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Editorial

Tuberculosis therapy in Mumbai: Critical importance of drug-susceptibility testing
Amrita Daftary, Madhukar Pai ...251

Original Articles

Possible impact of the standardized Category IV regimen on multidrug-resistant tuberculosis patients in Mumbai

Zarir F Udhwadia, Jai Bharat Mullerpattan, Kushal D Shah, Camilla S Rodrigues ...253

Relationship of epidermal growth factor receptor activating mutations with histologic subtyping according to International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society 2011 adenocarcinoma classification and their impact on overall survival

Venkata Nagarjuna Maturu, Navneet Singh, Amanjit Bal, Nalini Gupta, Ashim Das, Digambar Behera ...257

Management of chronic empyema with unexpandable lung in poor surgical risk patients using an empyema tube

Abhishek Biswas, Michael A Jantz, Andrea M Penley, Hiren J Mehta ...267

A randomized, double-blind study comparing the efficacy and safety of a combination of formoterol and ciclesonide with ciclesonide alone in asthma subjects with moderate-to-severe airflow limitation

Sundeep S Salvi, Abhijit J Vaidya, Rahul R Kodgule, Jaideep A Gogtay ...272

Clinical profile, etiology, and management of hydropneumothorax: An Indian experience

Vasunethra Kasargod, Nilkanth Tukaram Awad ...278

Comparison of oral montelukast with oral zileuton in acute asthma: A randomized, double-blind, placebo-controlled study

Rahul Magazine, Hameed Aboobacker Shahul, Bharti Chogtu, Asha Kamath ...281

And More....

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Tuberculosis therapy in Mumbai: Critical importance of drug-susceptibility testing

India is the ground zero for global tuberculosis (TB) epidemic, and Mumbai is the ground zero for India's epidemic of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). In this issue of Lung India, Udwadia *et al.*^[1] present data that highlight major concerns with the use of standardized, empiric treatment regimens for MDR-TB in Mumbai. The alarming rates of MDR-TB, heterogeneous drug-resistance patterns and disproportionate number of cases that are found to be pre-XDR and XDR, mandate the early and comprehensive drug-susceptibility testing (DST) of all TB patients, to allow for individualized, DST-guided drug regimens.

The rationale to impose a standardized drug regimen for MDR-TB and harmonize medical practice is not unfounded. As in many other high-burden settings, upfront, universal DST is uncommon in India and hinders opportunities to devise optimal regimens for patients with MDR-TB.^[2] Nearly half of all Indian TB patients are treated in the private sector^[3] where the quality of care is highly variable,^[4] and use of irrational drug regimens^[5] urges stricter antibiotic stewardship, and makes a case for standardized protocols. However, there is an undeniable risk of amplifying drug resistance by promoting one regimen for all, without taking the local epidemiology into account.

In the cohort of 1539 MDR-TB cases identified by the TB laboratory at Hinduja Hospital in Mumbai (which included samples from both public and private patients), only 30% were truly MDR-TB; remaining cases represented pre-XDR, XDR, and resistance beyond XDR-TB. In other words, nearly two-thirds of this sample would have received a suboptimal drug regimen and have been at risk for developing secondary resistance, had they been empirically treated under the recommended standardized regimen for MDR-TB.^[1] This is not unlike resistance profiles of cases reported by Dalal *et al.* and Dholakia and Shah, who have similarly suggested the need for individualized, DST-guided drug regimens in Mumbai.^[6,7] Other experts have argued that all TB patients in India deserve up-front DST,^[8] and there are large-scale, programmatic data to support this.^[9]

The importance of factoring in the local epidemiology of TB into empiric treatment regimens thus cannot be overemphasized. In India, a standardized empiric regimen for MDR-TB may perpetuate delays in DST and inadvertently feed into provider complacency in managing difficult cases. While patients' previous

treatment histories have guided empiric drug regimens in other settings, this option would be futile in Mumbai, where primary drug resistance is common, and previously treated patients lack a complete medical history due to their high rate of switching between providers.^[3,10] The alternative recommendation suggested by Udwadia and colleagues^[1] to use a tailored empiric drug regimen at their site based on data from their laboratory (and given their existing capacity to perform timely, comprehensive DST) is in line with the World Health Organization's most recent treatment guideline which emphasizes, "TB programs may need to adjust the (drug-resistant TB treatment) strategy to meet special circumstances and the local context."^[11]

The argument against a one-size-fits-all approach to MDR-TB management is also congruent with recent trends to shift away from rigid, inflexible TB management in general toward more individualized, patient-centered approaches to care.^[12,13] Patient retention is a major challenge to MDR-TB treatment completion and cure, and the administration of suboptimal drug regimens may be considered an important determinant of nonadherence and loss to follow-up.^[14,15] A patient-centered approach to MDR-TB management begins with early diagnosis and DST, but equally incorporates stable access to the second-line drugs, treatment literacy, individualized education and counseling, and efforts to meet the medical, economic, and social needs of patients throughout their treatment course.^[16] Alongside the push to tailor treatment regimens via DST, we cannot ignore the commensurate opportunity to refine current mechanisms of ensuring adherence and move beyond directly observed therapy-centered models of patient support.

The imposition of a standardized empiric drug regimen for MDR-TB, while feasible in lower burden settings with a more homogenous epidemic, may compound the existing challenges to MDR-TB management in settings with diverse patterns of TB drug resistance. It is time we shed universal dogmas when confronting strains of TB that are unpredictable, inconsistent, and increasingly untreatable. Given the profile of MDR-TB cases in Mumbai, DST-guided, individualized therapy is the safest option for patients and better aligned with the new End TB Strategy that calls for all countries to offer universal DST to all TB patients, at the time of diagnosis.^[17] To meet the End TB Strategy goals, however, India must invest more in TB care and control, increase the budget of the Revised National TB Control Program, roll-out improved molecular diagnostics and daily drug regimens and scale-up successful models of private sector engagement.^[18]

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