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TUBERCULOSIS CURRENT SCENARIO: MOVING TOWARDS ON TRACK AFTER COVID-19

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ABSTRACT

Tuberculosis (TB) is a serious infectious threat to the human being. Bacillus mycobacterium tuberculosis is the bacteria that causes deadly infectious tuberculosis (TB). It spreads through communication, coughs, or sneezes by infected people. Tuberculosis has been a prevalent disease since ancient times, which is found in our old scripture like the Indian traditional medicine text, 'Ayurveda'. Prior to the COVID-19 pandemic, TB remained the number one infectious cause of mortality worldwide. It ranked among the top 10 deadliest diseases, even surpassing HIV/AIDS in mortality. In the past, the high fatality rate was associated with tuberculosis (TB) but after the implementation of an intense program with currently recommended treatment it has been reduced up many times of people with TB can be successfully cured. Reports estimated millions of new cases and deaths among combined HIV-negative and TB with HIV patients past several years. From the Indian perspective, the conditions get more vulnerable if we see the notification rate and prevalence of TB patients. During the COVID-19 pandemic, the diagnosis process and new arrival

cases were off track, but the efforts made by authorities to move on track after the pandemic. Co-infection with HIV and TB is difficult to diagnose, prevent, and cure. MDR TB is also a threat to public health as it requires longer and more complex treatment regimens than drug-susceptible TB. During the COVID-19 pandemic, the diagnosis process and new arrival cases were off track but the efforts made by authorities tried to move on track after the pandemic. This paper aims to offer a comprehensive overview of global tuberculosis (TB) epidemiology, including the key challenges that need to be addressed to eliminate the disease as a public health issue worldwide.

Keywords: Tuberculosis, Epidemiology of Tuberculosis, Mycobacterium TB, MDR-TB, TB with HIV.

INTRODUCTION

Tuberculosis is a significant health threat to humankind since its inception **[1]**. It is spread by the Bacillus Mycobacterium tuberculosis, which can cause death due to infectious diseases globally **[2]**. The term "Tuberculosis" was indeed coined by J.L. Schönlein in 1839. He used the term to describe the characteristic tubercles or small nodules that form in the lungs and other affected organs during the disease **[3]**. It marked an important milestone in understanding and classifying TB as a unified disease entity. TB is strongly associated with poverty and disproportionately affects the most disadvantaged and marginalized populations. Providing diagnosis, care, and necessities for combating TB is incredibly challenging in these groups **[4]**. Until the COVID-19 pandemic, TB was the most significant factor of death from a single infectious agent. After that, HIV/AIDS was on that list **[5]**. The End TB Strategy and the UN Sustainable Development Goals (SDGs) aim to end the TB epidemic by setting milestones, targets, and strategies to reduce the TB incidence rate, deaths, and costs associated with TB treatment by 2030 and 2035 **[6]**.

The World Health Organization (WHO) generates annual estimates of tuberculosis (TB) burden using data collected from surveillance systems, special studies such as disease prevalence surveys, mortality surveys, surveillance and other data analyses, and expert opinions. The WHO formed the Task Force on TB Impact Measurement to aid this effort in June 2006. The task force's goal is to assist in accurately measuring and reporting TB incidence, prevalence, and mortality rates **[7]**.

Global scenario of TB

According to the WHO Report 2022, approximately 10.6 million individuals (with

a 95% UI range of 9.9 to 11 million) were reported to be ill with TB In 2021, and the count of individuals newly diagnosed with TB was 6.4 million, which corresponds to the statistics recorded during 2016-2017, while approximately 1.6 million individuals lost their lives due to TB **[5]**. Out of the total number of deaths caused by TB, 187,000 individuals were co-infected with HIV. The TB incidence rate (new cases per 100,000 population per year) increased by 3.6% between 2020 and 2021 **[8]**. Most cases are estimated to be in South-East Asia and Africa (45% and 23% respectively), with the highest incidence in India (28%), Indonesia (9.2%), and China (7.4%) **[5]**. There is a significant fall in TB case notifications due to the COVID-19 pandemic, with people newly diagnosed and reported with TB (i.e., officially notified) reduced to 18%, from 7.1 million to 5.8 million in 2020 and partial recovery in 2021, to 6.4 million. 90% of the worldwide reduction in the reported number of newly diagnosed tuberculosis cases between 2019 and 2020 was attributed to 10 countries, with the top three (India, Indonesia, and the Philippines) accounting for 67% of the decrease, as shown in Figure 1a. In 2021, the reduction compared to 2019 was mainly due to only five countries, which accounted for 90% of the decrease, as illustrated in **Figure 1(b) [5]**.

However, the global incidence rate of TB showed a slow decline from 1997 to 2001 but saw an increase in 2001 due to a rise in cases of HIV-infected patients in Africa. Since 2002, an average reduction rate of 1.3% per year increased to 2.2% between 2010 and 2011. While the absolute number of those cases decreased, this trend only started in 2006. As a result, the Millennium Development Goal contains six targets for tuberculosis, one of which is to halt and begin to reverse previous rate of incidence, which has already been achieved **[4]**. There has been a decrease in the overall incidence of TB, but the proportion of extrapulmonary tuberculosis (EPTB) cases has increased from 1991 to 2008 **[9]**. According to the World Health Organization's Tuberculosis Report 2021, the global incidence rate of TB has decreased by about 30% between 2000 and 2020. However, it is essential to note that progress has been slower in recent years and that the COVID-19 pandemic has brought new challenges to the fight against TB **[10]**.

"On the road to "WHO End TB Strategy 2025 Milestones." The global target set for the TB incidence rate milestone is 50% for 2015-2025, but reports illuminate that it will be reduced to 10% by 2021 from the base year of

2015. Likewise, the expected TB mortality reduction rate milestone was 75%, but it reached a 5.9% reduction in the same year. One more dimension that WHO added is the percentage of people with TB facing a catastrophic cost milestone of zero by 2025, which had achieved 48% by 2021 **[5]**.

"UN High-Level Meeting on TB Treatment Targets." Targets for treating and preventing tuberculosis were set during the 2018 conference of WHO member nations. These included a goal to treat 40 million individuals of all ages for TB between 2018 and 2022, of which 66% (26.3 million) were successfully treated by 2021. The MDR/RR-TB treatment target for all age groups was set at 1.5 million, of which 43% (0.64 million) were successfully treated. Additionally, a goal of providing TB preventive treatment to 30 million individuals of all ages between 2018 and 2022 was set, of which 42% (12.5 million) received treatment. The goal of treating 6 million individuals living with HIV between 2018 and 2022 was also established, and this target was exceeded with over 10.3 million patients treated **[5]**.

Global TB reduction in case notification, newly diagnosed with TB in 2020

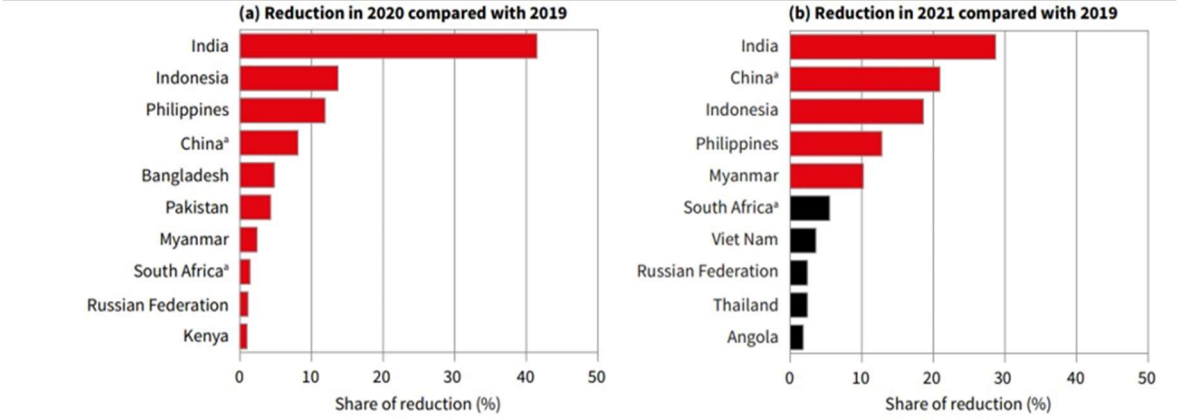

Figure 1: Top 10 countries that accounted for more than 90% of the global reduction in case notification of newly diagnosed with TB in 2020 and 2021, compared with 2019. "Adapted from WHO, request ID: 202300252"

Regarding geographic distribution, most individuals who developed TB were in regions mainly in Southeast Asia (45%), Africa (23%), and Western Pacific (18%), with minor proportions in the Eastern Mediterranean which is 8.1%, the Americas with 2.9% and Europe 2.2% in 2021. The 30 high TB prevalent countries accounted for 87% of all estimated incident cases globally. The 29 countries accounted for 66% of the estimated global incident cases in 2019 **[5]**. In 2021, the highest burden of tuberculosis cases in India was found among adult men, who accounted for 56.5% of all cases. In

comparison, adult women accounted for 32.5% of cases, and children accounted for 11%. The proportion of individuals with MDR/RR-TB among new tuberculosis cases was 3.6% (95% UI: 2.7-4.4%), while 18% (95% UI: 11-26%) among those who had previously received treatment. In comparison, the figures in 2015 were 3.9% and 20.5% for new and previously treated cases, respectively **[5]**.

Indian Scenario of TB

In India, tuberculosis has been referenced in the Vedas and ancient Ayurvedic scriptures, in which traditional prevention and treatment techniques have been included **[2]**. Several countries have carried out multiple drug and treatment programs in the modern era. India is one of those countries with a well-structured 'TB Elimination Programme' and TB Report, published annually by the Central TB Division of the Ministry of Health and Family Welfare. This report includes most of the dimensions related to the tuberculosis programs running in India and their target achievements. According to the India TB report, 2022 marks a significant milestone in India's tuberculosis (TB) surveillance efforts, with a record-high notification of 2.42 million cases. This represents a 13% increase from 2021. For the same year, the incidence rate was approximately 172 cases (per 1 lakh population) **[11]**. In 2020, the most apparent and immediate consequence of COVID-19 was a significant decrease in the reported number of newly diagnosed people worldwide with tuberculosis. The majority of the reduction in newly diagnosed tuberculosis cases occurred in three countries: India, Indonesia, and the Philippines (67% reduction of the global total) **[10]**. However, in 2021, there was a considerable recovery for India, nevertheless, not to 2019 levels **[5]**, but in 2022, it raised the record case notification to 24 lacks **(Figure 2) [11]**. **Figure 2** is plotted based on the India TB Report published from 2016 to 2023 **[11-18]**. India alone was responsible for 36% of the world's 82% TB fatalities among HIV-negative persons in 2021. Even then, India has fared far better on primary metrics than other major prevalent countries over time **[5]**. In 2019, mortality data from 123 countries represented 60% of the estimated number of TB deaths (among HIV-negative TB) globally 2019 **[19]**. The highest burden of tuberculosis cases in India was found among adult men, who accounted for 56.5% of all cases in 2021. In comparison, adult women accounted for 32.5% of cases, and children accounted for 11% of cases **[5]**.

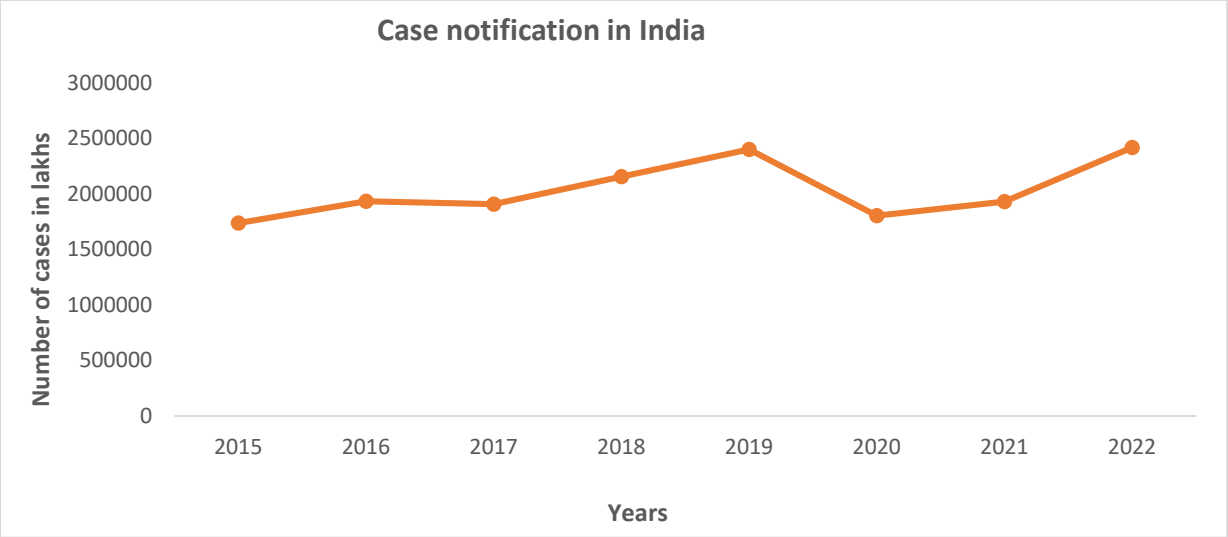

Figure 2. Case notifications of people newly diagnosed with TB, India, 2015-2022, during the COVID-19 pandemic Negative impact in 2020 but partial recovery in 2021, and considerable recovery in 2022

MDR/RR TB -

Multidrug-resistant tuberculosis (MDR-TB) is another form of tuberculosis resistant to at least two of the most potent first-line anti-TB drugs rifampicin and isoniazid **[4]**. The prevalence of multidrug-resistant tuberculosis (MDR-TB) is estimated by considering the reported proportion of MDR-TB cases in countries with an established routine drug resistance surveillance system or have conducted surveys. These proportions are then combined with global tuberculosis (TB) prevalence data. By using this information, estimates can be made regarding the prevalence of MDR-TB globally **[20]**.

Globally, the estimated number of people who developed MDR-TB or RR-TB (MDR/RR-TB) each year was stable between 2015 and 2020, but its enormous increase in 2021. There were an estimated 450000 incident cases (95%, 399,000–501,000) in 2021, an increase of 3.1% from 437000 in 2020 **[5]**. As per the Global TB Report 2022, the country's estimated incidence of multidrug-resistant tuberculosis (MDR/RR-TB) in 2021 was 119,000 cases, ranging from 93,000 to 145,000 cases. During the pandemic, there was a notable decrease in the total number of drug-resistant TB (DR-TB) patients detected compared to 2019 within the national TB control program. However, in 2022, there was a significant increase of 32% in the number of MDR/RR-TB cases detected under the National TB Elimination Program (NTEP) compared to 2021 **[11]**. we can see **(Figure 3)** the estimated incidence of MDR/RR TB worldwide distribution through the world map.

Estimated incidence of MDR/RR-TB, in countries with at least 1000 incident cases in 2021.

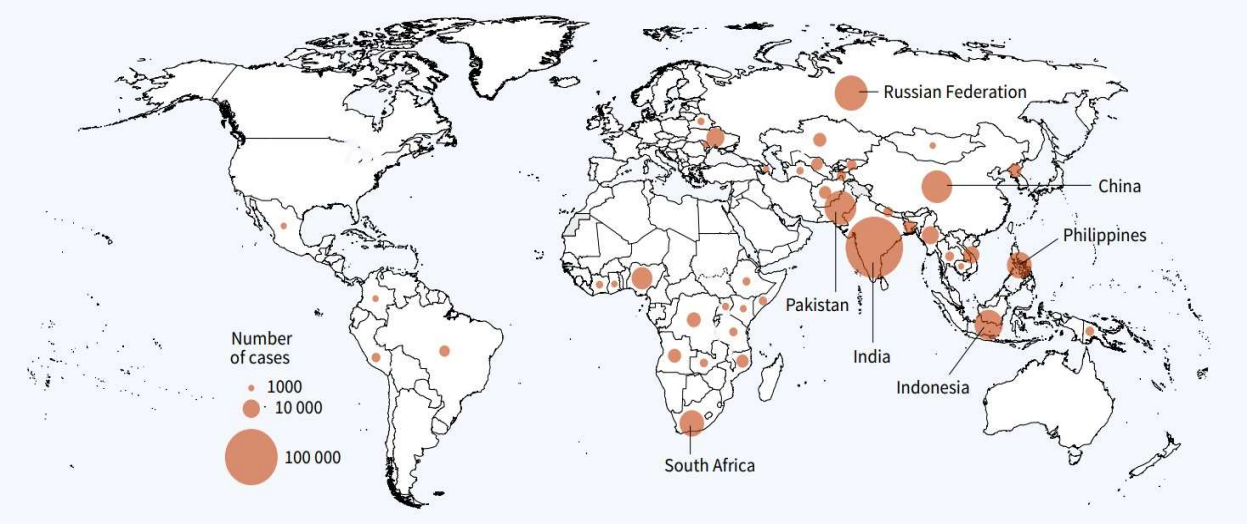

Figure 3: The seven countries with the highest burden in terms of numbers of MDR/RR-TB cases, and that accounted for two-thirds of global MDR/RR-TB cases in 2021, are labeled. "Adapted from WHO, request ID: 202300252"

TB with HIV

Infection with the Human Immunodeficiency Virus (HIV) significantly increases an individual's risk of developing active tuberculosis (TB) after exposure or experiencing reactivation of latent TB infection. The likelihood of TB disease progression increases as HIV-related immunosuppression advances **[21]**. For individuals who are not infected with HIV but have latent TB infection, there is an estimated 10% lifetime risk of developing active Tuberculosis disease. In contrast, for those co-infected with HIV, the risk is much higher, with approximately a 10% annual risk of developing active TB. This heightened risk is due to the compromised immune system caused by HIV infection, which makes individuals more susceptible to TB infection and progression to active disease **[22]**. These statistics highlight the importance of TB screening and preventive measures, especially in populations affected by HIV, to detect and treat latent TB infection before it progresses to active disease.

According to the WHO Report, 1,87,000 deaths (95% UI: 158 000–218 000) among TB and HIV-positive people in 2021. In India, 32% of these deaths were caused by HIV-positive patients. Although the global target for treating people living with HIV was surpassed **[5]**. In contrast to tuberculosis (TB), deaths from HIV/AIDS have declined between 2019 and 2021 **[23]**. This indicates positive progress in the management and treatment of HIV/AIDS.

Improved access to antiretroviral therapy (ART), prevention strategies, and healthcare services have reduced HIV/AIDS-related deaths. These advancements highlight the effectiveness of global efforts in controlling and managing the HIV/AIDS epidemic. However, it remains crucial to sustain these efforts to reduce further the impact of HIV/AIDS on global health **[23]**.

Furthermore, integrating the DOTS strategy with an existing HIV/AIDS home care program can facilitate better access to healthcare services and enhance the overall quality of care for individuals affected by both diseases. This integration helps to ensure that the unique needs and challenges of individuals co-infected with TB and HIV/AIDS are addressed holistically **[24]**.

Challenges and Control

TB is primarily a disease of poverty, which explains why it affects different population groups differently. One of the leading causes of TB is poor housing and environmental conditions, which impact a person's ability to receive healthcare services. Other key causes include food insecurity, financial hardships, illiteracy, and unfavorable psycho-social settings **[25-30]**. Social marginalization is often responsible for limited access to health services, leading to diagnostic delay, clinical worsening, poor adherence to treatment, and eventually to a less favorable outcome **[31-32]**. Some of the main challenges for the TB diagnosis process are Some of the main challenges for the TB diagnosis process are Limited Access to Healthcare, Treatment Adherence, Lack of Awareness, and Diagnostic Limitations. Many individuals affected by TB live in low-resource settings with limited access to quality healthcare facilities. This hampers timely diagnosis and appropriate treatment initiation, leading to the spread of the disease.

TB treatment requires a lengthy course of antibiotics, typically spanning several months. Ensuring patient adherence to the complete treatment regimen is critical to preventing treatment failure, relapse, and the development of drug resistance **[33]**. However, medication side effects, socioeconomic challenges, and a lack of support systems can affect treatment adherence. Societal factors, such as poverty, overcrowded living conditions, and inadequate nutrition, contribute to the spread of TB and make treatment outcomes more challenging **[34]**.

The commitment to UHC reflects a global effort to prioritize health as a fundamental human right and an essential component of sustainable development. It serves as a guiding principle for countries in their effort

to build inclusive and resilient health systems that can emphatically respond to the health needs of their populations **[35]**. After being primarily neglected for about two decades, Tuberculosis (TB) re-emerged on the global health agenda in the early 1990s. This resurgence was prompted by outbreaks of TB in high-income countries, which brought renewed attention to the disease. Recognizing the severity of the problem, the World Health Organization (WHO) declared Tuberculosis as a global emergency in 1993 **[3, 36]**. Over the past two decades, global strategies for TB control have been developed and recommended for adoption and adaptation in all countries. The first strategy – DOTS, for TB control, was launched in 1994-1995.

Of the total number of tuberculosis cases, 71% have pulmonary Tuberculosis **[37]**. Although the overall incidence of Tuberculosis (TB) has decreased, there has been an increase in the proportion of extrapulmonary TB (EPTB) cases. The rise in the proportion of extrapulmonary Tuberculosis (EPTB) can be attributed to several factors, including a rise in life expectancy, the majority of people being women, and a decline in the number of individuals vaccinated with the Bacillus Calmette-Guérin (BCG) vaccine **[9]**. In the early 20th century, North America and Western Europe experienced incidence rates of Tuberculosis (TB) similar to those currently observed in low- and middle-income countries with a very high burden of Tuberculosis. However, some countries in these regions have consistently documented significant reductions in TB case rates for over a century. It indicates that successful TB control and prevention efforts have substantially improved these regions, resulting in lower TB incidence rates over time **[38]**.

By increasing the percentage of cases confirmed bacteriologically, countries can enhance the accuracy of TB diagnoses, improve patient management, and enable appropriate treatment initiation. This, in turn, contributes to more effective TB control efforts, reduced transmission rates, and better patient outcomes **[27]**. WHO recommends expanded access to all-oral regimens for treating Tuberculosis (TB), accompanied by counseling and monitoring for adverse events. All-oral regimens refer to treatment regimens consisting of only oral medications without injectable drugs **[39]**.

CONCLUSION

Knowing that efforts are being made to fulfill the objectives for the treatment and prevention of TB set by the WHO member countries is energizing, and the National TB Elimination Programme of India is showing promise.

However, it is crucial to continue efforts to ensure that all people needing treatment and preventive care for TB can obtain it, especially those with MDR/RR-TB. It is encouraging to see that the target for treating people living with HIV has been met, but more efforts are needed to ensure that all people living with HIV who are also affected by TB receive the care they need. Despite TB prevalence, incidence, and mortality decreasing over the last decade, eliminating tuberculosis worldwide is still far from the impactful resources and milestones, and efforts at the governing level are still required. A dependable surveillance system is also necessary to monitor the epidemic's development and evaluate how well disease control strategies are being implemented. Without such a framework, TB management would be challenging. Another challenge is that progress has been deccelerated, paused, or reversed in the years prior to 2019, and global TB objectives are still not being met.

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