

TB patients get weak doses from new drugs, says study

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Chennai: Patients with drug-resistant tuberculosis in Chennai may be getting powerful new medicines at doses that are too weak to control the infection fully, even when lab reports show

the bacteria is "susceptible", a study by ICMR-National Institute for Research in Tuberculosis (NIRT) found.

After studying 220 samples of *Mycobacterium tuberculosis*, bacteria that cause TB in humans, NIRT scientists found that standard doses of several second-line drugs - including bedaquiline, clofazimine, pretomanid and the commonly used fluoroquinolones - may not reach pharmacologically effective levels against a large share of local strains.

The study, published in the journal *Frontiers in Microbiology* in March, used lab drug-sensitivity tests and dose-exposure modelling to show how often standard TB drug doses fail to reach effective levels in patients.

The team tested isolates from 110 patients with drug-susceptible TB and 110 with first-line drug-resistant disease, all collected in Chennai between 2020 and 2023, before treatment began. They tested how much of each newer second-line drug - bedaquiline, delamanid, clofazimine, linezolid, levofloxacin, moxifloxacin and pretomanid - was needed to stop the TB bacteria from growing in the lab.

Lab analysis showed that for bedaquiline and clofazimine, TB bacteria in Chennai often needed slightly higher drug levels to stop growing than what global cut-offs assume.

This means some local strains that behave like "normal" TB in the lab could still be reported as resistant if hospitals apply international thresholds without any adjustment.

For delamanid and levofloxacin, the pattern was reversed, with lower local thresholds raising the risk that true resistance could be missed if labs follow global charts too strictly.

Local TB strains may differ from global TB drug standards - risking both false alarms and missed resistance, highlighting the need for region-specific standards and cut-off levels, said study's lead and corresponding author Azger Dusthacker, who works in the department of bacteriology at NIRT.

"TB bacteria we see today are not the same as the global average that WHO cut-offs are based on. We need larger studies across India to develop standards for drug dosages specific to Indian strains," he said.

This, scientists said, will reduce resistance and improve treatment outcomes.

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