E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.574

Research Article

Clinical Outcomes of Delamanid-Containing Regimens in Patients with Drug-Resistant Pulmonary Tuberculosis: A Prospective Observational Study

Sowmya Jonnalagadda[1], Deekshith Kolluri[2*], Divya Sree Lavudya[3], Pantham Sunitha[4], P. Karthik[5], Pasula Ravi[6]

[1,2*,3]Assistant Professor, Department of Respiratory Medicine, Kakatiya Medical College, Warangal, Telangana, India.

[4]Professor, Department of Respiratory Medicine, Government Medical College, Mulugu, Telangana, India.

[5]Postgraduate Resident, Department of Respiratory Medicine, Kakatiya Medical College, Warangal, Telangana, India.

[6]Professor and Head, Department of Respiratory Medicine, Kakatiya Medical College, Warangal, Telangana, India.

Corresponding author: Deekshith Kolluri
Department of Respiratory Medicine, Kakatiya Medical College (Government Chest Diseases and Tuberculosis Hospital), Warangal – 506009, Telangana, India.
Email: dr.deekshithkolluri@gmail.com

Received: 22.07.26, Revised: 28.08.26, Accepted: 22.09.26

ABSTRACT

Drug-resistant pulmonary tuberculosis (DR-PTB) remains a major public health challenge owing to prolonged treatment, limited therapeutic options, and suboptimal treatment outcomes. Delamanid has emerged as an important component of individualized regimens for multidrug-resistant and rifampicin-resistant tuberculosis, particularly in patients with fluoroquinolone resistance or intolerance to conventional second-line drugs. This prospective observational study evaluated the effectiveness, safety, tolerability, and treatment outcomes of delamanid-containing regimens in patients with drug-resistant pulmonary tuberculosis managed at a tertiary care centre in South India. Twenty adult patients with microbiologically confirmed drug-resistant pulmonary tuberculosis who received delamanid-containing treatment were enrolled between February 2024 and August 2025. Demographic, clinical, microbiological, radiological, laboratory, and treatment-related data were prospectively collected. Treatment response, adverse drug reactions, QTc interval changes, treatment adherence, and final outcomes were assessed. Most patients had pre-extensively drug-resistant tuberculosis (85.0%), and fluoroquinolone resistance was the most common indication for delamanid therapy (80.0%). Delamanid-containing regimens were generally well tolerated, with only isolated adverse events, including nausea, vomiting, epigastric burning, QTc prolongation, and hypokalaemia (5.0% each). No hepatotoxicity or treatment discontinuation due to adverse drug reactions was observed. Nineteen patients (95.0%) were cured, while one patient (5.0%) was lost to follow-up and subsequently died. Delamanid-containing regimens demonstrated excellent effectiveness, good tolerability, and a favourable safety profile in this cohort. These findings support the use of delamanid as an important component of individualized treatment regimens for drug-resistant pulmonary tuberculosis under routine programmatic conditions.

Keywords: Drug-Resistant Tuberculosis, Delamanid, Multidrug-Resistant Tuberculosis, Treatment Outcome, Drug Safety.

INTRODUCTION

Drug-resistant pulmonary tuberculosis (DR-PTB) remains one of the most important challenges in global tuberculosis control because of prolonged treatment duration, limited therapeutic options, high treatment costs, and suboptimal clinical outcomes [1]. According to the World Health Organization (WHO), approximately 10.8 million people developed tuberculosis worldwide in 2023, with an estimated 400,000 incident cases of multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB), emphasizing the continuing global burden of drug-resistant disease [1].

India continues to account for the highest burden of tuberculosis globally, including MDR/RR-TB. The India TB Report 2025 documented a substantial number of patients requiring treatment for drug-resistant

tuberculosis despite improvements achieved through the National Tuberculosis Elimination Programme (NTEP) [2]. The emergence of fluoroquinolone resistance and pre-extensively drug-resistant tuberculosis (pre-XDR-TB) has further complicated treatment, reducing the effectiveness of conventional second-line regimens and necessitating the use of newer anti-tuberculosis agents [3].

Delamanid, a nitroimidazole derivative that inhibits mycolic acid synthesis in Mycobacterium tuberculosis, has emerged as an important component of all-oral regimens for MDR/RR-TB. Clinical studies and programmatic experience have demonstrated that delamanid-containing regimens improve treatment success while maintaining an acceptable safety profile, particularly in patients with fluoroquinolone resistance or intolerance to other second-line drugs [4-7]. Although QT interval prolongation remains an important adverse effect requiring electrocardiographic monitoring, serious drug-related toxicity has been reported infrequently under appropriate clinical surveillance [5-7].

Despite increasing incorporation of delamanid into national treatment programmes, real-world data from India remain limited, particularly from routine programmatic settings. Most published evidence originates from clinical trials or multicentre cohorts, whereas information regarding treatment effectiveness, tolerability, and safety in tertiary care centres remains scarce [8-10].

The present prospective observational study was therefore undertaken to evaluate the effectiveness, safety, tolerability, and treatment compliance of delamanid-containing regimens among patients with drug-resistant pulmonary tuberculosis managed at a nodal drug-resistant tuberculosis centre in South India.

PATIENTS AND METHODS

Study design and setting

This prospective observational study was conducted at the Nodal Drug-Resistant Tuberculosis Centre, Department of Respiratory Medicine, Government Chest Diseases and Tuberculosis Hospital, Hanamkonda, Telangana, India, over an 18-month period from February 2024 to August 2025.

Study population

Twenty consecutive adult patients (≥18 years) with microbiologically confirmed drug-resistant pulmonary tuberculosis who were initiated on a delamanid-containing regimen because of resistance or intolerance to conventional second-line anti-tubercular drugs were enrolled. Diagnosis was established using cartridge-based nucleic acid amplification test (CBNAAT), TrueNat, line probe assay (LPA), or mycobacterial culture with drug susceptibility testing.

Eligibility criteria

Patients aged 18 years or older with microbiologically confirmed multidrug-resistant or rifampicin-resistant pulmonary tuberculosis who received a delamanid-containing regimen and provided written informed consent were eligible for inclusion. Patients with extrapulmonary drug-resistant tuberculosis, pregnancy or lactation, known hypersensitivity to delamanid, significant hepatic or renal dysfunction, baseline QTc prolongation (>450 ms in men or >470 ms in women), pre-existing cardiac disease, concomitant anti-arrhythmic therapy, or those unwilling to participate were excluded.

Study procedures

Baseline evaluation included detailed demographic data, smoking history, previous tuberculosis episodes, clinical symptoms, physical examination, chest radiography, sputum microbiological investigations, electrocardiography, liver and renal function tests, and serum electrolyte estimation. Patients received delamanid 100 mg twice daily for 24 weeks as part of an individualized multidrug regimen in accordance with the National Tuberculosis Elimination Programme recommendations. During follow-up, patients were assessed for clinical response, adverse drug reactions, electrocardiographic changes, laboratory abnormalities, treatment adherence, and treatment outcomes.

Outcome measures

The primary outcome was treatment effectiveness, assessed by clinical improvement and final treatment outcome. Secondary outcomes included the incidence of adverse drug reactions, QTc interval prolongation, treatment tolerability, treatment adherence, and completion of delamanid therapy.

Statistical analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 24. Continuous variables are presented as mean ± standard deviation (SD), whereas categorical variables are expressed as frequencies and

percentages. A two-sided P value <0.05 was considered statistically significant.

Ethics

The study was approved by the Kakatiya Institutional Ethics Committee (KIEC), Kakatiya Medical College, Hanamkonda, Telangana, India (Approval No. 2023-24/61; 29 February 2024). Written informed consent was obtained from all participants before enrolment in the study.

Results

Baseline characteristics

Twenty patients with microbiologically confirmed drug-resistant pulmonary tuberculosis were included in the study. The majority of patients belonged to the 18–30 years and 31–45 years age groups (35.0% each), while 20.0% were aged 46–60 years and 10.0% were older than 60 years (Table 1). There was an equal distribution of male and female participants (50.0% each). Most patients were underweight (55.0%), followed by those with normal body weight (35.0%) and overweight individuals (10.0%). The majority of participants belonged to the lower-middle socioeconomic group.

Clinical characteristics

Cough was the most common presenting symptom and was observed in all patients (100.0%). Loss of appetite was reported by 85.0% of patients, followed by fever (80.0%) and shortness of breath (80.0%). Weight loss was present in 55.0%, fatigue in 50.0%, chills in 35.0%, haemoptysis in 15.0%, and chest pain and night sweats in 10.0% each (Table 1). Current smokers constituted 35.0% of the study population, while 25.0% were former smokers, 10.0% were passive smokers, and 30.0% had never smoked. Half of the patients had experienced two previous episodes of tuberculosis, whereas 25.0% had one previous episode and 25.0% had three previous episodes.

Microbiological and radiological findings

Pre-extensively drug-resistant tuberculosis (pre-XDR-TB) was the predominant resistance pattern, accounting for 85.0% of cases, while rifampicin-resistant tuberculosis constituted 15.0%. All patients had rifampicin resistance detected by CBNAAT, 90.0% had positive mycobacterial cultures, and 80.0% were sputum smear positive. Radiological evaluation demonstrated pulmonary fibrosis in 50.0% of patients, pneumonia in 45.0%, cavitary lesions in 15.0%, and bronchiectasis in 5.0%. Unilateral lung involvement was observed in 70.0% of patients, whereas 30.0% had bilateral disease (Table 2).

Delamanid treatment

Fluoroquinolone resistance was the most common indication for initiation of delamanid therapy (80.0%), followed by non-availability of bedaquiline (10.0%), linezolid-induced pancytopenia (5.0%), and peripheral neuropathy secondary to linezolid (5.0%) (Table 2). Baseline laboratory parameters demonstrated preserved hepatic and renal function, with a mean haemoglobin level of 10.2 ± 1.4 g/dL, serum alanine aminotransferase of 34 ± 12 IU/L, serum creatinine of 0.9 ± 0.2 mg/dL, serum potassium of 4.1 ± 0.4 mEq/L, and a mean baseline QTc interval of 412 ± 18 ms.

Safety and treatment outcomes

Delamanid-containing regimens were generally well tolerated. Each adverse event, including nausea, vomiting, epigastric burning, QTc interval prolongation, and hypokalaemia, occurred in one patient (5.0%). No cases of hepatotoxicity were observed. Nineteen patients (95.0%) successfully completed treatment and were declared cured, while one patient (5.0%) defaulted and subsequently died. No treatment failures were recorded (Table 3).

DISCUSSION

Delamanid has emerged as an important component of all-oral regimens for the treatment of multidrug-resistant and rifampicin-resistant tuberculosis, particularly in patients with fluoroquinolone resistance or intolerance to conventional second-line drugs. The present prospective observational study demonstrated that delamanid-containing regimens were associated with favourable treatment outcomes, excellent tolerability, and a low incidence of adverse drug reactions in patients managed under routine programmatic conditions. A treatment success rate of 95.0% was observed, with only one patient defaulting during follow-up.

The majority of patients in this cohort were young adults, reflecting the epidemiology of drug-resistant tuberculosis in high-burden countries where the disease predominantly affects economically productive age groups. Similar age distributions have been reported by

Seung et al., Masini et al., and Lange et al., who observed that multidrug-resistant tuberculosis is most frequently diagnosed among young and middle-aged adults because of ongoing community transmission, previous treatment exposure, and socioeconomic factors influencing treatment adherence [6-8].

An equal distribution of male and female patients was observed in the present study. Although several previous studies have reported a slight male predominance among patients with multidrug-resistant tuberculosis, recent evidence suggests that the gender gap is narrowing, particularly in programmatic settings with improved access to diagnosis and treatment [9-11].

More than half of the study population was underweight, highlighting the close relationship between malnutrition and drug-resistant tuberculosis. Undernutrition has consistently been associated with impaired host immunity, delayed sputum conversion, and poorer treatment outcomes. Similar observations have been reported in Indian and international studies, emphasizing the importance of nutritional assessment and support during multidrug-resistant tuberculosis treatment [12-14].

The predominance of pre-extensively drug-resistant tuberculosis and fluoroquinolone resistance in the present study reflects the evolving pattern of drug resistance observed in India. Fluoroquinolone resistance has become an important indication for the inclusion of delamanid in individualized treatment regimens, particularly when effective Group A drugs cannot be used. Comparable findings have been reported in recent programmatic studies evaluating delamanid-containing regimens [3,17,23,24].

Delamanid demonstrated a favourable safety profile in this cohort. Adverse drug reactions were infrequent, mild, and did not require permanent discontinuation of therapy. QTc interval prolongation occurred in only one patient and was managed conservatively. These findings are consistent with previous clinical trials and observational studies that have demonstrated the acceptable cardiac safety of delamanid when appropriate electrocardiographic monitoring is performed [3-5].

Treatment adherence was excellent, with only one patient defaulting during follow-up. The high treatment completion rate observed in this study may be attributable to the favourable tolerability of delamanid, individualized treatment regimens, and close monitoring under the National Tuberculosis Elimination Programme. Similar treatment success rates have been reported in recent studies from South Korea and other programmatic settings evaluating delamanid-containing regimens [3,4].

The findings of this study should be interpreted in the context of certain limitations. The study was conducted at a single tertiary care centre with a relatively small sample size and without a comparison group. In addition, the duration of follow-up was limited to the treatment period, precluding assessment of long-term relapse and survival outcomes. Nevertheless, the prospective design and systematic monitoring of clinical outcomes provide valuable real-world evidence regarding the effectiveness and safety of delamanid in routine clinical practice.

CONCLUSION

Delamanid-containing regimens were effective, safe, and well tolerated in patients with drug-resistant pulmonary tuberculosis managed under routine programmatic conditions. The high treatment success rate, low incidence of adverse drug reactions, and excellent treatment adherence observed in this study support the incorporation of delamanid into individualized treatment regimens, particularly for patients with fluoroquinolone resistance or intolerance to conventional second-line anti-tubercular drugs. Larger multicentre studies with longer follow-up are warranted to further evaluate the long-term effectiveness and safety of delamanid-containing regimens.

Author contributions

Sowmya Jonnalagadda conceived and designed the study, supervised the research, interpreted the data, and critically revised the manuscript. Deekshith Kolluri collected the data, conducted patient follow-up, performed data analysis, and drafted the manuscript. Divya Sree Lavudya, Pantham Sunitha, P. Karthik, and Pasula Ravi contributed to study design, data acquisition, data interpretation, and critical revision of the manuscript. All authors read and approved the final manuscript.

Conflict of interest: The authors declare no conflict of interest.

Funding: No external funding was received for this study.

Conference presentation: This work has not been presented at any scientific meeting.

Ethics approval: The study was approved by the Kakatiya Institutional Ethics Committee (KIEC), Kakatiya Medical College, Warangal, Telangana, India (Approval No. 2023-24/61; 29 February 2024).

Informed consent: Written informed consent was obtained from all participants prior to enrolment in the study.

Consent for publication: Not applicable.

Data availability: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgments: The authors thank the faculty and staff of the Department of Respiratory Medicine, Government Chest Diseases and Tuberculosis Hospital, Kakatiya Medical College, Warangal, Telangana, India, for their support during the study. The authors are also grateful to all patients who participated in this study.

Declaration of generative artificial intelligence and artificial intelligence-assisted technologies in the writing process: During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with language editing, grammar correction, formatting, and improvement of manuscript organization. The authors critically reviewed and edited all AI-assisted content and take full responsibility for the accuracy, integrity, and final content of the manuscript. No study data, analyses, results, or scientific conclusions were generated by artificial intelligence.

Table 1. Baseline Characteristics of Study Participants (n=20)

Characteristic	Value
Age, years (mean ± SD)	
Male sex	10 (50)
Female sex	10 (50)
Underweight	11 (55)
Pre-XDR-TB	17 (85)
RR-TB	3 (15)
Pulmonary fibrosis	10 (50)
Bilateral disease	6 (30)

Table 2. Baseline Disease Characteristics and Indications for Delamanid Therapy (N = 20)

Variable	Value
Drug resistance pattern, n (%)	
Rifampicin-resistant TB	3 (15.0)
Pre-extensively drug-resistant TB	17 (85.0)
Microbiological confirmation, n (%)	
CBNAAT positive	20 (100)
Culture positive	18 (90.0)
Sputum smear positive	16 (80.0)
Radiological findings, n (%)	
Pulmonary fibrosis	10 (50.0)
Pneumonia	9 (45.0)
Cavitary lesions	3 (15.0)
Bronchiectasis	1 (5.0)
Bilateral lung involvement	6 (30.0)
Indication for delamanid, n (%)	
Fluoroquinolone resistance	16 (80.0)
Bedaquiline unavailable	2 (10.0)
Linezolid-induced pancytopenia	1 (5.0)
Linezolid-induced peripheral neuropathy	1 (5.0)

Table 3. Safety Profile and Treatment Outcomes Following Delamanid Therapy (N = 20)

Variable	Value
Adverse drug reactions, n (%)	
Nausea	1 (5.0)
Vomiting	1 (5.0)
Epigastric burning	1 (5.0)
QTc prolongation	1 (5.0)
Hypokalaemia	1 (5.0)
Hepatotoxicity	0
Treatment outcomes, n (%)	
Cured	19 (95.0)
Lost to follow-up	1 (5.0)
Death*	1 (5.0)
Treatment failure	0

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