Editorial:

Tuberculosis control in India: the critical need for reducing diagnostic and treatment delays

Globally, tuberculosis (TB) continues to be major public health threat, with an estimated 8.7 million new cases per year, and an estimated 1.4 million deaths from TB. Early case detection and rapid treatment continues to remain the cornerstone of the "Stop TB strategy". With the incidence of TB declining very slowly, it is now becoming clear that TB cannot be eliminated by 2050.

India has the world's highest burden of TB. In India TB kills one person every two minutes and 750 people every day. Global TB control is unattainable without enhanced control of TB in India. Lately India has been in the news because of the international attention around the emergence of "totally drug-resistant" TB in Mumbai and the growing concern that routine TB control (i.e., the DOTS strategy) may not be sufficient for reducing TB incidence in the country.[1]

India's Revised National TB Control Programme (RNCTP) has made great strides in the last decade, and free, quality-assured TB diagnosis and treatment is available to all patients who seek care in the public sector. Over the past year, laudable political and administrative commitment has been demonstrated by major increases in the RNTCP budget, a ban of inaccurate, antibody-based serological tests for TB, a national order for mandatory notification of all TB cases, and initiation of a national web-based case notification and tracking system called *"Nikshay"*. The Government of India (GOI) recently approved the National Strategic Plan for 2012-2017 with an ambitious goal of universal access to quality TB diagnosis and treatment for all patients in India.[2]

While these are positive developments, TB control in India is at a critical juncture. The routine, basic DOTS program has been scaled-up and may have reached its limits because TB incidence is not declining. TB case finding has plateaued and many cases remain either undiagnosed or ineffectively treated. By the time TB cases are initiated on treatment in the RTNCP, they likely have already infected many others in the community.[3] Delays in diagnosis or ineffective treatment lead to ongoing transmission, facilitating the spread of the disease.

Patients often seek care in the informal and private sectors, and they remain outside the knowledge of the RNTCP.[4] In fact, more than 80% of India's health care is delivered through the private sector. Primary health care (first contact care) is mostly provided by non-medically trained providers. Overall quality of medical care is deficient on many counts, as shown by vignette and mystery client studies.[5]

A majority of TB patients begin by seeking advice in the informal private sector (chemists and unqualified practitioners), followed by care from qualified practitioners, before about 50% of them end up in the public sector for free treatment.[4,6,7] During this period (which can range from weeks to months, as shown by data from systematic reviews),[8,9] patients move from one provider to another and continue to transmit the infection to others. This convoluted pathway, coupled with the high cost of care in private sector pushes a lot of poor families into debt.

And yet, for all the money patients spend, they may receive suboptimal TB care, as illustrated by the use of inappropriate serological, antibody tests, growing use of interferon-gamma release assay as (IGRAs), such as, QuantiFERON-TB Gold for active TB (when they are meant for latent TB infection), and irrational TB drug regimens in the private and informal sectors.[10,11] This delayed/ incorrect diagnosis and treatment are major drivers of generation and transmission of drug resistance TB epidemic, and prevention of multidrug-resistant TB (MDR-TB) will require interventions to shorten delays and improve quality of care, especially in the private sector. So, it is clear that India will need to invest in new, more accurate diagnostics that can help reduce TB transmission. The biggest recent advance is the Xpert MTB/RIF

assay, using the GeneXpert technology (Cepheid Inc, California). This is a World Health Organization (WHO) endorsed, rapid, automated, 90 minute molecular test which can diagnose TB with great accuracy and can also detect MDR-TB at the same time. A recent Cochrane review[12] showed that this test has 88% sensitivity and 98% specificity when compared to culture. It can detect rifampicin resistance (which is a good surrogate marker of MDR-TB) with a specificity of 98% and sensitivity of 94%. Studies from India clearly shows substantially better performance of the Xpert MTB/RIF test over smear microscopy.[13,14] Recent data also suggest that Xpert MTB/RIF has value for childhood TB and extra-pulmonary TB (EPTB), especially TB meningitis and lymphadenitis, two common forms of EPTB.[15,16] A World Health Organization (WHO) policy on use of Xpert MTB/RIF for EPTB and childhood TB is expected this year.

By replacing inaccurate blood tests (serology and TB Gold) with accurate tests like Xpert MTB/RIF, TB can be diagnosed early and rapidly treated with anti-TB therapy. This should help reduce transmission in the community. But technologies alone cannot solve the problem. Innovative delivery approaches and business models are needed, especially to engage the dominant Indian private sector and to make good tests more affordable to private sector patients.[17]

A new initiative called Initiative for Promoting Affordable, Quality TB tests (IPAQT; www.ipaqt.org) has just been launched in India, to improve the affordability of WHO-endorsed TB tests.[18] Initiated by a coalition of accredited private labs in India, and supported by the industry, this project has made WHO-approved tests available at affordable prices to patients in the private sector. These labs have access to lower, negotiated prices for the quality tests in exchange of their commitment to pass on the benefits to patients.

By using a high-volume, low-margin model, the cost of Xpert MTB/RIF is now reduced to Rs 1700 (maximum price laboratories can charge patients), compared to Rs 3000 or higher in the private market. A WHO-endorsed line probe assay (Genotype MTBDR plus by Hain LifeScience, Germany) is now available at Rs 1600. Laboratories in the initiative cannot charge more than transparently advertised ceiling prices, and have to agree to stop doing TB serology. Laboratories will also participate in external quality assurance (EQA) programs. TB cases diagnosed by member labs will be notified to the RNTCP for linkages to free TB drugs, where necessary.

Since its launch in March of 2013, the IPAQT initiative has already achieved a pan-India presence - with 36 labs which encompasses over 3000 franchisee labs and greater than 10,000 collection centers committed to providing these tests at affordable prices. The number of labs is expected to increase significantly in the months ahead.

Thus, this initiative is expected to greatly increase affordability for private sector patients, and improve the quality of TB care in the country. Efforts are also necessary to link accurate diagnosis to correct TB treatment regimens, as recommended in the upcoming Standards for TB Care in India (STCI). It is also important to ensure that private sector patients get adequate support with treatment adherence. Only then will the benefits of accurate diagnosis be fully realized.

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REFERENCES

1. Udwadia ZF. MDR, XDR, TDR tuberculosis: ominous progression. Thorax 2012;67:286-8.
2. Sachdeva KS, Kumar A, Dewan P, Satyanarayana S. New vision for Revised National Tuberculosis Control Programme (RNTCP): universal access - "reaching the un-reached". Indian J Med Res 2012;135:690-4.
3. Pai M. As India grows, tuberculosis control must not be left behind. Lancet Infect Dis 2012;12:263-5.
4. Kapoor SK, Raman AV, Sachdeva KS, Satyanarayana S. How did the TB patients reach DOTS services in Delhi? A study of patient treatment seeking behavior. PLoS One 2012;7:e42458.
5. Das J, Holla A, Das V, Mohanan M, Tabak D, Chan B. In urban and rural India, a standardized patient study showed low levels of provider training and huge quality gaps. Health Aff (Millwood) 2012;31:2774-84.
6. Satyanarayana S, Nair SA, Chadha SS, Shivashankar SS, Sharma G, Yadav S, et al. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. PLoS One 2011;6:e24160.
7. Suganthi P, Chadha VK, Ahmed J, Umadevi G, Kumar P, Srivastava R, et al. Health seeking and knowledge about tuberculosis among persons with pulmonary symptoms and tuberculosis cases in Bangalore slums. Int J Tuberc Lung Dis 2008;12:1268-73.
8. Sreeramareddy CT, Kishore PV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. BMC Infect Dis 2009;9:91.
9. Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC public health 2008;8:15.
10. Jarosawlski S, Pai M. Why are inaccurate tuberculosis serological tests widely used in the Indian private healthcare sector? A root-cause analysis. J Epidemiol Global Health 2012;2:39-50.
11. Udwadia ZF, Pinto LM, Uplekar MW. Tuberculosis management by private practitioners in Mumbai, India: has anything changed in two decades? PLoS One 2010;5:e12023.
12. Steingart KR, Sohn H, Schiller I, Kloda LA, Boehme CC, Pai M, et al. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database Syst Rev 2013;Issue 1. Art. No.: CD009593.
13. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 2010;363:1005-15.
14. Boehme CC, Nicol MP, Nabeta P, Hillemann D, Nicol MP, Shenai S, et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. Lancet 2011;377:1495-505.
15. Nicol MP, Workman L, Isaacs W, Munro J, Black F, Eley B, et al. Accuracy of the Xpert MTB/RIF test for the diagnosis of pulmonary tuberculosis in children admitted to hospital in Cape Town, South Africa: a descriptive study. Lancet Infect Dis 2011;11:819-24.
16. Vadwai V, Boehme C, Nabeta P, Shetty A, Alland D, Rodrigues C. Xpert MTB/RIF: a new pillar in diagnosis of extrapulmonary tuberculosis? J Clin Microbiol 2011;49:2540-5.
17. Baloch NA, Pai M. Tuberculosis control: business models for the private sector. Lancet Infect Dis 2012;12:579-80.
18. Kay M. Private firms form initiative to offer accurate and affordable TB tests. BMJ 2013;346:f2161.