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How Plausible is Ending TB Scourge?

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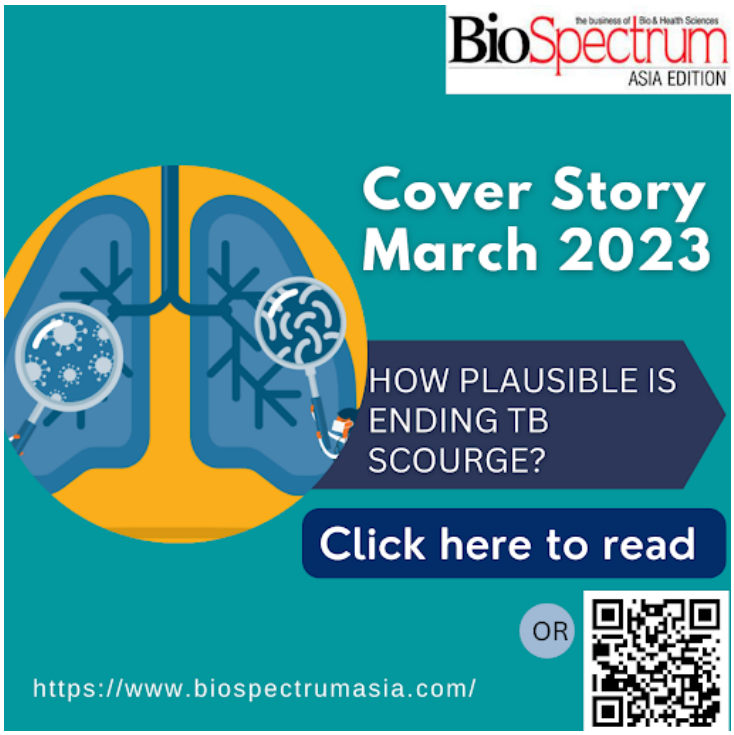
Tuberculosis (TB) has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS for a long time. And, presently, Asia Pacific is right in the thick of it. South-eastern Asia (SEA) is home to 26 per cent of the world's population with a 43 per cent burden of TB incidence, according to the World Health Organisation's (WHO) global TB report 2021.



Over the last three years, countries around the world, including in Asia and the Pacific, have faced double pandemics – COVID-19 and TB. Unfortunately, during this time, progress toward TB elimination stalled and, in some cases, reversed. COVID-19 made it harder for people to access TB diagnostics and care, leading to increases in cases and deaths since 2019. Four countries, India, Indonesia, the Philippines, and Myanmar accounted for most of the estimated increase in TB deaths, globally, in 2021.

Not all is lost though. The countries in the region, especially India and Indonesia, have renewed their efforts to eliminate TB. India launched the TB Free India campaign – a plan to eliminate tuberculosis by 2025, five years ahead of the target set by the UN's sustainable development goals. Indonesia received a $300 million loan from the World Bank to improve coverage, quality and efficiency of TB response in the country.

When observing World TB day this year on March 24, let's take stock of the progress made by Asian countries in eliminating this dreaded disease and the way forward.

Can we put an end to TB?

Despite countries making bold commitments to end TB by 2030, in the Sustainable Development Goals, the WHO End TB Strategy and the 2018 political declaration on the fight against TB, the epidemic shows no sign of slowing down. In 2021, approximately 10.6 million people fell sick with TB, and 1.6 million died. Drug-resistance continues to be a major problem with close to half a million people developing drug-resistant TB every year.

The burden of drug-resistant TB (DR-TB) also increased by 3 per cent between 2020 and 2021, with 450 000 new cases of rifampicin-resistant TB (RR-TB) in 2021.This is the first time in many years an increase has been reported in the number of people falling ill with TB and drug resistant TB.

According to Global TB Report 2022, the reported number of people newly diagnosed with TB fell from 7.1 million in 2019 to 5.8 million in 2020. There was a partial recovery to 6.4 million in 2021, but this was still well below pre-pandemic levels.

Reductions in the reported number of people diagnosed with TB suggest that the number of people with undiagnosed and untreated TB has grown, resulting first in an increased number of TB deaths and more community transmission of infection and then, with some lag-time, increased numbers of people developing TB.

The report notes a decline in global spending on essential TB services from $6 billion in 2019 to $5.4 billion in 2021, which is less than half of the global target of $13 billion annually by 2022. As in the previous 10 years, most of the funding used in 2021 (79 per cent) was from domestic sources.

The WHO report reiterates its call for countries to put in place urgent measures to restore access to essential TB services. It further calls for increased investments, multisectoral action to address the broader determinants that influence TB epidemics and their socioeconomic impact as well as the need for new diagnostics, drugs and vaccines.

The adverse impact of the COVID-19 pandemic on TB services has brought the urgency of vaccine development efforts into sharp focus. WHO, on January 17, announced plans to establish a new TB Vaccine Accelerator Council that will facilitate the licensing and use of effective novel TB vaccines catalysing high-level alignment between funders, global agencies, governments and end users in identifying and overcoming barriers to TB vaccine development.

Currently, BCG is the only licensed TB vaccine. While it provides moderate efficacy in preventing severe forms of TB in infants and young children, it does not adequately protect adolescents and adults, who account for close to 90 per cent of TB transmissions globally.

A recent WHO commissioned study, An investment case for new TB vaccines estimates that, over 25 years, a vaccine that is 50 per cent effective in preventing disease among adolescents and adults could avert up to 76 million new TB cases, 8.5 million deaths, 42 million courses of antibiotic treatment and $ 6.5 billion in costs faced by TB affected households, especially for the poorest and most vulnerable.

A vaccine that is 75 per cent effective could avert up to 110 million new TB cases and 12.3 million deaths. The study further suggests that every $1 invested in a 50 per cent effective vaccine could generate an economic return of $7 in terms of averted health costs and increased productivity.

As a quarter of the world's population is infected with TB, and, centred on WHO and the UN (United Nations) for funds, experts are pursuing the ambitious goal of ending TB by 2030. Majority of the countries in Asia have a national TB elimination programme. Let's look at what these are and what the status of these programmes is.

Progress so far

India

India carries one-fourth of the global TB burden and in 2021 notified 21 lakh TB cases. The government of India has developed the National Strategic Plan 2017-2025, which outlines approaches to eliminate TB by 2025. The plan has been divided into the four strategic pillars of Detect – Treat – Prevent – Build (DTPB).

The Indian government claimed that the overall notification of TB cases has improved by 55 per cent over the last 6 years.

In September 2022, India launched the Pradhan Mantri TB Mukt Bharat Abhiyaan. This has been envisioned to bring together all community stakeholders to support those on TB treatment and accelerate the country's progress towards TB elimination. The country also launched the Ni-kshay Mitra initiative to ensure additional diagnostic, nutritional, and vocational support to those on TB treatment and encourage elected representatives, corporates, non-profits, and individuals to come forward as donors to help the patients complete their journey toward recovery.

The programme has added 3,760 NAAT (A Nucleic Acid Amplification Test) machines across the nation until 2021, building on Universal Drug Susceptibility Testing (UDST) for all diagnosed TB cases, to ensure that patients are diagnosed with drug-

resistant TB at the outset and are promptly placed on appropriate treatment regimens.

The programme also launched initiatives to involve the communities and form a Jan Andolan against TB. More than 12,000 TB champions have been chosen through the initiative to support patients in receiving care and to reach out to the disadvantaged and marginalised. In order to enable dialogues between patients, clinicians, and their carers about common concerns in treatment, the initiative is also encouraging the formation of Patient Support Groups (PSGs).

The country plans to start sentinel surveillance for drug resistant TB using whole genome sequencing (WGS).

Indonesia

Indonesia is the third largest contributor to the global TB cases. In 2021, the country contributed around 9 per cent of the total 10.6 million new TB cases worldwide. The current National Strategy of TB Care and Prevention in Indonesia 2020-2024 aims to accelerate the TB elimination efforts in Indonesia by 2030 and to end it by 2050.

On December 19, 2022, the World Bank approved a $300 million loan to the Indonesian government to improve coverage, quality and efficiency of TB response. The first area is strengthening Indonesia's subnational TB response, such as case finding, treatment coverage, and timely response, and the performance in this area will be linked to a fiscal transfer. The second is strengthening TB response among primary health providers, including private healthcare providers. The third is enhancing digital systems for TB and well-informed policies through creating an ecosystem aimed at minimising the reporting burden and improving data availability and reliability.

In April 2022, to support the reduction of TB, the country's health minister prioritised the revision of national tobacco control regulation, with the goal to reduce the prevalence of one of TB's largest risk factors – smoking. In November 2022, the health minister urged all the stakeholders to find 60,000 cases of TB on a monthly basis in 2023 in order to eliminate TB by 2030. This is aimed at boosting the rate of TB screening that is currently still low in the country.

The Philippines

The Philippines accounts for 11 per cent of global TB cases, with an estimated 591,000 new TB cases emerging every year. Over the years, efforts have focused on TB treatment, testing, and diagnosis, but prevention has been neglected. From 2018 through 2020, TB preventive treatment (TPT) coverage declined from 11 to 2 per cent

The Philippines reacted quickly to COVID-19 and developed a strong comprehensive TB adaptive plan. Home-based testing and treatment had a big impact. Mass TB screening at key locations such as COVID-19 testing sites and vaccination sites to reach as many people as possible also helped.

In August 2021, Philippine Business for Social Progress (PBSP), the nation's largest business-led NGO, signed a Memorandum of Agreement (MoA) with provincial and local government units, health facilities, and TB partners nationwide. Through the ACCESS TB Project, PBSP will provide technical support, purchase drugs and diagnostics, provide laboratory equipment and supplies, and supply. The Global Fund allocated another $35.5 million to support and mitigate COVID-19 effects to the TB programme.

Vietnam

Vietnam has made significant progress in its commitment to end TB by 2030. However it is estimated that 170,000 people become sick from TB in Vietnam, but only around 100,000 are accounted for in the National TB system, leaving around 50,000 community TB cases undiagnosed, and the remaining 20,000 diagnosed but not reported.

In 2019, Vietnam developed the national action plan to end TB by 2030. In 2020,the United States Agency for International Development (USAID) and the Vietnam National TB Program (NTP) expanded the Ministry of Health/NTP's Double X Strategy for TB case identification, with the goal of ending TB in Vietnam by 2030. Double X is a new strategy to diagnose TB using chest X-rays and GeneXpert, a diagnostic method that detects TB bacteria.

New drugs in development

There's a lack of new research and drug development for TB. BCG, (which is almost 100 years old) is currently the only licensed TB vaccine. While it provides moderate efficacy in preventing severe forms of TB in infants and young children, it does not adequately protect adolescents and adults, who account for close to 90 per cent of TB transmissions globally.

To boost vaccine development for the disease, On January 17, 2023, WHO announced plans to establish a TB Vaccine Accelerator Council. The Council will facilitate the licensing and use of effective novel TB vaccines catalysing high-level alignment between funders, global agencies, governments and end users in identifying and overcoming barriers to TB vaccine development.

The University of Sydney and The Centenary Institute, together with collaborators have been awarded an AU$19 million contract from the National Institute of Allergy and Infectious Diseases, part of the US National Institutes of Health (NIH), to develop the next generation of TB vaccines.

Multidrug combination therapy is the standard for TB treatment, so it is not used alone, but at least three tuberculosis drugs must be used together. Patients have to take a cocktail of antibiotics, and even the easiest-to-treat form of the disease, drug-sensitive TB, takes six months of treatment and ongoing clinical monitoring.

In August 2022, Project to Accelerate New Treatments for Tuberculosis (PAN-TB) collaboration announced the execution of a joint development agreement (JDA) supporting the progression of two investigational TB combination treatment regimens into phase 2 clinical development. The collaboration will evaluate whether the novel regimens, which combine registered products and new chemical entities (NCEs), can effectively treat all forms of active pulmonary TB using substantially shorter treatment durations than existing drug regimens, with the goal of identifying a regimen suitable for phase 3 development.

However, one of the biggest roadblock is the increasing prevalence of multidrug resistance (MDR) and extremely-drug resistant (XDR) strains of Mtb. The WHO reported that Rifampicin resistant TB cases are increasing yearly, reaching over 70 per cent of TB cases in 2021. Because of this, the development of novel effective therapeutics is necessary to combat treatment times and drug-resistance.

“Compounds such as the first-in-class drug candidate Telacebec (Q203), which show activity against MDR- and XDR-TB strains can be used in new regimens for patients presenting with infections that are resistant to established therapeutics. The Q203 was identified by Institut Pasteur Korea and licensed out to the institute’s spin-off bio venture, Qurient, Co. Ltd. for further development. Recently, Telacebec was licensed out to the TB Alliance after successfully completing Phase IIa clinical trial, increasing hopes for TB elimination. Currently, IPK is developing new models of infection to better study the immune regulation of both active and latent TB infection. We hope to identify new pathways and targets which can be applied to the in-house candidate drug screening programmes run by IPK, " said **Dr Connor Wood, Head of Tuberculosis Research Lab, Institut Pasteur Korea (IPK)**.

Singapore scientists developed a series of chemical-based compounds against MDR-TB. US-based Neuro-Horizon Pharma licensed those promising compounds from NTU Singapore.

Additionally, in December 2022, the WHO released guidance on introducing a landmark treatment regimen for drug-resistant TB that will improve treatment outcomes and quality of life for thousands of people around the world.

“Considering past experiences in antibiotics development, we will need at least three drug combinations with novel distinct mechanisms of action (MoA). There are three new drugs in two classes (bedaquiline and delamanid/pretomanid) developed since 2010 with novel mechanisms of action. But there has not been ground breaking change in terms of regimen development since we are still short of new MoA drugs to make up the universal regimen. With new drug candidates like telacebec on the horizon the universal regime is not out of reach,” said **Dr Kiyean Nam, CEO, Qurient.**

The way forward

TB is curable and treatment options are available, then why does it remain a global problem and is still not yet defeated?

“There are several road-blocks on the path to defeating TB, including diagnosis and the lengthy treatment regimens, as well as poor vaccine protection,” said Dr Wood.

Many of the tools we need to tackle – and eventually defeat TB already exist, but they are not available to the people who need them. Barriers such as high prices, limited manufacturing, and slow registration mean that people who would benefit from new, highly effective drugs are never prescribed them.

“There is an urgent need to refocus global, regional and national attention back to TB, restore access to essential TB services, and increase investment in new diagnostics, drugs and vaccines. We are seeing promising diagnostic and treatment innovations but too often they do not reach the people who need them. This lack of access is holding back progress against TB in Asia and the Pacific, and around the world,” said **Hema Srinivasan, MedAccess’ Chief Access Officer, UK**.

MedAccess recently reached an agreement with Viatris to lower the price of pretomanid – part of the new WHO-recommended regimen for drug-resistant TB - by 34 per cent, with a volume guarantee agreement expected to be signed in the coming months. MedAccess also provided a volume guarantee to Macleods to reduce the price and increase supply of TB preventive therapy, enabling more people to access the short-course regimen through the IMPACT 4TB partnership, led by the Aurum Institute.

There are other key areas to focus on, such as financial needs to scale up implementation and speed up research and development of new tools, including a new TB vaccine, access to new rapid molecular diagnosis and to new shorter and more efficient treatment regimens, TB prevention, TB in children etc.

“As the largest international funder for TB programmes, the Global Fund is a critical partner in helping to achieve the goal of ending TB by 2030. In the Asia-Pacific region and everywhere, we must scale up efforts with public and private partners, civil society and communities affected by TB to find and treat all people with TB, mitigate the impact of the COVID-19 pandemic on TB programmes, address the socioeconomic barriers to care, and strengthen resilient, sustainable and inclusive health and community systems that can respond to current and future disease threats. At all levels of our action, we need to better include young people, in all their diversity, and facilitate youth-led action at global and national level to ensure that their ideas and perspectives are better reflected in the TB response,” said D**r Eliud Wandwalo, Head of Tuberculosis Programmes at the Global Fund**.

Asian countries have upped their strategies when it comes to TB, but there is still much to be done to end the disease for good. Advances in R&D, access to newer drug regimens, public private partnerships and efforts to address broader socioeconomic conditions that propel the disease are all required to reach TB elimination goals.

Ayesha Siddiqui