

Totally Drug-Resistant Tuberculosis in India

TO THE EDITOR—Three years after extensively drug-resistant (XDR) tuberculosis was first described in 2006, Velayati et al [1] drew attention to the emergence of totally drug-resistant (TDR) tuberculosis in a cohort of 15 patients from Iran, resistant to all first- and second-line drugs. Since the first cases of XDR tuberculosis in India were reported from the P. D. Hinduja National Hospital and Medical Research Centre [2], physicians here have grappled with increasingly resistant strains of tuberculosis. We describe the first patients from India with TDR tuberculosis. Drug susceptibility testing (DST) was performed at the Hinduja Hospital, the city's busiest referral laboratory and a Revised National Tuberculosis Control Programme (RNTCP) accredited

Table 1. Treatment and Resistance Details in 4 Patients Treated With First- and Second-Line Drugs for Tuberculosis

Patient No.	Age, Years/Sex	Physicians Visited, No. (Private or Government)	Drugs Used (Duration, Months)		Drug Susceptibility Test Results ^a	Hain Genotyping MTBDRplus and MTBDRsl
			First-Line Drugs	Second-Line Drugs		
1	37/Female	4 (private)	Isoniazid (1), rifampicin (1), ethambutol (11), pyrazinamide (1)	Moxifloxacin (7), para-aminosalicylate (6), clofazimine (12), kanamycin (3), linezolid (2), rifabutin (2)	Resistance to all first- and second-line drugs	<i>rpoβ</i> mutant 3, <i>katG</i> mutant 2, <i>gyrA</i> mutant 3D, <i>rrs</i> mutant 1
2	31/Female	5 (private)	Isoniazid (16), rifampicin (4), pyrazinamide (4), ethambutol (16)	Kanamycin (9), moxifloxacin (19), para-aminosalicylate (19), ethionamide (12), amikacin (9)	Resistance to all first- and second-line drugs	<i>rpoβ</i> mutant 3, <i>katG</i> mutant 1, <i>gyrA</i> mutant 3C, <i>rrs</i> mutant 1
3	20/Female	2 (1 government, 1 private)	Isoniazid (3), rifampicin (3), pyrazinamide (3), ethambutol (3)	Ofloxacin (1), para-aminosalicylate (12), kanamycin (12), ethionamide (12), terizidon (12), capreomycin (7)	Resistance to all first- and second-line drugs	Not done
4	57/Male	2 (private)	Isoniazid (24), rifampicin (6), ethambutol (6), pyrazinamide (6), streptomycin (1)	Kanamycin (13), ethionamide (3), levofloxacin (3), moxifloxacin (18), para-aminosalicylate (24), clofazimine (9)	Resistance to all first- and second-line drugs	<i>rpoβ</i> mutant 3, <i>katG</i> mutant 1, <i>inhA</i> mutant 1, <i>gyrA</i> mutant 3C, <i>rrs</i> mutant 1

Abbreviations: *gyrA*, gyrase subunit A; *inhA*, enoyl subunit A; *katG*, catalase peroxidase gene; *rpoβ*, RNA polymerase β subunit; *rrs*, 16S ribosomal RNA.

^a The first- and second-line drugs to which susceptibility was checked included isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin, amikacin, kanamycin, capreomycin, moxifloxacin, ofloxacin, para-aminosalicylate, and ethionamide.

laboratory for Mumbai. Each of the 4 patients was resistant to all first-line (isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin) and second-line (ofloxacin, moxifloxacin, kanamycin, amikacin, capreomycin, para-aminosalicylic acid, and ethionamide) drugs tested. All DSTs were performed by Mycobacterial Growth Indicator Tube 960 at critical concentrations for first-line and second-line drugs recommended by the World Health Organization (WHO). In addition, 3 of the patients underwent genotypic DST analysis using the MTBDRplus and MTBDRsl line probe assays (Hain Life Science). A careful audit of their prescriptions revealed that these 3 patients had received erratic, unsupervised second-line drugs, added individually and often in incorrect doses, from multiple private practitioners (mean, 4 physicians during a 18-month period) in an attempt to cure their multidrug-resistant (MDR) tuberculosis (Table 1). The latest WHO global resistance report estimated 110 132 cases of MDR tuberculosis from India in 2006, which accounts for 20% of the world's MDR tuberculosis load [3]. Although India's RNTCP has been a tremendous success, patients with MDR tuberculosis currently are not covered, with only 1% having access to Directly Observed Treatment, Short-course (DOTS)-Plus initiatives [4]. The vast majority of these unfortunate patients seek care from private physicians in a desperate attempt to find a cure for their tuberculosis. This sector of private-sector physicians in India is among the largest in the world and these physicians are unregulated both in terms of prescribing practice and qualifications. A study that we conducted in Mumbai showed that only 5 of 106 private practitioners practicing in a crowded area called Dharavi could prescribe a correct prescription for a hypothetical patient with MDR tuberculosis [5]. The majority of prescriptions were inappropriate and would only have served to further amplify resistance, converting

MDR tuberculosis to XDR tuberculosis and TDR tuberculosis. We would urge that patients with MDR tuberculosis only be treated within the confines of government-sanctioned DOTS-Plus programs to prevent the emergence and spread of this untreatable form of tuberculosis.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

**Zarir F. Udwadia, Rohit A. Amale,
Kanchan K. Ajbani, and Camilla Rodrigues**

P. D. Hinduja National Hospital and Medical Research
Centre, Mumbai, India

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Correspondence: Zarir F. Udwadia, MD, FRCP, P. D. Hinduja National Hospital and Medical Research Centre, Veer Savarkar Marg, Mahim, Mumbai 400 016, India (zarirfudwadia@gmail.com).

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