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Editorial

How to bend the curve of TB incidence downwards in India

During 2019 through 2021, the Indian Council of Medical Research (ICMR) conducted a national cluster sample survey, to document the point-prevalence of microbiologically confirmed pulmonary tuberculosis (MCPTB) among individuals of 15 years and above[1]. The average point prevalence was 316 (95% CI: 290-342) per 1,00,000 persons.

Typically, annual incidence is higher than point prevalence. Therefore, one may assume that the annual incidence is >300 cases of MCPTB/lakh population. The reported annual incidence of MCPTB in 2022 was recorded as 172/lakh population[2]. This suggests that the way data was being collected was incomplete and hence, inaccurate. If one adds up extra-pulmonary TB and cases below age of 15 yr, then the total number of new cases of TB may likely be much higher than the reported or derived annual incidence. In this context, given that India's population is 141 crores, our annual burden of new TB cases, an adult pulmonary and extra-pulmonary TB, and childhood TB may be over five million.

Two major lessons learnt from the survey results

The major lessons from the survey results are two, namely *(i)* our TB burden is huge and *(ii)* our present surveillance is grossly incomplete[1]. If one intends to bend the curve of annual incidence down then first a TB surveillance method must be designed to yield reliable information and also apply multiple interventions to decelerate its spread and lower its incidence.

TB is a communicable disease, majorly sustained among humans, 'anthroponosis' in other words and the frequency of transmission of the causative agent is determined mainly by the prevalence of MCPTB. *Mycobacterium tuberculosis* (*M.tb*) is transmitted by inhaling the microbe disseminated into the air directly from the infected persons or indirectly from dried sputum on the ground. After the COVID pandemic, people have become aware of the need to practice 'cough and sneeze etiquette' and 'no-spitting indiscriminately'.

We have our tasks cut out for us. First, a measuring tool needs to be developed to compare annual, denominator-based and objectively collected numbers of either infection or disease, or both. Such a measuring tool is essential for year-to-year comparisons such that the direction of transmission trajectory can be determined particularly when the curve of incidence bends downwards[3]. Second, we must design and deploy interventions to reduce disease, for which the frequency of infection must be slowed down. Both are formidable and challenging tasks, but we as a country have sufficient 'brain power' for planning TB control; the best way, in the best interest of our nation and people.

Like in all other respiratory-transmitted anthroponoses, the dynamics of transmission can be conceptualized with the 'basic reproduction number' denoted by R_0 and the 'effective reproduction number' denoted by R[4]. Assuming TB to be in an endemic steady state in India, its $R=1$. Our interventions must result in $R<1$ and sustain it over time. Sustaining progressively monitored graph showing $R<1$ is what we mean by bending the curve downwards[3,4].

History: Establishment of National Institutes and follow up actions

During the 1950s, the ICMR and the Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MoHFW), Government of India, had conducted a nationwide survey of pulmonary tuberculosis (PTB) using mass miniature chest X-rays and documented its high prevalence in all regions, and in response, designed two programmes and three institutions. The institutions were: *(i)* the Tuberculosis Research Centre (TRC) in Chennai (erstwhile Madras) currently named ICMR-National Institute for Research in Tuberculosis (ICMR-NIRT); *(ii)* the National TB Institute (NTI) in Bengaluru, under DGHS for training of staff; and *(iii)* the Bacillus Calmette-Guerin (BCG) and tuberculin manufacturing unit in the King Institute, Guindy, Chennai, under the Tamil

Nadu State Government. The two programmes were: *(i)* widespread BCG vaccination hoping for primary prevention of TB and *(ii)* a district-level National TB Control Programme (NTCP)[5]. For various reasons, TB could not be controlled. Therefore, a Revised NTCP (RNTCP), as designed by TB experts of the World Health Organisation (WHO), was launched in 1993, using directly observed treatment short-course (DOTS) as the main plank of intervention[6]. Actually, DOTS itself was developed and field-tested by TRC, for domiciliary management of PTB. Thirty years later, we find again that TB has not yet been controlled.

The results of a 15 yr follow up of a large randomized clinical trial of the BCG vaccine, in Chingleput district, Tamil Nadu, conducted by TRC confirmed the results obtained at 7.5 yr follow up, that BCG offered no overall protection in adults, and only a low (about 27%) degree of protection against pulmonary TB among children[7]. Without a tool for primary prevention, the strategy for TB control had to be re-designed[8].

Current focus on TB control

In November 2017, at the first WHO Global Ministerial Conference in Moscow, 75 ministers from various countries agreed to take urgent action to end TB by 2030 in the Sustainable Development Era[9] and in September 2018, the United Nations (UN) General Assembly held a High-level meeting on TB and endorsed ten key targets and commitments through a resolution that was endorsed by its Member States[10,11]. But, earlier that year, during the Delhi End Tuberculosis Summit on March 13, 2018, Indian Prime Minister Narendra Modi in the Delhi End Tuberculosis (TB) Summit declared the Government's goal for TB elimination by 2025, five years ahead of the UN target[12]. Soon RNTCP was re-designated as National TB Elimination Programme (NTEP).

Control and elimination are well defined terms in infectious disease epidemiology[13]. Disease control is a deliberate reduction of disease incidence (or burden) to a pre-determined low level, in a planned time frame, through interventions[13]. Elimination is extreme control to reach zero disease incidence[13]. The United Nations Sustainable Development Goals (SDG) include ending the TB 'epidemic' by 2030[14]. An epidemic denotes R>1, and indeed, developing countries have so far not bent the curve downwards to reach and sustain R<1[8]. TB elimination is defined for SDG as achieving an annual incidence of less than one case of infectious PTB per million population, or a prevalence of latent TB infection of <1 per cent of the population[14,15].

As mentioned above, under NTEP there were no reliable, denominator-based case numbers as a baseline benchmark. Hence ICMR, along with Central TB Division (CTD), conducted the national sample survey, financially supported by the MoHFW, Govt of India[1]. The survey is a landmark achievement in India's TB landscape, and it can hopefully become the harbinger of a watershed, if effective follow up actions are designed and deployed, to deflect the graph of R>1 to R<1, fulfilling the Prime Minister's vision of a TB-eliminated India, albeit delayed by several years.

The challenge given to CTD in 2018 was TB elimination in India by 2025, however, the progress towards TB control met a major setback during the COVID-19 pandemic. Post-pandemic, although NTEP has bounced back and achieved some of the pre-COVID targets, the two years that were lost during the pandemic cannot be compensated.

The result of the National TB Prevalence Survey (2019-2021) has however, dampened the hope of bending the trajectory downwards and to further document it convincingly any time soon. It is now clear that just incremental changes to NTEP alone will not lead to TB Control. There are several lessons in the well-designed and well-conducted ICMR national sample survey that are true 'eye-openers' for the CTD, MoHFW and the nation's community of infectious disease experts. TB elimination will take at least a decade of effective TB control. TB control must start with bending the curve. To bend the curve, first, the curve has to be drawn, which requires objective data collection – data that can be validated for reliability and used for year-to-year comparison. Bending the incidence curve is the beginning of TB control, followed by concerted efforts to accelerate the downward trend, and progress towards eventual elimination. This shift, however, cannot, be achieved or even hoped for, without a transformational re-design of the NTEP.

Epidemiology of PTB provides clues for early diagnosis

The National TB Prevalence Survey has revealed several previously unknown elements in the epidemiology of PTB and they offer many helpful hints for designing a proper TB control programme. The prevalence of MCPTB in various States is not uniform but varies widely. Eight States have a higher prevalence than the national average[1]. Among these, Delhi, Rajasthan, Uttar Pradesh, Haryana and Chattisgarh have above 400/lakh/year and Madhya Pradesh, Jharkhand, Bihar and the cluster of Himachal

Pradesh, Uttarakhand and Jammu-Kashmir have below 400[1]. Eleven States have a lower prevalence than the national average. Of these, Tamil Nadu, Telangana, Punjab, Karnataka, Andhra Pradesh and the cluster of north-eastern States have above 200/lakh/year and Kerala, Gujarat, Maharashtra and West Bengal have below 200[1]. Of these, all except Punjab and the northeast cluster are coastal States – this observation, however, deserves further scrutiny. The range between Kerala (115/lakh/year) and Delhi (534/lakh/year) is surprising and overall the lesson is that for TB control 'one size fits all' principle is quite inappropriate. One must assign greater responsibility with accountability to all States and Union Territories. The current role of States, *viz*. merely to implement NTEP guidelines irrespective of the outcome, must be revised. States must be empowered not only to support but also to supplement NTEP meaningfully and in a result-oriented manner. Goals must be set for individual States and Union Territories and they should be enabled to monitor progress regularly.

The prevalence of MCPTB is greater among men than in women[1]. When plotted on a graph, it is near-identical in the 15-24 yr age group, steadily diverging thereafter. This difference is most unlikely to be due to differential exposure to *M.tb* as, *(i)* the route of transmission is by respiration and *(ii)* the male-female prevalence is minimal or absent in adolescents and children. The biological determinants are researchable.

One risk factor for TB noted in the survey report was employment. While that may merely reflect the fact that more men than women were employed, nevertheless, it informs that there is an opportunity to systematize annual health checkups for all employed people in their workplace, with responsibility assigned to employers. Three major risk factors of MCPTB were low body mass index (BMI), diabetes and past history of TB treatment[1]. Habitual smoking and alcohol consumption were also risk factors. So, the annual checkup must include a brief self-administered questionnaire, documenting body weight, blood pressure and random blood sugar level. These are essential for early detection of non-communicable diseases (NCDs) for mitigating catastrophic outcomes as well as for early detection of TB.

The survey report showed that in the early stage, persons with MCPTB may be symptom-free or with symptoms that may not draw attention to TB, and also that chest X-ray is the most sensitive test for suspecting or diagnosing PTB. The employee's annual health checkup must, therefore, include a chest X-ray for everyone with a history record of the risk factors [low body mass index (BMI), diabetes, history of TB, smoking, habitual alcohol drinking]. Access to digital X-ray units must be made available in all districts. A digital chest X-ray on all persons with risk factors will help in early diagnosis of MCPTB. Further testing for *M.tb* in sputum can be done by NTEP. This method of 'active case search' for early case detection will be relatively easy as the responsibility is to be distributed to the employer-employee teams. Early detection of the infectious form of TB will help reduce the source of secondary transmission.

In every State, the district can be the unit of geography for active case search and all data (with confidentiality) received, collated and analyzed by the district units of the State Statistical Department. The benefits will be to the employees and employers. Early detection of NCDs and early treatment will benefit individuals and the institution by way of higher productivity. Once the systematic employee checkup is established, the design can be expanded to cover all self-employed people, organized labour force and university students.

The way forward

As said earlier, the tasks to bend the curve and to document it are challenging but unavoidable and essential for achieving TB control and progressing towards TB elimination. While CTD is responsible for the implementation of both tasks, the objective monitoring of progress requires a realistic and independently validatable method. Both early detection and cure of TB and its comprehensive surveillance overlap with the broader health management system.

When polio was identified for elimination in India, a unique supervisory system was created, under the title 'India Expert Advisory Group' (IEAG)[16]. It was chaired by an independent domain expert in the country and it took in representatives from all involved parties including programme functionaries, ICMR, WHO, other UN agencies, non-governmental organizations, and independent experts in infectious disease epidemiology and interventions. IEAG's recommendations were deemed to be binding on the MoHFW. This model was replicated when the MoHFW resolved to eliminate Measles and Rubella in India[16,17]. The IEAG MR has designed innovative district-by-district interventions and fever and rash surveillance, supported by laboratory confirmation.

Establishing an IEAG for TB control and elimination will allow a platform to be established for discussing and distilling all essential interventions and monitoring tools. The CTD will have an excellent and unprecedented opportunity to present reports for review and seek guidance on overcoming all barriers to TB control.

In the earlier IEAG models, the implementing agency acted as the Secretariat and an independent expert as the technical Chair; the same design is recommended for TB control and elimination. With interventions to bend the curve and monitoring and surveillance tools to reliably document the trajectory, India can look forward to the day when TB elimination becomes a reality.

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