Editorials

Tuberculosis Control in India: Time to get dangerously ambitious?

Thanks to a vastly improved, better funded and professionally managed Revised National Tuberculosis (TB) Control Programme (RNTCP), India has successfully scaled-up DOTS (directly observed treatment, short course), the global Stop TB strategy, to cover 100% of the population, and has done well to achieve the Stop TB Partnership's targets of 70% case detection and 85% cure rate ('70/85 targets'). A recent modelling study suggests that this scale-up has been a cost-effective strategy for improving the health of the Indian population, with exceptional return on investment from a societal perspective.[1] Yet, in 2009, over 2 million TB cases and 280 000 TB deaths occurred in India, with India maintaining its *numero uno* status among the highest TB burden countries in the world.[2] Even globally, despite the successes of DOTS, it is obvious that we are nowhere close to controlling TB. The facts are compelling—in 2009, more than 9 million new cases and 1.7 million TB deaths were reported.[2]

TB is a disease of poverty and there are probably many explanations for this complex problem. One important reason is that TB patients are not diagnosed and cured quickly enough, and/or they are mismanaged. Globally, in 2009, only about 63% of all TB cases were detected.[2] Several studies from around the world have shown that diagnostic delays are common, due in part to a reliance on ineffective tests, and also because of various patient and health system-related factors.[3] Regardless of the reasons for delay, the reality is that by the time a patient is diagnosed to have TB, he/she has already visited multiple healthcare providers, and infected several other people. Every doctor in India has seen this reality played out in various settings.

The human and sociopolitical aspects of this problem in India were nicely captured by Michael Specter, an internationally renowned journalist, in the *New Yorker* of November 2010.[4] In an article entitled 'Letter from India: A deadly misdiagnosis', Specter provided numerous examples of mismanagement of TB, especially in the private sector, and attempted to tease out the various possible reasons why mismanagement occurs. For example, inaccurate and inappropriate TB diagnostics are widely used in India, particularly in the private sector, where this is a big market. Serological (antibody-detection) tests for TB are known to be inaccurate, inconsistent and with no clinical value; this has been demonstrated in several meta-analyses and large-scale WHO studies.[5–7] No international guideline has ever recommended their use, and the RNTCP has never promoted or endorsed these tests. In fact, guidelines such as the International Standards for TB Care[8] and those by the Indian Academy of Pediatrics,[9] actually discourage their use. Despite the evidence and lack of any supporting policies, 1.5 million TB serological tests are estimated to be done in India every year at an expenditure conservatively estimated at US$ 15 million per year.[4,10] When compared with the entire RNTCP annual budget of US$ 65 million, this is substantial. Every major private laboratory in India offers TB serological tests, mostly ELISA kits imported from countries such as France and the UK. These countries, apparently, do not approve the same tests for clinical use on their own TB patients!

Of late, there is a worrisome trend of using tests such as interferon-gamma release assays (e.g. QuantiFERON-TB Gold) for active TB diagnosis, whereas these tests were intended for latent TB infection.

How did bad diagnostics become such a big business in India and what are the implications for TB control in the country? The *New Yorker* article[4] and a recent World Report in the *Lancet*[10] paint a serious picture of the diagnostic and treatment ecosystem in India which is dominated by the private sector, and characterized by systemic market failures throughout the value chain. These include dumping of useless diagnostics from rich countries into India because of weak regulation, doctors receiving incentives for tests ordered,[11] over-reliance on useless tests and under-use of good diagnostics, prescription of incorrect TB treatment regimens, and lack of accountability to ensure that patients complete TB treatment.[12] For Indian doctors, this cannot be news. Several older studies have documented poor TB management practices in the private sector, and indeed such studies were inspirational in developing the public–private mix (PPM) initiative.[13]

Mismanagement of TB is bad for the individual patient who may be put on unnecessary TB therapy or continue to suffer from TB without the correct treatment. It is equally bad from a public health perspective because every mismanaged or undiagnosed TB patient serves as a source for new infections in the community. To break this chain of transmission, we need to detect TB earlier, faster and get more TB patients on therapy. Widespread abuse of inappropriate tests can prevent the use of good diagnostics, and this is a major challenge for implementation of new WHO-approved diagnostics that are now available. Recognizing the gravity of the problem, the WHO recently announced its first negative policy regarding TB, *against* the use of TB serological assays.[10,14] The policy, however, is not intended to discourage research in serological tests, because of the potential for a useful, simple, point-of-care test based on immunodiagnosis.

Will the WHO policy change realities in India? Probably not, unless there are improvements in regulation of the private sector in general, and tighter regulation to prevent abuse of suboptimal diagnostics. India has the largest private health sector in the world, with 60%–80% of healthcare sought in the private sector, and a healthcare market that is worth billions of rupees. Despite its enormous size and importance, this sector is largely unregulated, although the Clinical Establishment Act 2010 attempts to address this tricky and controversial issue.

Weak regulation of health products is another area of concern. Unlike drugs, the regulation of *in vitro* diagnostics is weak in India, and this allows for bad diagnostics to enter the market despite lack of evidence or policies to support their use. TB tests are not classified as 'critical tests' by the Drug Controller General of India (DCGI), and this allows for entry and sale of suboptimal diagnostics with little independent validation. Once on the market, financial gains by various stakeholders keep such products profitable. If diagnostic companies (domestic as well as foreign), local distributors, laboratories and doctors earn money from suboptimal tests, then market logic dictates that irrational practices will continue to flourish. If any solution has to work in India, it must account for these market-based ground realities and address the financial incentives of all stakeholders that perpetuate bad medicine. This is true for all aspects of medicine in India, whether it is unnecessary caesarean sections and hysterectomies, widespread antibiotic abuse, kickbacks associated with diagnostic imaging services, linking of physician incomes to procedures/tests performed, or the well-acknowledged nexus between doctors and the pharmaceutical industry.

How do we address these challenges? To improve the landscape of TB diagnosis in India, several efforts are needed in parallel.[12] India must adopt new tools that are accurate, validated and WHO-endorsed, and replace suboptimal tests with good tests that can impact patient outcomes and reduce TB transmission in the community. Innovative tools and innovative delivery systems that engage both public and private sectors are essential for reaching this goal. The DCGI must tighten regulation of diagnostics and ensure that suboptimal tests are reviewed and removed from clinical use. New TB tests must be subjected to independent validation before approvals are

granted. This may require a rethink of the current system of classifying tests as 'critical' versus 'non-critical' where only a few tests (e.g. HIV, hepatitis B and C) related to blood safety are considered 'critical'. The RNTCP must set clear specifications for all TB diagnostics used in India, and collaborate with the DCGI in validating all TB tests before approval. Lastly, something must be done about the fact that an overwhelming majority of Indian laboratories have no formal quality accreditation or certification. Lack of laboratory quality assurance is a major threat to improving TB diagnosis in India, and this deserves serious attention.

In addition to improving diagnosis, we need to get ambitious, and think beyond the 70/85 targets. India has taken the lead in this area with its impending launch of RNTCP 3, an ambitious plan for 2012–17, that aims to provide *universal access* to quality diagnosis and treatment for the entire Indian population.[15] It is abundantly clear that the RNTCP alone cannot meet this goal of universal access. Everyone will need to pitch in, starting with the Indian government which must fund this groundbreaking TB control plan that will require much more resources. The Indian private sector and industry also has a unique opportunity here. India already makes a huge contribution through low-cost generic drugs, and it certainly has the economic, scientific and technological capacity to develop low-cost generic or novel TB diagnostics that can not only help India, but also other disease endemic countries.[16,17]

Greater engagement of the private sector is needed to effectively deliver innovative products and approaches. For example, because of the phenomenal growth and potential of private service laboratory networks in India, and the recent introduction and WHO endorsement of breakthrough technologies such as Xpert MTB/RIF,[18] a 2-hour molecular test for TB and drug-resistance, there are now emerging opportunities for private sector laboratories to not only contribute to improved case detection, but also ensure financial viability because of economies of scale. Small-scale pilot PPM projects will no longer be sufficient—the Indian private sector must be incentivised and engaged on a scale commensurate with its dominant role. This will require socially oriented, but economically viable business models.

There is probably no better time than now for all Indian healthcare providers, industry, civil society, donors, activists, journalists, politicians, philanthropists and patient groups to rally behind RNTCP 3 and make it a success story that can not only save lives of TB patients, but also inspire other high TB burden countries and pave the way for a more ambitious global TB control agenda.

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