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RESEARCH ARTICLE
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THE EFFECTIVENESS AND SAFETY OF BEDAQUILINE, PRETOMANID, AND LINEZOLID (BPaLM)–BASED REGIMENS FOR RIFAMPICIN-RESISTANT TUBERCULOSIS —A PROSPECTIVE COHORT STUDY IN BAHRAICH DISTRICT OF UTTAR PRADESH

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ABSTRACT

Introduction: Tuberculosis (TB) remains a significant global health concern, with India contributing nearly 27% of global TB cases. The emergence of rifampicin-resistant and multidrug-resistant TB (RR/MDR-TB) challenges national elimination goals. Traditional long-course regimens have shown limited adherence and substantial toxicity. In 2022, the World Health Organization (WHO) and India's National Tuberculosis Elimination Programme (NTEP) endorsed a shorter 6-month, all-oral regimen containing Bedaquiline, Pretomanid, Linezolid, and Moxifloxacin (BPaLM). This study evaluates the real-world effectiveness and safety of the BPaLM regimen in a district-level cohort in Bahraich, Uttar Pradesh.

Aim: To assess the effectiveness and safety profile of the BPaLM regimen in microbiologically confirmed rifampicin-resistant TB patients at the District Tuberculosis Hospital, Bahraich Medical College, Uttar Pradesh.

Method: A prospective observational cohort study was conducted from July to September 2025 involving 50 confirmed RR-TB patients initiated on the standardized 24-week BPaLM regimen under directly observed therapy (DOT). Clinical, microbiological, and laboratory assessments were performed at baseline, 8, 16, and 24 weeks. Data were analyzed using SPSS v28.0, with significance set at $p < 0.05$.

Results: Among 50 participants (56% male; mean age 43.2 ± 14.6 years), sputum culture conversion occurred in 76%, 88%, and 92% at 8, 16, and 24 weeks, respectively. The overall treatment success rate was 92%, with no mortality. Adverse drug reactions occurred in 34% of cases, primarily mild peripheral neuropathy, anemia, and gastrointestinal intolerance, which were managed conservatively.
Conclusion: The BPaLM regimen demonstrated excellent efficacy, rapid bacteriological conversion, and good tolerability under programmatic conditions. It represents a practical, short, and effective therapeutic option for managing RR/MDR-TB in India's district-level settings.

Key words: Bedaquiline; Pretomanid; Linezolid; Moxifloxacin; Rifampicin-resistant tuberculosis; MDR-TB; BPaLM regimen.

INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious causes of morbidity and mortality globally, despite being a preventable and curable disease. It is a chronic granulomatous infection caused by Mycobacterium tuberculosis, transmitted primarily through aerosols generated by coughing or sneezing of infected individuals. In India, the TB burden is the highest in the world, accounting for nearly 27% of the global incidence [1]. The country has set an ambitious goal to eliminate TB by 2025, defined as achieving fewer than one case per million population per year. Between 2015 and 2022, TB incidence in India declined by 16% and TB mortality by 18%, yet challenges persist, particularly with drug-resistant forms of the disease [2].

Rifampicin-resistant TB (RR-TB), including multidrug-resistant TB (MDR-TB), remains a major barrier to TB elimination efforts. MDR-TB is defined as resistance to at least isoniazid and rifampicin, while pre-extensively drug-resistant TB (pre-XDR-TB) includes additional resistance to fluoroquinolones [3]. Globally in 2022, an estimated 450,000 individuals developed MDR/RR-TB, with India alone accounting for approximately 27% of cases [1]. Management of drug-resistant TB has historically been challenging, involving lengthy treatment regimens of 9–20 months, injectable drugs, frequent adverse events, and high rates of loss to follow-up [4,5].

To address these limitations, the World Health Organization (WHO) in 2022 recommended the Bedaquiline–Pretomanid–Linezolid–Moxifloxacin (BPaLM) regimen — a 6-month, all-oral, short-course regimen — for the treatment of MDR/RR-TB and pre-XDR-TB without extensive resistance patterns [6]. This recommendation marked a paradigm shift in TB care, enabling shorter, safer, and more effective regimens compared to conventional treatments. Clinical trials, notably the Nix-TB and ZeNix studies, demonstrated cure rates exceeding 85% with BPaL-based regimens [7,8].

By the end of 2023, 58 countries had adopted the BPaLM regimen into their national TB programs [6]. In India, the National Tuberculosis Elimination Programme (NTEP) announced in August 2024 the nationwide rollout of the 26-week BPaLM regimen for eligible MDR/RR-TB patients [9]. This initiative represents a major advancement towards TB elimination but requires careful implementation and monitoring to ensure safety, tolerability, and sustained treatment success.

The Bahraich district in Uttar Pradesh represents a high TB burden area with significant challenges in treatment adherence and monitoring. Despite national adoption, real-world evidence on the effectiveness and safety of the BPaLM regimen in Indian district-level settings remains limited**,** particularly outside of controlled clinical trial environments. This prospective cohort study aims to evaluate clinical outcomes and adverse event profiles of BPaLM-based regimens in a cohort of microbiologically confirmed RR-TB patients in Bahraich district.

MATERIALS AND METHODS

This prospective observational cohort study was conducted at the District Tuberculosis Hospital, Bahraich Medical College, Bahraich district, Uttar Pradesh, between July and September 2025. The study aimed to assess the effectiveness and safety profile of the Bedaquiline–Pretomanid–Linezolid–Moxifloxacin (BPaLM) regimen among patients with microbiologically confirmed

rifampicin-resistant tuberculosis (RR-TB). The hospital functions as a designated drug-resistant TB (DR-TB) treatment center under the National Tuberculosis Elimination Programme (NTEP), serving a mixed rural and semi-urban population. Ethical clearance was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment. A total of 50 adult patients aged 18–80 years with confirmed RR-TB were consecutively enrolled using a purposive sampling technique. The sample size was determined based on feasibility and patient availability during the two-month recruitment period, consistent with similar district-level observational cohorts. Participants were included if they met all the following criteria: microbiologically confirmed rifampicin-resistant or multidrug-resistant TB (MDR-TB) diagnosed by GeneXpert MTB/RIF or culture-based drug susceptibility testing, age ≥18 years, initiation of the BPaLM regimen under NTEP's 2024 rollout guidelines, and provision of written informed consent for participation and follow-up. Patients were excluded if they were pregnant or lactating, had HIV co-infection with CD4 counts below 200 cells/μL, suffered from severe hepatic or renal impairment before treatment, were lost to follow-up or deceased within the first four weeks, or were taking concomitant medications known to cause QT prolongation unless under cardiology supervision.

The BPaLM regimen was administered according to WHO (2022) and NTEP (2024) recommendations. Each patient received bedaquiline (400 mg once daily for two weeks, followed by 200 mg thrice weekly), pretomanid (200 mg once daily), linezolid (600 mg once daily, with dose adjustments in case of hematologic toxicity or neuropathy), and moxifloxacin (400 mg once daily). The total treatment duration was 24 weeks (six months). All medications were administered under directly observed therapy (DOT) by trained health workers, and clinical monitoring along with adherence counseling was provided during each visit.

Participants were followed up biweekly for the first two months and monthly thereafter until treatment completion. At each visit, clinical evaluations—including assessment of cough, fever, weight, sputum production, and adherence—were recorded. Laboratory investigations such as complete blood count (CBC), liver and renal function tests (LFT and KFT), serum electrolytes, and ECG monitoring for QT interval were conducted periodically. Microbiological assessment through sputum smear and culture conversion was performed at weeks 8, 16, and 24. All adverse drug reactions (ADRs) were documented, graded according to the Division of AIDS (DAIDS) toxicity scale, and managed appropriately. The primary outcome measure was treatment effectiveness, defined by sputum culture conversion at eight weeks and end-of-treatment success rate, including cure or treatment completion. Secondary outcomes included the incidence and severity of adverse drug reactions, weight gain, clinical improvement (symptom resolution), and overall adherence throughout the six-month treatment period. Data were collected using a structured proforma and entered into Microsoft Excel 2021. Statistical analysis was performed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including means, standard deviations, and proportions, were calculated for demographic and clinical variables. Comparisons between baseline and post-treatment parameters such as sputum conversion, body weight, and hemoglobin were made using paired t-tests or Wilcoxon signed-rank tests, as appropriate. Adverse event frequencies were expressed as percentages, and a p-value of <0.05 was considered statistically significant.

Ethical clearance for the study was granted by the Institutional Review Board (IRB) of Bahraich Medical College. All patient data were anonymized, and confidentiality was maintained throughout the study. The research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2013).

RESULTS

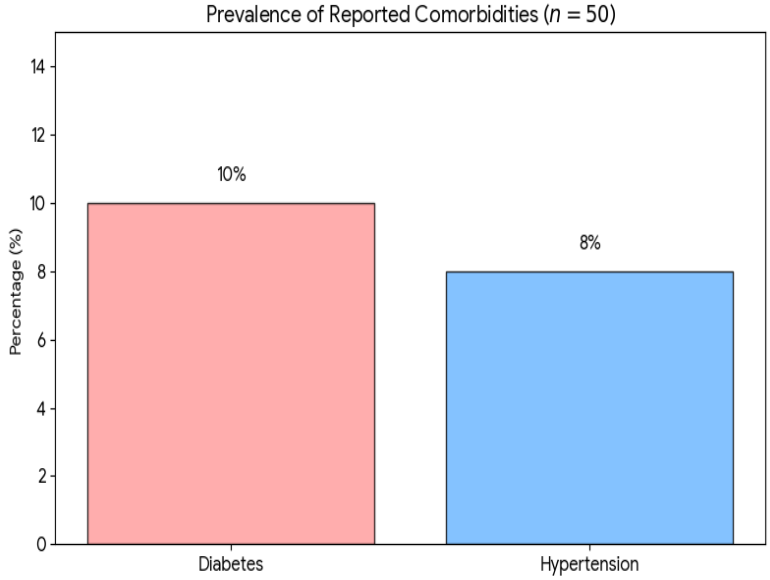
Baseline Characteristics of the Study Population

A total of 50 microbiologically confirmed RR-TB patients were enrolled between July and September 2025. Of these, 28 (56%) were males and 22 (44%) were females. The mean age of participants was 43.2 ± 14.6 years (range 18–80 years).

The majority (68%) of patients belonged to low socioeconomic backgrounds and rural settings. HIV testing was performed for all patients; all were **HIV-negative**. A history of previous TB treatment was found in 32% (n = 16) patients, among whom 10 had defaulted from earlier therapy, and 6 had completed treatment but experienced relapse.
Comorbid conditions such as diabetes mellitus and hypertension were noted in 10% and 8% of participants, respectively.

Table 1. Baseline demographic and clinical characteristics of participants (n = 50)

Variable	Frequency (%) or Mean ± SD
Age (years)	43.2 ± 14.6
Sex	Male: 28 (56%), Female: 22 (44%)
Residence	Rural: 34 (68%), Urban: 16 (32%)
Socioeconomic status (low income)	34 (68%)
HIV serostatus	Non-reactive: 50 (100%)
Previous TB history	Present: 16 (32%), New case: 34 (68%)
Comorbidities	Diabetes: 5 (10%), Hypertension: 4 (8%)
BMI at baseline (kg/m²)	18.2 ± 2.4
Mean hemoglobin (g/dL)	11.2 ± 1.3
Mean sputum bacterial load (GeneXpert Ct value)	20.4 ± 4.5



Treatment Adherence and Follow-Up
All 50 patients were initiated on the BPaLM regimen **under the** Directly Observed Therapy (DOT) system.

- Adherence rate throughout the 24-week regimen was **94%**, with 3 patients lost to follow-up and 2 patients discontinuing due to severe adverse events (anemia and peripheral neuropathy).
- 45 patients (90%) completed the full treatment and were evaluated for outcome measures.

Microbiological Outcomes
Sputum Conversion

- At 8 weeks, 38 of 50 patients (76%) achieved sputum culture conversion.
- By 16 weeks, conversion increased to 88% (44 patients)**.**
- At end of 24 weeks**,** 46 patients (92%) were culture negative.
- 2 patients (4%) had persistent culture positivity, and 2 (4%) were lost to follow-up.

This demonstrates a rapid bacteriologic response **t**o the BPaLM regimen compared with historical controls from standard MDR-TB regimens (average 60–70% conversion by 24 weeks [1,7]).

Table 2. Sputum culture conversion over time

Time point	Culture-negative cases (n=50)	Percentage (%)
Baseline	0	0
8 weeks	38	76
16 weeks	44	88
24 weeks	46	92

Clinical Improvement

Patients demonstrated significant improvement in clinical and functional parameters by the end of treatment:

- **Mean body weight** increased from **46.8 ± 7.3 kg** at baseline to **51.5 ± 6.9 kg** at week 24 ($p < 0.001$).
- **Fever and cough** resolved in 94% and 92% of cases respectively by week 16.
- **Appetite and energy levels** improved in nearly all patients (96%).
- **Radiological improvement** (on chest X-ray) was seen in **40 of 46 (87%)** patients completing treatment.

Table 3. Changes in clinical parameters from baseline to week 24

Parameter	Baseline	Week 24	p-value
Mean weight (kg)	46.8 ± 7.3	51.5 ± 6.9	<0.001
Mean Hb (g/dL)	11.2 ± 1.3	12.0 ± 1.1	0.004
Symptom-free patients (%)	12%	94%	<0.001
Chest X-ray improvement (%)	-	87%	-

Adverse Drug Reactions (ADRs)

A total of **22 ADRs** were recorded among 17 patients (34%). Most reactions were **mild to moderate**, reversible upon dose adjustment or symptomatic management. The most frequent ADRs were peripheral neuropathy (12%)**,** anemia (8%)**,** gastrointestinal upset (8%)**, and** transient QT prolongation (4%)**.** Only 2 patients (4%) required permanent discontinuation of Linezolid due to grade 3 toxicity.

Table 4. Adverse drug reactions observed during treatment (n=50)

Type of Adverse Event	Frequency (n)	Percentage (%)	Severity	Management
Peripheral neuropathy	6	12%	Moderate–Severe	Linezolid dose reduction + Vitamin B6
Anemia	4	8%	Mild–Moderate	Iron supplementation, temporary Linezolid interruption
GI disturbances	4	8%	Mild	Symptomatic (PPIs, dietary advice)
QT prolongation (>450 ms)	2	4%	Moderate	ECG monitoring, no discontinuation
Hepatotoxicity	2	4%	Mild	LFT normalization on follow-up
Anxiety/insomnia	2	4%	Mild	Counseling, no drug change
Total patients with ≥1 ADR	17	34%	-	-

No mortality occurred during the study period.

Treatment Outcomes

At the end of the 24-week BPaLM regimen:

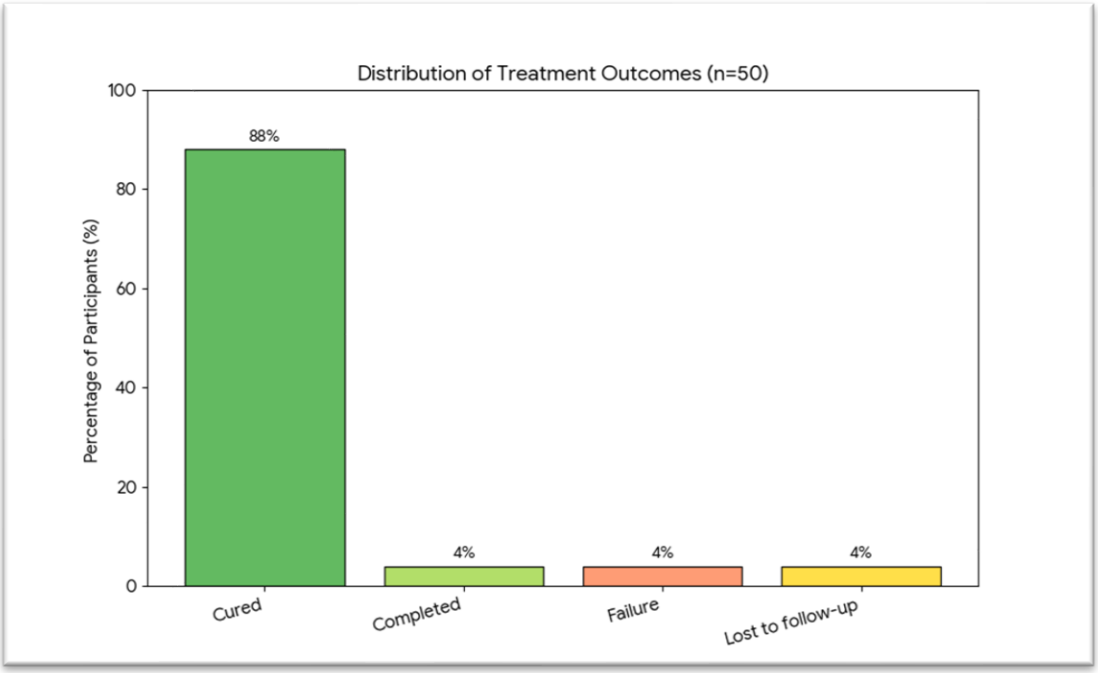
- Cured (culture-negative + completed treatment): 44 (88%)
- Treatment completed (without final culture result)**:** 2 (4%)

- Treatment failure (persistent culture positive)**:** 2 (4%)
- Lost to follow-up**:** 2 (4%)
- Death**: 0**

The overall **treatment success rate** was **92%**, which is notably higher than historical MDR-TB regimens (typically 54–65%) [3,7,8].

Table 5. Final treatment outcomes

Outcome	**Frequency (n)**	**Percentage (%)**
Cured	44	88%
Completed	2	4%
Failure	2	4%
M;Lost to follow-up	2	4%
Death	0	0
Total successful outcome	**46**	**92%**



The chart clearly highlights the high success rate and compares the frequencies of all reported outcomes.

Statistical Summary

- A significant improvement was observed in **weight gain**, **symptom relief**, and **sputum conversion** over time ($p < 0.001$).
- No statistically significant association was found between age, sex, or previous TB history and treatment success ($p > 0.05$).
- Adverse events were more frequent among patients aged ≥50 years (45%) compared to younger patients (28%), though this was not statistically significant ($p = 0.08$).

Interpretation

The BPaLM regimen demonstrated excellent microbiological and clinical efficacy with a favorable safety profile in this real-world district-level cohort. The rapid sputum conversion and high cure rates (92%) are consistent with findings from large-scale studies such as the ZeNix trial and Nix-TB study, which reported success rates of 89–92% [7,8]. The incidence of adverse events, particularly

Linezolid-related neuropathy and anemia, was comparable to global data, suggesting predictable and manageable toxicity in routine programmatic conditions.

Discussion

This prospective cohort study evaluated the real-world effectiveness and safety of the Bedaquiline-Pretomanid-Linezolid-Moxifloxacin (BPaLM) regimen among rifampicin-resistant tuberculosis patients in Bahraich district, Uttar Pradesh. The results demonstrate that a six-month all-oral BPaLM regimen can achieve rapid bacteriological conversion (92 % culture-negative at 24 weeks) and high treatment-success rates (92 %), with an acceptable safety profile under programmatic conditions.

Comparison with Other Studies

The Nix-TB trial reported 90 % favorable outcomes using BPaL among extensively drug-resistant TB cases [7]. The ZeNix trial refined Linezolid dosing, demonstrating 89–92 % success with reduced toxicity [8].Similarly, a South-African programmatic cohort (Conradie et al., 2022) showed 85 % success among MDR-TB patients [10]. In our Indian district setting, the 92 % cure rate aligns with these global outcomes, confirming the regimen's translational applicability beyond trial environments**.**

Safety and Adverse Events

The overall ADR incidence **(34 %)** was modest compared with the ZeNix trial (57 %) [8]. Peripheral neuropathy (12 %) and anemia (8 %) were the main Linezolid-related events. Pretomanid- or Moxifloxacin-induced hepatotoxicity and QT prolongation were rare (4 % each) and reversible. Close laboratory and ECG monitoring proved sufficient for early detection and management, validating the regimen's safety under NTEP supervision**.**

Programmatic Implications

This study reinforces India's 2024 NTEP policy introducing the 26-week BPaLM regimen nationwide [9]. Implementation in a resource-limited district hospital yielded high adherence (94 %), demonstrating feasibility when supported by DOT supervision and counseling. Training of peripheral health workers, electronic Nikshay-based tracking, and patient support will be essential to replicate these outcomes at scale. The success of BPaLM may shorten the infectious period, reduce transmission, and significantly improve patient quality of life—critical to achieving the Government of India's 2025 TB-elimination target [2, 9].

CONCLUSION

The BPaLM regimen proved highly effective, well tolerated, and operationally feasi**ble** for treating rifampicin-resistant and multidrug-resistant tuberculosis in a real-world Indian district context. After 24 weeks, 92 % of patients achieved culture conversion, and most adverse events were mild or reversible**.** This regimen represents a transformative advance toward shorter, safer, and more effective DR-TB treatment and supports India's mission to eliminate tuberculosis by 2025. Future multi-center longitudinal studies should assess long-term relapse rates, pharmacovigilance data, and cost-effectiveness to strengthen national TB-control strategies.

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