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# Extensively Drug-Resistant Tuberculosis Treated with Bedaquiline: A Case Report in the Particularly Vulnerable Tribal Group of Madhya Pradesh, India

Prashant Mishra<sup>1</sup>, Sharma R<sup>2</sup>, Yadav R<sup>1</sup>, Gaurav Bansal<sup>3</sup>, VG Rao<sup>1</sup>, Jyothi Bhat<sup>1</sup>

<sup>1</sup>Division of Communicable Diseases, ICMR-National Institute of Research in Tribal health, Jabalpur, <sup>2</sup>ICMR- National Institute of Medical Statistics, New Delhi, <sup>3</sup>District TB Centre, Ashoknagar, Madhya Pradesh, India

## Summary

The management of drug-resistant (DR) tuberculosis (TB) remains a challenge particularly in remote rural areas of the country. Although the treatment with wholly oral drug regimens, including bedaquiline (BDQ) and delamanid, is rolled out under the National TB Elimination Program, little is known about its coverage and the effectiveness in hard-to-reach tribal areas. The present report describes the early identification and successful management, through team effort, of a case of extensively DR TB belonging to the Saharia tribe – a Particularly Vulnerable Tribal Groups (PVTGs) of Madhya Pradesh, which has a very high prevalence of TB. The BDQ-containing regimen was well tolerated and found effective with minimal side effects and contributed to the reduced time to culture conversion and radiological improvements. The concerted efforts and strategies need to be adopted for effective implementation of Programmatic management of DR TB (PMDT) guidelines in remote tribal areas of the country.

**Key words:** Bedaquiline, Saharia, extensively drug-resistant tuberculosis

## INTRODUCTION

India reported the highest burden of tuberculosis (TB) and multidrug-resistant (MDR)-TB worldwide in 2018. In 2018, India diagnosed 45% of the estimated 130,000 MDR-TB cases, of these only 46,569 (36% of estimated cases) were put on treatment leaving 56% and 65% of estimated MDR-TB cases undiagnosed and untreated, respectively.<sup>[1]</sup>

The management of drug-resistant (DR)-TB in India through the National TB Elimination Programme is still a challenge. MDR-TB patients can be treated with wholly oral drug regimens, including bedaquiline (BDQ) and delamanid, the first new TB drugs found after 40 years. Still, <5% of eligible DR-TB patients in India get BDQ.<sup>[2]</sup>

Saharia, a Particularly Vulnerable Tribal Group (PVTG), is mainly located in the Gwalior and the Chambal Division of Madhya Pradesh, India. Although a high prevalence of TB has been reported among the Saharia tribe,<sup>[3,4]</sup> the proportion of DR cases reported are almost similar to that of other population.<sup>[5]</sup>

## CASE REPORT

A 38-year-old HIV nonreactive male exhibited productive cough, fever and reduced appetite for the past 8 months, and exertional shortness of breath. He had received treatment for pulmonary TB from private practitioners for 8 months in 2018. He had no history of diabetes or other medical conditions except for a chest augmentation procedure. The patient was a nonsmoker and nonalcoholic. The patient was detected through Intensified TB Control Project (ITCP) in Saharia tribe of Madhya Pradesh, which focuses on active case detection through the engagement of community volunteers, prompt

**Address for correspondence:** Dr. Jyothi Bhat, ICMR-National Institute of Research in Tribal Health, Nagpur Road, P.O. Garha, Jabalpur - 482 003, Madhya Pradesh, India. E-mail: bhatdr@gmail.com

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treatment, and follow-up of cases and awareness activities. The ITCP is ongoing in seven districts of the Chambal region of Madhya Pradesh state where this tribe predominantly resides and encompasses about 0.5 million population. The project team collected sputum sample for cartridge-based nucleic acid amplification test diagnosis through a door-to-door survey with patients being detected rifampicin resistant (RR-TB) the next day (October 18, 2018).

After confirmation of RR-TB, the team visited the patient's home for further investigation, counseling, and admission to DR-TB center to initiate relevant medication. However, the patient denied submitting a sputum sample for the second line-line probe assay (SL-LPA) to the survey team and even refused to visit the DR-TB center for starting the medication. After multiple visits and involving local key persons in the counseling of the patient regarding the importance of treatment continuation and seriousness of the disease, the patient agreed to start the medication. The project team promptly referred and admitted the patient to a public hospital for further management and medication. As per the programmatic management of DR-TB (PMDT) guideline of India, after completing preevaluation, the physician started medication, and a sputum sample was collected for SL-LPA. The patient was detected to be resistant to fluoroquinolone (FLQ) and SL injectable drug. The patient again refused to start extensively DR (XDR) medication and visit DR-TB Center, Gwalior, which is approximately 200 KM From the patient's village. However, with the help of community key persons and repeated visits by the project team, we could convince him of the XDR medication. He was also counseled about the importance of regular medication, the possible drug's side effects, and the diet. Finally, the patient visited the nearest DR-TB center, Gwalior, with project staff after 4 months of FLQ resistance detection.

At the DR-TB center, Gwalior, pretreatment evaluation tests were carried out along with baseline results, the electrocardiogram (ECG) was also normal with QTc 396 ms, and the patient was found fit for bedaquiline regimen. Chest radiograph demonstrated a bilateral apical and middle region consolidation. The baseline body mass index was 16.7. The treatment was started with an intensive phase regimen that included BDQ (200 mg) thrice a week, pyrazinamide (1250 mg), ethambutol (800 mg), ethionamide (500 mg), cycloserine (500 mg), pyridoxine (100 mg), clofazimine (100 mg), and linezolid (600 mg).

The patient started getting symptomatic relief after 2 weeks of therapy, which included the disappearance of fever and reduction in the frequency of cough. His appetite improved, and there was a gradual increase in weight. Monthly ECGs did not reveal any QTc prolongation (<500 ms). Monthly serum creatinine and electrolytes remained normal. After about 4 months of treatment, a chest radiograph demonstrated consolidation only in the right apical region. Postcompletion of BDQ (24 weeks) regimen, the QTc was 380 ms. His sputum

mycobacterial cultures remained negative since the 14<sup>th</sup> week of treatment.

## DISCUSSION

MDR and XDR-TB (XDR-TB) pose a critical public health challenge to TB control programs worldwide.<sup>[6]</sup> The management of DR-TB in rural and remote areas and resources limited countries like India is further a challenging task. The treatment of XDR-TB is associated with a higher rate of unfavorable treatment outcomes than MDR-TB.<sup>[7]</sup>

Saharia tribe is characterized by improvised socioeconomic milieu, geographical isolation, lack of formal education, and access to health-care services. Besides, there is still no information available related to the incidence and prevalence of XDR TB among this community.<sup>[8]</sup>

The present study showed that the BDQ-containing regimen was effective and well tolerated by the patient with minimal side effects and contributed to the reduced time to culture conversion and radiological improvements. Although the patient experienced common side effects particularly nausea, vomiting, and stomachache, no additional adverse events or QT prolongation were noted. It emphasizes that BDQs have the potential capacity to reduce the course of the treatment period and debilitating adverse drug effects as suggested earlier.<sup>[9]</sup>

In summary, the identification of XDR among the Saharia tribe was not unexpected, as resistance is a man-made problem. Further, the management of MDR-TB patients in the Saharia community is impeded by a lack of seriousness toward disease owing to poor health awareness, literacy, poverty, distance, and poor quality of health facilities in tribal areas.

Thus, concerted efforts and strategies are needed for the detection and implementation of PMDT guidelines among the marginalized community and in remote tribal areas of India to prevent the spread of TB and achieve the goal of TB elimination by 2025 in India.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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