Original Article

Temporal pattern and effect of COVID-19 on the trend of TB, DRTB, paediatrics TB and TB with HIV Coinfection: A decadal trend analysis

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Abstract

Background: India shares 2/3 of global TB burden. MDR and HIV coinfections are the main obstacle in achieving the successful TB control because it decrease the therapy effect. **Objective:** To analyze the long-term trends of incidence of tuberculosis cases and identify any differences between actual and projected cases after the COVID-19 pandemic. **Methodology:** A retrolective study was conducted in SMS medical college, Jaipur, and data were extracted from state TB cell and annual report published by central TB division. A multiplicative model was used for conducting time series analysis. The projected yearly number of cases were estimated using the line of best fit based on the least square method. **Result:** An increasing trend in the incidence of TB was observed, rising from 1,517,363 in 2008 to 2,404,815 in 2019. Similarly, DRTB also showed an increasing trend from 10,267 (0.67% of total new cases) in 2011 to 66,255 (2.75%) in 2019. The new cases of DRTB in 2020 were significantly lower than the projected number. The trend of HIV coinfection in TB cases fluctuated over the past decade. **Conclusion:** The findings reveal a concerning upward trajectory in TB incidence and DRTB cases over the decade. The fluctuating trend in HIV coinfection in TB cases emphasizes the complexity of addressing these interconnected health challenges.

Keywords: COVID-19, DRTB, paediatrics TB, TB, TB with HIV coinfection

Introduction

Tuberculosis (TB) remains a significant global public health concern, especially among vulnerable populations such as paediatric patients and those affected by drug-resistant strains and HIV coinfection.[1] Although tuberculosis is a preventable and curable disease, it constitutes a major proportion of health expenditure in developing countries.[2] Nevertheless, it remains the leading cause of death worldwide from infectious diseases, particularly in the context of HIV/AIDS.

According to the World Health Organization (WHO), more than 10 million people were suffering with tuberculosis disease; among them, 1.3 million died in 2021–22; 167,000 of them were infected with HIV.[3] On the other hand, COVID-19 pandemic has substantially reduced access to services for the diagnosis and treatment of tuberculosis, resulting in an increase in deaths due to tuberculosis, and a reversal in global progress.[4]

Similarly, the tuberculosis remains the leading cause of death among people living with HIV. It is estimated that in countries with

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high HIV prevalence, the risk of contracting HIV tuberculosis increases 20-fold compared to HIV seronegative people (World Health Organization, 2013). In 2019, TB accounted for an estimated 30% of the 690 000 AIDS-related deaths in the world. These 208 000 deaths represented approximately 15% of the 1.4 million TB deaths that year.[5]

India is the largest victim of tuberculosis in the world, with an estimated 2.5 million people suffering from it and 3.5 lakh deaths annually. Furthermore, about 38,000 TB patients also suffer from HIV infection.[6]

Paediatric TB poses unique challenges due to its distinct clinical manifestations, difficulties in diagnosis, and limited treatment options tailored for children. In addition, the emergence of drug-resistant strains of Mycobacterium tuberculosis complicates the landscape of TB control efforts.[7]

Since the launch of the first National Tuberculosis Control Programme in India in 1962, tuberculosis has remained a significant public health challenge. Primary objective of the study was to offer in-depth insights into the recent trends of tuberculosis incidence, drug resistance, HIV coinfection, and paediatric TB in India from 1990 to 2022. The secondary objective was to find out any difference between actual and projected cases of DRTB after the COVID-19 pandemic.

Material and Methods

Study design

A retrolactive record-based, descriptive type of observation study was conducted under the department of preventive and social medicine (PSM), Sawai Man Singh Medical College, Jaipur, Rajasthan.

Data collection and analysis

Year-wise data of TB were extracted from the state TB cell and annual report published by central TB division, India. Data from 2000 to 2022 were reviewed.

The data sets of yearly number of new cases of TB, DRTB, paediatric TB, and TB with HIV coinfection were divided into two segments. The data spanning from 2000 to 2022 were used to analyse long-term trends and forecasting of cases. In addition, projections for the yearly cases from 2020 to 2021 were made based on previous data to see the effect of COVID-19 pandemic on the trend of tuberculosis. The projected monthly number of cases from 2020 to 2021 was then compared with the actual number of cases during the same period, and the chi square test was applied to see if there was any significant difference between the actual and projected number of cases.

Data were entered into Microsoft Excel 2019, and the multiplicative model was used for conducting time series analysis. The projected number of cases for the period 2020 to 2022 was estimated using the line of best fit based on the least square method. Linear regression analysis was used to determine the magnitude of time trends in incidence rates. The equation of a straight line is typically represented as $y = mx + b$, where m is the slope, b is the y-intercept, and x is the independent variable. As individual data were not included in the study, ethical permission was not required.

Results

The temporal pattern of tuberculosis (TB) incidence per lakh indicates an upward trajectory from 2000 to 2022. However, during the surge of COVID-19 or the pandemic, the incidence of TB cases showed a significant dip (*P* value <0.05) as compared to expected cases. The yearly projection of TB incidence up to 2026 has been made using the least square method, and the trend of TB incidence over the period is depicted in Figure 1.

Similarly, the trend of drug-resistant TB (DRTB) cases and the proportion of DRTB among total cases of TB show an upward trajectory. The trends over the periods are depicted in Figures 2 and 3, respectively. The difference between observe cases and expected cases was not statistically significant (*P* value >0.05) during the period of COVID-19 pandemic.

Instances of HIV coinfection exhibited diverse trends from 2010 to 2022, with a decrease observed from 2014 to 2016, followed by an increase in 2016 and 2017. However, a subsequent decline occurred after reaching its peak in 2018. Furthermore, the number of cases during the COVID-19 period showed a significant decrease (*P* value < 0.05) compared to the expected cases [Figure 4].

The proportion of HIV coinfection among total TB cases was decreased over the period [Figure 5].

Similar to the incidence of TB cases, the number of paediatric TB cases shows an upward trend [Figure 6], while the proportion of paediatric cases relative to the total TB cases remains relatively stable over the observed period, as depicted in Figure 7. However, a sharp dip was observed in the period of 2020–2021, attributed to the COVID-19 pandemic.

Discussion

This study uses the report published by central TB division to analyse the incidence of Tuberculosis, Drug resistant TB, paediatric TB, and Tb HIV coinfection in the period from 2000–2022 in India.

According to the WHO 2019 Global TB report,[8] around the world, TB mortality was down about 3% every year, the incidence was down about 2% every year, and 16% of TB patients died of the disease. However, the rate of decline has not reached the pace of the 'stop TB Strategy Plan'. Therefore, it is necessary to strengthen the prevention and control of TB.

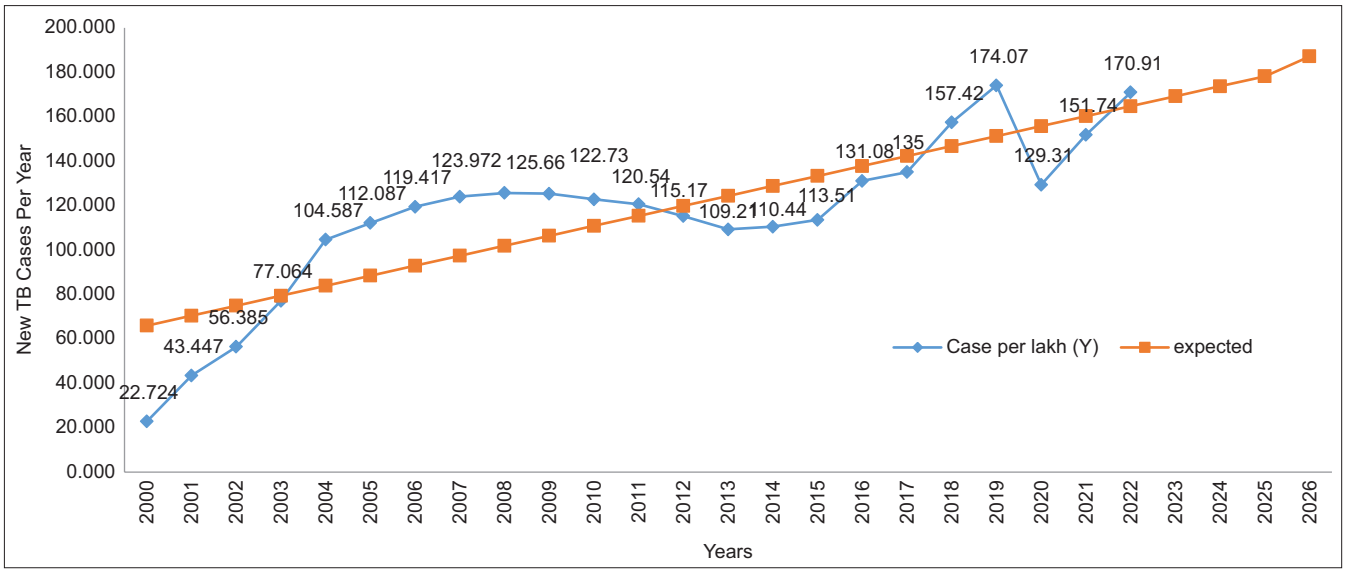

Figure 1: Trends of annual new cases of TB

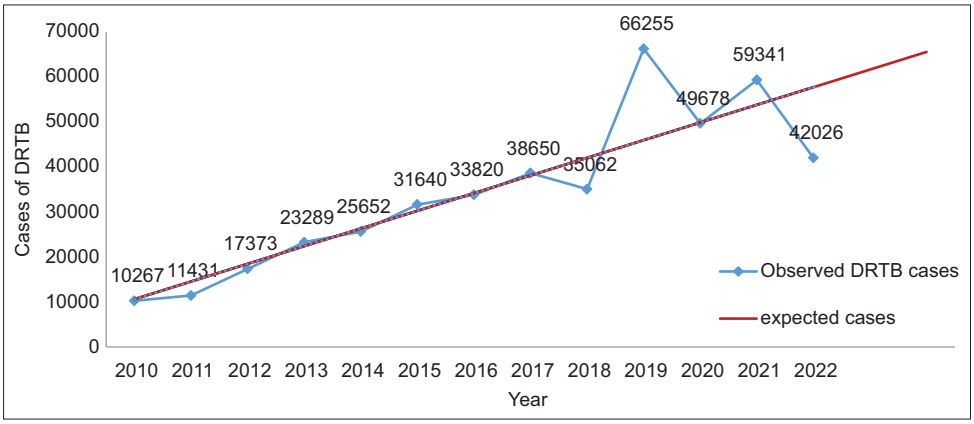

Figure 2: Trends of cases of DRTB (Observed Vs Expected cases)

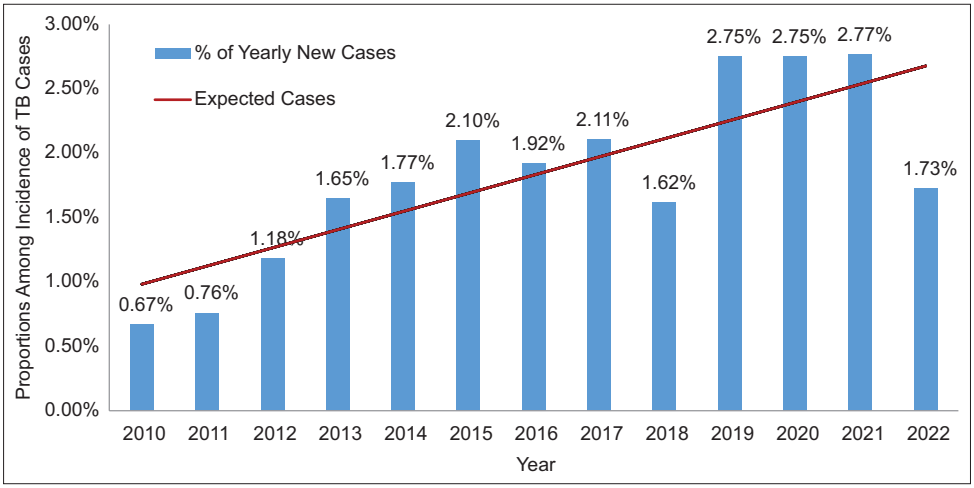

Figure 3: Trends of DR TB (% of incidence)

In our study, we observed a consistent increase in the number of TB cases per lakh of the population over the studied period. However, findings from Study of Dhamnetiya D. *et al.*[9] indicate an overall decline in the mortality rate, dropping from 122 deaths per 100,000 to 36 per 100,000 during the years 1990–2019. Their study aligns with our observations,

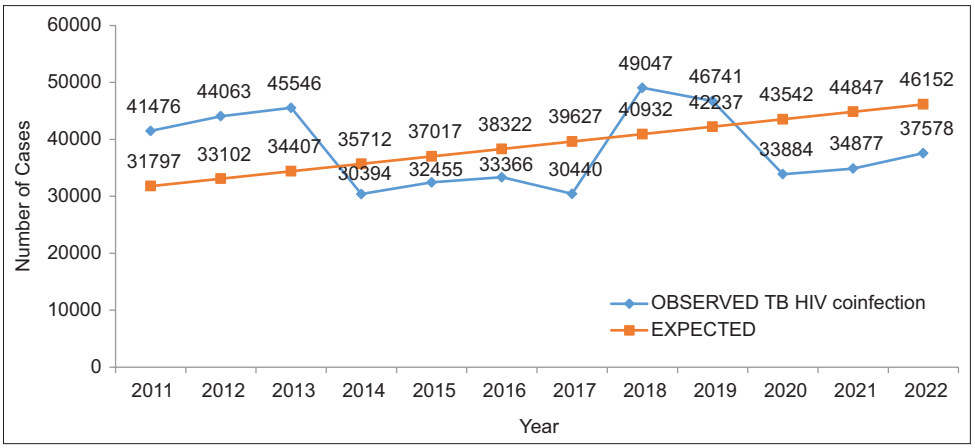

Figure 4: Trends of Tb HIV Co-infection

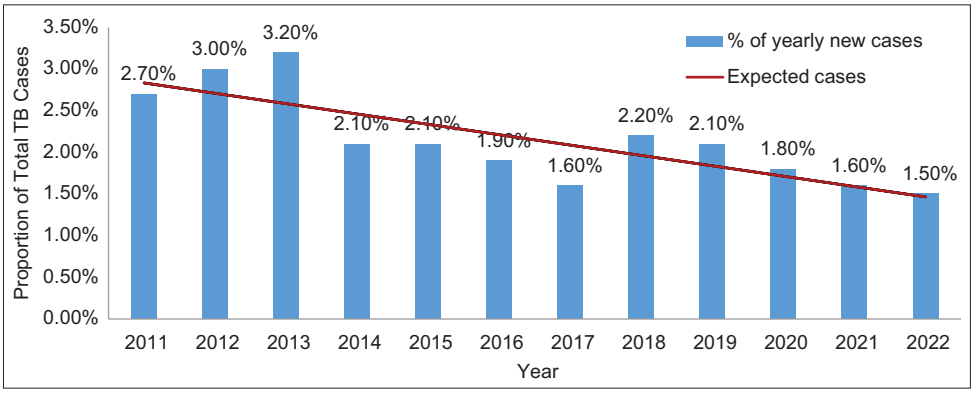

Figure 5: HIV co-infection (% of yearly new cases)

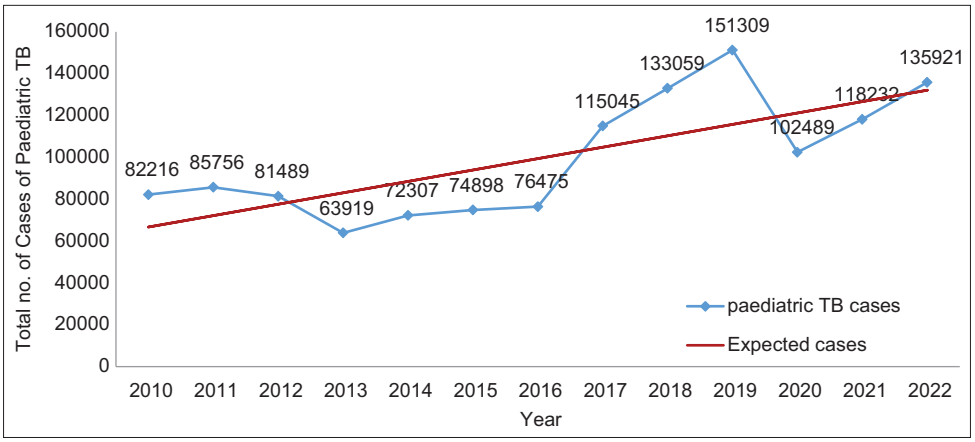

Figure 6: Trends of paediatric TB cases (Observed Vs expected cases)

highlighting a similar incidence trend of TB in India between 1990 and 2019.

Similarly, the annual report published by the World Health Organization reveals an increasing trend of TB in Pakistan over the period. When comparing this trend to that of Vietnam, the second National TB Prevalence Survey report (Nguyen HV *et al.*)[10] suggests no significant change in the burden over the 10-year period (from 307 in 2006–07 to 322 in 2017–18). However, it is noteworthy that the second survey in Vietnam used TB screening procedures and diagnostics recommended by the WHO, which were state-of-the-art in 2017–2018 but were not available during the initial survey in 2006–2007.[11] Similarly, in the study of Zheng Y *et al.*[12] in China, nonsignificant decline of incidence of TB cases in China was also concluded.

Despite the challenges mentioned earlier, countries like Sri Lanka have made significant strides in this field. They have significantly

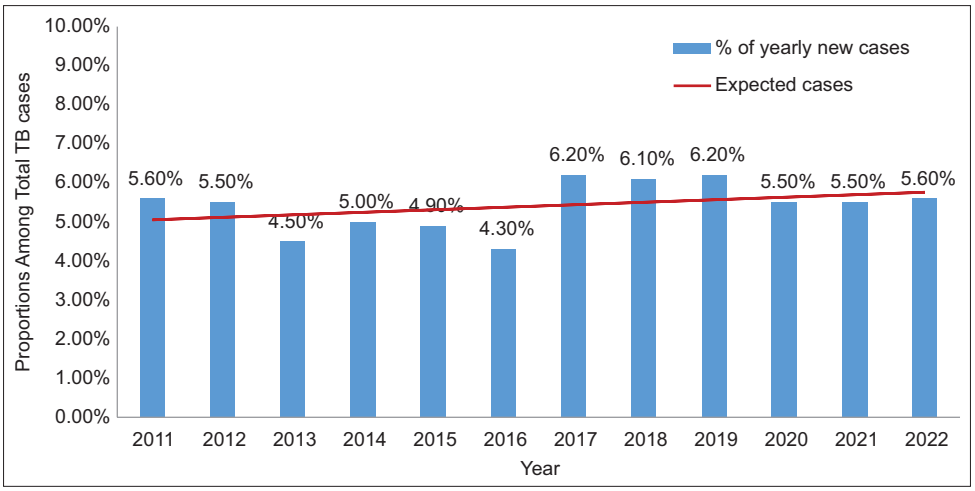

Figure 7: Paediatric TB (% of yearly new cases)

reduced the incidence rate of TB from 49 per 100,000 population in 2010 to 38.4 per 100,000 population in 2019. This achievement is reported in the review published by the Epidemiological Review of Tuberculosis Surveillance System in 2020.[13] However, countries like Singapore, United Kingdom, and United States show declining trend over decade in incidence of TB cases, but the decline was not significant.[14,15]

The rise in TB incidence in countries such as India, Pakistan, and Vietnam can be attributed to a complex interplay of social, economic, and healthcare factors. The emergence of drug-resistant TB strains adds a significant challenge to treatment efforts. In addition, the increased number of reported cases might reflect improved and more accessible reporting mechanisms rather than a sole increase in actual incidence. Understanding these multifaceted factors is crucial for devising comprehensive strategies to address and control TB in these regions.

In our study, we observed a rising trend in incidence of drug-resistant tuberculosis (DR-TB) cases, with the increasing relative proportion annually from 1.16% in 2010 to 1.76% in 2022. However, according to the WHO report in 2022,[3] the global proportion of DRTB cases was 3.4%, showing a gradual decrease from approximately 4% in 2015 to 3.4% in 2022.

A retrospective analysis by Lecai J *et al.*[16] in Shenzhen, China, also confirmed an upward trend of DRTB from 6.8% in 2012 to 7.5% in 2020. Despite the low incidence of tuberculosis (TB) cases in the United States, the proportion of drug-resistant TB (DRTB) cases is higher than in India, constituting approximately 8.4% of total TB cases. This proportion has remained relatively steady over the period from 1993 to 2020, fluctuating between 7.3% and 9.7%.[17]

The increasing incidence of DRTB in India can be attributed to several interconnected factors. The primary driver is the inconsistent or improper use of anti-TB medications, dropouts, and poor drug compliance. When patients do not adhere to the prescribed regimen or fail to complete the full course of medication, the bacteria can develop resistance to the drugs. Nonadherence often results from challenges such as limited access to healthcare facilities, insufficient education about the importance of completing the treatment, side effects, long duration of treatment course, and socioeconomic factors that impede patients' ability to follow through with the prescribed regimen.

Inadequate diagnostic practices and delayed detection also play a significant role in the rise of DRTB. Limited access to rapid and accurate diagnostic tools, coupled with delays in identifying drug-resistant strains, hinders timely intervention and appropriate management.[18] In addition, the widespread and sometimes indiscriminate use of antibiotics in various healthcare settings contributes to the emergence of drug-resistant strains.

Globally, 6.3% of incident tuberculosis cases in 2022 occurred among individuals living with HIV.[19] In India, this proportion was 1.5%, while compare with neighbouring developing countries like China reported 6%,[20] Vietnam 2.5%,[21] and Sri Lanka 0.6%.[22] These variations highlight the diverse rates of tuberculosis and HIV coinfection globally, underscoring the need for tailored strategies in different regions.

Based on our trend observation, the proportion of HIV coinfection in India has been decreasing over the period, declining from 2.5% to 1.5% between 2011 and 2022. A similar pattern is observed in the African Region from 2010 to 2022. However, a relatively steady pattern is being observed in the European and Americas regions.[3]

The study conducted in Russia by Yerramsetti S. *et al.* in 2022,[23] reporting a similar trend of new pediatric TB cases and a proportion that remains steady, contributes to the global understanding of pediatric TB dynamics. Comparing trends across different countries, such as India and Russia, can provide insights into common challenges or factors influencing the prevalence of pediatric TB.

In India, the proportion of paediatric TB is steady over the period from 2011 to 2022 (5.6%). This indicates a consistent prevalence

of paediatric TB during this timeframe, and understanding the factors contributing to this stability is crucial for effective disease management and prevention. Similar pattern is being observed in the region of America and Africa. However, it shows that upward trend is observed in the western and south Asia pacific.[3]

Globally, progress in reducing TB incidence varies widely. Eight-three countries, mainly in WHO's African and European regions, achieved a minimum 20% reduction from 2015 to 2022, meeting the 2020 End TB Strategy milestone. Twenty one nations, including South Africa, saw reductions exceeding 50%. Conversely, some countries, particularly in the America and Asia (Indonesia, Mongolia, Myanmar, India, and the Philippines), experienced more than a 5% increase in TB incidence in 2022 compared to 2015. The disparities highlight the diverse trajectories in combating TB across nations.[3]

End TB strategy goal and achievement

In line with the objectives of the END TB strategy, there is a mandate for an annual reduction of 10% in global tuberculosis incidence rates by 2025. Simultaneously, the projected case–fatality ratio for individuals with TB must decrease from 15% in 2015 to 6.5% by the same year. Achieving these reductions in both mortality and incidence by 2025 poses challenges. In addition to the aforementioned considerations, it is noteworthy that the incidence of TB cases in India has experienced an upward trend, escalating from 113 per lakh to 170.91 per lakh from 2015 to 2022. Conversely, mortality rates in the same context are on a declining trajectory at a rate of 15 to 18% per annum.

Conclusion

Despite notable advancements in the diagnosis and treatment of drug-resistant tuberculosis (TB) over the past 25 years, efforts in India to eliminate TB face significant challenges. The current progress falls short of the targets set in the national strategic plan for 2017–2025, aiming for an 80% reduction in TB incidence by 2030, and the End TB Target of the SDG for 2030, which aims for a 90% reduction. The emergence of multidrug-resistant TB (MDR-TB) poses a considerable hurdle.

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Conflicts of interest

There are no conflicts of interest.

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