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VIEWS & REVIEWS

PERSONAL VIEW

India should screen all tuberculosis patients for drug resistant disease at diagnosis

India's national programme needs to embrace comprehensive screening and test for the isoniazid monoresistance that precedes multidrug resistant disease, says **Yogesh Jain**

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Drug resistant tuberculosis attracts attention because of poor outcomes, the risk of transmission to others, and the financial implications of multidrug resistant tuberculosis (MDR TB). In India the programmatic management of drug resistant TB,[1] with a focus on MDR TB, started in 2007 and covered the country by 2012.

The national programme prioritises case finding and treatment of MDR TB even though only half of patients with MDR TB are cured with the existing treatment regimen.[2] The programme rightly notes that preventing MDR TB in the community is more important than treatment, but this recognition needs more attention than it currently gets.

Inadequate screening for drug resistance

A first step in prevention is early screening for drug resistance in all patients with TB.[3] With improved screening from 2011 to 2013 the number of notified cases of MDR TB in India each year increased nearly sixfold to 25 244.[4] However, this is still far short of the estimated 62 000 incident cases of MDR TB each year.[2]

India plans to offer drug susceptibility testing, first to patients with presumptive MDR TB,[1] such as those who have previously received treatment, and by 2015 to all adult patients with pulmonary disease.[1] Adults with extrapulmonary disease and children are not yet included in the patients to be investigated.

Only 248 341 of 1 415 617 patients (17.5%) who were registered with the national programme up to 2013 underwent drug susceptibility testing[5]; this needs to be scaled up much more quickly. A diagnostic strategy that investigates only presumptive MDR cases will miss out as much as half of patients[2 4] with MDR TB. Screening should be offered to all patients with TB at the time of diagnosis and not only when they fail to improve.

The World Health Organization recommends testing for drug resistance either to isoniazid and rifampicin or to rifampicin alone.[4] In many countries, including India, the current focus is on promoting cartridge based nucleic acid amplification tests (CBNAATs) to pick up rifampicin resistance alone as a surrogate for MDR TB .[6] This strategy misses out isoniazid monoresistance.

In India 2.2% of previously untreated patients and 15% of those with a history of previous TB treatment are estimated to have MDR TB. The proportion of patients who have isoniazid resistance diagnosed is much higher, measured at 11% and more than 37% in sub-national studies.[6 7] MDR TB develops first with resistance to isoniazid and then the acquisition of resistance to rifampicin. In fact, isoniazid resistant TB could be called pre-MDR TB.[8]

So, to diagnose MDR TB it seems logical to do a CBNAAT, but to prevent MDR TB it is advisable to screen for isoniazid resistance as well as rifampicin resistance in all patients at diagnosis—for example, by using a rapid test such as a line probe assay. This may be the most cost effective testing strategy, even at very low levels of resistance, for averting deaths and preventing acquired MDR TB.[4] Recent advocacy for testing drug resistance only to rifampicin is based on only deterministic modelling with limited data for key parameters and insufficient sensitivity analyses.[9]

Inappropriate treatment regimens

The presently prescribed intermittent regimens in the Indian national programme for new and re-treatment cases of TB are of suboptimal effectiveness in curing patients with isoniazid resistance. Intermittent regimens are likely to lead to more relapse and increase the risk of developing drug resistance.[10] If isoniazid monoresistance is documented, WHO[11] and the International Union Against Tuberculosis and Lung Disease[12] recommend regimens containing three drugs other than isoniazid (any three of rifampicin, pyrazinamide, ethambutol, or levofloxacin) that should be given daily for at least nine months to prevent the emergence of subsequent MDR TB. Also, the choice of the three drugs can be improved with availability of information on resistance to ethambutol and pyrazinamide. India

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should align its TB regimens with the latest guidelines to prevent the development of MDR TB.[10]

The acquisition of MDR TB in India and elsewhere is exacerbated by a political economy of poor resources for poor people, coupled with poor programme implementation.[13] National control programme staff have responded bravely to the news of a 30% slash in the TB budget this year.[14] Aside from scarce resources the epidemic is fuelled by underpowered treatment regimens; inadequate supervision; mechanical clinical care that disregards the side effects of drugs and leads to interrupted drug regimens; and ignoring the role of synergistic emaciation.

Most importantly, we need an attitude that escapes the construct of scarcity and demands equitable and holistic solutions for people with TB.

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