

DRUG RESISTANCE TB IN INDIA: CHALLENGES, ISSUES AND SOLUTIONS

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Multi Drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) are emerging as a major challenges across globe including in India as narrated by the World Health Organization (WHO) for success the Stop TB strategy, launched in 2006.^[1] **MDR-TB** is defined as tuberculosis disease where the bacilli is resistant to isoniazid (H) and rifampicin (R), with or without resistance to other drugs. Irregular consumption and frequent interruption in taking treatment for TB is the most common cause of acquiring multidrug resistance.^[1] In India, MDR-TB amongst new cases are estimated at 2-3% and amongst re-treatment cases at 14-17%. **Extensively Drug Resistant TB (XDR-TB)** is a subset of MDR-TB where the bacilli, in addition to being resistant to R and H, are also resistant to fluoroquinolones and any one of the second-line injectable drugs (namely Kanamycin, Capreomycin or Amikacin).^[1] Although XDR-TB has been reported in India, its magnitude remains undetermined as yet due to the lack of laboratories being capable of conducting quality assured second line drug susceptibility testing.

TB resistance is now being reported form different parts of world to combat this growing resistance, in April 2009, WHO urged member states to take action on multiple fronts towards achieving universal access to diagnosis and treatment of M/XDR-TB by 2015.^[1] Despite the important progress being made, severe bottlenecks are limiting the responses to the M/XDR-TB epidemic. Indeed, only 10% (24511/ 250000) of the estimated MDR-TB cases among notified TB cases in 2009 in the high MDR-TB countries, and 11% (30475/280000) globally were enrolled on treatment.^[1] Some countries are making progress by implementing policy changes that rationalize the use of hospitals, such as South Africa, or treating patients through community-based models of care, such as the Philippines. However, diagnostic capacity remains

limited. Furthermore, the price of some quality-assured second-line drugs has not fallen, and shortages of drugs still occur.

In India where the annual TB incidence rate is approximately 2 million cases per year—the highest of all countries and fourth in the global burden of TB—the extent of MDR-TB incidence is staggering. About 3% of new cases and 12-17% of previously treated cases in India are MDR-TB. Moreover, the WHO ranked India at the bottom among all developing countries in terms of their TB management and control and performance.^[2] There is no doubt that the development of multidrug-resistant (MDR)-TB and XDR-TB narrates the apparent weaknesses in primary care services; both diagnostic and treatment services, but it also reflects a failure to country on adhering to the WHO's directly observed treatment, short course (DOTS) strategy. One of the main reasons hypothesized is selective preference of the suspected TB cases to private practitioners.^[3] Most TB patients first seek help from one of India's 10 million private practitioners. It is estimated that for most of these patients it is up to 4–6 weeks before they are diagnosed as having TB.^[4] In addition to this, the TB cure rates for patients who remain with private practitioners are low^[3-5]; it is also estimated that 99,000 MDR-TB cases occur in the country annually^[6]. Although the true incidence of both MDR and XDR-TB is impossible to gauge for India, only estimates could be modelled from the reported incidence of known Multi-Drug Resistant Tuberculosis (MDR-TB) cases. To compound the problem further, India has now also been diagnosed with Total Drug Resistant TB.^[6]

To address the challenge of MDR-TB, the Revised National Tuberculosis Control Programme (RNTCP) of India has initiated MDR-TB services, at a sub-national

level, in 2007 in a limited geographical area and is in the process of expanding these services, in a phased manner, to cover the entire country by 2012.^[7] However, due to limited quality assured laboratory capacity in India the program presently enrolls only those patients identified to be at a high risk of MDR-TB (MDR suspects) for diagnostic assessment and subsequent treatment.⁷ RNTCP has limited information on the proportion of MDR-TB suspects amongst TB patients on first line treatment within the program, whether all these MDR-TB suspects are identified and undergo diagnostic assessment and whether all those diagnosed as MDR-TB are initiated on treatment according to the program guidelines.^[7]

Several International responses in terms of providing funds has been worth appreciating, presence of donor agencies like The Global Fund to Fight AIDS, Tuberculosis and Malaria, as well as UNITAID, are major – if not only – source of funding for programmatic management of MDR-TB in several countries, demonstrating commitment to in response to M/XDR TB. However, developing and adapting to newer tools will help in accelerating the scale up of adequate M/XDR-TB management; the introduction of new rapid diagnostic tests which was found promising in Ethiopia, India and South Africa needs to be accelerated. It is also important that the rapid diagnostic tests to should bring diagnosis closer to patients, this reflects the need for increased research investment into novel rapid tests. WHO Five candidate anti-TB drugs are being evaluated in clinical trials, and preliminary results are encouraging: a new anti-TB drug is anticipated on the market in a few years.^[6] Besides scaling up implementation of available and new tools, research providing evidence countries can use to reach the global target of achieving universal access to MDR-TB care in line with resolution World Health Assembly. The involvement of civil society organizations and communities in global and national responses to M/XDR-TB also remains very limited.^[3] Hence, there is an urgent priority to strengthen their active involvement in the response to MDR TB. It is high time to focus advocacy efforts at not only global level but also at country level or state level to ensure that the health sector receives the necessary resources and the M/XDR-TB response remains high on the global health-policy agenda.

With emergence of XDR and TDR in Indian a new debate has also began on the existing DOTS treatment especially for those with drug resistance to continue with the DOTS or initiate Hospital based treatment of

resistant cases. However, findings of a systematic review on cost and cost effectiveness of TB narrates that outpatient-based models of care can greatly enhance the efficiency of treatment for MDR-TB.⁸ Considerable amounts could be invested in incentives and enablers (such as food packages and transport vouchers) to minimize the risk of default from outpatient treatment before costs would come close to those for inpatient care. Empirical evidence on the cost effectiveness of MDR-TB treatment is currently limited to one middle-income country in Latin America, two upper-middle-income countries that were part of the former Soviet Union and one lower-middle income country in Asia.^[8] More country specific data are needed, especially from the two countries that, in combination, account for about 50% of the world's cases of MDR-TB – China and India. Operational research are also suggested to identify the conditions under which outpatient-based models of care specially for migrant populations, HIV TB co-infection and populations with high default rates needs to be considered. Further research on involvement of the different stake holders like private labs, private providers, DOTS providers and convergence with other programs will be required to tackle the menace of MDR TB in India.

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