

The tip of the iceberg: Alarming increase in the detection of MDR-TB

In this issue of *SARJ*, Narsingh *et al.*^[1] highlight the alarming and burgeoning problem of multidrug-resistant tuberculosis (MDR-TB).^[2] More recently, this has been supplanted by an increasing burden of extensively drug-resistant TB (XDR-TB),^[3] and resistance beyond XDR-TB.^[3] The problem of programmatically incurable TB and its spread, in our communities, from home-discharged index cases has recently been highlighted.^[4]

In their study, Narsingh *et al.*^[1] found that almost 11% of patients assessed, had MDR-TB. Although there are several drawbacks to this estimate, including the study design, this highlights the alarming increase in the detection of MDR-TB in many of our urban centres. In 2014 almost 20 000 cases of MDR-TB were detected nationally.^[5] The disease prevalence, given that 220 000 cases were tested, was ~8.5%. These data and clinical observations in urban areas are discordant with the recent prevalence survey indicating a much lower rate of MDR-TB nationally. Nevertheless, this still represents an alarming burden of MDR-TB given that 50 - 60% of the MDR-TB caseload remains undetected.

Drug-resistant TB represents a serious threat to TB control for several reasons. The mortality, as demonstrated in this study, is surprising high; ~30 to 40% for MDR-TB and 60 to 70% for XDR-TB (prior to the use of bedaquiline).^[5,6] This is worse than the mortality rates for many cancers. There is also considerable long-term morbidity due to chronic lung disease. If this were not enough, drug-resistant TB is already consuming almost 40 - 50% of the total National TB Programme budget,^[7] which is not sustainable.

Drug-resistant TB is also a major threat to healthcare workers. Indeed, Narsingh *et al.*^[1] show that only ~50 - 60% of patients were isolated. Recent reports indicate that healthcare workers in KwaZulu-Natal have a rate of drug-resistant TB almost six-fold higher than the general population, strongly suggesting that it is nosocomially contracted.^[8] Drug-resistant TB in healthcare workers has also been reported in the Western Cape Province.^[9] This highlights the poor infection control protocols and interventions that are available in our clinics and hospitals. Both the constitution of the country and the Occupational Health and Safety Act are openly being flouted.

How can we address this MDR-TB epidemic? Clearly, as the authors^[1] point out, proper education of healthcare workers is important to ensure that patients are appropriately treated. However, first and foremost, we need to address the extremely high burden of TB itself. This requires eradication of poverty and overcrowding, addressing the socioeconomic inequalities in the country, addressing the epidemic of HIV that fuels TB, and also addressing other major drivers such as smoking, exposure to indoor air pollution, and the growing epidemic of type II diabetes.^[2] Next we need to address the transmission of drug-resistant TB. Approximately 80% of the MDR-TB burden is due to person-to-person spread. As 60 - 70% of the caseload remains undetected, transmission will not be addressed unless active case finding is adopted.^[10] Recently it has been shown that molecular tools can greatly improve case detection when using a mobile van staffed by healthcare workers.^[10] Innovative strategies are

also required to address transmission in congregate settings such as schools, churches, beer halls, and taxis.

We also need better diagnostic tests. There is a need to move towards 'precision medicine' for TB, where simultaneous multi-drug readouts are obtained so patients can be treated with bespoke therapy rather than the 'kitchen sink' approach that is currently being used. Wider access to newer and repurposed drugs, such as bedaquiline, delamanid, and linezolid are required. The issue of infection control to protect healthcare workers also needs urgent attention. Most importantly, we need to understand the pathogenesis of MDR and XDR-TB. More recent data suggest that, in contradiction to blaming the patient and healthcare workers, several other factors are important, including population-based pharmacokinetic (PK) variability, various mycobacterial-related factors including efflux pumps, and PK mismatch due to suboptimal penetration of drugs into tuberculous TB cavities.^[3] If we do not understand and address these factors, we will continue to lose the precious new anti-TB drugs, which is already happening, given the increasing number of treatment failures being seen despite the use of bedaquiline.

Our national TB control programme, and the healthcare system as a whole, is akin to the Titanic, which is on course for a deadly collision. Only the tip of the iceberg is visible but will anyone take heed? Evasive action is urgently needed, but can we respond in time?

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