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Editorial

Strengthening the response to XDR-TB in India: A call for enhanced diagnostics and treatment strategies

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Extensively drug-resistant tuberculosis (XDR-TB) continues to represent a major challenge for global TB control, particularly in low- and middle-income countries. XDR-TB, defined as resistance to rifampicin, any fluoroquinolone, and at least one of the newer agents-bedaquiline or linezolid—remains a challenging condition to treat, with treatment success rates typically being poor. In 2023, a total of 28,982 cases of pre-XDR or XDR-TB were reported worldwide.[1] With rising resistance to key drugs such as bedaquiline and linezolid, the threat to TB treatment outcomes and public health is escalating. Against this backdrop, the recent study by Kherabi et al., published in *The Lancet Regional Health – Europe*, highlights the grave reality in Europe, where only 40% of XDR-TB patients achieved treatment success.[2] These findings raise important questions about the effectiveness of current treatment protocols and diagnostics, offering valuable lessons for countries like India, where XDR-TB is prevalent. In this editorial, we examine the implications of these findings for India and propose urgent actions needed to enhance the management and treatment of XDR-TB.

The study revealed a striking variability in treatment outcomes for XDR-TB patients, with only 40.2% achieving successful outcomes, compared to a much higher success rate for multidrug-resistant TB (MDR-TB) and pre-XDR-TB patients. The highest rates of resistance were observed to bedaquiline (48.4%) and linezolid (34%), with a pooled proportion of treatment failure at 37.1% and death at 21.3%. The study emphasized the importance of incorporating a higher number of effective drugs into treatment regimens to improve outcomes. Moreover, the stark contrast between upper-middle-income countries (UMICs) and high-income countries (HICs) in terms of treatment success calls for urgent reforms in low-resource settings.[2]

India carries a substantial burden of XDR-TB, further compounded by the emergence of resistance to key drugs such as bedaquiline and linezolid. Despite the introduction of newer regimens such as BPaLM, their effectiveness is undermined by limited access to comprehensive drug susceptibility testing (DST). A recent Indian study by Singla et al. underscores this concern: among 117 patients previously exposed to bedaquiline, 42(36%) developed bedaquiline resistance. Of those with resistance who initiated treatment, 87% (33/38) experienced unfavorable outcomes, including death (40%), treatment failure (40%), and loss to follow-up (8%). Notably, clofazimine resistance was also found to be significantly associated with bedaquiline resistance, further complicating treatment outcomes. These findings highlight the urgent need to implement routine bedaquiline DST, develop affordable and accurate rapid diagnostics for detecting resistance, and accelerate research into novel anti-TB agents to safeguard treatment success.[3]

India's efforts to combat TB have made progress, but the challenge of managing XDR-TB remains formidable. A key limitation is the inadequate availability of rapid, molecular-based DST for all second-line drugs, including bedaquiline

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and linezolid. With only 34 intermediate reference laboratories in India performing Line Probe Assays (LPA), diagnostic delays are a significant obstacle, leading to missed opportunities for timely intervention.[4] With 780 medical colleges functioning nationwide, systematic upgrading and integration of advanced TB diagnostic and management facilities at these tertiary referral centers represents a scalable and pragmatic strategy to address the growing burden of drug-resistant TB in India.[5]

In response to these challenges, India must prioritize the following actions:

1. Expand Diagnostic Infrastructure: Rapid genotypic DST for all Group A drugs, including bedaquiline and linezolid, should be developed & integrated into medical college laboratories across India.[6] This will ensure early identification of drug resistance, enabling timely treatment adjustments.
2. Implement Therapeutic Drug Monitoring (TDM): Subtherapeutic drug levels can be an important cause of lack of response to anti-TB treatment. TDM can play a critical role in optimizing treatment regimens by adjusting dosages based on drug levels in the patient's system.[6] TDM has recently been incorporated in the national essential diagnostic list of India (2025).[8] Including TDM in the National Essential Diagnostic List and utilizing biochemistry departments in medical colleges for individual dosing would significantly improve treatment outcomes.
3. Reinstate Respiratory Medicine Departments in medical college hospitals: Respiratory Medicine departments were recently removed from the mandatory list for undergraduate medical college hospitals in India. Their reinstatement is crucial to ensure that specialists are available to manage complex TB cases, including XDR-TB, especially in these referral centers.[9]
4. Utilize Artificial Intelligence for Risk Stratification: Migration, alcoholism, unwillingness to follow treatment, and side effects are common factors that contribute to treatment interruptions and, as a result, poor treatment outcomes in tuberculosis management.[9] These challenges must be addressed through targeted interventions. AI-based tools can play a crucial role in this effort by helping identify high-risk patients early, enabling proactive interventions such as personalized counseling, digital adherence tools, and socio-economic support. By flagging cases with a lower likelihood of successful outcomes, these tools can help prevent treatment interruptions and loss to follow-up, ensuring more effective and timely care for patients.
5. Enhanced Patient Support and Community Engagement: Comprehensive patient support systems that address migration, addiction, and socio-economic challenges are essential. Community outreach programs and the use of digital tools can help improve treatment adherence and prevent the development of resistance.
6. Airborne Infection Control in XDR-TB: A Critical Aspect of Management: Airborne infection control practices are crucial in managing TB, including drug-resistant forms like XDR-TB. Administrative controls focus on swiftly identifying and managing TB risks, with dedicated infection prevention and control (IPC) staff, facility risk assessments, isolating symptomatic TB patients, providing surgical masks, and screening healthcare personnel. Environmental controls aim to reduce airborne Mycobacterium tuberculosis, primarily through good natural ventilation that ensures adequate air exchanges (atleast 12 air changes per hour), ideally via cross-ventilation. Assisted ventilation can be used if natural ventilation is insufficient. HVAC (Heating, Ventilation, and Air Conditioning) systems can be installed in intensive care units (ICUs) catering to TB patients to enhance air quality and ensure proper ventilation, reducing the risk of airborne transmission of Mycobacterium tuberculosis, including drug-resistant forms like XDR-TB. These systems can support natural and assisted ventilation methods and integrate with ultraviolet germicidal irradiation (UVGI) and high-efficiency particulate air (HEPA) filtration as per assessment and requirement to maintain a safe environment for both patients and healthcare workers. Ultraviolet germicidal irradiation (UVGI) and high-efficiency particulate air (HEPA) filtration systems may enhance air quality in high-risk areas, such as isolation rooms. Personal controls require healthcare workers to wear fit-tested N95 respirators or powered air-purifying respirators (PAPRs), with proper seal checks before entering isolation rooms or performing aerosol-generating procedures. Patients must wear surgical masks and follow proper cough hygiene practices during transport or when leaving isolation rooms.[11]
7. TB Preventive treatment: Currently, Indian guidelines do not recommend preventive treatment for latent pre-XDR or XDR-TB infections.[12] Although individualized regimens tailored to the drug susceptibility patterns of the index case have been suggested, there is limited evidence to guide their use.[13] Operational research is necessary to evaluate and establish the feasibility of such regimens within the programmatic setting in India.
8. Safeguarding New Anti-TB Drugs Through Controlled Access: In India, the private sector continues to manage a considerable proportion of TB patients.[14] In such a scenario, the use of newer anti-TB drugs such as bedaquiline, pretomanid, and delamanid must be carefully regulated under programmatic access. Unrestricted availability risks dosing errors, inappropriate prescriptions, poor adherence, treatment interruptions, and loss to follow-up—factors that could accelerate resistance and compromise the effectiveness of these critical drugs. Ensuring access through standardized programmatic channels is therefore

essential to safeguard their efficacy and sustain long-term TB control efforts.

The treatment success rate for XDR-TB in Europe, as reported in *The Lancet*, paints a grim picture, but it also presents an urgent call to action for India. National tuberculosis programmes worldwide need to develop and scale up facilities for rapid diagnostic techniques to detect drug resistance to important second-line anti-tuberculosis drugs, including bedaquiline, in a manner similar to their acceptance of the WHO-recommended bedaquiline-based treatment regimens for multidrug-resistant tuberculosis.[6] The current infrastructure, diagnostic limitations, and treatment approaches must be transformed to ensure that the promise of newer regimens like bedaquiline is not wasted. XDR-TB will not wait for the system to catch up. India must act swiftly to strengthen diagnostics, clinical management, and patient support, ensuring that those affected by this deadly disease are not abandoned. If these critical gaps are not addressed, the progress we've made in the battle against TB could be severely undermined. The time to act is now, and India must lead the way in safeguarding the future of TB treatment globally.

The treatment success rate for XDR-TB in Europe, as reported in *The Lancet Regional Health – Europe*, highlights a troubling scenario, and similar patterns are observed in India, where bedaquiline-resistant strains show markedly poor treatment outcomes.[2,3] Together, these findings serve as a critical call to action to strengthen diagnostics, optimize treatment regimens, and ensure programmatic oversight of newer anti-TB drugs. In response to the growing threat of drug resistance, national tuberculosis programs worldwide must prioritize the development and scaling up of rapid diagnostic techniques, especially for detecting resistance to essential second-line anti-tuberculosis drugs like bedaquiline. This approach should be adopted in the same way that WHO-recommended bedaquiline-based treatment regimens for multidrug-resistant tuberculosis (MDR-TB) have been embraced.[6] India's current infrastructure, diagnostic capacity, and treatment strategies are not sufficient to fully leverage the potential of newer regimens such as bedaquiline. XDR-TB will not wait for the healthcare system to catch up. India must act decisively and immediately to enhance diagnostics, clinical management, and patient support. Failure to address these critical gaps will jeopardize the progress made in controlling TB, potentially reversing years of hard-earned gains. The time to act is now, and India must take the lead in ensuring that the future of global TB treatment is secured.

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