing the need for better adherence strategies.

The high proportion of previously treated cases and significant drug resistance burden underline the necessity of **early detection, tailored treatment regimens, and improved follow-up mechanisms** to enhance treatment success and minimize recurrence.

REFERENCES

1. Oelofse S, Esmail A, Diacon AH, Conradie F, Olayanju O, Ngubane N, et al. Pretomanid with bedaquiline and linezolid for drug-resistant TB: A comparison of prospective cohorts. Int J Tuberc Lung Dis. 2021;25:453– 60.
2. World Health Organization. Global tuberculosis report 2023. Geneva: WHO Press; 2023.
3. Central TB Division, Ministry of Health and Family Welfare, Government of India.Training modules (1–4) for programme managers and medical officers.New Delhi: MoHFW; 2020. Module 1:4. PMID: 21420161. S2CID: 208791546.
4. World Health Organization.Global Tuberculosis Report 2020.Geneva: WHO Press;2020.
5. *Nahid P,Mase SR,Migliori GB, et al. Treatment of drug-resistant tuberculosis. an official ATS/CDC/ERS/IDSA clinical practice guideline. Am J Respir Crit Care Med 2019; 200:e93–e142.* [DOI] [PMC free article] [PubMed] [Google Scholar]
6. World Health Organization.Consolidated guidelines on tuberculosis treatment. 2019.
7. Nunn AJ, Phillips PPJ, Meredith SK, et al. ; STREAM Study Collaborators. A trial of a shorter regimen for rifampin-resistanT
8. Burhan E, Karyana M, Karuniawati A, Kusmiati T, Wibisono BH, Handayani D, Riyanto BS, Sajinadiyasa IGK, Sinaga BYM, Djaharuddin I, Indah Sugiyono R, Susanto NH, Diana A, Kosasih H, Lokida D; Siswanto; Neal A, Lau CY, Siddiqui S. Characteristics of Drug-sensitive and Drug-resistant Tuberculosis Cases among Adults at Tuberculosis Referral Hospitals in Indonesia. Am J Trop Med Hyg. 2022 Oct 17;107(5):984-991.doi:10.4269/ajtmh.22-0142.PMID: 36252800; PMCID: PMC9709011.
9. World Health Organization. Frequently asked questions on the WHO rapid communication: key changes to the treatment of multidrug- and rifampicin-resistant TB [Internet]. Geneva: WHO; 2019 [cited 2025 Jan 27].Available from:https://www.who.int/docs/default- source/documents/tuberculosis/mdr-rr-tb-taskforce-faqs-updated- june2019.pdf