KEY DRIVERS OF HIGH TB BURDEN IN TOP 10 COUNTRIES: A SYSTEMATIC REVIEW

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ABSTRACT

Tuberculosis (TB) is the second leading cause of death from infectious diseases globally, with 10.6 million cases and 1.3 million deaths, largely concentrated in India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, the Democratic Republic of the Congo, South Africa, and Myanmar, in 2022.This study aimed to identify key socioeconomic and environmental factors, assess TB-related healthcare and policies, and examine the impact of the COVID-19 pandemic in these countries. A systematic review was conducted by searching major databases for studies related to the key drivers of high TB burden. After screening 3,660 studies, 62 relevant papers were analyzed for inclusion in this review.Thematic analysis was employed to systematically identify, analyze, and interpret patterns within the data extracted from the selected studies. This approach enabled the categorization of key drivers and contextual factors contributing to the high TB burden, facilitating a comprehensive understanding of recurring themes across different settings.The review found that factors such as income loss, financial hardship, high out-of-pocket healthcare costs, and regional economic disparities significantly contribute to the TB burden, with comorbidities and poor sociodemographic conditions amplifying these challenges. Insufficient healthcare infrastructure, staffing shortages, and heavy reliance on external funding further weaken TB control efforts. Additionally, delayed diagnosis, limited access to quality healthcare services, stigma associated with TB, and low awareness about disease prevention were frequently identified as barriers. Political instability, population displacement, and gaps in treatment adherence also play critical roles in sustaining high TB rates in these countries.These findings can inform the development and implementation of integrated healthcare strategies, improvements in living conditions, and targeted interventions aimed at effectively reducing TB rates and addressing dual health burdens in high-prevalence settings.

KEYWORDS

Tuberculosis, Top Ten TB Burden Countries, Drivers of High TB Burden, After 2015

1. INTRODUCTION

Tuberculosis (TB), a highly contagious airborne disease, continues to pose a major public health challenge globally. In 2022, TB ranked as the second leading cause of death from infectious diseases worldwide, following only COVID-19. It remains the foremost cause of mortality among people living with HIV and is a significant contributor to deaths associated with antimicrobial resistance. During this period, it was estimated that 10.6 million individuals contracted TB worldwide, with men constituting 5.8 million cases, women 3.5 million, and children 1.3 million. Moreover, people living with HIV accounted for 6.3% of the total TB cases. Alarmingly, the TB incidence rate increased by 3.9% between 2020 and 2022, reversing the previous trend of a 2% annual decline over the past two decades. In total, TB was responsible for approximately 1.3 million deaths globally in 2022, including 167,000 among people living with HIV. Although this number represents a decrease from the estimated 1.4 million deaths recorded in 2020 and 2021, it is still close to the levels reported in 2019. Notably, the burden of TB remains overwhelmingly concentrated in ten countries: India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, the Democratic Republic of the Congo, South Africa, and Myanmar. The demographic data of these countries underscore their diversity and the unique challenges they face in TB control [1].

Population size and density are critical factors influencing TB transmission and management strategies in these high-burden countries. India, with a population of 1.417 billion and a high density of 473.42 individuals per square kilometre, faces significant risks of TB transmission in its densely populated regions. China, with the most populous country at 1.426 billion, has a lower density of 150.44 individuals per square kilometre, posing distinct

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epidemiological challenges. Likewise, Indonesia (275.5 million people, 144.65 people/km²), the Philippines (115.6 million, 381.98 people/km²), and Pakistan (235.8 million, 300.18 people/km²) must grapple with the dual challenges of large populations and substantial population densities. Nigeria (218.5 million, 234.31 people/km²) and Bangladesh (171.2 million, 1301.14 people/km²) exhibit high transmission potential due to both their population size and density. Meanwhile, the Democratic Republic of the Congo, with a smaller population of 5.97 million and a density of 42.3 people per square kilometre, faces unique challenges related to healthcare access. South Africa (59.9 million, 48.96 people/km²) and Myanmar (54.2 million, 82.43 people/km²) also confront moderate challenges associated with population distribution. These disparities underscore the necessity for country-specific and contextually tailored TB control strategies [1].

The distribution of TB cases is not uniform across these countries. India bears the highest proportion, accounting for 27% of global cases, which is significantly greater than Indonesia's 10%. China follows with 7.1%, closely trailed by the Philippines at 7%. Pakistan contributes 5.7%, while Nigeria reports 4.5%. Bangladesh adds 3.6%, and both the Democratic Republic of the Congo and South Africa account for 3% each. Myanmar has the lowest share among these countries at 1.91% [1]. Over the past decade, TB incidence rates have displayed varying trends. Globally, the TB incidence rate decreased from 163 per 100,000 in 2010 to 128 in 2020, but rose slightly to 133 in 2022. India mirrored this trend, with a decline from 276 per 100,000 in 2010 to 197 in 2020, and a marginal increase to 199 in 2022. Indonesia experienced notable fluctuations, with a peak in 2018, a drop in 2020, and a sharp rise to 257 in 2022. In contrast, China consistently reduced its incidence from 76 in 2010 to 52 in 2022. The Philippines saw a steady increase, reaching 638 in 2022. Pakistan's rates declined gradually, with a slight increase to 258 in 2022. Nigeria and Bangladesh exhibited stable rates around 219 and 221, respectively, while the Democratic Republic of the Congo's incidence fell modestly from 386 in 2010 to 369 in 2022. South Africa achieved a substantial reduction from 1,234 to 468 over the period, while Myanmar experienced fluctuations, including a resurgence to 475 in 2022 [2].

Despite various efforts, the ten countries face significant challenges in reaching the TB control targets set by the Global Plan 2023–2030. According to the WHO, these nations are encountering substantial obstacles in reducing TB incidence and deaths relative to 2015 benchmarks (UNOPS, 2023). Some countries, such as India and China, have made considerable progress, but still have considerable gaps to bridge before meeting their targets. Others, notably Indonesia and the Philippines, have seen setbacks, with incidence and mortality rates trending away from their intended goals. Such disparities reflect not only differences in the pace of public health advancements but also highlight the pressing need for intensified and targeted approaches tailored to each country's epidemiological and socioeconomic context [3].

Beyond epidemiological trends, the economic and health system characteristics of these countries significantly affect their ability to control TB. India and China, given their large populations, stand to benefit most from public health improvements, but they also face enormous challenges in resource allocation and service delivery. Economic disparities are pronounced, with China demonstrating robust health investment and low poverty rates, while Nigeria, the Democratic Republic of the Congo, and Myanmar continue to struggle with high poverty and limited healthcare expenditure. The impact of COVID-19 has further complicated TB control, with China and India recording the highest case numbers among these ten nations, and Nigeria having the lowest. Another crucial component is BCG vaccination coverage, which ranges widely: China and Bangladesh maintain consistently high rates, while the Philippines, Congo, and other countries experience significant fluctuations. This variability in vaccination underscores the ongoing need for sustained and targeted immunization programs [2,3].

TB remains a leading cause of death in many of these high-burden countries, with India, Indonesia, Nigeria, Myanmar, and the Democratic Republic of the Congo ranking TB among the most common causes of mortality. The fight against TB is further complicated by the high prevalence of HIV-associated TB and multidrug-resistant TB (MDR-TB), particularly in South Africa, India, and Nigeria, which face substantial burdens of HIV-positive TB cases and related mortality. India, China, the Philippines, and Indonesia also report the highest numbers of MDR-TB cases. Trends in TB notifications indicate both progress and ongoing challenges: while countries such as China and South Africa have succeeded in reducing incidence and deaths, others like Indonesia, the Philippines, and Myanmar have experienced increases that jeopardize progress toward the 2030 targets [2,3]. Treatment coverage and success rates vary as well, with some nations excelling in pediatric or adult coverage, and others requiring intensified interventions. Financing for TB control also differs, with some countries primarily relying on domestic resources, while others depend on international assistance [3].

Given these complex and intersecting challenges, there is an urgent need for a systematic review to identify and analyze the key drivers of the high TB burden in these countries. Socioeconomic determinants, such as poverty, inadequate living conditions, and income inequality, significantly fuel TB transmission and progression. It is also essential to assess health system factors, including infrastructure, healthcare workforce, and access to diagnostic and treatment services, to uncover existing gaps. Evaluating the effectiveness of public health policies, including vaccination and preventive therapy coverage, will help determine the most impactful strategies. Additionally, biological and environmental factors, such as HIV prevalence, MDR-TB, and overcrowding, must be considered. Cultural attitudes and health-seeking behaviors also influence diagnosis and treatment adherence, making it necessary to tailor interventions to diverse populations. Finally, the impact of global events such as the COVID-19 pandemic must be analyzed to strengthen the resilience of TB control programs. By systematically reviewing and synthesizing the existing literature, this study aims to provide a comprehensive understanding of the factors contributing to high TB incidence and mortality in these settings. The insights gained will inform the development of more targeted and effective interventions, supporting these countries in achieving the Global Plan 2023–2030 targets for TB control.

This study is organized into several key sections to ensure a comprehensive and systematic presentation of the research findings. The abstract provides a concise summary of the study's objectives, methodology, main findings, and implications, accompanied by a set of relevant keywords to facilitate indexing and retrieval. The introduction outlines the background, context, and significance of the research, highlighting the global and regional burden of tuberculosis (TB) and the rationale for the systematic review. The materials and methods section details the systematic review protocol, including the literature search strategy, inclusion and exclusion criteria, data extraction, and analytical approach. The results section presents the main findings, focusing on the key drivers of high TB burden in the top ten affected countries. This is followed by the discussion, which interprets the results in the context of existing literature, explores the implications for policy and practice, and suggests areas for future research. The limitations section acknowledges the constraints and potential biases of the study, providing context for the interpretation of findings. Lastly, the references section lists all sources cited throughout the study, ensuring transparency and enabling readers to consult the original literature.

2. MATERIAL AND METHOD

This study utilized a systematic review design to comprehensively examine the factors underlying the high tuberculosis (TB) burden in the top ten countries with the mostnew TB cases in 2022. The primary research question focused on identifying socioeconomic, environmental, healthcare, and policy-related contributors to TB incidence and understanding how these elements interact. The review was grounded in established frameworks using clear inclusion criteria to ensure validity and reproducibility; studies included adults of all genders, TB patients and healthcare providers, those with TB and common comorbidities, all ethnicities, and a range of healthcare settings in the ten high-burden countries. Both quantitative and qualitative primary studies (with mixed methods as well) published in English after 2015, with a minimum sample size of 50, low attrition rates, and peer-reviewed, full-text accessibility were selected to ensure methodological rigour. Exclusion criteria eliminated grey literature and non-purchased articles to improve reliability. Key outcomes measured included socioeconomic and environmental factors, healthcare system weaknesses, policy issues, and the impact of global events such as COVID-19 on TB control efforts. The literature search, conducted independently by multiple reviewers, covered databases such as PubMed, Google Scholar, and ResearchGate, using a combination of predefined core and related search terms with Boolean operators to maximize comprehensive coverage. Study selection followed PRISMA guidelines, with independent screening of titles, abstracts, and full-texts to minimize bias.The selection of eligible papers for this systematic review followed a rigorous and transparent process. An initial search was conducted across three major databases: PubMed (n = 1,011), Google Scholar (n = 1,668), and ResearchGate (n = 981), yielding a total of 3,660 records. Before screening, 772 duplicate records were removed, while automation tools did not mark any records as ineligible, and a further 69 were excluded for other reasons, resulting in 773 unique records for screening. During the screening phase, 209 records were excluded based on their titles and abstracts, leaving 564 reports for full-text assessment. Of these, 502 reports were excluded due to reasons such as irrelevant population (n = 101), publication date outside the inclusion period (n = 201), language barriers (n = 6), study design incompatibility (n = 66), methodological issues (n = 51), non-human studies (n = 12), inadequate outcome data (n = 33), geographical mismatch (n = 17), and insufficient details (n = 15). Ultimately, 62 studies met all eligibility criteria and were included in the final review, ensuring a robust and focused synthesis of the evidence relevant to the high TB burden in the top ten affected countries (Figure 1).Data extraction captured study characteristics and key variables using a structured template, and both descriptive statistical and manual qualitative analyses were performed. The quantitative data were summarized using measures of central tendency and variability, while qualitative findings were coded deductively and inductively, then grouped into thematic categories such as socioeconomic, environmental, healthcare, and policy factors. The review employed CASP tools for critical appraisal, ensuring that only high-quality, methodologically sound studies informed the synthesis. Throughout, ethical standards were rigorously maintained, with particular attention to participant confidentiality and reviewer transparency regarding conflicts of interest.

3. RESULTS

Selection of Eligible Papers

The following figure (1) is illustrated to show the selection process of the eligible papers for the review analysis.

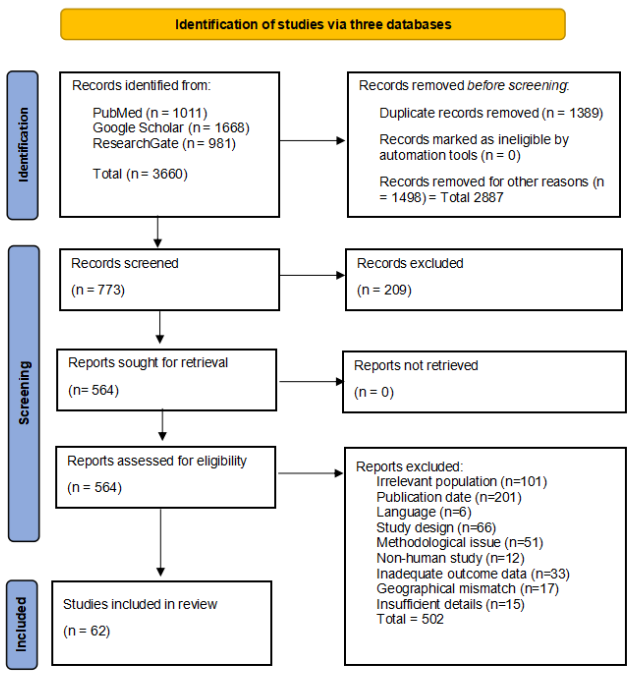

Figure 1. Flow Diagram of Paper Selection Process

Characteristics of Included Studies

Table 1 Summary of the Characteristics of the Included Studies

Characteristics of the Included Studies	Frequency	Percentage
Year of Publication		
2016	3	4.8%
2017	8	12.9%
2018	6	9.7%
2019	5	8.1%
2020	10	16.1%
2021	11	17.7%
2022	9	14.5%
2023	6	9.7%
2024	4	6.5%
Total	**62**	**100.0%**
The Origin of the Study		
India	12	19.4%
China	7	11.3%
Indonesia	14	22.6%
Pakistan	3	4.8%

Nigeria	6	9.7%
Bangladesh	3	4.8%
Philippines	4	6.5%
DR Congo	4	6.5%
South Africa	3	4.8%
Myanmar	6	9.7%
Total	**62**	**100.0%**
Research Design		
A Cross-sectional study	39	62.9%
A Cohort study	10	16.1%
A Longitudinal Analysis Study	1	1.6%
A case-control study	3	4.8%
Time-Series Analysis with Statistical Modeling	1	1.6%
A Qualitative Study	8	12.9%
Total	**62**	**100.0%**
Data Collection Technique		
Patients’ registers and electronic medical records	12	19.4%
Combined interview and patients’ records	9	14.5%
Interview alone	20	32.3%
Interview and Observation	1	1.6%
Patients’ records and blood sample collection	6	9.7%
Self-administering	4	6.5%
Observation and Standardized Patients' Interactions	1	1.6%
Combined observation and patients’ records	2	3.2%
Interview and Discussion	4	6.5%
Interview, observation and measurement.	3	4.8%
Total	**62**	**100.0%**
Focus Area of Study		
Cost burden for Tuberculosis	10	16.1%
Awareness and Perception of Tuberculosis on TB Incidence	6	9.7%
Diabetes Comorbid Conditions on TB incidence	9	14.5%
HIV Comorbid Conditions on TB Incidence	7	11.3%
Environmental impacts on TB incidence	6	9.7%
COVID-19 impacts on TB incidence	6	9.7%
Socioeconomic impacts on TB incidence	7	11.3%
Impacts of health system weakness on TB incidence	5	8.1%
Impacts of TB control policies on TB incidence	6	9.7%
Total	**62**	**100.0%**
Different sizes of Samples		
<= 200	17	27.4
201-400	5	8.1
401-600	3	4.8
601-800	1	1.6
801-1000	11	17.7
>1000	25	40.3
Total	**62**	**100%**

Major Drivers of High TB Burden

Socioeconomic Factors

This review revealed that major socioeconomic factors contributing to the high TB burden encompassed notable income reduction and financial instability, extensive out-of-pocket and catastrophic health expenditures, geographical cost disparities, severe impacts on employment and economic standing, considerable direct and indirect costs, healthcare access and adherence expenses, demographic influences, and coexisting health conditions.

Income Loss and Cost Burden

In Indonesia, both TB and MDR-TB patients saw their median incomes fall to zero, with increased numbers lacking formal income and facing high diagnosis and treatment costs. TB-affected households had median expenses of USD 133, while MDR-TB households faced USD 2,804, causing catastrophic costs, especially for the poor and unemployed. In India, 69% of TB patients incurred pre-treatment costs averaging USD 39.74, higher among younger people, diabetics, and those using private care. In China, median TB care costs ranged from USD 965.5 to USD 1,185.5, with rural, older, divorced, less-educated, uninsured, and low-income patients most affected. In Myanmar, 60% of TB-affected households experienced costs of USD 759, mainly from patient time, food, and medical expenses, with low wealth and MDR-TB as key predictors. Nigeria's DR-TB guidelines led to per-patient costs between USD 9,425 and 18,528, driven by hospitalization and outpatient care. In Congo, 56.5% of TB households faced costs exceeding 20% of annual expenditure, averaging USD 400 for first-line TB and USD 1,224 for drug-resistant TB. In South Africa, average TB expenses were USD 3,430 per patient, rising to USD 4,530 with successful treatment, primarily due to medication and staffing. In the Philippines, TB treatment costs USD 601, with DR-TB five times higher and catastrophic costs affecting 42.4% of households. In Bangladesh, TB and MDR-TB patients faced costs of USD 265 and USD 437, respectively. In Pakistan, patients incurred direct and indirect costs totalling USD 762.05, with 65.3% experiencing catastrophic expenditures.

Table (2) Major Drivers for Experiencing Catastrophic Cost for TB

Major Drivers	**Studies**	**Strength of Association**
Income Quantiles -Poorest (Wealthiest) -Less poor (Wealthiest) -Average (Wealthiest) -Less wealthy (Wealthiest)	-Si Thu Aung et al., 2021[4]	-cOR = 2.36 (1.5-3.7)*** -cOR = 1.86 (1.2-2.9)** -cOR = 1.36 (0.9-2.1) -cOR = 1.06 (0.7-1.6)
	-Kaswa M, *et al*., (2021) [5]	-aOR = 10.14 (6.32–16.27) -aOR = 5.45 (3.48–8.53) -aOR = 3.72 (2.39–5.79) -aOR = 1.85 (1.19–2.87)
- Less wealthy (Wealthiest) -Average (Wealthiest) -Less poor (Wealthiest) -Poorest (Wealthiest)	-Florentino JL, *et al*., (2022) [6]	-aOR = 1.27 (0.90–1.82) -aOR = 1.31 (0.93–1.84) -aOR = 2.41 (1.71–3.43)*** -aOR = 3.85 (2.73–5.46)***
-Poor (Non-poor) -Job loss (No job loss) -Working (non-working) -Employed informal (Formal) -Unemployed (Formal) -Employed (Unemployed)	-Fuady, A., *et al*., (2018) [7] -Van den Hof, S., *et al*., (2016) [8] -Kaswa M, *et al*., (2021) [5] -Florentino JL, *et al*., (2022) [6]	-aOR = 3.68 (1.74–7.78)** -aOR =21.17 (8.31–53.90)*** -aOR = 1.39 (0.94±2.06) -cOR = 1.97 (1.06–3.64) -cOR = 1.55 (0.80–3.02) -aOR = 2.26 (1.74–2.93)***
-Male (Female) - Female (Male)	-Si Thu Aung et al., 2021 [4] -Fuady, A., *et al*., (2018) [7] -Florentino JL, *et al*., (2022)[6] -Van den Hof, S., *et al*., (2016) [8] -Kaswa M, *et al*., (2021) [5]	-OR = 1.06 (0.81, 1.39) -cOR = 1.10 (0.66–1.82) -cOR = 1.09 (0.90–1.32) -cOR = 1.19 (0.86±1.63) -cOR = 1.06 (0.76–1.46)
-Sub-urban (Urban) -Rural (Urban) -Urban (Rural) - Urban (Rural)	-Fuady, A., *et al*., (2018) [7] - Kaswa M, *et al*., (2021) [5] - Florentino JL, *et al*., (2022) [6]	-cOR = 0.54 (0.25–1.19) -cOR = 1.47 (0.69–3.16) -cOR = 0.88 (0.54–1.42) -aOR = 1.37 (1.10–1.71)**
-Intermediate Education (Low) -Higher Education (Low) -Secondary and above (Less than Secondary) -No Education (Some Education)	-Fuady, A., *et al*., (2018) [7] -Van den Hof, S., *et al*., (2016) [8]	-cOR = 0.78 (0.45–1.33) -cOR = 0.60 (0.14–2.51) - aOR = 1.19 (0.79±1.79) -aOR =2.13 (1.18–3.85)

	- Kaswa M, *et al*., (2021) [5]	
-Income-earning job (No)	-Fuady, A., *et al*., (2018) [7]	-aOR = 1.08 (0.40–2.92)
-No Health Insurance (Yes)	-Fuady, A., *et al*., (2018) [7]	-cOR = 1.26 (0.74–2.15)
-Previous TB Treatment (No)	-Fuady, A., *et al*., (2018) [7]	-aOR = 2.86 (1.35–6.05)**
-Private facility (Pubic)	-Fuady, A., *et al*., (2018) [7] -Van den Hof, S., *et al*., (2016) [8]	-cOR = 1.14 (0.68–1.89) -aOR = 17.2 (11.1±26.4)
-Hospitalization (No)	-Fuady, A., *et al*., (2018) [7] -Kaswa M, *et al*., (2021) [5] -Florentino JL, *et al*., (2022) [6]	-cOR = 1.16 (0.56–2.38) -aOR = 21.83 (9.27–51.39) -aOR = 9.47 (4.65–21.01)***
DR-TB (DS-TB)	-Florentino JL, *et al*., (2022) [6] -Kaswa M, *et al*., (2021) [5]	-aOR = 8.27 (5.27–13.28)*** -aOR = 5.10 (3.37–7.74)
-Food Supplement (No)	-Fuady, A., *et al*., (2018) [7]	-cOR = 0.78 (0.5–1.3)
-Adverse effects (No)	-Fuady, A., *et al*., (2018) [7]	-aOR = 1.77 (0.92–3.40)
-HIV Positive (Negative) -HIV Unknown (Negative) -HIV Negative (Positive) -HIV unknown (Positive) -HIV not tested (Positive)	-Si Thu Aung et al., 2021 [4] -Fuady, A., *et al*., (2018) [7] -Van den Hof, S., *et al*., (2016) [8] - Kaswa M, *et al*., (2021) [5]	-OR = 1.18 (0.66, 2.10) -cOR = 0.00 (0.00~) -cOR = 0.46 (0.26–0.82) -cOR = 1.36 (0.67±2.77) -aOR = 0.90 (0.53–1.54) -aOR = 0.76 (0.42–1.40) -aOR = 0.66 (0.19–2.28)
-Diabetes (No)	-Van den Hof, S., *et al*., (2016) [8]	-aOR = 1.63 (1.08±2.44)
-Smear Negative (Positive)	-Van den Hof, S., *et al*., (2016) [8]	-cOR = 1.20 (0.86±1.67)

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses (HIV = human immunodeficiency virus, DR-TB = Drug Resistant Tuberculosis, DS-TB = Drug Sensitive Tuberculosis)

Comorbid Conditions (Diabetes)

TB patients with diabetes consistently faced higher out-of-pocket medical expenses, increasing their financial burden. In India, 48% of those screened for latent TB infection (LTBI) were positive, and diabetes-TB patients were more likely to be male, manual laborers, smokers, alcohol users, and insulin-dependent. In Indonesia, TB incidence was higher in people with diabetes (PLWD) with LTBI. In China, 40.47% of diabetics had LTBI, with low education increasing risk. In the Philippines, 22.6% of TB patients had diabetes, while in Pakistan the rate was 39.6%, with more cases among women. Nigeria reported 9.4%, Bangladesh 19.1% with diabetes and 34.3% with prediabetes, Congo 11.4%, South Africa 52.8%, and Myanmar 11%. Across all countries, the co-existence of TB and diabetes led to pronounced financial hardship.

Table (3) Major Drivers for Comorbidity of Diabetes among Tuberculosis Patients

Major Drivers	Studies	Strength of Association
- Age > 40 years (> 40 years) - Age ≥ 60 years (< 60 years) - Age 41-64 years (18-40 years) - Age ≥ 65 years (18-40 years)	-Ekeke, N., *et al.,* (2017) [9] -Rajaa S, et al. (2021) [10] -Cox SE, *et al*. (2021) [11]	- aOR = 2.8 (2.1–3.9) - aPR = 1.13 (0.86 -1.48) - aOR = 2.58 (1.61- 4.14) - aOR = 2.51 (1.31–4.81)
- Female (Male) - Male (Female)	- Kyaw Soe, *et al*. (2020) [12] - Rajaa S, et al. (2021) [10]	- aRR = 1.05 (0.96–1.15) - aPR = 1.18 (0.89 - 1.57)
- Primary Education (No Formal Education) - Secondary Education (No Formal Education) - Higher Education (No Formal Education)	- Rajaa S, et al. (2021) [10]	- aPR = 1.04 (0.72 - 1.51) - aPR = 1.18 (0.84 - 1.65)
- Rural residence (Urban)	-Ekeke, N., *et al.,* (2017) [9]	- aOR = 2.3 (1.6–3.2)
- Currently married (Never married) - Widowed/Separated/Divorced (Never married)	- Rajaa S, et al. (2021) [10]	- aPR = 3.77 (2.20 - 6.49)*** - aPR = 3.66 (1.96 - 6.83)***

- Currently married (Never married) - Separated/Divorced (Never married) - Widowed (Never married)	- Cox SE, *et al*. (2021) [11]	- aOR = 2.09 (1.31–3.31) - aOR = 0.75 (0.23–2.48) - aOR = 0.85 (0.40–1.84)
- Private Facility (Public)	-Ekeke, N., *et al.,* (2017) [9]	- aOR = 2.0 (1.4–2.7)
- Vigorous Occupation (Non-vigorous) - Employed (Unemployed) - Unemployed (Employed)	-Ekeke, N., *et al.,* (2017) [9] -Rajaa S, et al. (2021) [10] -Kakisingi, C., et al. (2024) [12]	- aOR = 0.6 (0.4–0.9) - cPR = 1.16 (0.83 - 1.62) - aOR = 0.314 (0.102–0.968)
TB incidence among - PLWD with baseline LTBI - PLWD without baseline LTBI	-McAllister SM, et al., (2020) [13]	- 17.13 (5.25-29.00/1000 person-years) - 4.79 (0.63-10.21/1000 person-years)
-Smear Positive (Negative) -Not Recorded (Negative)	- Kyaw Soe, *et al*. (2020) [14]	-aRR = 0.90 (0.74–1.08) -aRR = 1.21(0.72–2.03)
GeneXpert at Diagnosis ("MTB not detected" as Reference) -MTB detected Rifampicin Sensitive -MTB detected Rifampicin Resistant -Not recorded -MDR-TB (DS-TB)	- Kyaw Soe, *et al*. (2020) [14] - Cox SE, et al. (2021) [11]	-aRR = 0.97 (0.86–1.10) -aRR = 1.62 (1.07– 2.46)* -aRR = 0.86 (0.52–1.41) -aOR = 2.48 (1.55–3.95)
("HIV Negative" as Reference) -HIV positive and on CPT and ART -HIV positive and not on either CPT and/or ART -HIV unknown/not recorded	- Kyaw Soe, *et al*. (2020) [14]	 -aRR = 0.92 (0.75–1.130) -aRR = 1.27 (0.88–1.83) -aRR = 1.45 (0.80–2.62)
-Alcohol Use (No Alcohol Use)	- Rajaa S, et al. (2021) [10]	-cPR = 0.96 (0.79 to 1.15)
-Normal (Underweight) -Over weight (Underweight) -Obesity (Underweight) -Underweight (Normal) -Over weight/Obese (Normal) - Underweight (Normal)	- Rajaa S, et al. (2021) [10] - Cox SE, *et al*. (2021) [11] - Kakisingi, C., et al. (2024) [12]	-aPR = 3.26 (2.55 to 4.16)*** -aPR = 3.86 (2.69 to 5.52)*** -aPR = 4.08 (2.81 to 5.94)*** -aOR = 0.50 (0.33–0.75) -aOR = 1.53 (0.83–2.82) -aOR = 7.484 (2.684–20.865)

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses. (DM = diabetes mellitus, TB = tuberculosis, MTB = mycobacterium tuberculosis, AFB = acid fast bacilli, DS-TB = Drug Sensitive Tuberculosis, MDR-TB = Multidrug Resistance TB, HIV = human immunodeficiency virus, ART = anti-retro viral treatment, CPT = cotrimoxazole prophylaxis therapy, PLWD = People living with Diabetes)

Comorbid Conditions (HIV)

The overlap of HIV and tuberculosis (TB) significantly increased the TB burden across countries. In India, multidrug-resistant TB (MDR-TB) was 12.5%, with higher rates in relapsed patients (23.1%) compared to new cases (8.8%); TB relapse was a major contributor to MDR-TB and drug resistance. In Indonesia, HIV prevalence among TB patients ranged from 5.1% to 11.5%. China saw an increase in HIV among TB patients from 0.8% in 2015 to 1.1% in 2019. In the Philippines, HIV-positive MDR-TB cases rose sharply from 0.5% in 2011 to 15% in 2015. Pakistan showed higher HIV prevalence in extra-pulmonary TB among males. Nigeria reported HIV among TB patients at 13.1–26.7%, while Bangladesh had just 0.1%. In Myanmar, previously treated TB patients had a high HIV prevalence of 28.2%.

Table (4) Major Drivers for Comorbidity of Tuberculosis among PLHIV

Studies	Major Drivers	Outcomes	Strength of Association
- Kashongwe,M., et al. (2017) [15]	- Age 31–60 years (<30 years) - Age > 60 years (<30 years)	-DRTB -MDRTB -RRTB -INH mono-resistance -DRTB -MDRTB -RRTB -INH mono-resistance	- aOR = 1.0 (0.2–4.3) - aOR = 0.4 (0.1–4.5) - aOR = 0.3 (0.1–2.9) - aOR = 1.4 (0.3–6.0) - aOR = 1.2 (0.3–4.4) - aOR = 0.4 (0.1–3.9) - aOR = 0.4 (0.1–3.3) - aOR = 1.4 (0.4–5.1)
- Saldanha N, *et al*. (2019) [16]	HIV Duration - 6–10 years (<= 5 years)	 -DRTB -MDRTB	 - aOR = 0.8 (0.3–2.3) - aOR = 0.6 (0.2–2.4)

	- > 10 years (<= 5 years)	-RRTB -INH mono-resistance -DRTB -MDRTB -RRTB -INH mono-resistance	- aOR = 0.7 (0.3–2.3) - aOR = 0.8 (0.2–2.4) - aOR = 1.6 (0.5–4.7) - aOR = 1.1(0.3–5.1) - aOR = 1.3 (0.5–4.7) - aOR = 1.5 (0.3–4.9)
- Saldanha N, *et al.* (2019) [16]	CD4 counts - 51-100 (< 50) - > 100 (< 50)	-DRTB -MDRTB -RRTB -INH mono-resistance -DRTB -MDRTB -RRTB -INH mono-resistance	- aOR = 0.6 (0.2–1.8) - aOR = 0.2 (0.1–1.2) - aOR = 0.3 (0.1–1.2) - aOR = 0.6 (0.2–1.8) - aOR = 0.7 (0.3–1.6) - aOR = 0.5 (0.1–1.2) - aOR = 0.5 (0.1–1.5) - aOR = 0.7 (0.3–1.7)

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses. (PLHIV = People living with HIV, DRTB = Drug-resistant Tuberculosis, MDRTB = Multi-drug resistant Tuberculosis, RRTB = Rifampicin-resistance Tuberculosis, INH = Isoniazid)

Poor Sociodemographic Conditions

Adverse socio-demographic factors significantly worsen TB prevention and treatment. In India, 14% of actively screened TB patients were 65 or older, 57% lacked formal education, 92% lived in rural areas, and many lived far from care centers, all linked to a higher TB burden. In Indonesia, nonadherence was associated with smoking, low education, rural residency, and initial care from private providers. In China, unemployment and large households increased TB risk. The Philippines saw treatment challenges due to poor referral systems and work or household conflicts. In Pakistan, low BMI, female gender, being single, middle income, and smoking were significant TB risk factors. In Nigeria, lower TB burden was associated with higher income and proximity to treatment, while widowhood, marriage, and certain therapies raised TB risk. In Bangladesh, TB was linked to overcrowded housing, recent TB contact, and employment status. In Congo, chronic diseases, depression, undernutrition, alcohol addiction, and smoking increased the TB burden. In South Africa, substance use, male-headed and overcrowded households, and poor water and sanitation access were key factors. In Myanmar, delayed care-seeking was associated with low education, low income, poor TB knowledge, and long travel distances.

Table (5) Sociodemographic Characteristics of Tuberculosis Burden

Studies	Major Drivers	Outcomes	Proportions/ Strength of Association
-May Chan Oo et al., (2020) [17] -Adisa, R, et al.(2021) [18] -Mujtaba MA et al. (2022**)** **[19]**	- 18-33, 34-49, ≥ 50 years -18–34, 35-54, ≥ 55 years - Older (Younger)	-Delay in seeking TB care -Successful TB Treatment -Experiencing TB Recurrence	- 62.8%, 69.1%, 68.3% - 46.3%, 41.4%, 21.3% -OR=1.01 (1.004–1.02)***
-Kashongwe M, et al. (2017) [15] -Shewade HD, *et al*. (2019) [20] -May Chan Oo et al., (2020) --Adisa, R, et al.(2021) -Mujtaba MA et al. (2022**)** [19] -Kapwata, T, et al., (2022) [21]	- Male, Female -Female (Male) -Male (Female)	-Experiencing MDR/RR-TB -New Smear Positive TB -Delay in seeking TB care - Successful TB Treatment -Experiencing TB -Experiencing TB	- 57.1%, 42.9% -66%, 34% -66.7%, 66.9% -57.4%, 42.6%** -OR=2.07 (1.92–2.22)*** -aOR= 1.46 (1.31-1.64)***
-Shewade HD, *et al*. (2019) [20]	- Urban, Rural	-New Smear Positive TB	- 12%, 87%
- Shewade HD, *et al*. (2019) [20] -May Chan Oo et al., (2020) [17]	- No formal Education - Less than Primary - Up to Secondary - Higher Secondary and above - Illiterate/ No formal Education - Primary School Level - Middle School Level	-New Smear Positive TB -Delay in seeking TB care	- 47% - 14% - 32% - 7% - 88% - 81.2% - 72%

- Lolong DB, *et al.* (2023) [22]	- High School Level - University/College - Low Education (High Education)	- TB Medication Non-Adherence	- 53.7% - 36.2%*** -aOR=1.60 (1.27–2.03)***
- Shewade HD, *et al.* (2019) [20] - May Chan Oo et al., (2020) [17] -Kapwata, T, et al., (2022) [21]	- Unemployed - Studying - Homemaker - Daily wage Worker - Employed, nota daily wage - Government Staff - Private Employee - Self-Employee - Manual Worker - Dependent - Retired - A member of the household employed (No)	- New Smear Positive TB -Delay in seeking TB care -Experiencing TB	- 13% - 5% - 18% - 38% - 24% - 76.5% - 45.9% - 54.0% - 80.4% - 71.7% - 42.9% -aOR=0.67 (0.57-0.78)***
-Kashongwe M, et al. (2017) [15] -May Chan Oo et al., (2020) [17] -Iweama CN, et al. (2021) [23] -Mujtaba MA et al. (2022) [19]	- Married, Single, Widow - Single, Married, Widow - Widowed (Single) - Separated/divorced (Single) - Married (Single) - Unmarried (Married)	-Experiencing MDR/RR-TB - Delay in seeking TB care - TB Medication Adherence -Experiencing TB	- 34.4%, 60.5%, 5.0% - 57.8%, 70.2%, 71.7% - aOR= 26.74(2.92-232.90)* - aOR= 19.93 (0.64-617.74) - aOR=120.5 (5.4-271.1)* -OR = 1.21 (1.11–1.32)**
- May Chan Oo et al., (2020) [17] - Iweama CN, et al. (2021) [23] - Lolong DB, *et al.* (2023) [22] -Mujtaba MA et al. (2022) [19]	- ≤ 100,000 MMK/month -100,001-200,000 MMK/month -> 200,000 MMK/month - #18,000–#99,999.00 (<#18,000.00) - #100,000–#199,999 (<#18,000.00) - #200,000–#299,999 (<#18,000.00) -Middle Income Status (High Income)	-Delay in seeking TB care -TB Medication Adherence -Experiencing TB	- 62.8%, 69.1%, 68.3%*** -aOR = 0.59 (0.04-9.85) -aOR = 0.01 (0.00- 0.13)** -aOR = 1.10 (0.05- 25.04) -OR= 1.94 (1.62–2.3)***
-Kashongwe M, et al. (2017) [15] -Shewade HD, *et al.* (2019) [20] -Iweama CN, et al. (2021) [23]	- No Alcohol use (Alcohol Use) - Current Alcohol intake, No -Current Drinker (No Current Drinker)	-Experiencing MDR/RR-TB -New Smear Positive TB -TB Medication Adherence	- 4.75 (1.56 - 14.50)** - 28%, 70% - aOR = 0.54 (0.26 1.12)
-Shewade HD, *et al.* (2019) [20] - Iweama CN, et al. (2021) [23] -Mujtaba MA et al. (2022) [19] -Lolong DB, *et al.* (2023) [22]	- Current Smoking, No Smoking - Current Smoker (No Smoker) - Ex-Smoker (No Smoker) - Smoking (No Smoking)	-New Smear Positive TB -TB Medication Adherence -Experiencing TB - TB Medication Non-Adherence	- 24%, 74% - aOR = 2.24 (0.61-8.16) - aOR = 2.21 (0.27-18.35) -aOR = 1.57 (1.44–1.7)*** -aOR- 1.78 (1.47–2.16)***
-Kapwata, T, et al., (2022) [21]	- Substance Use (No)	-Experiencing TB	-aOR=5.26 (3.94 -7.03)***
-Kashongwe M, et al. (2017) [15] - Shewade HD, *et al.* (2019) [20]	-Undernutrition (No) -History of weight loss, no history	-Experiencing MDR/RR-TB	- 1.24 (0.38 - 4.04) - 73%, 24%*
- Mujtaba MA et al. (2022) [19]	- Lower BMI (Higher BMI)	-Experiencing TB	- OR =0.96(0.95–0.97)***
-Shewade HD, *et al.* (2019) [20]	- TB household, No TB household	-New Smear Positive TB	- 25%, 75%
-Shewade HD, *et al.* (2019) [20]	- TB death, No TB death	-New Smear Positive TB	- 11%, 89%
-May Chan Oo et al., (2020) [17]	- Previous History of TB, No	-Delay in seeking TB care	- 54.3%, 68.7%
- Iweama CN, et al. (2021)	->5km Distance to DOTS center	-TB Medication Adherence	- aOR= 0.06 (0.00-0.01)**

[23]	(<5km)		
-Iweama CN, et al. (2021) [23]	-Fair TB and DOT Knowledge (Poor) - Good TB and DOT Knowledge (Poor) -TB awareness (No awareness)	-TB Medication Adherence	- aOR = 0.04 (0.01-1.63)*** - aOR = 0.01 (0.18-0.30)*** -OR=1.91 (1.49–2.44)***
-Iweama CN, et al. (2021) [23]	-DOTS treatment duration ⩾6 months (< 6months)	-TB Medication Adherence	- aOR = 0.07 (0.00-12.24)
- Iweama CN, et al. (2021) [23] - Adisa, R, et al. (2021) [18]	-TB/HIV co-infection status (No) -HIV Positive, HIV Negative	-TB Medication Adherence -Successful TB Treatment	-aOR= 0.01 (0.12- 0.35)*** -17.8%, 82.2%***
- Iweama CN, et al. (2021) [23]	-ART and CPT use (No)	-TB Medication Adherence	-aOR=24.9 (19.6-304.3)***
-- Iweama CN, et al. (2021) [23]	-Severe TB drugs side effects (No)	-TB Medication Adherence	-aOR=0.10 (0.00-3.24)
- Mujtaba MA et al. (2022) [19]	-Diabetes (No Diabetes)	-Experiencing TB	-OR= 1.14(1.017–1.278)*
-Mujtaba MA et al. (2022) [19]	-Smear Positive (Negative)	-Experiencing TB Recurrence	-OR= 2.38 (1.65–3.54)***
-Mujtaba MA et al. (2022) [19]	-DR-TB (DS-TB)	-Experiencing TB Recurrence	-OR- 5.62 (4.27–7.39)***

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses. (MDR/RR-TB = Multidrug Resistant/Relapse Regime Tuberculosis, DR-TB = Drug Resistant Tuberculosis, DS-TB = Drug Sensitive Tuberculosis)

Awareness and Perception Regarding Tuberculosis

Patient awareness and perceptions of tuberculosis (TB) are critical for effective disease control and treatment adherence, yet significant gaps persist. In India, nearly half of TB patients lacked knowledge about symptoms, prevention, and causes, with many holding misconceptions such as TB not being curable or affecting only certain groups. In Indonesia, while most recognized TB's contagiousness and practiced preventive measures, some relied on traditional healers, avoided masks due to discomfort or misconceptions, and practiced inappropriate sputum disposal. Chinese patients who had completed treatment also had knowledge gaps regarding next steps if TB was suspected and where to access affordable care. In Bangladesh and South Africa, misconceptions included believing TB could be prevented by avoiding handshakes or sharing food, and associating TB with marginalized groups or sexual transmission. In Nigeria, medication burden discouraged adherence, with some patients overwhelmed by the number and size of tablets.

Table (6) Awareness and Perception Regarding Tuberculosis

Studies	Major Drivers	Outcomes	Proportions/ Strength of Association
-Sagir G, et al. (2018) [24] -Jing, R., et al., (2024) [25]	Age Groups -< 30 years, 31-45 years<>45 years -36–55 years (15–35 years) -56–65 years (15–35 years) -≥ 65 years (15–35 years)	-Good Tuberculosis Knowledge -TB Awareness Rate	-73.8%, 48.5%, 21.6%* -0.77(0.51,1.17) -1.03(0.60–1.79) -0.43(0.28,0.68)***
-Sagir G, et al. (2018) [24]	-Male, Female	-Good Tuberculosis Knowledge	-52.3%, 34.8%
-Sagir G, et al. (2018) [24] -Jing, R., et al., (2024) [25]	-Rural, Urban -Urban (Rural)	-Good Tuberculosis Knowledge -TB Awareness Rate	-18.2%, 69.8% -OR =1.92(1.09,3.38)*
-Sagir G, et al. (2018) [24] -Sharma SK, et al., (2020) [26]	Education -Primary and below, Secondary and above Educational status -No Formal Education -Primary -Higher Secondary -Graduation and above	-Good Tuberculosis Knowledge -Different TB Knowledge Score	-35.1%, 86.0% -Mean±SD=7.25 ± 3.14*** -Mean±SD=77.41 ± 3.32*** -Mean±SD=8.57 ± 3.75*** -Mean±SD=9.60 ± 3.45*** -Mean±SD=50.04±3.93*** -Mean±SD=49.90±4.03***

-Jing, R., et al., (2024) [25]	Education (Junior High School or lower) -High School/Middle School -University level or higher	-TB Awareness Rate	-Mean±SD=50.90±4.25*** -Mean±SD=51.33±5.17*** -1.51(1.01,2.26)* -2.05(1.38,3.05)***
-Sharma SK, et al., (2020) [26]	Religion -Hindu -Muslim -Christian -Sikh	-Different TB Knowledge Score	-Mean±SD=8.74 ± 3.39*** -Mean±SD=7.38 ± 3.37*** -Mean±SD=6.15 ± 4.06*** -Mean±SD=7.98 ± 4.44***
-Sharma SK, et al., (2020) [26] -Jing, R., et al., (2024) [25]	Occupation -Government Service -Self-Employed -Agriculture/Domestic Worker -Unemployed/Housewife Occupation (Domestic and unemployed) -Farmers -Workers -Managers and employees -Pensioners -Others	-Different TB Knowledge Score -Different TB Perception Score -TB Awareness Rate	-Mean±SD=8.57 ± 3.83 *** -Mean±SD=8.15 ± 3.61*** -Mean±SD=7.18 ± 3.24*** -Mean±SD=8.81 ± 3.48*** -Mean±SD=50.68±4.80** -Mean±SD=50.51±4.33** -Mean±SD=49.63±3.87** -Mean±SD=51.11±4.51** -OR=1.14(0.69,1.88) -OR=1.59(0.81,3.01) -OR=1.00(0.53,1.39) -OR=0.61(0.33,1.14) -OR=1.53(0.72,3.26)
-Sharma SK, et al., (2020) [26] -Jing, R., et al., (2024) [25]	Family income per month (Rs) . -≤2000 -2001.4000 -4001.6000 ->6000 Monthly Income (RMB) (< 2000) -2000-3999 -4000-5999 -More than 6000	-Different TB Knowledge Score -Different TB Perception Score -TB Awareness Rate	-Mean±SD=7.34 ± 3.39 *** -Mean±SD=7.50 ± 3.27*** -Mean±SD=6.97 ± 3.39*** -Mean±SD=9.46 ± 3.45*** -Mean±SD=50.15±4.39 * -Mean±SD=50.55±4.00* -Mean±SD=50.11±4.04* -Mean±SD=50.98±4.68* -OR= 0.99(0.63,1.55) -OR= .50(0.97,2.33 -OR= 1.89(1.10,3.25)*
-Sharma SK, et al., (2020) [26]	Type of Family -Joint -Nuclear -Extended	-Different TB Knowledge Score -Different TB Perception Score	-Mean±SD=8.52 ±3.10 *** -Mean±SD=8.34 ± 3.83*** -Mean±SD=6.29 ± 3.55*** -Mean±SD=50.33±4.01*** -Mean±SD=51.03±4.66*** -Mean±SD=48.45±3.96***
-Sharma SK, et al., (2020) [26]	Source of Health Information -Media -Health Personnel -Friends and Neighbors -Relatives	-Different TB Knowledge Score -Different TB Perception Score	-Mean±SD=8.89±3.04 *** -Mean±SD=8.70±3.92*** -Mean±SD=6.60±3.48*** -Mean±SD=7.77±3.50*** -Mean±SD=50.88±4.05 -Mean±SD=50.61±4.83 -Mean±SD=50.02±4.50 -Mean±SD=50.51±4.18
-Sharma SK, et al., (2020) [26]	Religion -Hindu -Muslim -Christian -Sikh	-Different TB Perception Score	-Mean±SD=50.74±4.36 ** -Mean±SD=50.03±4.07** -Mean±SD=49.41±4.28** -Mean±SD=51.85±5.68**

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses.

Environmental Influence

Environmental conditions play a significant role in TB occurrence and transmission. In China, TB hotspots were concentrated in the northwest provinces and shifted from central to the northwest regions over time, while cold spots persisted in eastern districts. TB cases peaked from late winter to spring and correlated strongly with higher population density, atmospheric pressure, temperature, humidity, and precipitation. Annual average relative humidity and mean temperature were the most influential meteorological factors, while air pressure and wind speed also contributed. Pollutants like PM10, O3, and NO2 were notably associated with TB incidence. In India, exposure to second-hand smoke, using mud walls, shared toilets, daily smoke exposure, solid fuel for cooking, and lack of separate cooking areas increased TB risk, while finished walls were protective. Poor home ventilation, lighting, high occupancy density, and floor type further raised TB risk. Indonesian studies confirmed that dense housing, room temperatures outside 20-25°C, firewood use for cooking, and high population density significantly increased pulmonary TB risk. In Myanmar, risk factors included male gender, living with or caring for a TB patient, smoking, and alcohol use.

Table (7) The Environmental factors for the risk of Tuberculosis Incidence

Studies	Major Drivers	Outcomes	Proportions/ Strength of Association
- Guo C, et al. (2017) [27] - Li, H. et al. (2021) [28]	-Temperature (°C) -Wind speed (m/s) -Atmospheric pressure (hPa) -Relative humidity (%) -Spring (Winter) -Summer (Winter) -Autumn (Winter) -Annual average temperature -Annual average wind speed -Annual average relative humidity -Annual mean pressure -NDVI	-The excess risk of Tuberculosis incidence -The determining power on the TB incidence	**-ER%= -0.77 (-0.79, -0.75)***** **-ER%=−1.94 (−2.11, −1.77)***** **-ER%=−0.92 (−0.94, −0.90)***** -ER%=0.06 (0.05, 0.07)*** -ER%=24·8(24·5, 25·1)*** -ER%= 8·1(7·7, 8·5)*** -ER%= -6·1 (-6·3, -5·8)*** -q=0.162*** -q=0.031*** -q=0.254*** -q=0.035*** -q=0.011***
Atillah, CN, et al, (2023) [29]	-Coverage of healthy houses -Coverage of households with PHBS -Population density	-Number of Tuberculosis Cases	-r =-0,317*** -r = -0,013 -r = 0,78***
-Kapwata, T, et al., (2022) [21]	-Flat Dwelling (House) -Shack Dwelling (House) -Room (House) -Hut (House)	-Experiencing TB	-aOR=0.44 (0.18 – 1.04) -aOR=0.75 (0.58 – 0.98)* -aOR=0.96 (0.71 – 1.29) -aOR=0.95 (0.40 – 2.24)
-Kapwata, T, et al., (2022) [21] -Singh, S.K, et al, (2018) [30]	Room used for sleeping - > 2 people per room (<2) -3 to 4 people (<3 people) -5 to 6 people -7 people and above	-Experiencing TB	-aOR=2.15 (1.66 -2.78)*** -aOR=0.95 (0.88-1.03) -aOR=0.87 (0.70-1.09) -aOR=0.83 (0.49-1.41)
-Aditama W, et al. (2019) [31]	-Occupancy density of the house (Control) -Ventilation of the house (Control)	-Incidence of Pulmonary Tuberculosis	-aOR=30.8 (2.8 – 336.4)** -aOR=17.2 (1.6 – 178.9)*
-Kapwata, T, et al., (2022) [21] -Singh, S.K, et al, (2018) [30]	(Flush toilet connected to sewage system) -Flush toilet with septic tank -Flush toilet with septic tank -Chemical Toilet -Pit Toilet - Share toilet with other household (No)	-Experiencing TB	-aOR=1.01 (0.77 -1.31) -aOR=1.33 (0.84 -2.08) -aOR=0.91 (0.74 -1.11) -aOR= 0.91 (0.74 -1.11) -aOR=1.23 (1.13-1.36)*
-Kapwata, T, et al., (2022) [21] -Singh, S.K, et al, (2018) [30]	(Water Source -Piped water in the house) -Piped water in the yard -Piped water outside the yard -Borehole/well -Spring/stream/river/dam -Rainwater tank -Water tank - Potability of water (No)	-Experiencing TB	-aOR=0.92 (0.64-1.32) -aOR=1.40 (0.95-2.05) -aOR=1.24 (0.78 - 1.98) -aOR=1.70 (0.96 - 3.00) -aOR=1.45 (0.86 –2.41) -aOR=1.16 (0.76 – 1.77) --aOR=1.1 (1.03 – 1.18)*
-Kapwata, T, et al., (2022) [21]	-Non-electric Source of Energy (Electric)	-Experiencing TB	-aOR=1.06 (0.91 – 1.24)
-Singh, S.K, et al, (2018) [30]	Smoking inside the house -Less than daily (Never) -Daily (Never)	-Experiencing TB	-aOR=1.38 (1.25-1.52)* -aOR=1.49 (1.39-1.61)*
-Singh, S.K, et al, (2018) [30]	Fuel used for cooking -Solid Fuel (Non-solid Fuel)	-Experiencing TB	-aOR=1.03 (0.94-1.14)

-Singh, S.K, et al, (2018) [30]	Separate kitchen -Yes (No)	-Experiencing TB	-aOR=0.95 (0.88-1.03)
-Singh, S.K, et al, (2018) [30]	Material of floor -Rudimentary (Natural) -Finished (Natural)	-Experiencing TB	-aOR=1.27 (1.13-1.43)* -aOR=1.12 (1.01-1.25)*
-Singh, S.K, et al, (2018) [30]	Material of roof -Rudimentary (Natural) -Finished (Natural)	-Experiencing TB	-aOR=0.82 (0.66-1.02) -aOR=0.90 (0.79-1.04)

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses. (ER = Excess risk, q = Determinant Power, NDVI = The Normalized Difference Vegetation Index, PHBS = households practicing clean and healthy living behavior)

Weaknesses of the TB-care System

A qualitative study in India identified major deficiencies in the TB-care system, including non-compliant drug storage lacking essential features like air conditioning, humidity control, and pest management, leading to 80% patient dissatisfaction. Staff worked in unsafe conditions with risks from deteriorating buildings. Impoverished patients often traveled long distances to higher-level centers with limited sample collection days, reducing compliance and delaying detection of drug-resistant TB. The 30-kilometer gap between District TB Centers and sub-centers delayed timely treatment. Staff shortages and inadequate Directly Observed Therapy (DOT) providers were common, and job dissatisfaction was fueled by salary disparities and lack of benefits for contractual staff. Further challenges included poor team communication, lack of certified training, insufficient equipment, irregular support, and unpaid salaries. TB health assistance heavily relied on external funding, often halting when funds were depleted, and lacked cohesive management, with customs issues and fragmented models undermining effectiveness. Traditional training did not meet global health needs, highlighting a need for multidisciplinary approaches. Surveillance gaps persisted due to the exclusion of non-governmental and cross-border TB cases, and inconsistent screening protocols complicated data integration. Migrant patients faced limited treatment options and missed follow-ups, increasing drug resistance. Funding deficits, exacerbated by more cases detected via GeneXpert, led to patient concern over treatment access. Remote areas suffered from poor infrastructure, restricting healthcare access. Overall, TB services often lacked person-centered care, emphasizing the need for improved patient-provider interactions and enhanced provider training.

Weaknesses of Tuberculosis Control Policies

Studies in Indonesia and India reveal significant challenges in TB control policies, stemming from their complexity and the need for effective collaboration among healthcare professionals. Key issues include the careful selection of skilled staff, comprehensive health system responses, and addressing financial and resource constraints. The advancement and consistent use of GeneXpert technology are vital for detecting drug-resistant TB; however, obstacles such as selection bias, power and internet interruptions, and equipment repair delays limit progress. Policies should mandate Xpert testing for all TB suspects, ensure strict quality control, and improve clinician-laboratory communication to align diagnostics with treatment. In India, policy deficiencies include weak public health infrastructure, poor TB awareness, limited healthcare access, malpractice in the private sector, ineffective programs, insufficient drug supplies, inadequate budgets, and corruption. Addressing root causes, enhancing primary care, combating malnutrition, and improving access to affordable medication and diagnostics are essential. Disparities between public and private sectors, such as patient time, costs, and antibiotic use, highlight the need for better integration and standardized care. Financial weaknesses are evident in the wide variation in community-based TB care costs and the lack of uniform assessment tools, complicating nationwide implementation and planning. Leadership and management weaknesses, especially resource shortages and poor coordination, further hinder TB control. Inadequate staff training, facility limitations, inconsistent diagnostic practices, drug shortages, and poor patient education contribute to low treatment adherence, misdiagnosis, and rising MDR-TB rates.

Impact of COVID-19 on Tuberculosis

The COVID-19 pandemic severely disrupted TB programs, affecting notifications, healthcare resources, and treatment adherence. In China, TB patient notifications sharply declined after the Spring Festival, requiring 10 weeks to recover, compared to two weeks in previous years. Many health workers and laboratory staff were reassigned to COVID-19 tasks, causing temporary closures of TB clinics and labs, as well as shortages of reagents and drugs. Travel restrictions led to 26.9% of TB patients missing follow-up exams and widespread reliance on self-administered therapy. In India, decreased mobility and surging hospital admissions resulted in fewer reported TB cases, highlighting reduced access to care. In Indonesia, TB case notifications fell by 26%, with treatment coverage dropping 11%. Higher COVID-19 rates were linked to further reductions in TB notifications and treatment. Healthcare system weaknesses, such as insufficient primary health centers and low doctor-to-population ratios, were exposed. In the Philippines, TB patients faced over twice the risk of mortality and a 25% lower recovery rate during the pandemic. In Nigeria, lockdowns led to temporary closures of healthcare facilities, reduced screenings, supply disruptions, and increased patient fees. In Bangladesh, suspected TB notifications and sputum tests dropped by over 30%, with DOTS patients reporting transport barriers, fear of infection, income loss, and dissatisfaction with crowded, delayed, and understaffed services.

Table (8) COVID-19 and the risk of Tuberculosis Burden

Studies	Major Drivers	Outcomes	Proportions/ Strength of Association
-Sy KTL., et al., (2020).[32]	-TB with COVID-19 (without COVID-19)	-Death -Risk of recovery -Shortertime-to-death -Longer time-to recovery	-RR=2.17 (1.40-3.37) -RR=0.75 (0.63-0.91) -P=0.0031 -P=0.0046
- Fei, H.,et al. (2020) [33]	-COVID-19 Epidemic	-Reallocation CDC and primary health care workers to fight the COVID-19 epidemic -Reallocation TB laboratory staff to work forCOVID-19 testing -Temporarily closed TB outpatient clinics and TB laboratory -Shortage of laboratory reagents for TB -Shortage of anti-TB drug -Strict of intra-county and inter-city travel restrictions -Postponed or missed going for their follow-up examinations	-75.2% (221/294) of counties -37.8% (111/294) of counties -14.6% (43/294) and 13.6% (40/294) of counties -4.4% (13/294) of counties -8 .2%(24/294) -84.0% (247/294) and 71.1% (209/294) -26.9% (725/2694) of TB patients
-Mihika, F. A., (2022) [34]	-COVID-19 Epidemic	Challenges told by them due to CVOID-19 pandemic (n = 16) -Lack of manpower -Increased workload -Interruption regular follow-up -Interruption TB diagnosis -Interruption in the drug supply -Interruption sample collection -Reduced patient's visit -Interruption in performing test -Interruption report delivery	 -16 (100%) -15 (94%) -10 (63%) -10 (63%) -4 (25%) -16 (100%) -16 (100%) -10 (62%) -7 (44%)
-Oga-Omenka C, et al. (2023) [35]	- COVID-19 Epidemic	Closure of clinic -Not closed -Closed once -Closed more than once Reasons for closure -Government mandate/lockdown -Low clinic visits -Not enough PPEs or other medical supplies -Not enough staff available -Citizen protests -Other reasons Change in hours of operation -No change -Fewer hours -More hours Compared to pre-COVID, how have client numbers changed? -Fewer patient visits per day -More patient visits per day -Missing Staff layoffs due to COVID	 -69% -29% -1%*** -93% -1% -1% -0% -1% -3%*** -74% -21% -5%*** -55% -20% -25%

		-No -Yes -Not sure Shortages of medical supplies since COVID -No -Yes	-88% -11% -1%*** -83% -17%***

*< 0.05, ** < 0.01, *** < 0.001: Reference Groups are enclosed in parentheses.

4. DISCUSSION

Income Loss and Cost Burden

The financial burden of tuberculosis (TB) is a major global challenge, especially in high-prevalence countries [7]. In Indonesia, TB and multidrug-resistant TB (MDR-TB) patients frequently faced total income loss and high out-of-pocket expenses for diagnosis and treatment. Indian TB patients, particularly younger individuals, those with diabetes, and users of private healthcare, also incurred significant pre-treatment costs [36]. In China, TB care expenses were substantial for rural residents and those under certain healthcare schemes, with older adults, the divorced or widowed, and less-educated individuals bearing greater financial strain [37]. Catastrophic health expenditures due to TB were common in South Africa, the Philippines, Bangladesh, Myanmar, Nigeria, Congo, and Pakistan. Direct medical costs, income loss, and caregiving duties worsened the economic impact, forcing vulnerable households to borrow, sell assets, or reduce essential spending. Comprehensive health financing and social protection are urgently needed.

Comorbid Conditions (Diabetes) and Their Impact on TB

TB patients with comorbidities like diabetes face significantly higher out-of-pocket medical expenses, intensifying their financial burden, especially in India, Indonesia, and China [13,38]. These costs restrict access to healthcare and can drive families into poverty, undermining progress toward SDG 3 (Good Health and Well-being) and SDG 1 (No Poverty) [39]. In the Philippines, TB diabetes comorbidity further raises costs and highlights the need for integrated care. Targeted interventions such as subsidized healthcare, improved access to affordable medicines, and education for high-risk groups are essential. Strengthening TB policies by including diabetes screening and management, particularly for lower-income and less educated populations, is crucial [40]. The Health Belief Model and Social Determinants of Health theory underscore the importance of addressing both health behaviors and socioeconomic factors to reduce this dual burden.

Comorbid Conditions (HIV) and Their Impact on TB

The convergence of HIV and tuberculosis (TB) significantly increases the TB burden, making it harder to achieve Sustainable Development Goal 3 on health and well-being [39]. High rates of HIV co-infection among TB patients require enhanced TB policies and integrated TB-HIV services, especially in countries like India, Indonesia, and China. In India, the prevalence of multidrug-resistant TB (MDR-TB) and resistance to isoniazid and rifampicin underscores the need for robust drug resistance monitoring and treatment protocols. Rising HIV rates among TB patients in the Philippines, Pakistan, and Nigeria highlight the need for targeted interventions, resource allocation, and stronger health systems. Public health frameworks emphasize adopting integrated care models and fortifying health systems to better manage dual TB-HIV challenges and support SDG achievement [41].

Poor Sociodemographic Conditions

Overcoming tuberculosis (TB) in areas with poor sociodemographic conditions is critical for achieving Sustainable Development Goal 3, which promotes health and well-being for all [39]. High TB rates are driven by low income, limited education, and poor healthcare access. In India, 57% of screened TB patients lacked formal education, and 92% lived in rural areas. In Indonesia, smoking, private healthcare, and rural residence increased non-adherence to TB treatment. China’s TB burden was linked to unemployment and large households, while the Philippines struggled with referral system issues and work conflicts. Pakistan’s TB incidence is related to low BMI, female gender, and smoking. In Nigeria, income, proximity to care, and TB/HIV co-infection were key factors. Overcrowding, recent TB contact, chronic illness, and substance use also worsened the TB burden in Bangladesh, Congo, South Africa, and Myanmar. Addressing these disparities requires integrated care, stronger health systems, and community-based interventions [42].

Awareness and Perception Regarding Tuberculosis

Achieving health-related Sustainable Development Goals, especially SDG 3, requires addressing gaps in TB awareness and perception [39]. Robust educational campaigns are essential for strengthening TB policies. Public health frameworks stress the need for comprehensive health education to dispel myths and improve TB prevention, treatment, and management [42]. Studies from India and China show that poor knowledge among TB patients leads to lower treatment adherence and increased transmission. In Indonesia and South Africa, misconceptions and stigma hinder effective TB control. Integrating culturally sensitive education into TB policies can empower communities, improve outcomes, and reduce disease burden. Partnerships with local leaders and health workers are vital to extend the reach of these programs, ensuring accurate information even in remote areas. Addressing these educational gaps will accelerate progress toward the SDGs and support healthier populations.

Environmental Influence

Addressing environmental factors is critical for achieving SDG 3, which aims for health and well-being for all [39]. Improving TB policies requires better living conditions, reduced environmental pollutants, and stronger public health infrastructure. Studies from China, India, and Indonesia show that population density, poor ventilation, high humidity, second-hand smoke, and use of solid fuels for cooking all raise TB risk. Public health frameworks emphasize integrated care and stronger health systems to combat TB effectively [42]. Policies should focus on better housing, reducing indoor air pollution, and ensuring adequate ventilation and lighting. Community education campaigns are also needed to highlight the importance of environmental factors in TB prevention. By implementing targeted policies and involving communities, countries can significantly reduce TB incidence and progress toward health-related SDG targets.

Weaknesses of TB-care System

Achieving SDG 3 on health and well-being requires addressing healthcare system weaknesses that hinder effective TB control [39]. Strengthening TB policies involves improving drug storage, infrastructure, and addressing staff shortages. In India, unsafe facilities and poor drug storage harm both staff and patients, leading to dissatisfaction and poor treatment adherence. Workforce inefficiencies, low job satisfaction, and salary disparities further weaken TB control efforts [28]. In Indonesia, inadequate management, poor communication, lack of sputum examination tools, and insufficient training highlight the need for better support systems. Reliance on external funding and fragmented management causes project stagnation when funds run out. Data gaps, especially for cases treated outside formal systems or by NGOs, hinder surveillance. Public health frameworks emphasize integrated care and system strengthening [28]. Improving infrastructure, sustainable financing, and provider training is essential for effective TB control and SDG progress.

Weaknesses of Tuberculosis Control Policies

Addressing shortcomings in TB control policies is vital to achieving SDG 3, which promotes health and well-being [39]. In Indonesia, complex TB policies require collaboration between academics, health staff, and broader systems. Effective policy demands qualified personnel and solutions to financial and resource constraints. Expanding advanced diagnostics like GeneXpert is essential, but power outages and maintenance issues must be resolved. In India, poor public health infrastructure, low TB awareness, limited healthcare access, and weak government implementation hinder TB control. Strengthening primary care, combating malnutrition, and improving access to affordable medicines and diagnostics are critical [42]. Disparities between public and private providers highlight the need for better care integration and standardization. In Myanmar, financial gaps and a lack of assessment tools complicate community-based TB care. Leadership weaknesses, staff shortages, coordination failures, and poor drug planning demand policy reforms and stronger public–private collaboration, supported by integrated care models.

Impact of COVID-19 on Tuberculosis

The COVID-19 pandemic severely disrupted TB control efforts, posing major challenges to achieving SDG 3 on health and well-being. In countries like China, India, Indonesia, the Philippines, Nigeria, and Bangladesh, pandemic-driven resource reallocation, clinic closures, and travel restrictions led to reduced TB case notifications and poor treatment adherence. Interruptions in routine TB services and shortages of essential supplies highlighted weaknesses in existing TB policies. Public health frameworks emphasize the need for integrated care models and stronger health systems to address these challenges [42]. Strengthening TB policies is crucial to ensure uninterrupted care during crises, including leveraging technology for remote patient monitoring, securing drug supply chains, and coordinating TB and COVID-19 responses. Addressing workforce shortages and improving provider training are also essential for resilient TB management and progress toward the SDGs.

5. CONCLUSION

This review highlights key socioeconomic factors driving the high tuberculosis (TB) burden in several countries, including major income loss, financial instability, high out-of-pocket spending, and employment impacts. In Indonesia, TB and MDR TB patients' median incomes fell to zero, with high diagnosis and treatment costs. Indian TB patients faced average pre-treatment costs of USD 39.74, especially among younger, diabetic, or private care users. Rural TB patients in China faced median costs of USD 965.5, with higher expenses for those with lower education or income. Myanmar's TB-affected households spent USD 759, while Nigeria's drug-resistant TB (DR TB) treatment costs ranged from USD 9,425 to 18,528 due to hospitalization. In Congo, over half of TB-affected households spent more than 20% of their income on TB, impacting employment and poverty. South African TB treatment averaged USD 3,430, rising for successful treatment. The Philippines, Bangladesh, and Pakistan saw many TB patients borrowing or selling assets to manage costs. Coexisting diabetes and HIV further intensified financial strain, complicating treatment and adherence. Poor sociodemographic conditions, such as low education, unemployment, rural living, and weak healthcare access, worsened TB incidence and nonadherence. Misconceptions and low TB awareness in many countries impede disease management, calling for improved public education. Environmental factors, including poor housing, inadequate ventilation, and pollution, significantly impacted the spread of TB. Weaknesses among DOT providers and broader healthcare system challenges, including inadequate facilities, staff shortages, and underfunding, further hindered TB control. Effective TB management, therefore, requires integrated, well-funded strategies and strengthened health systems.

6. RECOMMENDATIONS

To effectively reduce the high burden of tuberculosis (TB) in the most affected countries, a multifaceted approach is essential, drawing on evidence from economic, clinical, social, and policy perspectives. Addressing income loss and the substantial financial burden linked to TB requires comprehensive health financing mechanisms and robust social protection programs to shield patients and families from catastrophic expenditures, as seen in Indonesia, India, China, and beyond. Integrated care models that prioritize the management of comorbidities such as diabetes and HIV must be adopted, with targeted subsidies, improved access to affordable medicines, and provider training to enhance early detection and treatment, especially for vulnerable and hard-to-reach populations. Public health systems should be strengthened through sustainable funding, improved drug and diagnostic supply chains, staff training, and better infrastructure, reducing reliance on external funding and preventing service disruptions during crises like COVID-19. Community-based interventions, health education campaigns, and partnerships with local leaders are crucial to raising TB awareness, dispelling stigma, and improving health-seeking behaviors, particularly in rural and low-education settings. Environmental interventions, including better housing, improved ventilation, and reduction of indoor air pollutants, should be prioritized, while policy reforms must focus on integrating public and private TB care, expanding access to advanced diagnostics, and ensuring policy implementation and monitoring at all levels. Ultimately, these recommendations highlight the importance of coordinated, context-sensitive interventions that address the socioeconomic, clinical, environmental, and systemic factors driving TB, and stress the need for ongoing research, policy innovation, and collaboration to achieve global TB control and the Sustainable Development Goals.

To address tuberculosis (TB) comprehensively, it is vital to adopt a global perspective that encompasses not only the highest-burden countries but also regions with emerging TB threats and diverse socioeconomic dynamics. Enhanced genomic surveillance and the application of advanced molecular epidemiology can facilitate early detection of TB transmission patterns and drug-resistant strains in both established and newly affected areas. Expanding the use of digital health technologies, including electronic treatment monitoring, mobile health applications, and telemedicine, can improve case detection, treatment adherence, and patient support, especially in resource-limited settings. Integrating TB surveillance with broader public health data systems will enable real-time monitoring of epidemiological shifts and the rapid deployment of targeted interventions. Research investments should prioritize operational studies in underrepresented regions to identify context-specific drivers and barriers to TB control, while fostering regional laboratory capacity for rapid diagnostics and resistance testing. Multilateral collaboration and data sharing between countries can accelerate the development and implementation of innovative interventions, such as new vaccines, shorter treatment regimens, and AI-driven risk stratification tools. By combining these scientific advances with community engagement and tailored public health strategies, the global response to TB can become more agile, equitable, and effective across a wider range of settings.

To strengthen TB management, it is essential to spotlight and replicate successful strategies from high-burden countries. For example, India’s use of digital adherence technologies, such as 99DOTS and video-observed therapy, has significantly improved treatment monitoring and patient engagement. South Africa’s integration of TB and HIV services, including co-located clinics and joint treatment protocols, has enhanced case detection and reduced mortality among co-infected patients. China’s expansion of rapid molecular diagnostics like GeneXpert across rural and urban settings has enabled earlier detection of drug-resistant TB, while Indonesia’s community-based active case finding has improved early identification and linkage to care. Bangladesh’s robust community health worker network, supported by mobile health tools, serves as a model for patient follow-up and health education. Nigeria’s public-private mix approach, which involves engaging private providers in TB notification and treatment, has led to increased case reporting and treatment success. These modernized, evidence-based strategies, ranging from digital health innovations and integrated care models to community engagement and public-private collaboration, demonstrate practical pathways for overcoming TB management challenges and should be adapted and scaled based on local needs and resources.

7. LIMITATION

This review relies primarily on cross-sectional data, which limits the ability to assess the long-term socioeconomic effects of TB on families and communities. The study also does not explore cultural and behavioural factors in depth, despite their crucial importance for understanding TB prevention and treatment adherence. While weaknesses in healthcare systems are highlighted, there is less attention given to system strengths and successful strategies that could be scaled or replicated elsewhere. Additionally, findings from specific countries may not be easily applicable to other regions with different healthcare infrastructures, economic situations, or cultural backgrounds. Finally, the review is based on reported cost data, which may be affected by reporting bias or inaccuracies, potentially impacting the reliability of the estimated cost burden.

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