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THE NEED FOR DISCLOSURE

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Last June, Sunil Kumar, 28, a Delhi-based vegetable vendor, was diagnosed with drug-resistant tuberculosis (DRTB). The government hospital he visited for treatment prescribed a drug called bedaquiline. That year, even though India was giving bedaquiline to patients as part of a conditional access programme, there were questions about the medicine's toxic effects. There was no Phase 3 data, which is mandatory under the Indian regulatory regime for establishing a drug's safety. The only large randomised trial data on the drug came from a limited 161-patient Phase 2b study, which threw up paradoxical results.

While on the one hand patients on bedaquiline had shown TB-negative sputum more often compared to controls, on the other, comparatively more patients died in the Bedaquiline arm, suggesting that the drug might be killing patients. After an investigation did not find any link between the deaths and bedaquiline, the U.S. Food and Drug Administration fast-tracked the drug's approval on the condition that the drugmaker, Janssen Pharmaceuticals Inc, provide Phase 3 data by 2022. Given this, the World Health Organisation has suggested that all patients be told of bedaquiline's mortality risk as seen in the Phase 2b trial.

Kumar doesn't remember being told all this. "They didn't tell me anything. Nor did I sign any form," he says. Even if he had been given the patient-information booklet (designed by India's Central TB division) for bedaquiline, he may not have learnt about the mortality risk.

"While the patient information booklet mentions side-effects such as dizziness, it does not disclose the Phase 2b results. Such a lack of disclosure is egregious," says Jennifer J. Furin, an infectious diseases clinician at Harvard Medical School.

When questioned about the inadequacy of the patient booklet, V.S. Salhotra, the additional deputy director general (TB) at Delhi's Directorate General of Health Services, says the booklet mentions all risks. He did not respond to a follow-up question about the phase 2b results.

Unfortunately, Kumar's experience is not uncommon. Interviews conducted by *The Hindu* show that Indian TB patients are frequently ignorant of drug side-effects. This is a problem because DRTB medicines can be highly toxic. Kanamycin, which belongs to the aminoglycoside class of antibiotics, can cause permanent hearing loss and is toxic to the kidneys. Another DRTB drug, cycloserine, can trigger suicidal thoughts, while the drug isoniazid has been linked with peripheral neuropathy (nerve damage).

Informing patients about these side-effects, or informed consent, is critical for several reasons. First, the patient has a right to know. Second, advance knowledge of risks makes it more likely that the patient will act to mitigate them. In the case of kanamycin, deafness is sometimes preceded by warning symptoms such as tinnitus, giving doctors an opportunity to intervene.

A third advantage is that it helps patients plan for painful side-effects. This, in turn, ensures they complete the treatment — something that often does not happen in DRTB. In the case of cycloserine, for example, a patient could choose to move in with her family during the treatment. "If you can't sleep for nights, and you have crazy dreams, what are you going to do? You have got to know that you need to put in place a support system before you jump into treatment," says Aditi Krishnamurthy, an independent community health consultant in Bengaluru.

Unfortunately, one of the biggest barriers to informed consent in India is patient literacy, say

experts. Some poorly educated patients think of TB as a death sentence and do not see the point of taking medicines. Convincing them to do so is already an uphill task. Telling them about drug adverse effects without fully explaining the risk-benefit ratio is likely to push them further away, Krishnamurthy points out. “Informed consent is a double edged sword.”

Take the case of journalist Nandita Venkatesan, who was diagnosed with intestinal tuberculosis for the second time in 2013. She was admitted to a large private hospital in Mumbai where her doctors gave her kanamycin.

One afternoon, about a week after Venkatesan finished her course of the drug, she took a nap. When she woke up, she could hear absolutely nothing. Eventually, a ear-nose-throat specialist diagnosed her with over 90% hearing loss, and told her it was a side-effect of the drug.

Today, Venkatesan does not rue that she was prescribed the drug, given how ill she was. “I know the doctors who treated me did terrific work,” she recounts. What still rankles is that no one told her about the catastrophic impact it could have on her life. “I didn’t even hear a whisper about this,” she says.

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