

Prevalence and Factors Associated with HIV Infection Among Tuberculosis Patients aged below 15 years Across regions with High TB burden in Tanzania: A Six-year Retrospective Cross-Sectional Study

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Abstract

Background

TB-HIV co-infection disproportionately affects children in sub-Saharan Africa. Scale-up of PMTCT, ART, and TB Preventive Therapy (TPT) aims to reduce this burden. This study estimated HIV prevalence among TB-registered children aged < 15 years across ten high-burden Tanzanian regions (2018–2023) and identified factors associated with HIV co-infection.

Methods

A cross-sectional retrospective review of records was conducted using secondary data extracted from the National TB and Leprosy System, District Health Information System-2 Electronic TB and Leprosy (DHIS2-eTL). All children aged < 15 years who were diagnosed with TB and had documented HIV status across ten regions with high a TB burden between January 2018 and December 2023 were included. Binary logistic regression was used to identify factors associated with HIV co-infection, and results are reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI) at 5% statistical significance

Results

Among 25,449 children with TB, 3,667(14.4%) had a documented HIV-positive status. HIV prevalence declined markedly from 28.5% in 2018 to 8.9% in 2023 ($p < 0.001$). Pediatric TB-HIV co-infection increased with age: 9.0% in children aged below 5 years, 17.7% in those aged 5–9 years, and 22.6% in those aged 10–14 years ($p < 0.001$), with noticeable regional variations. After multivariable adjustment, older age groups (aOR = 2.32 95% CI 2.11–2.55 and 2.99 95% CI 2.72–3.29 for 5–9 and 10–14 years, respectively), residence in Njombe (aOR = 1.73, 95% CI 1.46–2.04), Mbeya (aOR = 1.53, 95% CI 1.31–1.78), and Iringa (aOR = 1.37, 95% CI 1.17–1.61), and a history of prior TB treatment (aOR: 3.75–4.68) were independently associated with higher odds of co-infection. The COVID-19 era (2020–2023) was associated with substantially lower odds of co-infection (aOR = 0.42, 95% CI 0.39–0.46).

Conclusions

HIV prevalence among children with TB in Tanzania declined from 28.5% to 8.9% between 2018 and 2023, temporally coinciding with scaled-up PMTCT, ART and TPT interventions, though this cross-sectional analysis cannot establish causality, the trend is consistent with programmatic success. However, persistent regional disparities, higher risk in older children, and a strong association with prior TB treatment underscore ongoing vulnerabilities that may require more nuanced attention.

Background

Tuberculosis (TB) and HIV are among the most consequential infectious diseases of the twenty-first century, and their co-occurrence produces outcomes worse than either infection alone. Globally, an estimated 10.8 million people developed TB in 2023, and the African Region accounted for approximately 23.6% of all new cases, with nearly one in five (18%) attributable to immunosuppression secondary to HIV infection (1). In 2023, approximately 662,000 new TB cases were co-infected with HIV, accounting for 6.1% of all new TB cases worldwide, while TB-associated deaths among people living with HIV (PLHIV) numbered approximately 161,000 (2).

Children aged below 15 years carry a substantial and frequently underestimated share of the global TB burden, accounting for approximately 12% of all new TB cases globally, equivalent to 1.3 million new pediatric TB cases in

2023 (1). In 2024, it was estimated that approximately 337,000 children under 15 years of age in the African Region alone will develop TB, of those 40–60% will develop TB-HIV coinfection, reflecting persistent gaps in prevention, early diagnosis, and child-friendly treatment (1). HIV infection is the strongest known risk factor for progression from latent TB infection to active TB disease, increasing an individual's lifetime risk by 16- to 27-fold, with children and adolescents living with HIV (CALHIV) being 8–20 times more likely to develop TB disease than their counterparts(3). For children, the consequences of TB-HIV co-infection are particularly severe: co-infected children experience higher mortality, with TB claiming 33% of deaths among CALHIV globally, resulting in 21,000 pediatric HIV-related deaths (4). This is due to accelerated immune deterioration, more complex treatment, and an amplified risk of drug resistance in CALHIV with TB (4).

Sub-Saharan Africa (SSA) accounts for approximately 75% of the global HIV/AIDS burden and harbors 17 of the 30 countries with the highest pediatric TB prevalence, contributing to 46% of global pediatric TB-related deaths (5, 6). In 2024, an estimated 1.4 million children globally were living with HIV, with 120,000 new infections and 75,000 AIDS-related deaths among children, the lowest count since the 1980s, reflecting the impact of the PMTCT scale-up (7). Despite this progress, a significant proportion of HIV-positive children in high-burden countries remain undiagnosed or unlinked to care, with an estimated 48% of CALHIV with TB accurately diagnosed, treated, and unreported, sustaining a pool of immunocompromised children at risk of TB (3). A sub-Saharan African systematic review estimated the TB incidence rate among HIV-positive persons at 4.17 per 100 person-years in high-burden settings, specifically 3.42 per 100 person-years among CALHIV (3).

Tanzania, located in East Africa has a population of approximately 61 million, and is classified among the top 30 countries with a high TB burden (1). The Tanzania HIV Impact Survey (THIS) 2022–2023 predicted a national adult HIV prevalence of 4.4%, with marked regional heterogeneity ranging from below 0.2% to over 12.7% in the Njombe region. This situation has directly increased pediatric TB-HIV coinfection risk, resulting in 10 to 60% pediatric TB-HIV co-infection prevalence (8, 9). Although PMTCT programs under the Option B+ strategy have significantly reduced vertical transmission, the uptake of confirmatory HIV testing among HIV-exposed infants remains suboptimal, with only 34.6–44.2% of HIV-exposed infants returning for the 18-month confirmatory test, resulting in a large proportion of children with unidentified HIV and, therefore, unprotected from TB infection/disease (10).

TB-HIV co-infection in children was further compounded by the COVID-19 pandemic, which severely disrupted health services across SSA from 2020. Studies have documented significant declines in TB case notifications and HIV testing services during the pandemic, with modelling estimates projecting up to 6 million excess TB deaths by 2025 if diagnostic and treatment gaps are not addressed (11, 12). An interrupted time series analysis in Ghana demonstrated that COVID-19 negatively impacted TB case notification and HIV testing, while ART initiation remained broadly preserved (13). The resulting diagnostic gap disproportionately affected children, among whom the underdiagnoses of TB was estimated at 53–69% in the pre-pandemic era (14) .

Despite the well-documented global and regional burden of pediatric TB–HIV coinfection, evidence on its prevalence, temporal trends, geographical distribution, and associated factors across multiple regions of Tanzania remains limited. Tanzania's NTLP reports national pediatric TB-HIV co-infection annually but lacks region and age-stratified trend data needed to allocate PMTCT and TPT resources efficiently. Single-facility studies (3, 4, 15–17), provide clinical detail but cannot inform regional prioritization. This study fills that gap by analyzing six years of surveillance data across ten high-burden regions, enabling evidence-based targeting of interventions. Furthermore, previous research has seldom explored the impact of the COVID-19 pandemic on the continuum of TB–HIV care among children, including potential disruptions in case detection, treatment initiation, and outcomes (18, 19). Consequently, important evidence gaps remain regarding the epidemiology and determinants of pediatric TB–HIV

coinfection in Tanzania, particularly in high-burden regions and during periods of major health system disruption. To inform NTLP resource allocation and targeting of integrated TB-HIV services, this study aimed to (i) estimate the prevalence of HIV among TB patients < 15 years of age across ten high-HIV-burden regions of Tanzania from 2018 to 2023, (ii) describe temporal and geographic trends, and (iii) identify factors independently associated with HIV co-infection.

Methods

3.1. Study Design

This study adopted a retrospective cross-sectional design to estimate the prevalence of HIV infection and identify the associated factors among children diagnosed with TB between January 2018 and December 2023. The study utilized programme-scale secondary data of children < 15 years of age, extracted from the District Health Information System 2 Electronic TB and Leprosy (DHIS2-eTL). The DHIS2-eTL is the official national TB surveillance system that provides standardized facility-level records across all registered health facilities. The study covered the period from January 2018 to December 2023, deliberately selected to enable temporal comparisons between the pre-COVID-19 (2018–2019) and the COVID-19 disruption (2020–2023) periods.

3.2. Study Setting

Records were extracted from the ten regions with high TB burden in Tanzania as documented in DHIS2-eTL surveillance data. These regions include Njombe, Iringa, Mbeya, Songwe, Kagera, Tabora, Shinyanga, Mara, Ruvuma, and Geita, which together account for 21,591,809 people according to the 2022 National Population and Housing Census, with individual regional populations ranging from 889,946 in Njombe to 3,391,679 in Tabora. Children aged below 15 years constitute approximately 9,755,430 (44.0%) of the total population (20). Nationally, Tanzania has a population of approximately 61 million and is among the WHO's 30 high TB/HIV burden countries (1, 20, 21), with an adult HIV prevalence of 4.4%(9) and children under 15 years accounting for 17% of all notified TB cases in 2022(21). All ten study regions exceed this national adult HIV prevalence, ranging from 4.9% in Geita and Ruvuma to 12.7% in Njombe, the highest in the country, reflecting their selection as priority regions for integrated TB-HIV programming (9). The National Tuberculosis and Leprosy Programme (NTLP) operates under the Ministry of Health (MOH), which coordinates TB and Leprosy diagnosis, treatment, and surveillance through a network of public and private health facilities across the country.

3.3. Study Population

The study population comprised all children aged < 15 years diagnosed with TB and registered in the DHIS2-eTL during 2018–2023 with documented HIV status. The < 15 years cutoff aligns with WHO and NTLP definitions for pediatric TB. Children with all forms of TB (pulmonary and extrapulmonary) and all diagnostic categories (bacteriologically confirmed and clinically diagnosed) were included. HIV status (positive vs. negative) served as the binary outcome variable. Children with unknown or missing HIV status were excluded, as were adults (≥ 15 years). This approach enabled identification of factors associated with HIV co-infection across the full TB-registered cohort.

3.4. Sample Size

A total of 163,476 records were reviewed from the DHIS2-eTL across ten regions. Of the records reviewed, 159,809 records were excluded from the analysis for the following reasons: 137,877 were adult cases, 21,782 were HIV negative, 150 had incomplete records, such as 4 missing age, and 146 had unknown HIV status. The final sample

included in the analysis consisted of 3,667 records. Post-hoc power assessment confirmed adequacy, with 3,667 HIV-positive cases across 20 predictor variables yielding an events-per-variable ratio of approximately 183 (3,667/15), substantially exceeding the recommended minimum threshold of 10 (22).

3.5. Data Sources and Variables

Secondary data were obtained from the DHIS2-eTL using a structured extraction checklist covering demographics (age and sex), referral source, and method of diagnosis, TB disease classification, treatment regimen, HIV status, collaborative TB-HIV services, and history of prior treatment.

The primary outcome was HIV status (positive or negative), as documented at the time of TB registration. Covariates included age (categorized as < 5, 5–9, and 10–14 years), sex (male/female), region (ten study regions), DSTB treatment regimen (2HRZE/10RH, 2RHZE/4RH, 2RHZE/4RH-KID), disease classification (pulmonary, extra-pulmonary, or both), and history of treatment (new case, relapse, treatment after loss to follow-up, or other previously treated).

3.6. Statistical Analysis

Data were cleaned using Microsoft Excel Professional 2021, with quality checks for duplicate entries, missing values, and logical inconsistencies. All statistical analyses were performed using R software (version 4.5.1) at a significance level of 5%. Descriptive statistics were computed for all variables. Continuous variables were summarized as means with standard deviations (or medians with interquartile ranges for non-normally distributed data), and categorical variables as frequencies and percentages.

The Mann-Kendall test was used to assess monotonic trends in the annual HIV prevalence. Associations between HIV status and participant characteristics were assessed using Pearson's chi-squared test (or Fisher's Exact Test as applicable) for categorical variables and the Wilcoxon rank-sum test for continuous variables. Binary logistic regression was performed to identify factors associated with HIV co-infection, with results reported as unadjusted and adjusted odds ratios (OR/aOR) with 95% confidence intervals (CIs). Variables with $p < 0.2$ in the bivariate analysis and those with biological plausibility were included in the multivariable model. The COVID-19 period was defined as 2020–2023 and the pre-COVID period as 2018–2019.

Results

4.1. Participant Characteristics and HIV Prevalence

Among 25,449 children aged below 15 years diagnosed with TB across the ten study regions between 2018 and 2023 with documented HIV status, the overall prevalence of HIV co-infection was 14.4% (3,667/25,449). HIV prevalence declined markedly over the six years, from 28.5% in 2018 to 8.9% in 2023 ($p < 0.001$). In the bivariate analysis (Table 1), TB-HIV co-infection increased progressively with age: 9.0% in children aged below 5 years, 17.7% in those aged 5–9 years, and 22.6% in those aged 10–14 years ($p < 0.001$). No significant difference in HIV prevalence was observed between the sexes (female 14.5% vs. male 14.4%; $p = 0.814$). Regional variation was evident ($p < 0.001$), with the highest crude HIV prevalence in Njombe (29.7%), Mbeya (25.9%), and Iringa (23.5%), and the lowest in Ruvuma (6.7%), Mara (7.4%), and Kagera (8.2%). The full participant characteristics are presented in Table 1.

Table 1
Sociodemographic and clinical characteristics of children aged < 15 years with tuberculosis by HIV co-infection status, Tanzania, 2018–2023

Characteristic	Total N = 25,449	HIV Negative N = 21,782	HIV Positive N = 3,667	p-value
Age (years) – mean (SD)	5.7 (4.5)	5.4 (4.4)	7.4 (4.5)	< 0.001
<5 years	13,047 (51.3%)	11,873 (91.0%)	1,174 (9.0%)	< 0.001
5–9 years	6,325 (24.9%)	5,207 (82.3%)	1,118 (17.7%)	
10–14 years	6,077 (23.9%)	4,702 (77.4%)	1,375 (22.6%)	
Sex				0.814
Female	12,134 (47.7%)	10,379 (85.5%)	1,755 (14.5%)	
Male	13,315 (52.3%)	11,403 (85.6%)	1,912 (14.4%)	
Region				< 0.001
Geita	3,102 (12.2%)	2,532 (81.6%)	570 (18.4%)	
Iringa	1,381 (5.4%)	1,056 (76.5%)	325 (23.5%)	
Kagera	3,632 (14.3%)	3,335 (91.8%)	297 (8.2%)	
Mara	3,661 (14.4%)	3,391 (92.6%)	270 (7.4%)	
Mbeya	1,472 (5.8%)	1,091 (74.1%)	381 (25.9%)	
Njombe	1,112 (4.4%)	782 (70.3%)	330 (29.7%)	
Ruvuma	2,777 (10.9%)	2,592 (93.3%)	185 (6.7%)	
Shinyanga	3,596 (14.1%)	3,090 (85.9%)	506 (14.1%)	
Songwe	871 (3.4%)	745 (85.5%)	126 (14.5%)	
Tabora	3,845 (15.1%)	3,168 (82.4%)	677 (17.6%)	
Year of Registration				< 0.001
2018	2,688 (10.6%)	1,922 (71.5%)	766 (28.5%)	
2019	3,404 (13.4%)	2,670 (78.4%)	734 (21.6%)	
2020	4,536 (17.8%)	3,840 (84.7%)	696 (15.3%)	
2021	4,907 (19.3%)	4,380 (89.3%)	527 (10.7%)	
2022	5,421 (21.3%)	4,877 (90.0%)	544 (10.0%)	
2023	4,493 (17.7%)	4,093 (91.1%)	400 (8.9%)	
DSTB Regimen				< 0.001
2HRZE/10RH	477 (1.9%)	435 (91.2%)	42 (8.8%)	
2RHZE/4RH	15,201 (60.4%)	12,728 (83.7%)	2,473 (16.3%)	
2RHZE/4RH-KID	9,477 (37.7%)	8,369 (88.3%)	1,108 (11.7%)	

HIV = Human Immunodeficiency Virus; SD = Standard Deviation; N = Number of participants; DSTB = Drug-Susceptible Tuberculosis; H = Isoniazid; R = Rifampicin; Z = Pyrazinamide; E = Ethambutol; 2HRZE/10RH = 2 months of Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol followed by 10 months of Rifampicin and Isoniazid; 2RHZE/4RH = 2 months of Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol followed by 4 months of Rifampicin and Isoniazid; 2RHZE/4RH-KID = pediatric formulation of 2RHZE/4RH regimen; SD = standard deviation. Values are expressed as n (%) unless otherwise stated. p-values from the Wilcoxon rank-sum test (continuous) and Pearson's chi-squared test (categorical).

4.2. Factors Associated with HIV Infection Among Tuberculosis Patients under 15 Years of Age

In multivariable logistic regression, compared with children aged below 5 years, those aged 5–9 years had more than twice the adjusted odds of HIV co-infection (aOR = 2.32, 95% CI 2.11–2.55), while those aged 10–14 years had nearly three times the odds (aOR 2.99, 95% CI 2.72–3.29). After adjustment for age, sex, region, year of registration, and DSTB regimen, Njombe (aOR = 1.73, 95% CI 1.46–2.04), Mbeya (aOR = 1.53, 95% CI 1.31–1.78), Iringa (aOR = 1.37, 95% CI 1.17–1.61), and Tabora (aOR = 1.15, 95% CI 1.01–1.30) were associated with higher odds of co-infection. At the same time, Kagera (aOR = 0.45; 95% CI 0.38–0.52), Mara (aOR = 0.35; 95% CI 0.30–0.41), and Ruvuma (aOR = 0.40; 95% CI 0.33–0.48) had significantly lower odds compared to Geita (reference region).

The COVID-19 era (2020–2023) was associated with substantially lower odds of HIV co-infection than 2018–2019 (aOR = 0.42, 95% CI 0.39–0.46). Children receiving the standard adult-formulation regimen 2RHZE/4RH (aOR = 1.62, 95% CI 1.17–2.29) or the child-friendly dispersible formulation 2RHZE/4RH-KID (aOR = 1.76, 95% CI 1.37–2.51) had higher odds than those on 2HRZE/10RH. Extrapulmonary TB (aOR = 2.10, 95% CI 1.14–4.35) and pulmonary TB (aOR = 2.37, 95% CI 1.29–4.91) were each associated with higher odds than having both forms simultaneously. Children with a history of prior treatment had markedly elevated odds: other previously treated (aOR = 4.50, 95% CI 2.16–9.45), relapse (aOR = 4.68, 95% CI 3.04–9.45), and treatment after loss to follow-up (aOR = 3.75, 95% CI 2.18–6.35). The full regression results are presented in Table 2.

Table 2

Factors associated with HIV infection among TB patients aged below 15 years (binary logistic regression)

Characteristic	Unadj. OR	95% CI	p	Adj. OR	95% CI	p
Age:						
< 5 years (Ref)	Ref	–	–	Ref	–	–
5–9 years	2.17	1.99–2.37	< 0.001	2.32	2.11–2.55	< 0.001
10–14 years	2.96	2.72–3.22	< 0.001	2.99	2.72–3.29	< 0.001
Sex:						
Female (Ref)	Ref	–	–	Ref	–	–
Male	0.99	0.92–1.06	0.814	0.99	0.92–1.07	0.796
Region						
Geita (Ref)	Ref	–	–	Ref	–	–
Iringa	1.37	1.17–1.59	< 0.001	1.37	1.17–1.61	< 0.001
Kagera	0.40	0.34–0.46	< 0.001	0.45	0.38–0.52	< 0.001
Mara	0.35	0.30–0.41	< 0.001	0.35	0.30–0.41	< 0.001
Mbeya	1.55	1.34–1.80	< 0.001	1.53	1.31–1.78	< 0.001
Njombe	1.87	1.60–2.19	< 0.001	1.73	1.46–2.04	< 0.001
Ruvuma	0.32	0.27–0.38	< 0.001	0.40	0.33–0.48	< 0.001
Shinyanga	0.73	0.64–0.83	< 0.001	0.82	0.72–0.94	0.005
Songwe	0.75	0.61–0.92	0.007	0.95	0.76–1.18	0.638
Tabora	0.95	0.84–1.07	0.407	1.15	1.01–1.30	0.038
Period						
Pre-COVID (Ref)	Ref	–	–	Ref	–	–
During COVID	0.39	0.36–0.42	< 0.001	0.42	0.39–0.46	< 0.001
Regimen						
2HRZE/10RH (Ref)	Ref	–	–	Ref	–	–
2RHZE/4RH	2.01	1.48–2.81	< 0.001	1.62	1.17–2.29	0.005
2RHZE/4RH-KID	1.37	1.01–1.92	0.055	1.76	1.37–2.51	0.001
Disease						
Both (Ref)	Ref	–	–	Ref	–	–

Adj. OR = adjusted odds ratio; CI = confidence interval; COVID-19 = Coronavirus Disease 2019; HRZE = isoniazid, rifampicin, pyrazinamide, and ethambutol; RH = rifampicin and isoniazid; KID = child-friendly tuberculosis formulation; LTFU = lost to follow-up; OR = odds ratio; Ref = reference category. *p*-values were derived from logistic regression analyses. The referral source and calendar year were excluded from the final multivariable model because of sparse cell counts in some categories.

Characteristic	Unadj. OR	95% CI	p	Adj. OR	95% CI	p
Age:						
Extra-pulmonary	1.90	1.07–3.74	0.041	2.10	1.14–4.35	0.029
Pulmonary	2.26	1.28–4.45	0.009	2.37	1.29–4.91	0.011
History on Treatment:						
New (Ref)	Ref	–	–	Ref	–	–
Other	5.75	2.99–11.0	< 0.001	4.50	2.16–9.45	< 0.001
Relapse	5.85	4.02–8.53	< 0.001	4.68	3.04–9.45	< 0.001
After LTFU	4.05	2.43–6.62	< 0.001	3.75	2.18–6.35	< 0.001
Adj. OR = adjusted odds ratio; CI = confidence interval; COVID-19 = Coronavirus Disease 2019; HRZE = isoniazid, rifampicin, pyrazinamide, and ethambutol; RH = rifampicin and isoniazid; KID = child-friendly tuberculosis formulation; LTFU = lost to follow-up; OR = odds ratio; Ref = reference category. p-values were derived from logistic regression analyses. The referral source and calendar year were excluded from the final multivariable model because of sparse cell counts in some categories.						

Discussion

This study characterized the prevalence and factors associated with HIV infection among 25,449 children with TB across ten high-burden regions of Tanzania over six years' period (2018–2023). Tanzania has achieved remarkable progress in scaling up HIV and TB prevention interventions, including PMTCT, ART, and TPT programs, and this study presents critical findings in the context of these efforts. The findings showed an HIV prevalence of 14.4%, with a notable decline of more than two-thirds, from 28.5% in 2018 to 8.9% in 2023, a testament to the programme's efforts to reduce TB-HIV co-infection. Children aged 10–14 years had three-fold higher odds of HIV co-infection (aOR 2.99, 95% CI 2.72–3.29), and those with prior TB treatment had 4–5-fold higher odds. These findings suggest that routine repeat HIV testing for all children with TB aged ≥ 5 years and intensified TPT for children with prior TB could reduce co-infection burden. Regional disparities (aOR 1.73 in Njombe vs. reference) indicate that Njombe, Mbeya, and Iringa should be prioritized for integrated TB-HIV services.

The overall HIV prevalence of 14.4% is consistent with WHO estimates that HIV prevalence among children with TB in countries with moderate-to-high HIV prevalence ranges from 10% to 57%, with substantial variation by setting (4, 14, 23). The marked decline in HIV prevalence among pediatric TB patients between 2018 and 2023 temporally coincides with the progressive scale-up of PMTCT services, and expansion of pediatric ART and TPT coverage in Tanzania (10, 21, 24–26). The increased TB-HIV coinfection among older children may reflect a survivor bias or aging-up effect, whereby children who missed PMTCT or TPT intervention survived into early adolescence and presented with childhood TB disease later (27, 28). The 2022–2023 THIS survey documented a decline in national adult HIV prevalence from 4.9% (2016–2017) to 4.4%, reflecting the impact of the sustained national HIV response (8, 9). Since children predominantly acquire HIV through vertical transmission, the successful implementation of Option B+, which provides lifelong ART to all HIV-positive pregnant women regardless of CD4 count, has been instrumental in reducing the number of perinatally infected children who would later present with TB (10).

ART has been shown to reduce TB incidence in HIV-positive children by 70–92%, directly explaining lower TB-HIV co-infection rates in settings with high ART uptake (29, 30). However, the mechanisms underlying continued HIV

acquisition among older children in the context of scaled-up PMTCT remain incompletely understood(27, 31). Studies from neighboring countries have documented "breakthrough" infections despite nevirapine prophylaxis, missed steps along the PMTCT cascade (including undiagnosed maternal HIV, poor retention, and limited follow-up testing for older children with infrequent health system contact), and possible horizontal or postnatal transmission routes that are not captured by standard PMTCT surveillance(31). Disentangling testing gaps, breakthrough vertical transmission, and other transmission pathways among older children remains an important area for further research in Tanzania.

The strong and graded association between age and HIV co-infection, with nearly three-fold odds in the 10–14-year age group compared with children below 5 years, is consistent with evidence from sub-Saharan Africa. Mandalakas et al, 2020. demonstrated in a multi-country SSA cohort that increasing ART uptake was associated with declining TB prevalence, and that severe immunosuppression, rather than age per se, was strongly associated with poor TB outcomes(15). This is consistent with the hypothesis that the age gradient observed in our cohort reflects accumulating immune deterioration among perinatally infected children who were not diagnosed early or who experienced ART coverage gaps, leading to progressive immunosuppression by the time TB is diagnosed in later childhood(15, 32).

Additionally, older children, particularly those aged 10–14 years, were largely born before or during Tanzania's October 2013 Option B+ rollout (33), when lifelong maternal ART was not yet universal. Many may have had undiagnosed HIV for years, missed early infant diagnosis, or experience breakthrough infections from incomplete PMTCT cascades. Nationally, only 34.6–44.2% of HIV-exposed infants return for the 18-month confirmatory test (10), leaving many undiagnosed until later presentation with advanced diseases including TB. These findings reinforce the need for routine, repeat HIV testing of all children presenting with TB, particularly those aged ≥ 5 years, regardless of prior HIV status.

Substantial geographic variation in HIV co-infection rates was observed, with Njombe, Mbeya, and Iringa consistently showing the highest adjusted odds of co-infection. This is concordant with the THIS 2022–2023 regional data, which identified these same regions as having the highest adult HIV prevalence in mainland Tanzania: 12.7%, 9.6%, and 11.1%, respectively (9). High community HIV prevalence translates directly into higher rates of perinatal exposure among children and a higher background risk of sexually acquired HIV among older adolescents in the 10–14-year group (4, 34). In contrast, Kagera, Mara, and Ruvuma had significantly lower odds, consistent with their comparatively lower adult HIV prevalence. These regional disparities highlight the need for geographically targeted intensification of integrated TB-HIV services, including enhanced tracing of HIV-exposed infants, scaling up of TB preventive therapy, and community-level ART adherence support in high-burden regions.

The substantially lower odds of HIV co-infection during 2020–2023 (aOR = 0.42) likely reflect diagnostic disruptions rather than true declines. Studies from Malawi, Ghana, and Zambia document 20–45% drops in TB notifications and HIV testing during COVID-19, with disproportionate under-detection of HIV-positive TB cases (11–13, 35).

The markedly elevated odds of HIV co-infection among children with a history of prior TB treatment, particularly relapse cases (aOR = 4.68) and those previously lost to follow-up (aOR 3.75), underscore the bidirectional relationship between HIV and poor TB treatment outcomes. HIV-positive children are more likely to experience treatment failure, loss to follow-up, and relapse due to inadequate immune reconstitution, suboptimal ART adherence, and the added complexity of managing dual infections(4). These findings are consistent with prior evidence that TB treatment outcomes are substantially worse in HIV-co-infected children(3, 15). Therefore, children presenting with retreatment TB in Tanzania should be considered a high-priority group for HIV testing and integrated

care. Moreover, children with HIV should be routinely monitored for possible recurrence of TB, which may be devastating to treatment outcomes, as it may result in failure or development of resistance (36, 37).

Both pulmonary and extrapulmonary TB were associated with higher odds of HIV co-infection than having both forms simultaneously. This may reflect that the reference category (having both) represents children with the most advanced and disseminated disease, possibly including severely immunocompromised children already known to be HIV-positive and under treatment. Extrapulmonary TB, in particular, is well recognized as an AIDS-defining illness and a marker of severe immunosuppression, and its association with HIV co-infection in this cohort is biologically plausible(4).

The primary strength of this study is the use of six years of complete programme-level data across ten high-burden regions, providing high statistical power and broad generalizability across Tanzania's HIV-endemic areas; routinely collected data further minimized recall bias. Of 27,831 eligible children, 25,449 (91.4%) had documented HIV status and were included. The 8.6% excluded due to missing HIV status were anticipated, and a detailed study profile was provided in the sampling section to maintain transparency. Although a census of all available records was used to limit selection bias, children without documented HIV status may differ systematically from those included, and this possibility cannot be fully excluded. The cross-sectional design precludes causal inference; the observed temporal decline in co-infection prevalence cannot be directly attributed to PMTCT, ART, or TPT scale-up without further evidence. The ten-region selection, guided by adult HIV prevalence, may not fully represent Tanzania's national pediatric TB-HIV burden, though these regions bear the greatest programmatic burden. Absence of CD4 counts, viral loads, and ART status at TB diagnosis restricted characterization of immunological profiles among co-infected children, limiting clinical inference from the observed age and regional risk gradients. Prospective cohort studies with individual-level programme data linkage, or interrupted time-series analyses aligned with intervention roll-out timelines, are needed to test causal hypotheses.

Conclusion

HIV co-infection was found in approximately one in seven children diagnosed with TB across the ten high-HIV-burden regions of Tanzania, with a marked and encouraging decline from 28.5% to 8.9% between 2018 and 2023. This trend likely reflects the cumulative impact of preventive and treatment interventions. Nonetheless, significant regional disparities persist, particularly in Njombe, Mbeya, and Iringa, and older children, those with prior TB treatment, and those with extra-pulmonary disease remain at substantially higher risk of HIV co-infection. To further reduce the burden of TB-HIV co-infection among Tanzanian children, stakeholders need to intensify geographically targeted TB-HIV integration, prioritizing Njombe, Mbeya, and Iringa regions, routinize HIV testing for all children presenting with TB, with particular attention to older children, expand TPT for children living with HIV in high-burden regions and strengthen tracking and follow-up of HIV-exposed infants to close the confirmatory testing gap. A continued investment in pediatric ART coverage and PMTCT programme fidelity will consolidate recent gains, Sustained commitment to these integrated strategies will be critical to protecting recent gains and accelerating progress toward the elimination of childhood TB-HIV co-infection in Tanzania.

Abbreviations

Abbreviation	Full Term
aOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CTC	Care and Treatment Clinic
DSTB	Drug-Susceptible Tuberculosis
EID	Early Infant Diagnosis
HIV	Human Immunodeficiency Virus
IPD	Inpatient Department
LTFU	Lost to Follow-Up
MOH	Ministry of Health
NaTHREC	National Health Research Ethics Committee
NIMR	National Institute for Medical Research
NTLP	National Tuberculosis and Leprosy Programme
OR	Odds Ratio
PLHIV	People Living with HIV
PMTCT	Prevention of Mother-to-Child Transmission
RCHS	Reproductive and Child Health Services
SD	Standard Deviation
SSA	Sub-Saharan Africa
TB	Tuberculosis
THIS	Tanzania HIV Impact Survey
TPT	Tuberculosis Preventive Therapy
WHO	World Health Organization

Declarations

Ethics Approval and Consent to Participate

Ethical approval was granted by the National Institute for Medical Research (NIMR) through the National Health Research Ethics Committee (NaTHREC) (Reference: NIMR/HQ/R.8a/Vol.IX/4988) in Dodoma, Tanzania. Administrative clearance was obtained from the Cavendish University School of Postgraduate Studies. Permission to utilize programmatic data was obtained from the Tanzania Ministry of Health through the NTLP (Reference: GA.154/425/05/111/9). As this study involved secondary analysis of de-identified, routinely collected programmatic data, the requirement for individual informed consent was waived by the ethics committee in accordance with

national ethical guidelines. All patient identifiers were removed during data extraction, and only anonymized data were used for analysis. This study was conducted in accordance with the Declaration of Helsinki and adhered to the STROBE guidelines for reporting cross-sectional studies.

Consent for Publication

Not applicable. No individual-level identifiable data are presented.

Competing Interests

The authors declare no competing interests.

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Author Contribution

ENM: Conceptualization, methodology, analysis, writing, original draft, project administration. STW: Data review, analysis, and interpretation. DN, DK, and FSK: Technical oversight throughout study development, analysis, interpretation, writing, and review. DK, OGO, AR, JK, KMR, PS, RFB, and GAS: Critical review and editing of the manuscript. All authors read and approved the final manuscript.

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Data Availability

The datasets analyzed during this study are not publicly available due to patient privacy considerations and institutional data protection policies. Aggregated data supporting the findings are available from the corresponding author upon reasonable request. Researchers may also request data access directly from the Tanzania NTLP. All supporting data necessary to interpret the study findings are included within the manuscript and its supplementary materials.

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