BMC Infectious Diseases

SYSTEMATIC REVIEW

Open Access

Prevalence, clinical characteristics, and treatment outcomes of childhood tuberculosis in Nigeria: a systematic review and meta-analysis

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Abstract

Background Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is a leading cause of infection-related deaths worldwide. Children with underdeveloped immune systems are particularly vulnerable, experiencing symptoms akin to common childhood illnesses. Early diagnosis and treatment typically yield positive outcomes. In Nigeria, childhood TB is underreported, complicating accurate burden assessment. This review synthesises and presents evidence on the disease prevalence among children in Nigeria, identifies clinical characteristics, and evaluates the effectiveness of treatment regimens and outcomes.

Methodology A comprehensive systematic search across electronic databases was conducted to retrieve studies on the prevalence, characteristics, diagnostic criteria, and treatment outcomes of childhood tuberculosis in Nigeria. Study registration, data extraction and quality assessment followed standardized guidelines. The meta-analysis used a random-effects model to determine prevalence and mean treatment outcomes. Statistical heterogeneity was assessed using the I^2 statistic, and publication bias was evaluated with Egger's test ($p=0.127$) and a funnel plot.

Results This review and meta-analysis of 22 studies, primarily retrospective (77%) and cross-sectional (18.20%), involving 1,162,936 participants aged 0–18 years, found a pooled prevalence of 20.82% (95% CI: 8.55–36.64)) with high heterogeneity ($I^2=99.88\%$). Pulmonary tuberculosis is the most common form in children 62.70% (95%: 43.57–80.03) diagnosed using sputum smear microscopy, GeneXpert MTB/RIF assays, chest radiographs, and tuberculin skin tests. Clinical diagnosis based on symptoms, contact history, and radiological findings is crucial for younger children unable to produce sputum, as laboratory tests confirm only 6% of cases. Treatment involves the use of rifampicin, isoniazid, pyrazinamide, and ethambutol per national and international guidelines. The meta-analysis showed an average treatment success rate of 75.47%%, but challenges such as loss to follow-up (11.40%)) and increasing mortality rates (6.76%) persist.

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Conclusion The burden of childhood tuberculosis in Nigeria is significant, even as diagnostic limitations pose constraints. The findings highlight the need for stronger health system collaborations to improve the quality of care offered to children diagnosed with TB. Future research should standardize diagnostic criteria and methodologies for consistent and reliable prevalence estimates. More longitudinal studies are necessary to comprehend the trend and pattern for the heightened prevalence and subpar treatment outcomes of childhood tuberculosis in Nigeria.

PROSPERO ID CRD42024586765.

Keywords Tuberculosis, Childhood tuberculosis, Prevalence, Treatment outcome, Nigeria

Introduction

Tuberculosis (TB) remains a leading cause of infection-related deaths globally despite being declared a public health emergency by the World Health Organization (WHO) about three decades ago [1]. Infections in children present with even worse prognoses and outcomes due to the underdeveloped immune response mechanism common among children. Childhood TB is an infection by *Mycobacterium tuberculosis* in individuals under 15 years old, primarily affecting the lungs but potentially involving organs like the kidneys, spine, or brain [2]. The disease presentation and progression differ slightly from those in adults, and among the pediatric age bands, with under-fives disproportionately affected [3]. Multi-organ manifestations are also common in children with an increased tendency for active disease after a latent infection [3, 4].

Prevalence reports indicate high case numbers and associated fatalities in endemic areas and resource-limited settings. In 2022, there were approximately 10.6 million cases of active TB globally, with 1.3 million children affected [5]. Africa has seventeen of the 30 countries accounting for the highest global TB prevalence, with approximately 322,000 cases reported among children and young adolescents (0–15 years) in each country [5, 6]. However, two-thirds of these cases were either undiagnosed or unreported, and only around 32% of children under five were diagnosed and treated [6]. In Nigeria, 9% of 361,000 reported TB cases in 2023 occurred in children, indicating a 26% increase in the number of cases in 2022 [7]. Nigeria, as an endemic region, grapples with multiple risk factors for increased TB infection, which is not limited to overpopulation and overcrowding – that favors increased spread– but also poor living conditions, economic strains and food insecurity, and poor healthcare and diagnostic systems, among others [8].

Clinical presentations may mimic common childhood illnesses [9]. Asymptomatic patients with a positive Tuberculin Skin Test (TST) are typically identified during routine medical checks or contact tracing after exposure to infected individuals. Once diagnosed, disease presentation, severity, and progression vary per site of infection, whether pulmonary or extrapulmonary. Pulmonary TB results in focal lymphadenopathy, progressive pulmonary disease, pleural involvement, and reactivated pulmonary disease, with symptoms such as fever, night sweats, anorexia, nonproductive cough, failure to thrive, and poor weight gain. Extrapulmonary TB affects other organs, causing peripheral lymphadenopathy, meningitis, skeletal TB, and abdominal TB [1]. Disseminated TB, or miliary TB, is a severe form that spreads through the bloodstream to multiple organs. Early diagnosis and prompt treatment usually yield favourable outcomes. Most children fully recover with early detection and therapy. Quality supportive care enhances prognosis, minimising long-term complications, recurrence, or drug resistance [10, 11]. However, poor treatment outcomes are seen in cases of HIV co-infection due to immunosuppression and drug interaction between antiretroviral medication and anti-TB medication [12].

Childhood TB is poorly reported in Nigeria, with inconsistent data reporting limiting understanding of the actual disease burden. With the ambitious target by WHO to attain 90% treatment coverage, treatment success rate, preventive treatment coverage, and uptake of new diagnostics and drugs by 2025 [13], it is pertinent to understand the disease prevalence, patterns, and treatment trends across endemic regions such as Nigeria. Thus, this review and meta-analysis aims to systematically synthesise existing evidence to determine the prevalence of childhood TB in Nigeria, identify common characteristics, and assess the outcomes and effectiveness of current treatment regimens.

Methodology

Study reporting and registration

This review was conducted and reported per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline covering all parts of the article items, including the title, abstract, introduction, method, results, discussion, and funding (S1) [14]. The study protocol was registered with PROSPERO (International Prospective Register of Systematic Reviews) with registration number CRD42024586765 and provided details of the research question and objectives, inclusion and exclusion

criteria, and the methodological approach for this systematic review.

Research questions

1. What is the pooled prevalence of childhood tuberculosis in Nigeria?
2. What are the clinical characteristics and disease patterns of childhood tuberculosis in Nigeria?
3. What are the treatment options and outcomes in Nigeria?

Search strategy

A systematic search of available literature was conducted across electronic databases to identify all studies on the study theme. The search retrieved studies from PubMed, Google Scholar, Science Direct, DOAJ, AJOL, and Cochrane Library using relevant BOOLEAN strings from our inclusion and exclusion criteria (Fig. 1). The search on PubMed was carried out using a combination of Medical Subject Headings (MeSH) in the search string ("tuberculosi"[All Fields] OR "tuberculosis"[MeSH Terms] OR "tuberculosis"[All Fields] OR "tuberculoses"[All Fields] OR "tuberculosis s"[All Fields]) AND ("nigeria"[MeSH Terms] OR "nigeria"[All Fields] OR "nigeria s"[All Fields]). The search included studies published from inception to August 2024 (S2). Additionally, the reference list of all relevant studies was searched based on the eligibility criteria to identify additional studies for the review. The literature search was conducted by two authors (A.E.B. and B.M.U.) through a detailed examination of various databases. The focus was on studies reporting the prevalence, characteristics, and

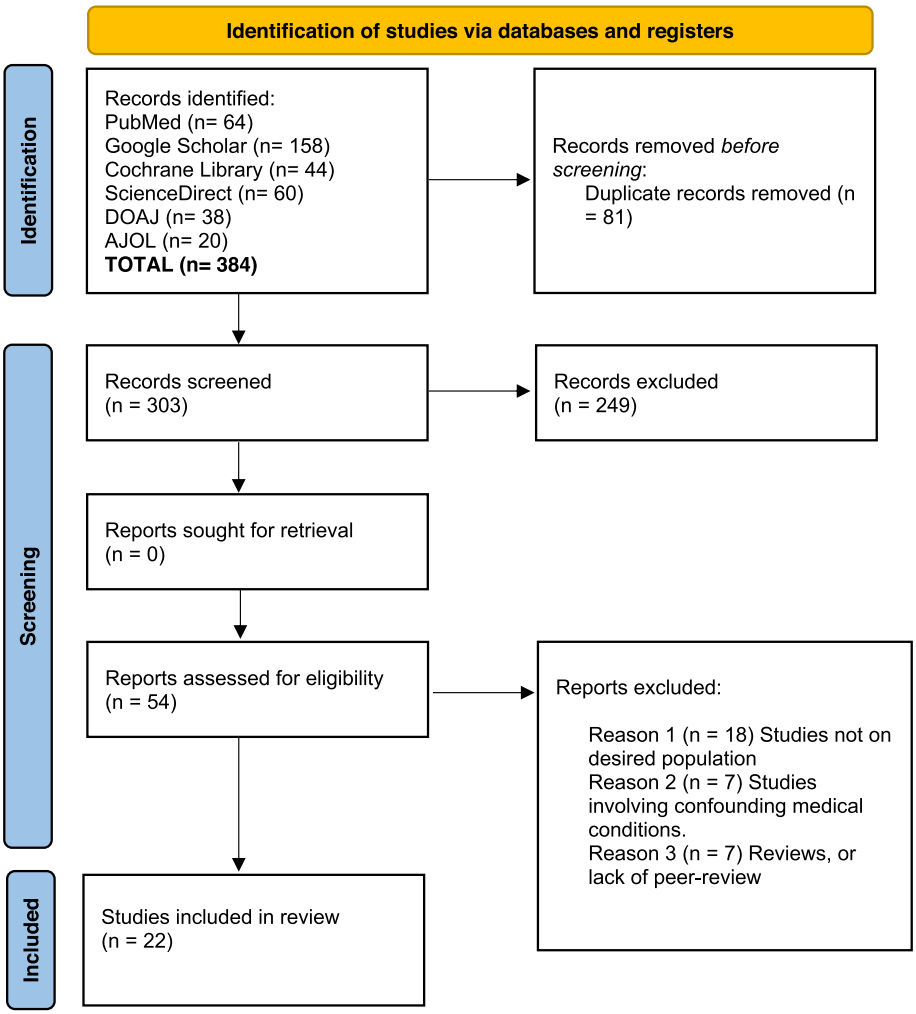

Fig. 1 The PRISMA flow chart for selecting studies for systematic review

management outcomes of children diagnosed with tuberculosis in Nigeria.

Eligibility criteria

To be included in this review, the study should have utilized an observational (cohort, case-control, cross-sectional) or intervention (randomized controlled trials, controlled clinical trials) study design. The inclusion criteria were drawn according to population, exposure, comparison, and outcome (PECO) framework:

- Population: individuals aged 0 to 18 years in Nigeria.
- Exposure: Mycobacterium tuberculosis infection.
- Comparison: none.
- Outcome:
- Prevalence of childhood tuberculosis.
- Clinical characteristics of childhood tuberculosis.
- Treatment outcomes of tuberculosis.

Studies reporting data on the prevalence, characteristics, and treatment outcomes of childhood tuberculosis in Nigeria were included. In addition, the included studies should have been published in English and conducted before 22nd August 2024, when the study search was done.

Research conducted outside Nigeria and studies that did not provide relevant data on childhood tuberculosis outcomes were excluded. Additionally, the review excluded qualitative studies, preprints, narrative and systematic review articles, editorials, commentaries, conference abstracts, and data from grey and unpublished sources due to inconsistency in reporting. Only pediatric-specific data were extracted for studies involving adult and pediatric populations, while adult subpopulation data were excluded from the review.

Study selection

Two independent reviewers (A.E.B. and T.A.W.) screened titles and abstracts to determine eligibility following the predetermined inclusion and exclusion criteria registered in the PROSPERO protocol after article duplicates were removed using the Rayyan tool. Eligible studies were subjected to a full-text review, and disagreements were resolved through discussion and involvement of a third reviewer (B.M.U).

Measurements

This systematic review and meta-analysis determined the prevalence, clinical characteristics, and treatment outcome of tuberculosis among individuals aged 0 to 18 years. Treatment outcomes were measured from primary studies, which were categorized as:

1) Cured: Sputum smear-positive patient who was sputum negative in the last month of treatment and on at least 1 previous occasion.
2) Treatment completed: Patients who have completed treatment but who do not meet the criteria to be classified as a cure or a failure.
3) Treatment failure: Any TB patient who is sputum smear positive at 5 months or later during treatment.
4) Died: Patient who died during the period of treatment (regardless of the cause of death).
5) Defaulted/Lost to follow-up: Patient whose treatment was interrupted for two consecutive months or more after registration.
6) Transferred out: A TB patient who has been transferred to another local government area to continue his/her treatment and for whom treatment outcome is unknown.

Data extraction

Data extraction was conducted independently by two researchers (T.A.W and B.M.U) using a pre-tested form developed in Microsoft Excel, which involved gathering relevant details from each study included in the analysis. The extracted information encompassed the primary author's name, year of publication, the state/region in which the study was conducted, study design, sample size, and infection prevalence. Furthermore, the extraction process captured data on the diagnostic approach utilized for TB diagnosis in children, clinical characteristics of infection, treatment modality, adherence, duration of treatment, successful outcomes, and failure rates, including mortality (Tables 1, 2, 3 and 4).

Quality assessment

Two authors (B.M.U. and F.M.D.) independently evaluated the quality of the included studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies (S3) [38]. This checklist assessed methodological quality based on eight questions, with responses categorized as yes, no, unclear, or not applicable. A score of 1 indicated 'yes,' while 0 represented the other responses. Scores ranged from 0 to 8 and were converted to percentages. Only studies scoring at least 50% were included in the final meta-analysis. Disagreements during the appraisal were resolved through scientific consensus and discussion.

Data synthesis and statistical analysis

A systematic synthesis and meta-analysis were used to synthesize extracted data. Data from the Microsoft spreadsheet file was imported for analysis into STATA version 15 software. Studies with substantial

Table 1 Prevalence and characteristics of included studies

Authors	References	Publication Year	Study Design	Sample Size	Study objective(s)	Prevalence of TB(%)	Study location (region)
Adejumo OA et al.	[15]	2016	Retrospective study	535	To assess the treatment outcomes of Childhood TB in Lagos state, Nigeria.	6.3	Lagos (Southwest)
Daniel OJ et al.	[16]	2015	Retrospective study	2396	To assess the trend of childhood TB cases notified in Lagos, Nigeria from 2011 to 2014.	6.8	Lagos (Southwest)
Oloyede IP et al.	[17]	2019	Retrospective study.	3276	To assess the pattern of diagnosis, type of tuberculosis and treatment of childhood tuberculosis in Uyo, Southern Nigeria	1.	Uyo (Southsouth)
Mado SM et al.	[18]	2017	Retrospective study	1392	To determine the prevalence and pattern of TB in children at Federal Medical Centre, Gusau.	4.8	Gusau (Northwest)
Surajudeen B et al.	[19]	2021	Retrospective study	1243	To determine the burden and treatment outcome of childhood TB	7.1	Lafia (Northcentral)
Olusola O.	[20]	2019	Retrospective cohort study	28	To examine the response of tuberculosis-infected HIV-infected children to the standard recommended anti-TB regimens.	HIV/TB co-infection = 28	Osogbo (Southwest)
Imam, TS and Oyeyi, TI.	[21]	2008	Retrospective study.	291 Children 0- <15years	To ascertain the prevalence of pulmonary tuberculosis amongst patients attending the Infectious Diseases Hospitals in Kano.	7.0	Kano (Northwest)
Ebonyi et al.	[22]	2020	Observational study.	90	To determine the prevalence of LTBI in HIV-1-infected children on ART in a pediatric HIV clinic of the Jos University Teaching Hospital (JUTH), Jos, Nigeria.	4.4	Jos (Northcentral)
Alex-Hart Balafama A et al.	[23]	2019	Retrospective cross-sectional study	202	To evaluate the pattern and outcome of childhood Tuberculosis at the University of Port Harcourt Teaching Hospital.	-	Port Harcourt (Southsouth)

Table 1 (continued)

Authors	References	Publication Year	Study Design	Sample Size	Study objective(s)	Prevalence of TB(%)	Study location (region)
Onubogu C et al.	[24]	2019	Retrospective study	501	To examine the outcomes as well as factors that influence the outcomes of children TB treatment at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, South-East, Nigeria	New TB cases = 89.6 Pulmonary TB = 73.3	Nnewi (Southeast)
Fetuga BM et al.	[25]	2009	Retrospective study	2097	To determine the epidemiological and clinical features of childhood tuberculosis in Sagamu.	2.48	Sagamu (Southwest)
Attah C. Joseph et al.	[26]	2018	Cross sectional study	150	To determine the associated risk factors for Pulmonary TB among children aged 18 months to 15 years in an endemic setting	32	Nasarawa (Northcentral)
Ahmed PA et al.	[27]	2014	Descriptive and retrospective study	192	To describe the clinical presentation and outcome of adolescent tuberculosis at National Hospital Abuja (NHA), Nigeria.	18.8	Abuja (Northcentral)
Alex-Hart et al.	[28]	2019	Retrospective cross-sectional study	140	To evaluate the proportion of childhood TB cases seen in school-age children attending the DOTS clinic in the University of Port Harcourt Teaching Hospital.	41.79	Port Harcourt (Southsouth)
Ewa AU et al.	[29]	2015	Prospective study	128	To identify TB in children who were either living with adults who have TB or in the environment of adults with TB.	57	Eku (Southsouth)
Joseph AC et al.	[30]	2018	Cross-sectional study	150	N/A	32	Nasarawa (Northcentral)
Ogbudebe CL et al.	[31]	2018	Retrospective cohort study.	724	To determine the case category distribution of childhood TB in Nigeria and assess which clinical and demographic factors are associated with different treatment outcomes in childhood TB.	-	Lagos, Ondo, and Osun (Southwest)

Table 1 (continued)

Authors	References	Publication Year	Study Design	Sample Size	Study objective(s)	Prevalence of TB(%)	Study location (region)
Garba MA et al.	[32]	2023	Retrospective study	1463	To assess the use of Xpert MTB/RIF test as a modality for diagnosis of childhood TB across Tertiary Health Institutions in Nigeria	-	N/A
Ilah BG et al.	[33]	2018	Retrospective study	415	To determine the pattern and outcome of childhood tuberculosis managed at the DOTS clinic in Gusau, Nigeria.	18.3	Gusau (Northwest)
Bamidele J et al.	[34]	2021	Retrospective cohort study	759	To determine TB/HIV prevalence and treatment success of children with tuberculosis attending clinics in two tertiary institutions in Ogun State, Nigeria and to determine factors associated with treatment success	14.8	Ogun (Southwest)
Oleyede IP et al.	[35]	2013	Descriptive Cross-sectional study.	204	To determine the prevalence, and risk factors associated with pulmonary paragonimiasis and pulmonary tuberculosis among school children in Mbo Local Government Area (LGA) of Akwa Ibom State Nigeria.	2.9	Mbo (Southsouth)
Alao MA et al.	[36]	2020	Retrospective study	1,146,560	To evaluate 25 years of data from a continuous TB treatment program, focusing on outcomes and insights to inform progress toward SDG3 targets.	14.2	Iwo (Southwest)

Table 2 Clinical characteristics of childhood TB in Nigeria

References	Demographics of participants	Diagnostic modality	Clinical characteristics			
			PTB(%)	ETB(%)	DTB(%)	Others(%)
[15]	Males (51.8%) and females (48.2%) from 0–15 years.	AFB test, score charts and other clinical test and chest x-ray. Diagnosed by smear microscopy (20.6%), chest radiographs (69.9%), diagnosed clinically (3.7%)	91	9	-	New TB cases – 92.5 TB/HIV coinfection = 29
[16]	Males (46%) and females (54%) of 0–15 years.	AFB test, other diagnostic tests, such as chest radiograph, tuberculin test, and ESR. Use of a score chart according to the national TB guidelines	17–20	19–27.80	-	-
[17]	Males (53.96%) and females (46.04%) of 0–15 years. Mean age = 5.35 years ± 5.32 years.	Chest radiograph, sputum AAFB, sputum GeneXpert, ymph node aspirate and histology, GeneXpert, lymph node aspirate AAFB, gastric aspirate GeneXpert, cerebrospinal fluid AAFB, and TST.	67	13	-	TB/HIV cinfection – 29
[18]	Males (59.7%) and females (40.3%). Mean age of 5.6 ± 3.2 years	Diagnosis of TB was based on WHO criteria for the diagnosis of TB in resource-poor setting	26.9	Spinal TB – 13.40 Abdominal TB – 6.0 Renal TB – 1.50 Tuberculous meningitis – 1.50	50.70	TB/HIV co-infection – 9
[19]	Males (56%) and females (44%). The mean age of the study population was 7.72 ± 3.24	Gene Xpert testing on sputum sample. Gastric aspirate Gene Xpert analysis conducted for children without sputum.	84.1	3	13	-
[20]	Males (46.4%) and females (53.6%). Aged 3 months to 17 years. Mean age of 6.7 years.	An NTB score of 7 or above, suggestive chest radiograph findings, a positive Mantoux test, and therapeutic trial responses. Cerebrospinal fluid findings were also considered.	64.3	Abdominal TB – 10.7 TB meningitis – 3.6 Miliary TB –1	17.90	TB/HIV co-infection – 28
[21]	Males (54.53%) and females (45.73%) of 0–15 years.	Acid-fast Bacilli (AFB Test WHO, 2000).	14.7	-	-	-
[22]	Males (54.4%) and females(45.6%) of 6 months – 18 years.	LTBI diagnosed using an interferon-gamma release assay, the ELISpot test, T-SPOT®.TB assay was done on freshly collected whole blood.	-	-	-	LTBI – 4.4
[23]	Males (53.9%) and females(46.04%) of 0–18 years. Most \ were 1–4 years of age	Positive sputum smear for AFB (by Ziel Nelson) or a confirmed positive Xpert MTB/RIF test which also detects rifampicin resistance.	80.69%	TB Adenitis – 11.39, TB spine – 4.95, TB abdomen – 1.49, TB meningitis – 1.49	-	New cases – 96.04 TBHIV co-infection – 48.45
[24]	Males (50.5%) and females(49.5%) of 2 months to 14 years with a median and mean age of 5.0 and 6.15 ± 4.49 years, respectively.	Diagnosis done per standard guidelines by the NTBLCP. Further evaluation conducted with TST (Mantoux test), radiologic investigations and Ziehl–Neelsen stain for acid-fast bacilli (AFB. Gastric aspirate, cerebrospinal fluid, lymph node fine needle, peritoneal or pleural aspirates were also used in instances.	73.3	-	26.70	New TB cases – 89.6 TBHIV co-infection – 42.5
[25]	Males(61.5%) and females(38.5%) of 4 months to 14 years and median age, 96 months.	Per the NTBLCP guidelines with presenting clinical features and one of either AFB positivity in in smears of sputum or gastric washings, histology of granulomatous lesions, radiographs, clinical and radiological improvement of presenting features and supported lab investigations: PCV, ESR, ELISA test for HIV I and II	57.7	-	-	TBHIV co-infection – 60
[26]	Males(48%) and females(52%) of aged 18 months to 15 years. Mean age of 9.12 ± 4.66 years and median age of 10 years.	Chest X-ray, sputum or gastric aspirate acid-fast bacilli microscopy and mycobacterium culture.	-	-	-	TBHIV co-infection – 31.2

Table 2 (continued)

References	Demographics of participants	Diagnostic modality	Clinical characteristics			
			PTB(%)	ETB(%)	DTB(%)	Others(%)
[27]	Males (25%) and females (75%) aged 10–15 years The mean (SD) age was 12.3(1.76).	Direct smear microscopy (auramine-rhodamine and Kinyoun stain) in symptomatic patients. Clinical diagnosis was based on symptoms, TST results, contact history, or suggestive radiological/histopathological findings. A history of contact, radiological and/ or histopathological finding from lymph node biopsy were suggestive.	61.1	38.9	-	TBHIV co-infection – 25
[28]	Males(50.71%) and females(49.29%) of 6 to 18 years, with a mean age of 12.06 ± 3.86 years.	Sputum smear positivity, clinical evaluation, and radiological findings.	-	-	-	TB/HIV co-infection – 35
[29]	Males (53%) and females (47%) under 19 years of age. Mean age of 9.3 years and a median of 9.9 years	Physical examination, TST, chest radiograph and gastric aspirate (AFB)	-	-	-	-
[30]	Males (48%) and females (52%) mean age of 9.12 years (± 4.66) and a median age of 10 years	Diagnosis based on either culture-positive or AFB microscopy-positive results in two samples, or a combination of positive results from both tests.	-	-	-	New TB infection – 98.5 TB/HIV co-infection – 10
[31]	Males(44.8%) and females (55.2%) of 0–15 years.	Diagnosis per standard WHO/NTP methods, using sputum microscopy, clinical examination, chest X-ray, or GeneXpert. For those unable to produce sputum, alternative samples (gastric lavage, cerebrospinal fluid, and pleural biopsy) were collected for GeneXpert.	58.0	42	-	New TB cases – 98.5 TB/HIV co-infection – 14.9
[32]	Males(56%) and females (44%) of 0–14 years.	The Xpert MTB/RIF test, histologic diagnosis (Ziehl-Neelsen staining and microscopy of lymph node biopsy specimens). Xpert MTB/RIF testing also rose steadily from 56.65–64%	66.8	33.2	-	New TB cases – 98.7 TB/HIV co-infection – 25
[33]	Males (39.5%), females (60.5%). Mean ± SD age was 8.89 ± 5.38 years, with 38.2% being in the 0–5 years age group.	Diagnosis made with sputum smear microscopy/ gastric washout AFB and GeneXpert MTB/RIF	76.3	23.7	-	TB/HIV co-infection – 1.3
[34]	Males (44.64%), females (55.36%). Mean age was 6.26 ± 4.3 years	Diagnosis made with Gene Xpert or AFB test (bacteriological diagnosis) for patients who could produce sputum or alternatively gastric lavage/washout	95.54	4.5	-	TB/HIV co-infection – 46.4
[35]	Males(44.6%) and females (55.4%) aged 5–18 years. The mean age (± SD) of the subjects was 11.6 ± 3.1 years.	Diagnosis done with while the ZN stain for AAFB.	-	-	-	-
[36]	Males(39.6%) and females (60.4%).	Diagnosis made with either TST, chest and spinal X-rays, sputum microscopy for AFB stain and culture, fine needle aspirate for cytology, histology, and GeneXpert, white blood cell count, and erythrocyte sedimentation rate.	65.7	34.3	-	New TB cases – 95.2% TB/HIV co-infection – 4.5

AFB acid fast bacilli test, *TST* tuberculin skin test (Mantoux test), *ART* anti-retroviral therapy, *PTB* pulmonary tuberculosis, *ETB* extra-pulmonary tuberculosis, *DTB* disseminated tuberculosis

Table 3 Sites of Extrapulmonary Tuberculosis (EPTB)

Author	Extrapulmonary TB site	Prevalence (%)
Adejumo OA et al. [15]	-	9
Daniel OJ et al. [16]	-	19–27.80
Mado SM et al. [18]	Thoracic spine Abdomen Kidney Meninges	13.40 6.00 1.50 1.50
Surajudeen B et al. [19]	-	6.25
Ahmed PA et al. [27]	Lymph nodes (TB adenitis) Meninges Pericardium Spine Miliary TB	11.10 8.30 8.30 2.80 2.80
Illah BG et al. [33]	-	23.70
Bamidele J et al. [34]	-	4.50
Alao MA et al. [36]	Pleurae Joint Spine Abdomen Lymph nodes Endometrium Meninges Pericardium Miliary	13.50 3.10 59.70 6.90 12.70 0.30 0.30 0.70 2.80

homogeneity among study regions and selected characteristics were considered for a meta-analysis. The study pool prevalence was determined using the random-effects model due to the heterogeneity among included studies and study characteristics. Odds ratios (OR) or prevalence ratios (PR) were calculated to determine the prevalence. At the same time, mean differences (MD) or standardized mean differences (SMD) were used for continuous outcomes such as treatment outcomes. Statistical heterogeneity was assessed using the I^2 statistic. Outputs of 0, 25, 50, and 75% were used to declare no, low, moderate, and high heterogeneity, respectively [39].

Publication bias

Publication bias was assessed using Egger's test and a funnel plot [40, 41]. Sensitivity analysis determined how individual studies influenced the overall pooled prevalence. The meta-analysis results were presented and illustrated using tables and figures.

Results

Study overview

Our initial search generated 384 studies, of which 54 were selected for full-text screening (Fig. 1). After further evaluation, 22 studies met the eligibility criteria and were included in this systematic review and meta-analysis (Table 1). These studies span multiple regions across Nigeria to investigate the prevalence, characteristics, and treatment outcomes of childhood tuberculosis. Details of the included studies with their references are summarized in Tables 1, 2, 3 and 4.

Study characteristics

This review included 22 studies on childhood tuberculosis in Nigeria [15–36], with a total of 1,162,936 participants aged 0–18 years. Approximately 17 (77%) of the studies utilized a retrospective study design [15–21, 23–25, 27, 28, 31–34, 36], 4 (18.20%) were cross-sectional observational studies [22, 26, 30, 35]. Only 1 study (4.50%) was a prospective study [29] (Table 1) (Fig. 2). These studies were conducted between 2008 and 2023 with the location of studies spanning the major cities in Nigeria. Based on geopolitical zones, the Southwest had the highest number of publications on childhood tuberculosis (7), followed by South-south and North-central with five publications each. The Northwest region reported three studies, while the Southeast reported one (Fig. 3). There was a nationwide study across DOT centers [32], whereas no study was reported from the Northeastern region. These studies collectively provided a comprehensive view of the prevalence, characteristics, and treatment outcomes of childhood tuberculosis in Nigeria, with a special focus on pulmonary TB and TB/HIV co-infection.

Participant demographics

The total sample size was 1,162,936, with males accounting for 39.78% of the total sample size (462,652) and females constituting 60.22% (700,284). The age range of the participants varied significantly, from 2 months to 18 years, with most studies concentrating on children aged 0–15 years (Table 2) [15–17, 21, 24–26, 31–33]. The mean age is 8.44 ± 2.34 years, indicating a predominance of school-aged children in most populations. Few studies reported on the socioeconomic status of the sample and noted a trend. Ahmed PA et al. noted that 83.30% of adolescents with tuberculosis belonged to lower socioeconomic groups [27]. This review's findings span urban areas, such as Lagos and Port Harcourt, and rural regions in Northwestern Nigeria, providing a diverse perspective on the sociodemographic patterns of childhood TB.

Prevalence and regional distribution

We analyzed Nineteen studies reporting childhood tuberculosis prevalence. The pooled prevalence of tuberculosis in children was 20.82% (95% CI: 8.55–36.64) (Fig. 4). A subgroup analysis based on the geopolitical zone showed the highest prevalence of 89.62% in a single study from the Southeast [24], followed by 21.45% pooled prevalence from 6 studies in the Southwest [15, 16, 20, 25, 34, 36]. 19.49%

Table 4 Treatment modalities and outcomes of childhood tuberculosis in Nigeria

References	Treatment approach	Treatment adherence	Treatment outcomes	Follow-up duration
[15]	2RHZE, then 4RH TB/HIV co-infected had CPT along with their anti-TB medications and were offered ART within 8 weeks of anti-TB commencement.	-	Treatment successful – 77.4% (more among 5–14 age band). Dead – 6.0%, Defaulted – 15.0%, Transferred out – 1.3% Treatment failure – 0.03%, (Children less than 1 year had worst treatment outcomes)	6 months.
[16]	2RHZE then 4RH	-	Progressive increase in the proportion of children treated for TB from 5.9 – 7.6% within the study period	6 months.
[17]	2RHZE (intensive phase) 4RH (consolidation phase)	-	Completed treatment – 78% Absconded (LTFU) – 13% Transferred out – 9% Treatment complication (drug-induced hepatitis) – 3%	6 months.
[18]	All patients received RHZE or streptomycin according to Nigerian TB and leprosy treatment guidelines	-	Treatment successful – 59.7% LTFU – 22.4% Defaulted – 4.5% Transferred out – 3% Dead – 10.4%	-
[19]	N/A	-	Treatment successful (cured or completed treatment) – 66% LTFU – 26% Dead – 8%	
[20]	Involved category I and II anti-TB drugs according to Nigerian guidelines, with HAART administered either before or concurrently	-	Treatment successful – 85.7% Dead – 14.3%	2 to 63 days, with a mean duration of 16.8 days.
[22]	Children with a positive test were treated with INH after first excluding TB by chest X-ray and clinical evaluation.	-	-	2 months
[23]	Treatment and follow up of TB cases were conducted per the National guidelines on TB and leprosy management	-	Treatment successful – 58.41% Defaulted – 22.77% Transferred out – 4.95% Dead – 10.89%	6 months and 12 months.
[24]	Children with pulmonary and some extrapulmonary TB (except TB meningitis, miliary TB, and osteoarticular TB) were treated with R6 regimen – 2RHZE/4HR On the other hand, those with TB meningitis, miliary, or osteoarticular TB were treated with R12 regimen – 2RHZE/10RH.	-	Treatment successful – 62.9% Transferred out – 7% LTFU – 21.4% Treatment failure – 0.4% Dead – 8.4%	-

Table 4 (continued)

References	Treatment approach	Treatment adherence	Treatment outcomes	Follow-up duration
[25]	Per the NTBLCP guidelines - a combination of RHZ, and streptomycin (or ethambutol for children older than 6 years) in initial phase, while only RH were used in the continuation phase.	-	Treatment successful – 92.3% Discharged against medical advice – 3.8% TB-HIV co-infection death – 3.8%	-
[27]	-	-	Treatment successful – 75.0% LTFU – 19.4% Re-treatment relapse – 11.1% Dead – 5.6%	-
[28]	2RHZE then 4RH	Treatment adherence was ensured through the National Tuberculosis and Leprosy Control Programme's directly observed treatment short course (DOTS) strategy.	Treatment successful – 64.29% Transferred out – 34.29% Dead – 1.43%	6 months
[31]	Treatment followed the NTP guidelines which aligns with the WHO-recommended Directly Observed Therapy, Short Course (DOTS) strategy for TB treatment [37]	-	Treatment successful – 83.0% Unsuccessful outcomes (died, failure, and not evaluated) – 17.0%	6 months.
[32]	N/A	-	Treatment successful – 84.6%	-
[33]	Treatment was based on WHO and NTBLCP guidelines	About 67.1% adhered to treatment as measured by children who completed their treatment.	Treatment successful - 82.9% Transferred out – 11.8% LTFU – 1.3% Dead – 3.9%	30 months
[34]	2RHZE (intensive phase) 4RH (continuous phase) For TB spine/bone or TB meningitis: 2RHZE (intensive phase) 10RH (continuous phase)	-	Treated successfully – 81.3% LTFU – 4.5% Dead – 6.3% Treatment failure – 1.8% Not evaluated – 6.3%	6 to 10 months
[36]	RHZE for drug-sensitive MTB.	The annual mean measured treatment adherence was 91.4(± 5.8) %	Treatment success – 84% Transfer out – 0 LTFU – 3% Failure – 5%	-

AFB acid-fast bacilli test, *TST* tuberculin skin test (Mantoux test), *RHZE* Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol, *RH* Rifampicin, Isoniazid, *2RHZE* regimen for 2 months, *4RHZE* 4 months, *10RHZE* 10 months, *CPT* cotrimoxazole preventive therapy, *ART* anti-retroviral therapy, *PTB* pulmonary tuberculosis, *ETB* extra-pulmonary tuberculosis, *DTB* disseminated tuberculosis, *LTFU* loss to follow up

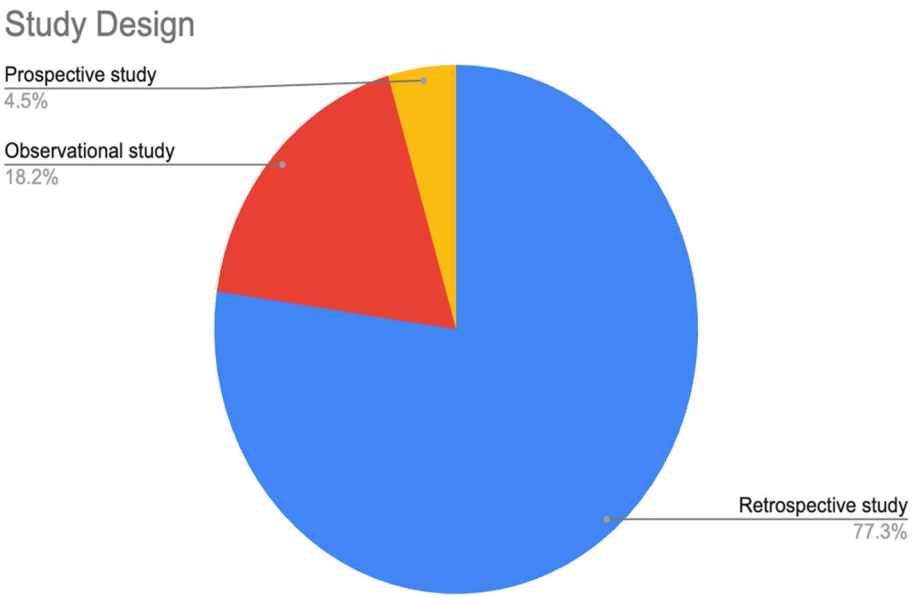

Fig. 2 Study design

was reported in the South-south, 17.15% in the North-central, and 9.24% in the Northwest (Fig. 5). There is considerable heterogeneity (I^2 = 99.88%), suggesting significant variability across regions and study settings (Fig. 5). For instance, in Lagos, childhood TB cases comprised 6.30% of all tuberculosis cases [15], while in Zamfara State, the prevalence was lower at 4.80% among pediatric hospital admissions [18]. A study from Nasarawa State reported a higher prevalence of 32% among children with suspected tuberculosis [30].

Clinical presentation and diagnostic approaches

Pulmonary tuberculosis is the predominant form of TB among children, with a prevalence of 62.70% (95% CI: 43.57–80.03) from 12 studies across the 5 geopolitical zones (Table 2) (Figs. 6 and 7) [15–18, 21, 24, 25, 27, 33, 34, 36]. Extrapulmonary manifestations have also been documented, including TB adenitis, spinal TB, abdominal TB, and TB meningitis. A combined prevalence of 15.86% (95% CI: 5.96–29.11) from 8 included studies accounted for extrapulmonary tuberculosis (ETB)

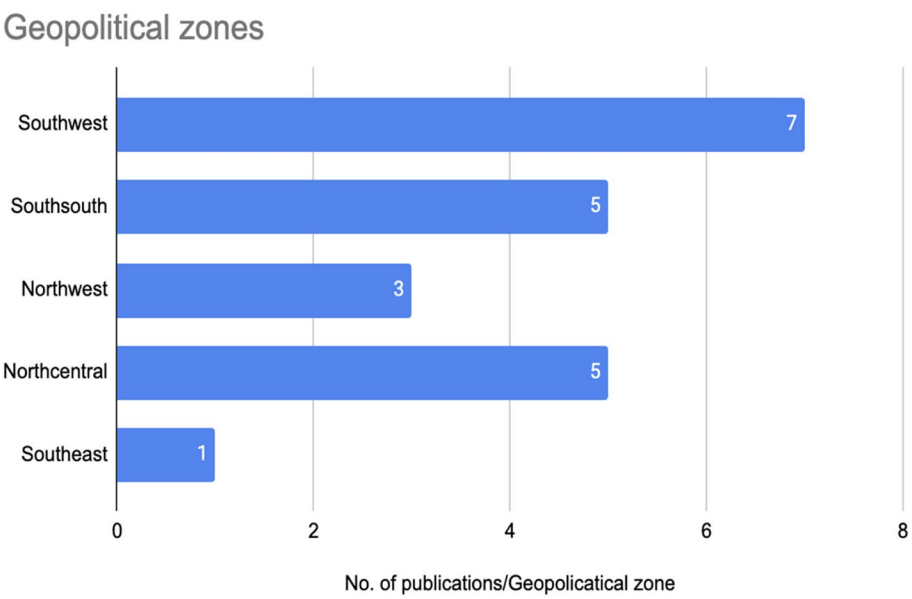

Fig. 3 Number of publications by geopolitical zones

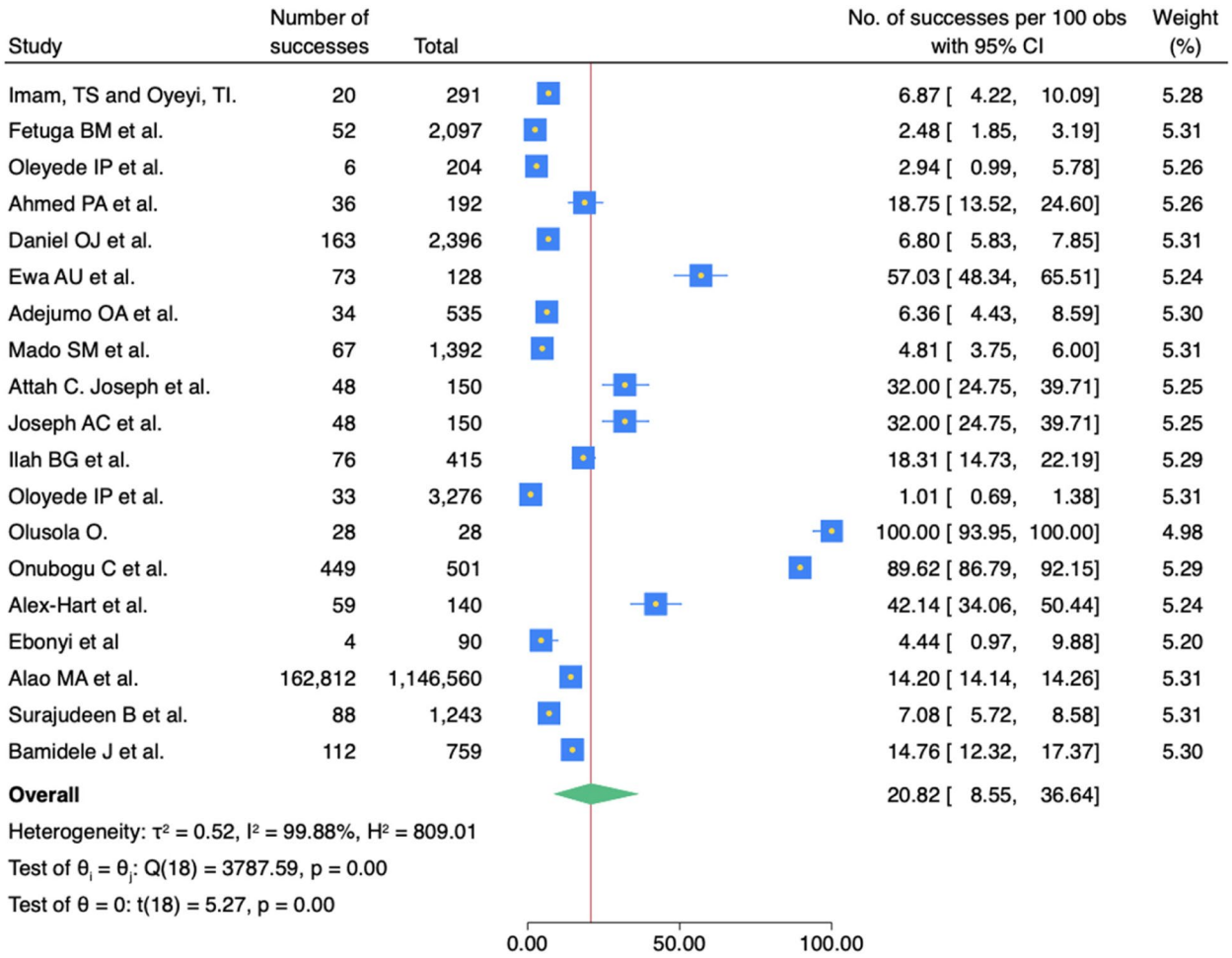

Fig. 4 Prevalence of childhood tuberculosis

(Table 3) (Fig. 8). Disseminated tuberculosis was also found across 3 studies, with an overall prevalence of 28.56% (95% CI: 0.00–78.49) (Fig. 9) [22,2328,].

TB/HIV co-infection

Thirteen studies report the TB-HIV co-infection (Fig. 10) [15, 17, 18, 20, 23–27, 30, 33, 34, 36]. The pooled prevalence of TB/HIV co-infection was 24.59% (95% CI: 13.59–37.25), with a degree of heterogeneity at $I^2 = 96.92\%$) (Fig. 10). There is a significant variation across reported studies, ranging from 13.77 to 37.25%.

Diagnostic modalities

Diagnostic approaches generally followed guidelines provided by the World Health Organization, with sputum smear microscopy for acid-fast bacilli (AFB), GeneXpert MTB/RIF assays, chest radiographs, and tuberculin skin tests being widely used [15, 27, 32–35]. GeneXpert testing has shown improved diagnostic capability, with its usage increasing from 56.50 to 64% between 2017 and 2020 [32]. Clinical diagnosis based on symptoms, contact history, and radiological findings were also reported among younger children who could not produce sputum for sample analysis [20]. Confirming tuberculosis through bacteriological methods is problematic, as laboratory tests only verify 6% of cases, underscoring the challenges in diagnosing TB in children [34].

Treatment approach and outcomes

Childhood tuberculosis across reported studies was managed according to the guidelines set by WHO and the National Tuberculosis and Leprosy Control Program (NTBLCP). The standard treatment regimen for pulmonary TB reported comprised a two-month intensive treatment course with rifampicin, isoniazid, pyrazinamide, and ethambutol (RHZE), followed by a four-month continuation phase with rifampicin and isoniazid (RH) (Table 4) [28, 34]. This would be extended to a 10-month course for other extrapulmonary manifestations such as spinal, abdominal, or bone

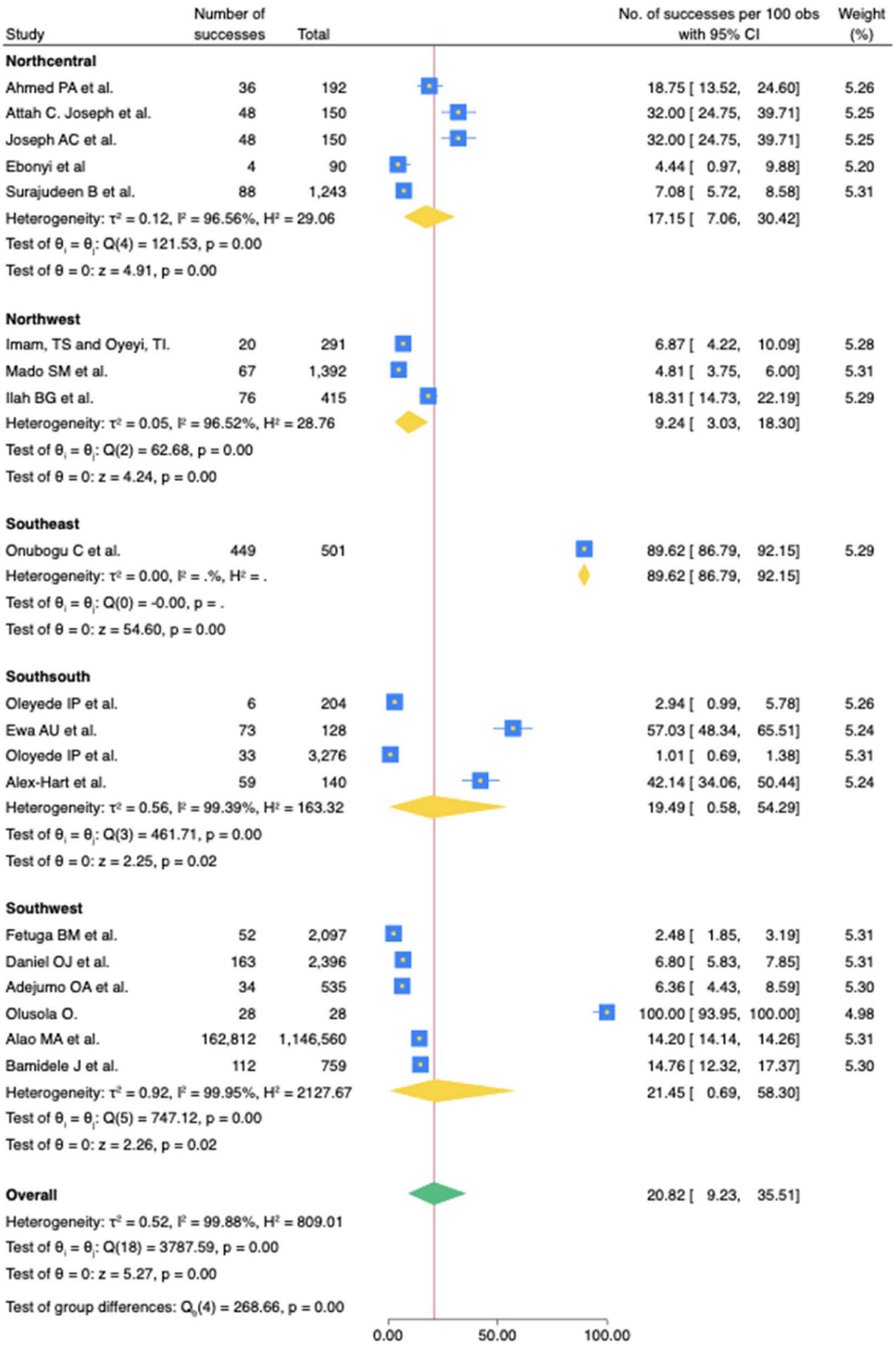

Fig. 5 Prevalence of childhood tuberculosis by geopolitical zone

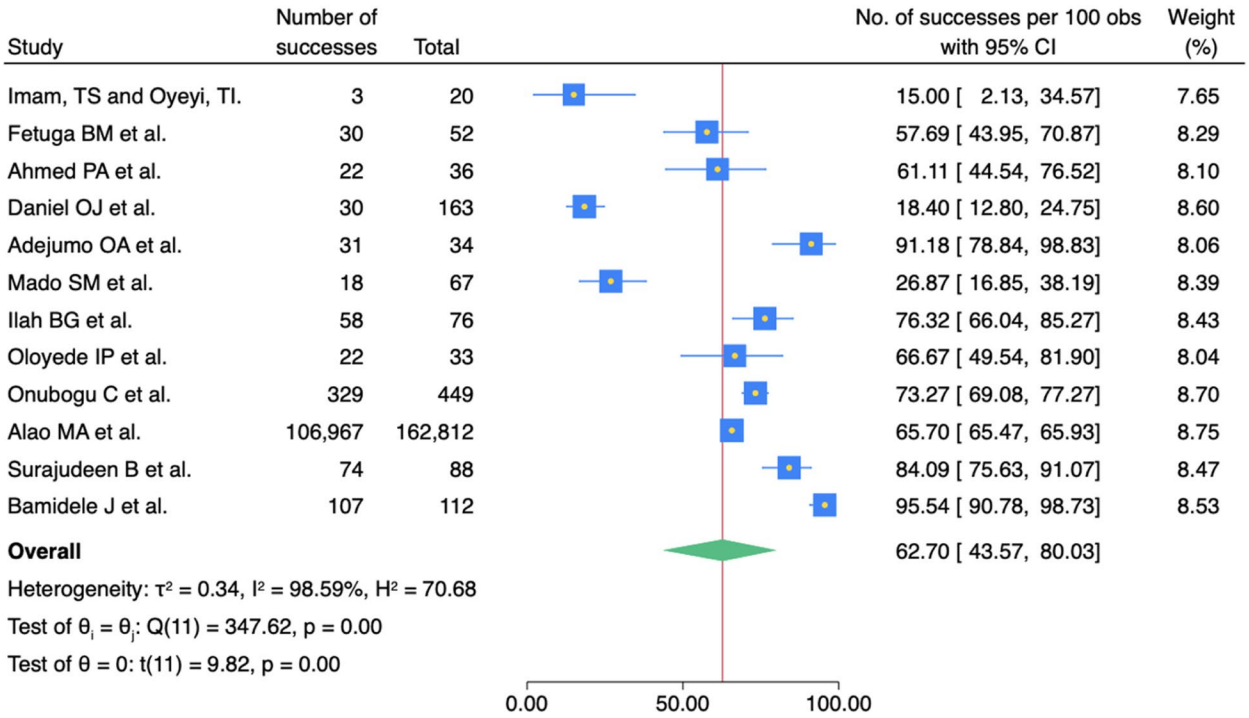

Fig. 6 Prevalence of pulmonary TB

TB. The meta-analysis showed an overall treatment success rate of 75.47% (95% CI: 67.47–82.53) (Figs. 11 and 12), suggesting favorable outcomes. Adherence to treatment, socioeconomic status, and comorbidities, such as HIV, influenced treatment success rates [15, 27]. Alao MA et al. reported adherence rates as high as 91.40% over a 25-year period [36]. The treatment duration typically spans from 6 to 12 months, with longer durations prescribed for more complex cases such as extrapulmonary manifestations, disease complications, or drug-resistant TB [33, 34]. The meta-analysis showed 11.40% (95% CI: 4.87–19.99) of the population were lost to follow-up from 10 studies (Fig. 13), while treatment failure was reported across 13 studies, with a prevalence of 2.12% (95% CI: 0.0–12.06) (Table 4) (Fig. 14). The pooled mortality rate was 6.76% (95% CI: 4.75–9.06), with a low degree of heterogeneity ($I^2 = 3.44\%$), signifying low variation between the studies and across the geopolitical zones (Figs. 15 and 16). Challenges such as loss to follow-up and reported mortality rates remained prominent and impacted treatment outcomes.

Publication bias

The risk of publication bias was assessed using a funnel plot and Egger's test. The funnel plot was asymmetrical (Fig. 17) with Egger's test of 0.0005, showing publication bias.

Discussion

This systematic review assessed the prevalence, characteristics, and treatment outcomes of childhood tuberculosis in Nigeria. Analyzing 22 studies across different regions showed notable findings on childhood tuberculosis in Nigeria. The pooled prevalence of TB among children in Nigeria was 20.82% (95% CI: 8.55–36.64) from 19 studies. There was study heterogeneity among the included studies. This broad variation suggests the impact of methodological differences, population selection, and actual geographical differences on the findings of this review.

There were differences in tuberculosis prevalence across the regions. The study by Ilah Bilikisu et al. in Gusau, Northern Nigeria, had the highest prevalence rate with a staggering 76.32% [33]. This heightened prevalence may be attributed to socio-demographic factors characterized by poor educational attainment and low socioeconomic class in most families in the region. Notably, Northern Nigeria is dominated majorly by indigenes of the lower echelon and the economically disadvantaged [33]; this poses a major risk factor for the acquisition and spread of tuberculosis. The lowest prevalence

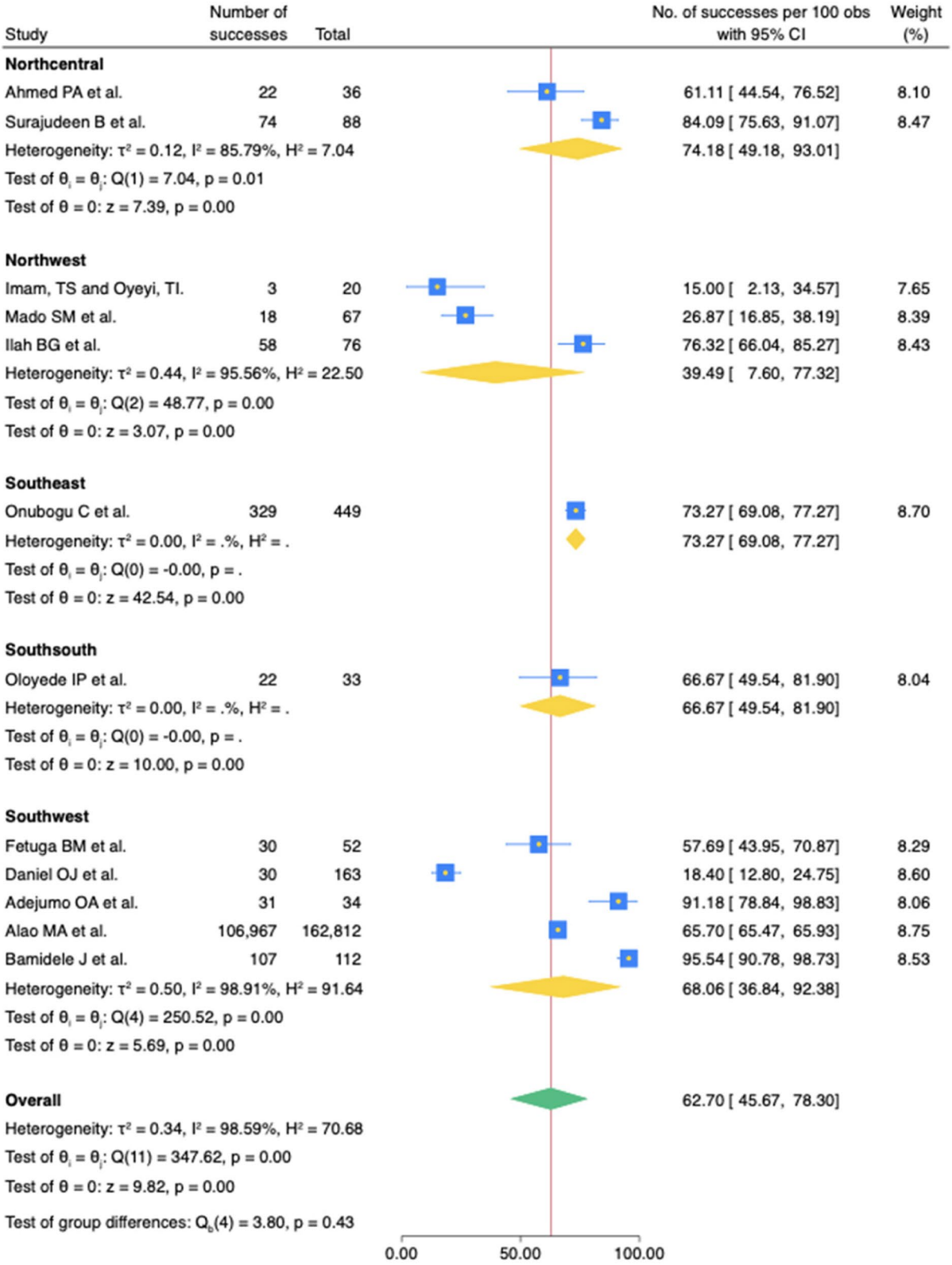

Fig. 7 Pulmonary TB rates by geopolitical zone

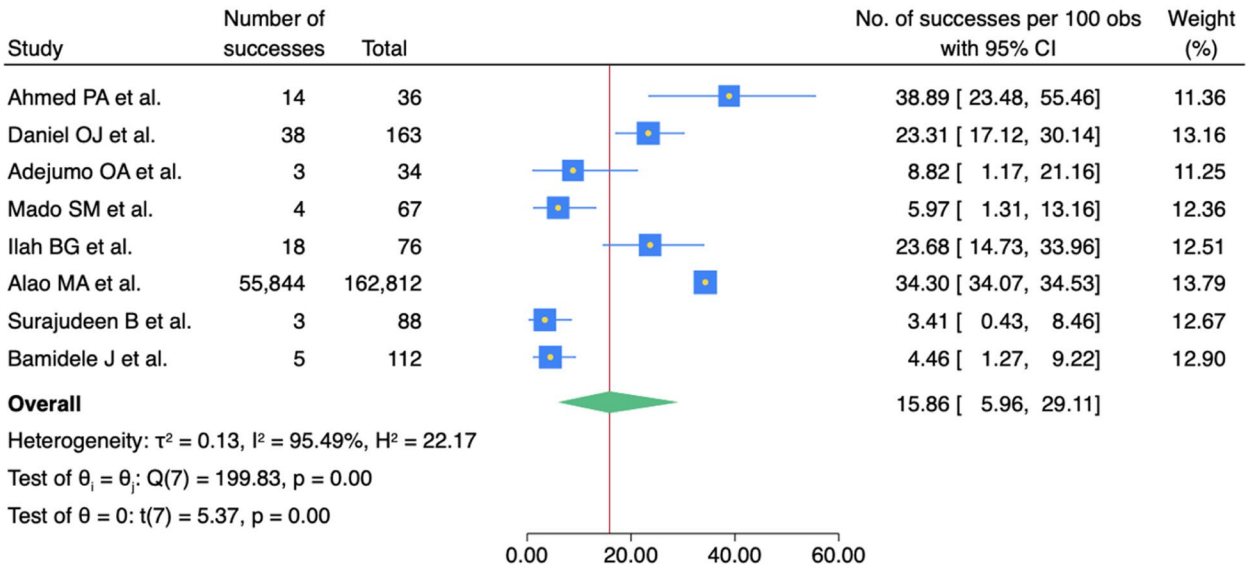

Fig. 8 Prevalence of extrapulmonary TB

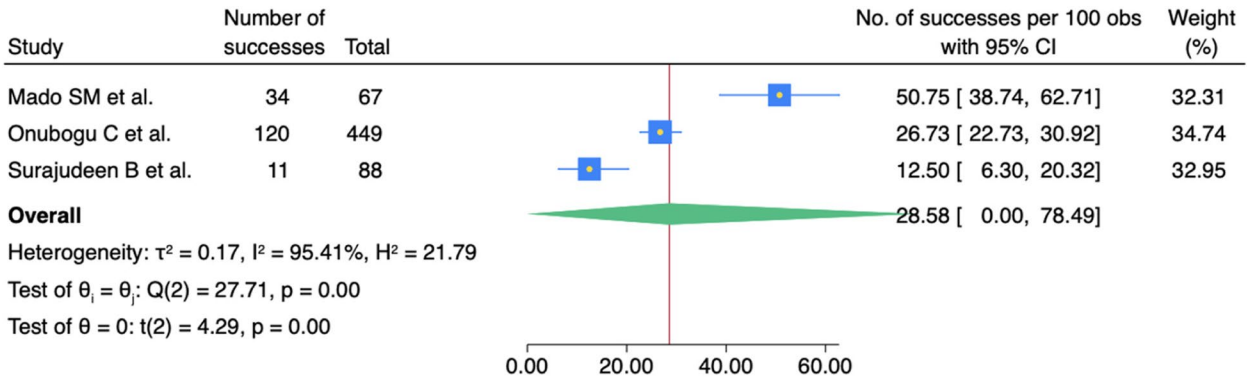

Fig. 9 Prevalence of disseminated TB

of TB was recorded in the Niger Delta region, located in Southern Nigeria [35]. This finding corroborates our earlier hypothesis that geographical, cultural nuances, and socio-economic class impact childhood tuberculosis prevalence and should be factored into intervention strategies and policymaking. Nigeria and other African countries, such as the Central African Republic, Namibia, Gabon, and Ethiopia, contribute to the world's major childhood tuberculosis burden, according to the WHO's Global Tuberculosis Report [42, 43]. Children between the 5–14 age bands are commonly reported to be more infected than the under-fives and those aged 15–18 [42]. This is partly due to the diagnostic challenges for the under-five age band, which may not be able to produce sputum for Xpert/MTB RIF assay.

Across reviewed studies, pulmonary TB was the most common presentation observed, which is in keeping with global findings, with varying levels of male-to-female preponderance [23, 31, 44]. However, studies in our review reported more females being infected than males. For the diagnosis of TB, clinical tests in conjunction with different combinations of radiologic, microscopic, and immunologic investigations, including acid alcohol fast bacilli (AAFB) test, chest radiograph, gene Xpert diagnostic test, Interferon-gamma release assay, ELISpot assay, T-SPOT test, tuberculin skin test (Mantoux) were used [20, 22, 30, 35]. While some studies used standard WHO diagnostic criteria, the diagnostic tools were based on available resources across centers, communities, and regions. No study reported the use of other specialized techniques

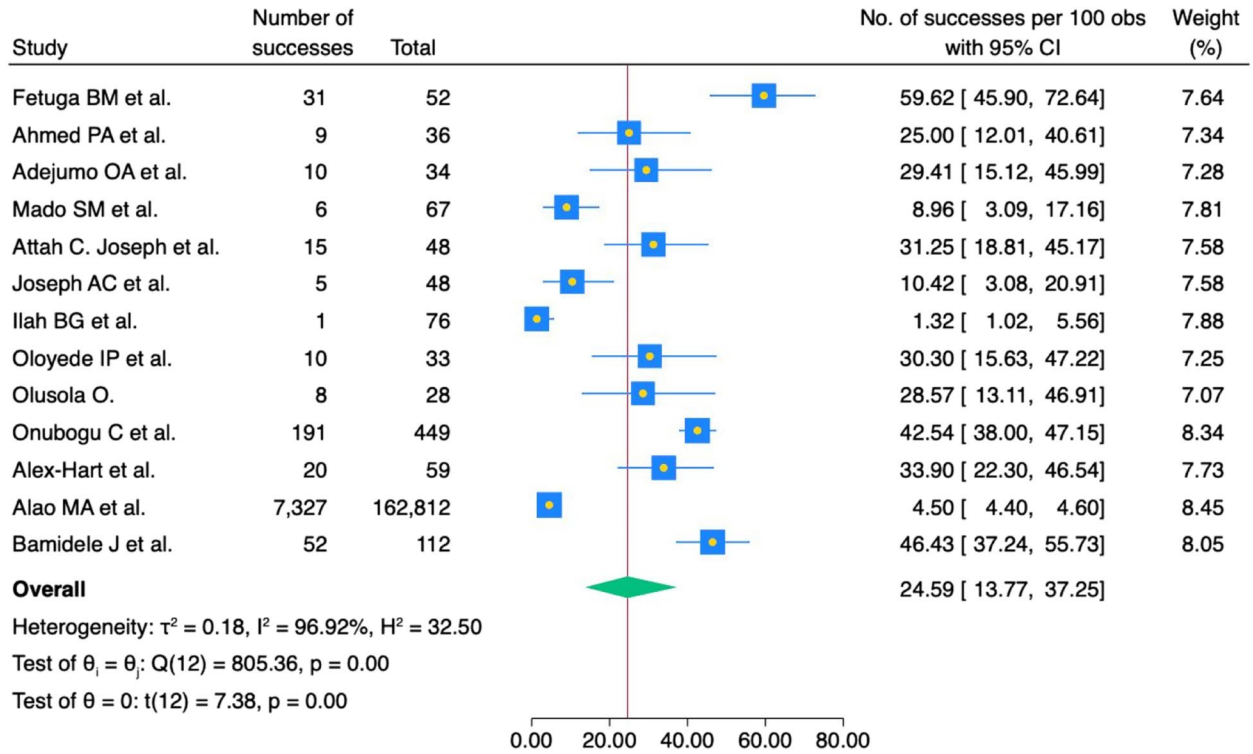

Fig. 10 TB/HIV co-infection rates

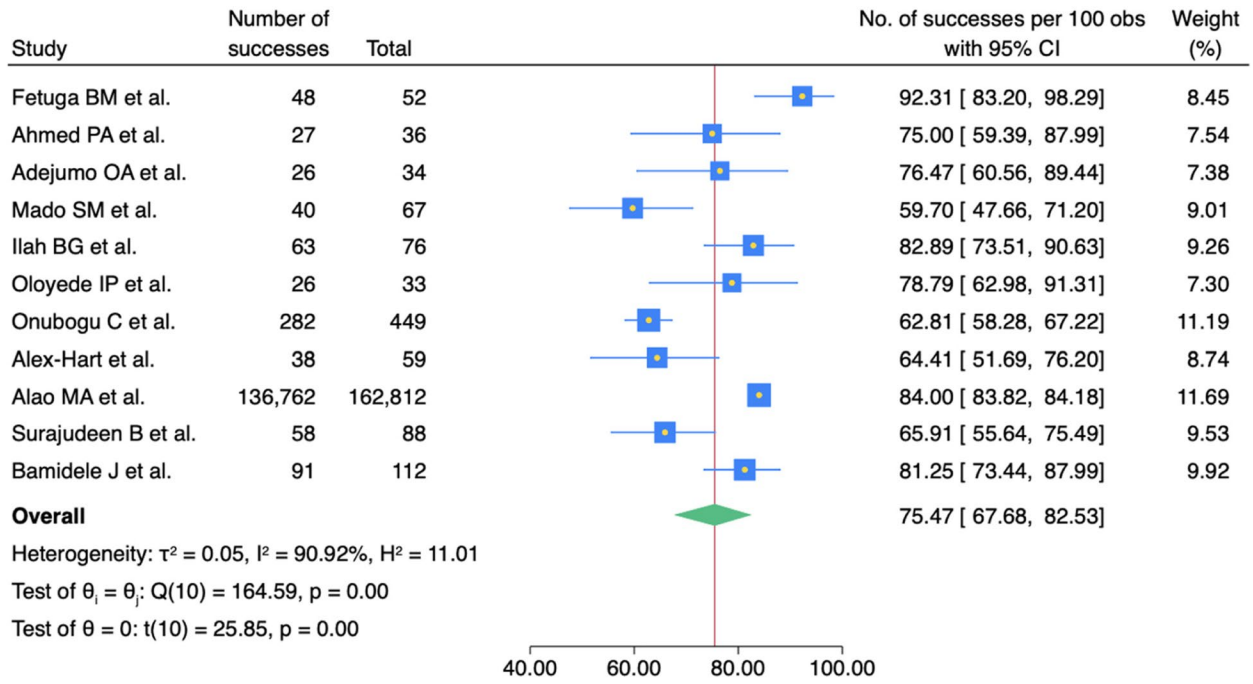

Fig. 11 Treatment success rates

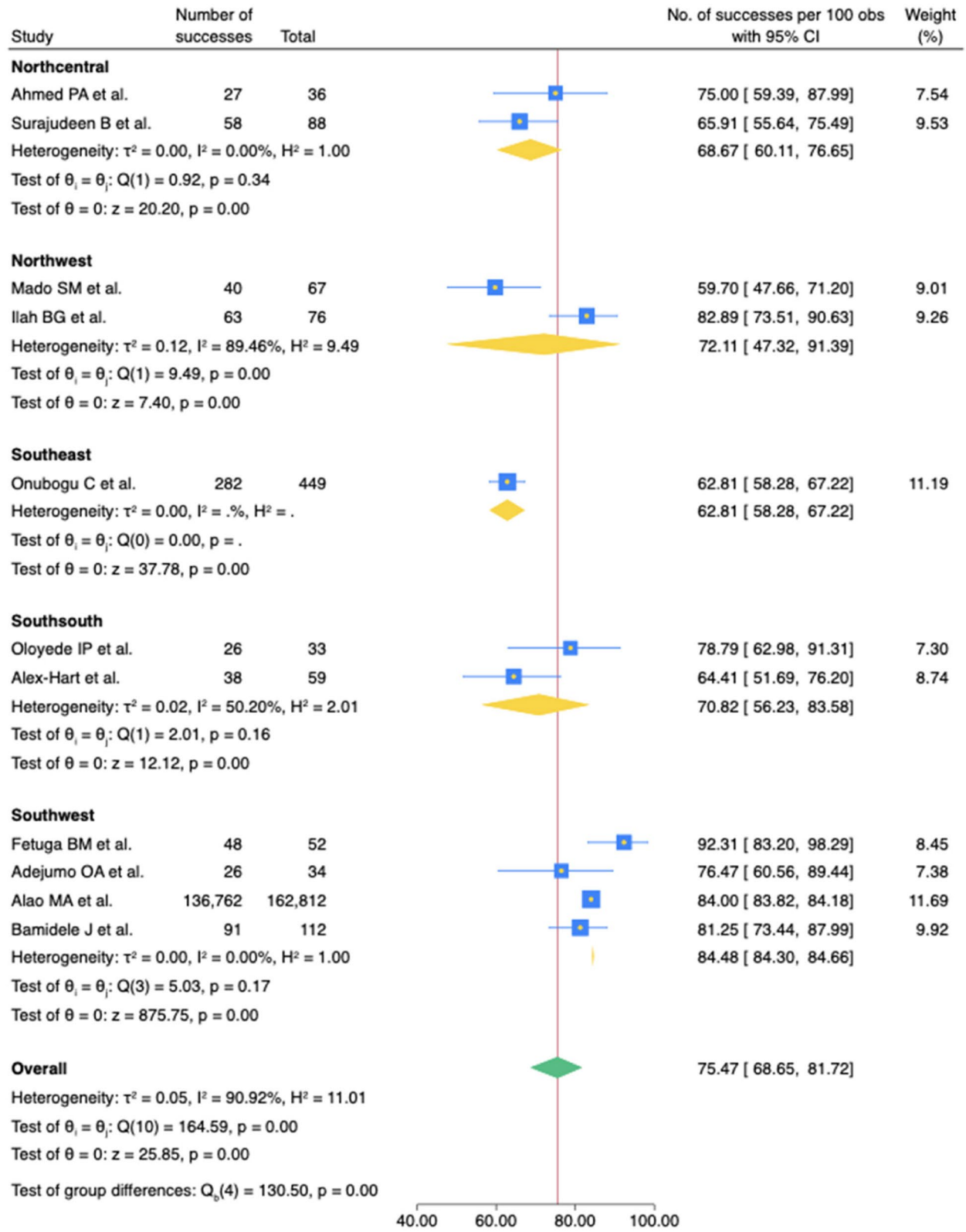

Fig. 12 Treatment success rates by regions

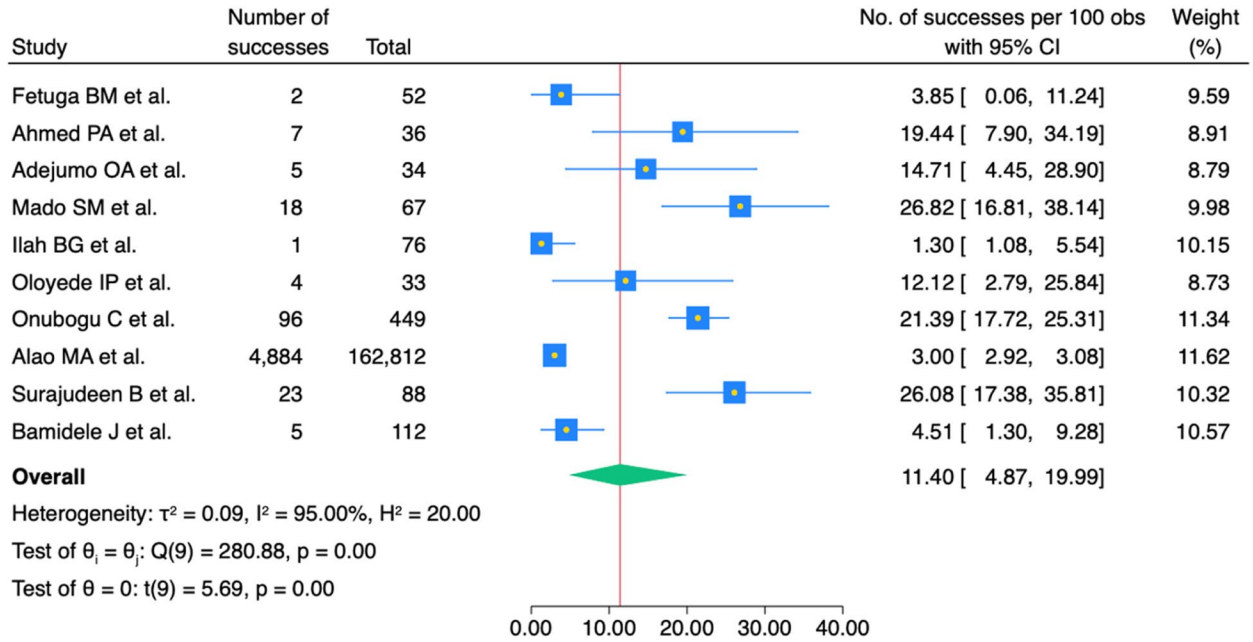

Fig. 13 Number loss to follow-up

such as Truenat MTB-RIF Dx, culture and drug susceptibility testing (DST), first and second-line Line Probe Assay (LPA) as outlined in the NTBLCP 2021 updated guidelines, underscoring the need for targeted intervention towards scaling up diagnosis. Additionally, TB/HIV co-infection was noted across studies, with a pooled prevalence of 24.59% (95% CI: 13.59–37.25). TB remains the leading opportunistic infection and major cause of death among HIV co-infected patients and was shown in this review to pose a major threat to children living with HIV, in other cases causing mortality. A study by Addo et al. reported a lower prevalence of TB/HIV co-infection at 14.7% in Ghana, compared with that observed in our study [45]. HIV co-infection not only worsens morbidity but also increases chances for mortality, complicates treatment options, and increases treatment failure rates. Reduced co-infection rates and burdens are attainable if preventive measures are targeted towards early screening and diagnosis and immediate initiation of directly observed therapy short course (DOTS) upon diagnosis.

Management protocols across the reviewed studies adhered to national treatment guidelines, recommending a 6- or 12-month regimen with rifampicin, isoniazid, pyrazinamide, and ethambutol based on disease severity [15, 46]. These guidelines align with international TB treatment standards and recommendations and follow the DOTS protocol [47]. DOTS has been widely adopted for TB treatment globally to facilitate treatment efficiency and mitigate the incidence of treatment failure and anti-TB drug resistance [28]. In the event of interruption,

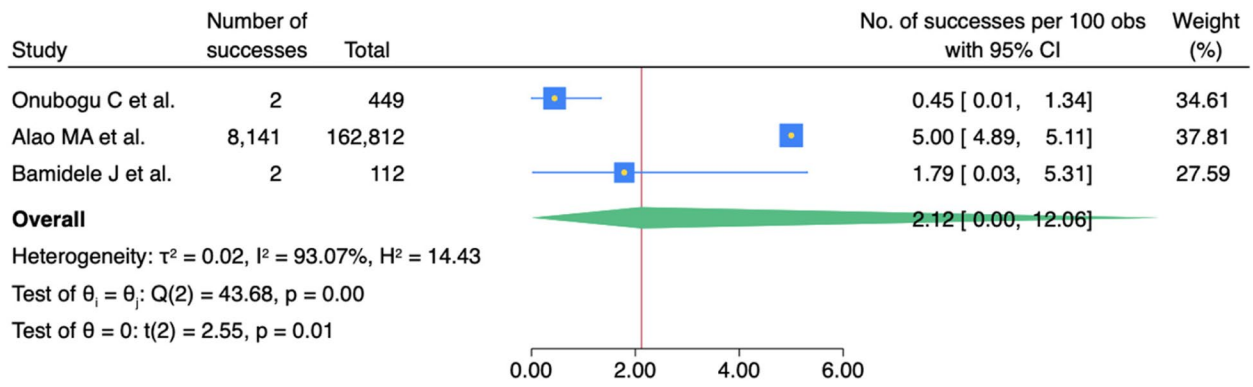

Fig. 14 Treatment failure rates

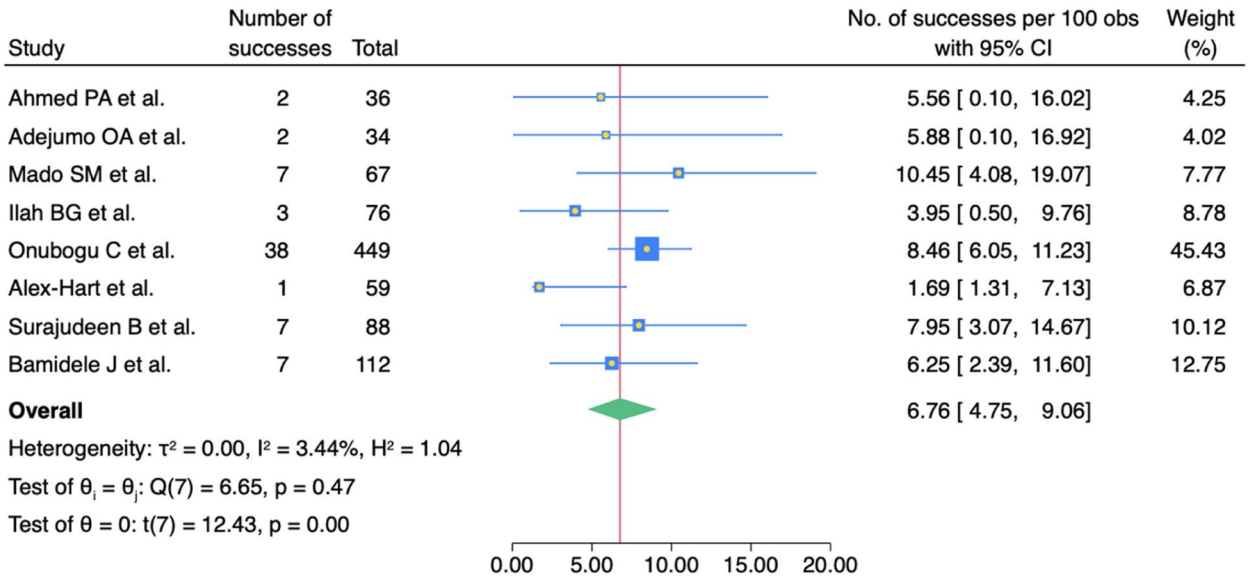

Fig. 15 Mortality rates among infected children

modifications to the routine have yielded positive results. One study in our review reported the use of a 3-month course of streptomycin in addition to rifampicin, isoniazid, and pyrazinamide among children who defaulted treatment [18]. This was followed by a 4-month continuous phase of rifampicin and isoniazid, and successful treatment outcomes were noted. The seven-month treatment course was the recommended protocol for those who had defaulted treatment when the study was conducted; current treatment guidelines do not recommend streptomycin therapy [46].

From our analysis, the overall treatment success rate was 75.47%, leaving more to be expected compared to the WHO targets. According to a recent study, Nigeria's average treatment success rate is 75.3% [48], although previous studies have reported a higher success rate. Adejumo et al. evaluated childhood TB treatment outcomes, noting a 77.40% success rate, with anti-TB medications administered per national guidelines and ART commenced within 8 weeks of anti-TB treatment initiation [15]. Most of the pooled studies reported > 70% positive treatment outcomes; however, few studies reported lower success rates attributed to defaulters, HIV-coinfection, patients lost to follow-up, and deaths occurring during treatment [15, 18, 23, 34]. Compared with the average treatment success rate (86%) obtained worldwide, according to WHO, Nigeria still falls short of the expected global standard [49], this underscores the need to ramp up treatment efficiency strategies geared at improving treatment success outcomes among children. We recognize the crucial role of health system managers and policymakers in addressing the drivers of poor treatment success, and the responsibility of parents and guardians in supporting children throughout the tuberculosis management process. Treatment options should prioritize improving adherence, early diagnosis, and prompt commencement of treatment especially in the setting of a co-infection. Age was a significant factor impacting treatment outcomes. Children 0 to 5 years old had negative treatment outcomes compared to older children [23, 31]. This is possibly due to the relatively immature immune systems among younger children, predisposing them to more severe complications and treatment failure [50]. Therefore, early detection of signs and symptoms, especially among younger children who cannot produce sputum, is important in improving treatment outcomes in Nigeria. Our findings highlight the burden of tuberculosis among children, delineating the patterns and treatment outcomes such as successful treatment outcomes, death, and defaults. A trend linking treatment completion rates with cure and overall success highlights the necessity of aligning management protocols with international TB treatment and follow-up standards to enhance treatment success rates in Nigeria and globally.

Limitations

This review addresses the peculiarities of childhood TB in Nigeria by evaluating the prevalence, clinical characteristics, and treatment outcomes across 22 studies. Our review, despite reporting promising and useful results, recorded significant limitations. Significant heterogenicity exists across reviewed studies, which could be attributed to variability in diagnostic methodology, study population, geographical disparity, and

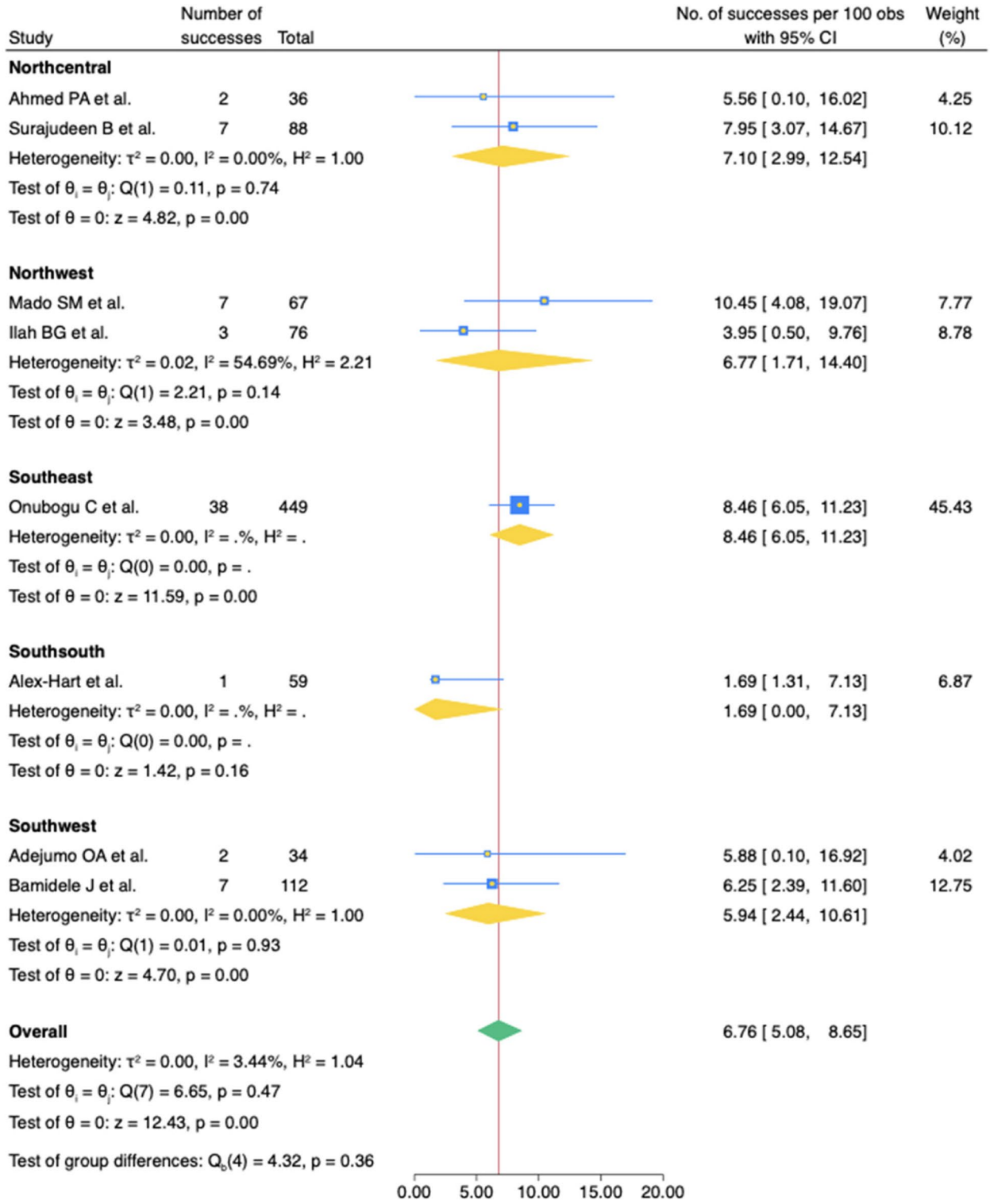

Fig. 16 Mortality rates among infected children across regions

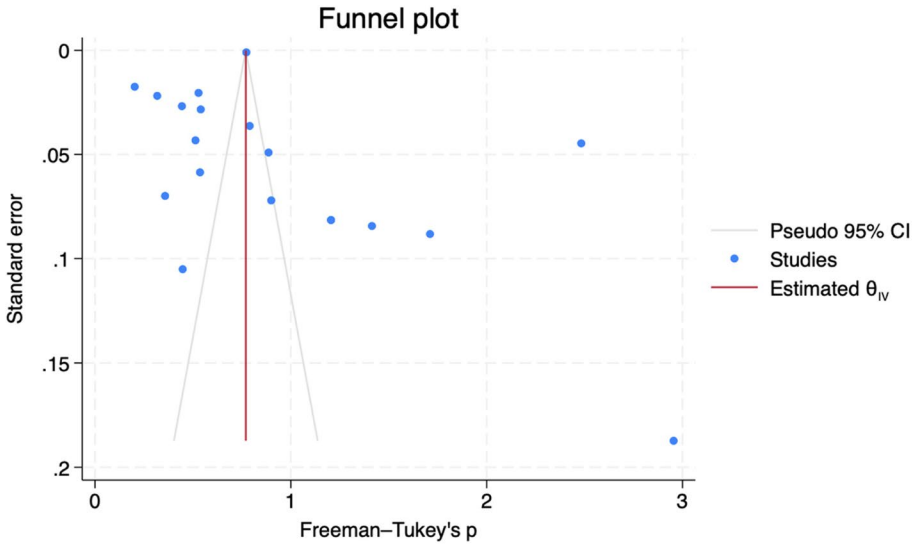

Fig. 17 Funnel plot for publication bias

socio-economic status. This is a notable limitation of this meta-analysis. Additionally, our study could not deduce causality as most studies utilised a retrospective or cross-sectional study design. Due to inconsistent reporting, the review could not include data from grey literature and unpublished sources. Methodological variations in calculating the prevalence rate were detected across studies. This may have impacted the overall prevalence, highlighting the need for standardised diagnostic methodologies.

Conclusion

The burden of childhood tuberculosis in Nigeria is significant even as diagnostic limitations pose constraints. This systematic review and meta-analysis assessed the prevalence, clinical characteristics, and treatment outcomes of childhood tuberculosis in Nigeria, synthesizing data from 22 studies reported across various geographical regions. The pooled prevalence, as observed, stands at 20.82%, indicating a rather substantial burden of childhood tuberculosis in the region. The disease characteristics vary significantly, and considerable TB/HIV coinfection was also noted. Our review shows an overall treatment success rate of approximately 75.47%, which is lower than global expectations. This study recognizes the crucial role of health system managers and policymakers in addressing the drivers of poor treatment success rates, and the responsibility of parents and guardians in supporting children throughout the tuberculosis management process. The availability and accessibility of advanced diagnostic techniques across locations in the country continue to limit early diagnosis and treatment, impeding precise prevalence estimates and treatment success rates. There is a need to strengthen available collaborations between systems to improve the quality of care offered to children diagnosed with TB and placed on the TB treatment cascade. Future research should aim to standardize diagnostic criteria and methodologies for consistent and reliable prevalence estimates. More longitudinal than retrospective studies are necessary to comprehend the disease trend, pattern, and causative factors for the heightened prevalence and subpar treatment outcomes of childhood tuberculosis in Nigeria.

Abbreviations

TB	Tuberculosis
WHO	World Health Organisation
TST	Tuberculin skin test
PECO	Population, Exposure, Comparison, and Outcome
NTBLCP	National Tuberculosis and Leprosy Control Program
RHZE	Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol
DOTS	Directly Observed Therapy Shortcourse

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10321-3.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Acknowledgements

None.

Authors' contributions

B.M.U. conceptualized and designed this study. A.E.B. and B.M.U. conducted a literature search to put together relevant studies. B.M.U and T.A.W. conducted the data extraction table, which two external reviewers reviewed. B.M.U. and F.M.D. conducted the quality assessment. S.A. conducted the data analysis. P.M.W., M.M.A, N.G.U., O.J.O., R.A.U., I.G.P. and L.A.M wrote the initial draft, which B.M.U. and F.M.D. edited. B.M.U. is the corresponding author and is responsible for the work's credibility.

Funding
No funding was sourced for this study.

Data availability
Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 8 October 2024 Accepted: 6 December 2024
Published online: 19 December 2024

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