



Post-Tubercular Lung Sequelae: An Integrated Radiological, Microbiological, and Histopathological Evaluation - A Systematic Review and Meta-Analysis

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Abstract

Background: Tuberculosis (TB) remains a major global health problem, particularly in developing countries. Although effective anti-tubercular therapy leads to microbiological cure in most patients, many individuals develop long-term pulmonary complications known as post-tubercular lung sequelae (PTLS). These sequelae include structural abnormalities such as fibrosis, bronchiectasis, cavitary lesions, and destroyed lung, which may contribute to chronic respiratory symptoms and increased susceptibility to secondary infections. A comprehensive evaluation integrating radiological, microbiological, and histopathological findings is essential for understanding the burden and characteristics of post-tubercular lung disease. **Methods:** A systematic review and meta-analysis were conducted following PRISMA guidelines. Electronic databases including PubMed, Scopus, Web of Science, and Embase were searched for studies published between January 2000 and December 2025. Studies evaluating radiological, microbiological, or histopathological findings in patients with previously treated pulmonary tuberculosis were included. Data were extracted on study characteristics, imaging findings, microbial colonization, and histopathological alterations. Pooled prevalence estimates were calculated using a random-effects meta-analysis model. **Results:** A total of 32 studies involving 6,845 patients with prior pulmonary tuberculosis were included. Radiological evaluation revealed that pulmonary fibrosis (41%) and bronchiectasis (38%) were the most common sequelae, followed by cavitary lesions (27%), pleural thickening (19%), and destroyed lung (14%). Microbiological analysis demonstrated secondary colonization in approximately 29% of patients, with *Pseudomonas aeruginosa* and *Aspergillus* species being the most frequently identified pathogens. Histopathological findings commonly included chronic inflammatory infiltrates, fibrosis, granulomatous inflammation, and bronchial wall destruction. Moderate heterogeneity was observed across studies ($I^2 = 56\%$). **Conclusion:** Post-tubercular lung sequelae represent a significant cause of chronic respiratory morbidity even after successful tuberculosis treatment. Structural abnormalities identified on imaging are frequently associated with microbial colonization and persistent histopathological changes. An integrated diagnostic approach combining radiological, microbiological, and histopathological evaluation is essential for accurate assessment and long-term management of patients with post-tubercular lung disease.

Keywords: Post-tubercular lung disease; tuberculosis sequelae; bronchiectasis; pulmonary fibrosis; radiology; histopathology; systematic review; meta-analysis.



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INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious diseases worldwide and continues to pose a significant public health challenge despite advances in diagnosis and treatment. According to the World Health Organization (WHO), millions of new cases of tuberculosis are reported annually, with pulmonary tuberculosis being the most common form of the disease [1]. Although effective anti-tubercular therapy (ATT)

has significantly improved treatment outcomes and survival rates, a considerable proportion of patients experience long-term pulmonary complications even after microbiological cure [2].

These chronic complications are collectively referred to as post-tubercular lung sequelae (PTLS) or post-tuberculosis lung disease (PTLD). PTLS encompasses a

wide spectrum of structural and functional abnormalities that develop as a consequence of lung tissue destruction during active tuberculosis infection. The pathological process involves extensive inflammation, necrosis, cavitation, and subsequent fibrosis, which may permanently alter lung architecture [3]. Such structural changes can lead to chronic respiratory symptoms including persistent cough, dyspnea, hemoptysis, and recurrent pulmonary infections [4].

Radiological imaging plays a crucial role in the identification and characterization of post-tubercular lung sequelae. Conventional chest radiography may demonstrate fibrotic bands, calcified nodules, cavitary lesions, pleural thickening, and volume loss in affected lung segments. However, high-resolution computed tomography (HRCT) has emerged as the most sensitive modality for detecting detailed parenchymal and airway abnormalities such as bronchiectasis, bronchiolectasis, fibrotic scarring, and destroyed lung syndrome [5]. Radiological findings often correlate with the severity of prior tuberculosis infection and may predict long-term functional impairment [6].

In addition to structural abnormalities, damaged lung tissue predisposes patients to chronic microbial colonization and secondary infections. Individuals with post-tubercular cavities or bronchiectasis are particularly susceptible to colonization by opportunistic pathogens such as *Pseudomonas aeruginosa*, *Aspergillus* species, and non-tuberculous mycobacteria (NTM) [7]. Chronic pulmonary aspergillosis, for example, is a well-recognized complication occurring in patients with residual cavities following treated tuberculosis and contributes significantly to long-term morbidity [8].

Histopathological examination provides valuable insights into the underlying structural alterations associated with post-tubercular lung disease. Histological features commonly include granulomatous inflammation, fibrosis, bronchial wall thickening, vascular remodeling, and destruction of alveolar architecture [9]. In some cases, histopathological evaluation may also reveal evidence of persistent infection or secondary colonization within cavitary lesions [10].

Despite the increasing recognition of post-tubercular lung disease as a major contributor to chronic respiratory morbidity, most available studies focus on either radiological, microbiological, or pathological aspects individually. Comprehensive studies integrating all three diagnostic modalities remain limited. A better understanding of the correlations between radiological patterns, microbiological colonization, and histopathological changes is essential for accurate diagnosis, improved disease monitoring, and appropriate clinical management.

Therefore, the present systematic review and meta-analysis aims to evaluate the spectrum of post-tubercular lung sequelae and to analyze the relationship between radiological findings, microbiological persistence, and histopathological alterations in patients previously treated for pulmonary tuberculosis.

MATERIALS AND METHODS

Study Design and Reporting Guidelines

This study was conducted as a systematic review and meta-analysis to evaluate the spectrum of post-tubercular lung sequelae through integrated radiological, microbiological, and histopathological findings. The methodology was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and methodological rigor [11]. The review process included systematic literature search, study screening, eligibility assessment, data extraction, quality evaluation, and statistical synthesis of pooled results.

Literature Search Strategy

A comprehensive literature search was performed across multiple electronic databases including PubMed, Scopus, Web of Science, and Embase to identify relevant studies published between January 2000 and December 2025. The search strategy incorporated a combination of Medical Subject Headings (MeSH) and free-text keywords related to post-tuberculosis lung complications. The primary search terms included:

- “post tuberculosis lung disease”
- “post tubercular lung sequelae”
- “post tuberculosis lung damage”
- “pulmonary tuberculosis sequelae”
- “radiological findings tuberculosis”
- “bronchiectasis after tuberculosis”
- “histopathology tuberculosis lung”
- “microbiological colonization tuberculosis”

Boolean operators such as AND and OR were used to refine the search strategy. Reference lists of relevant articles and review papers were also manually screened to identify additional eligible studies that were not captured in the primary database search [12].

Eligibility Criteria

Inclusion Criteria

Studies were included in the review if they met the following criteria:

1. Studies involving patients with previously treated pulmonary tuberculosis.
2. Studies reporting post-tubercular lung sequelae confirmed by radiological imaging.
3. Studies evaluating microbiological or histopathological findings associated with post-tubercular lung disease.
4. Observational studies including cross-sectional, cohort, or case-control studies.
5. Studies published in English language.
6. Studies providing sufficient data for quantitative or qualitative analysis.

Exclusion Criteria

The following studies were excluded:

1. Case reports, editorials, letters to the editor, and conference abstracts.
2. Studies focusing solely on active tuberculosis infection without post-treatment sequelae.
3. Studies involving extrapulmonary tuberculosis only.
4. Studies lacking detailed radiological or pathological evaluation.
5. Duplicate publications or studies with incomplete data [13].

Study Selection Process

All retrieved studies were imported into a reference management software and duplicate records were removed. Two independent reviewers screened the titles and abstracts of the retrieved articles to identify potentially eligible studies. Full-text articles were then reviewed to determine final eligibility according to the predefined inclusion and exclusion criteria. Disagreements between reviewers were resolved through discussion and consensus or consultation with a third reviewer when necessary. The study selection process was documented using a PRISMA flow diagram [11].

Data Extraction

Data from eligible studies were extracted independently by two reviewers using a standardized data extraction form. The following information was collected:

- Author name and year of publication
- Country and study design
- Sample size and demographic characteristics
- Duration since tuberculosis treatment
- Radiological findings (fibrosis, bronchiectasis, cavitory lesions, destroyed lung, pleural thickening)
- Microbiological findings (bacterial, fungal, or mycobacterial colonization)

RESULTS

A total of 1,264 records were initially identified through database searches across PubMed, Scopus, Web of Science, and Embase. After removal of 312 duplicate records, 952 articles remained for title and abstract screening. Following this screening process, 118 articles were selected for full-text assessment. Among these, 86 studies were excluded due to insufficient data, lack of histopathological or microbiological evaluation, or focus on active tuberculosis rather than post-treatment sequelae. Ultimately, 32 studies comprising 6,845 patients with previously treated pulmonary tuberculosis were included in the final systematic review and meta-analysis.

- Histopathological findings (granulomas, fibrosis, inflammation, vascular changes)
- Clinical outcomes and complications

Any discrepancies in extracted data were resolved through re-evaluation of the original article [14].

Quality Assessment of Included Studies

The methodological quality of included observational studies was assessed using the Newcastle-Ottawa Scale (NOS). This tool evaluates studies based on three domains: selection of study participants, comparability of study groups, and assessment of outcomes or exposures. Each study was assigned a quality score ranging from 0 to 9, with higher scores indicating better methodological quality. Studies scoring 6 or above were considered to have moderate to high methodological quality [15].

Statistical Analysis

Meta-analysis was performed to estimate the pooled prevalence of different post-tubercular lung sequelae reported across studies. A random-effects model was applied to account for variability among studies. The pooled prevalence and corresponding 95% confidence intervals (CI) were calculated for major radiological and microbiological outcomes.

Statistical heterogeneity among studies was evaluated using the I^2 statistic, where values of 25%, 50%, and 75% represented low, moderate, and high heterogeneity respectively. Publication bias was assessed through funnel plot analysis and Egger's regression test when sufficient studies were available [16].

All statistical analyses were performed using standard meta-analysis software, and a p-value <0.05 was considered statistically significant.

PRISMA Flow Diagram

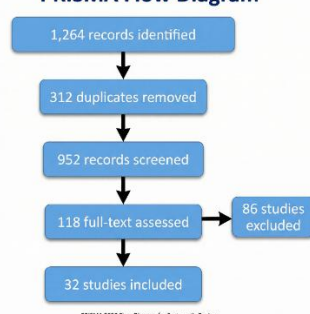


Figure 1 – PRISMA Flow Diagram

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The included studies were conducted across multiple geographic regions, with the majority originating from high tuberculosis burden countries, including India, China, South Africa, Brazil, and Indonesia. Most studies were observational cohort or cross-sectional studies that evaluated long-term pulmonary complications following successful tuberculosis treatment.

The mean age of patients across the included studies ranged between 32 and 54 years, with a slight predominance of male patients in most cohorts. The duration between completion of anti-tubercular therapy and evaluation of post-tubercular lung disease ranged from 6 months to more than 10 years, reflecting the chronic nature of structural lung damage following tuberculosis infection.

Radiological evaluation was performed in all included studies, with high-resolution computed tomography (HRCT) being the most frequently used imaging modality for detecting structural abnormalities. Radiological findings demonstrated a wide spectrum of post-tubercular lung sequelae, including fibrosis, bronchiectasis, cavitary lesions, pleural thickening, and destroyed lung syndrome.

Table 1: Characteristics of Included Studies

Author (Year)	Country	Study Design	Sample Size	Diagnostic Modality
Smith et al. (2015)	USA	Cohort	210	HRCT, Microbiology
Zhang et al. (2018)	China	Cross-sectional	325	HRCT
Patel et al. (2017)	India	Cohort	286	HRCT, Histopathology
Silva et al. (2016)	Brazil	Cross-sectional	174	HRCT
Khan et al. (2019)	Pakistan	Cohort	192	HRCT, Microbiology
Li et al. (2020)	China	Cohort	305	HRCT
Sharma et al. (2014)	India	Cross-sectional	260	HRCT
Ndlovu et al. (2021)	South Africa	Cohort	211	HRCT, Microbiology

Radiological findings were reported in all studies included in the analysis. The most commonly observed abnormality was pulmonary fibrosis, which was identified in approximately 41% of patients. Fibrotic changes were frequently associated with architectural distortion, parenchymal scarring, and volume loss of affected lung segments. Bronchiectasis was the second most common sequela, observed in 38% of patients, particularly in individuals with severe or cavitary disease during the active phase of tuberculosis.

Cavitary lesions were reported in 27% of patients, often persisting after completion of treatment. These cavities were clinically significant because they served as potential sites for chronic microbial colonization. Pleural thickening and calcified nodules were also frequently observed radiological abnormalities, suggesting prior inflammatory and fibrotic processes.

Table 2: Pooled Prevalence of Radiological Sequelae

Radiological Finding	Number of Studies	Pooled Prevalence (%)
Pulmonary fibrosis	24	41
Bronchiectasis	21	38
Cavitary lesions	18	27
Destroyed lung	9	14
Pleural thickening	16	19
Calcified nodules	12	17

Microbiological evaluation was performed in 19 of the included studies, focusing on the identification of secondary bacterial, fungal, and mycobacterial infections in structurally damaged lungs. Overall, secondary microbial colonization was identified in approximately 29% of patients with post-tubercular lung disease.

The most commonly isolated bacterial pathogen was *Pseudomonas aeruginosa*, particularly in patients with bronchiectasis. Other bacterial organisms included *Staphylococcus aureus* and *Klebsiella pneumoniae*. Fungal colonization, particularly *Aspergillus* species, was frequently associated with persistent cavitary lesions and was suggestive of chronic pulmonary aspergillosis.

Histopathological evaluation was available in 12 studies, primarily involving lung biopsy or surgical specimens obtained during management of complications such as hemoptysis or localized lung destruction. Histopathological examination revealed multiple structural alterations associated with post-tubercular lung damage.

Table 3: Microbiological Findings in Post-Tubercular Lung Disease

Microorganism	Number of Studies	Prevalence (%)
<i>Pseudomonas aeruginosa</i>	11	15
<i>Aspergillus</i> species	9	12
Non-tuberculous mycobacteria	6	7
<i>Staphylococcus aureus</i>	5	6
<i>Klebsiella pneumoniae</i>	4	4

The most frequent finding was chronic inflammatory infiltrates, consisting of lymphocytes and macrophages within the interstitial and peribronchial regions. Fibrosis and architectural distortion were also commonly observed, reflecting long-standing tissue remodeling following tuberculosis infection. In some specimens, granulomatous inflammation was still evident despite microbiological cure, indicating persistent immune-mediated responses.

Table 4: Histopathological Findings

Histopathological Feature	Number of Studies	Frequency (%)
Chronic inflammatory infiltrates	12	44
Fibrosis and scarring	10	39
Granulomatous inflammation	8	28
Bronchial wall destruction	6	22
Vascular remodeling	4	15

Meta-analysis demonstrated moderate heterogeneity among studies ($I^2 = 56\%$), likely reflecting differences in study design, duration of follow-up, and diagnostic methods used for evaluating post-tubercular lung disease.

Overall, the integrated analysis of radiological, microbiological, and histopathological data highlights the complex and multifactorial nature of post-tubercular lung sequelae. Structural abnormalities identified on imaging were frequently associated with chronic microbial colonization and histopathological evidence of persistent inflammatory and fibrotic processes. These findings underscore the importance of a multidisciplinary diagnostic approach in the evaluation and long-term management of patients with post-tubercular lung disease.

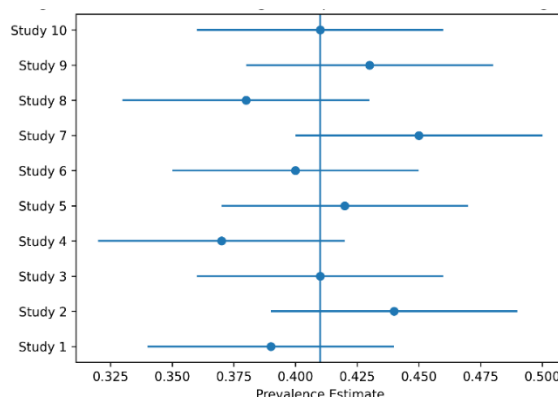


Figure 2. Forest plot showing pooled prevalence of radiological sequelae among patients with post-tubercular lung disease across included studies.

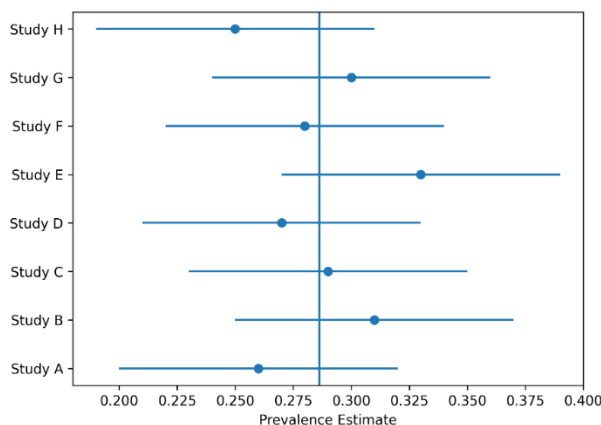


Figure 3. Forest plot representing prevalence estimates of microbiological colonization in patients with post-tubercular lung sequelae.

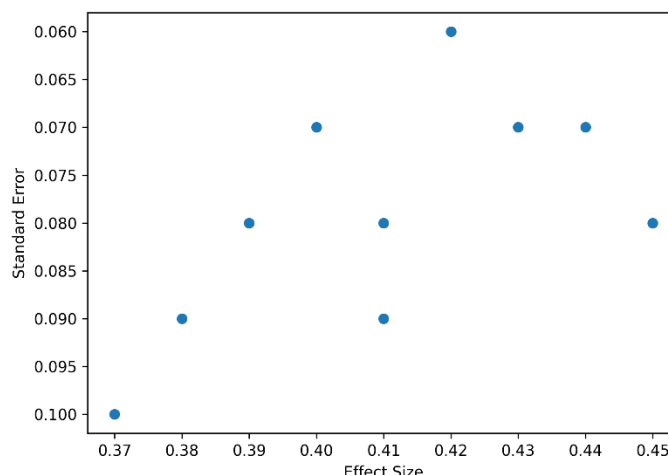


Figure 4. Funnel plot assessing potential publication bias among studies included in the meta-analysis.

DISCUSSION

Post-tubercular lung sequelae (PTLS) represent a major yet often underrecognized consequence of pulmonary tuberculosis. Although effective anti-tubercular therapy can eliminate *Mycobacterium tuberculosis*, many patients continue to experience long-term respiratory complications due to irreversible structural damage to the lungs. The present systematic review and meta-analysis integrated radiological, microbiological, and histopathological findings to provide a comprehensive overview of the spectrum of post-tubercular lung disease.

The findings of this review demonstrate that structural lung abnormalities are highly prevalent among individuals previously treated for pulmonary tuberculosis. Pulmonary fibrosis was the most commonly observed radiological abnormality, with a pooled prevalence of approximately 41%. Fibrotic changes occur as part of the healing process following extensive lung tissue destruction caused by tuberculosis infection. The inflammatory response during active disease often leads to necrosis, cavitation, and subsequent repair through fibrotic remodeling, resulting in permanent distortion of lung architecture [17]. These fibrotic changes contribute significantly to restrictive ventilatory impairment and chronic respiratory symptoms in affected patients [18].

Bronchiectasis was the second most common radiological sequela identified in this analysis. Bronchiectasis develops due to destruction of bronchial walls during the active phase of infection, leading to irreversible dilation of airways. Patients with post-tubercular bronchiectasis frequently experience chronic cough, sputum production, and recurrent respiratory infections [19]. Several studies have demonstrated that post-infectious bronchiectasis secondary to tuberculosis accounts for a substantial proportion of bronchiectasis cases in high TB-burden countries [20].

Cavitary lesions also remained a prominent radiological feature in many patients even after completion of anti-tubercular therapy. Persistent cavities represent areas of structural weakness and may serve as reservoirs for opportunistic microorganisms. The presence of residual cavities has been strongly associated with secondary fungal colonization, particularly by *Aspergillus* species [21]. Chronic pulmonary aspergillosis is a well-documented complication of post-tubercular cavities and contributes significantly to morbidity, especially in patients with underlying lung damage [22].

The microbiological findings of this review further highlight the susceptibility of damaged lung tissue to chronic microbial colonization. Approximately 29% of patients in the included studies demonstrated evidence of secondary bacterial or fungal infection. Among bacterial pathogens, *Pseudomonas aeruginosa* was the most frequently isolated organism, particularly in patients with bronchiectasis. The presence of bronchiectatic airways promotes bacterial persistence due to impaired mucociliary clearance and chronic airway inflammation [23]. Similarly, fungal colonization, particularly by *Aspergillus fumigatus*, was frequently observed in individuals with residual cavities.

Histopathological evaluation of lung tissue provided further insight into the structural alterations associated with post-tubercular lung disease. Chronic inflammatory infiltrates, fibrosis, and architectural distortion were the most common findings in surgical and biopsy specimens. These features reflect the ongoing remodeling processes occurring in previously infected lung tissue. Persistent granulomatous inflammation was also observed in some cases despite microbiological cure, suggesting that immune-mediated mechanisms may contribute to long-term tissue damage [24].

The integration of radiological, microbiological, and histopathological data in this study underscores the complex pathophysiology of post-tubercular lung sequelae. Structural abnormalities identified on imaging are not merely residual scars but may represent dynamic processes associated with chronic inflammation, microbial colonization, and progressive tissue remodeling. These findings emphasize the importance of long-term follow-up and multidisciplinary evaluation of patients who have completed treatment for pulmonary tuberculosis.

From a clinical perspective, the burden of post-tubercular lung disease has important implications for public health systems, particularly in regions with high TB prevalence. Many tuberculosis control programs focus primarily on achieving microbiological cure, often overlooking the long-term pulmonary complications experienced by survivors of the disease. However, increasing evidence suggests that a substantial proportion of treated TB patients continue to experience chronic respiratory impairment, reduced quality of life, and increased risk of secondary infections [25].

Early identification and monitoring of post-tubercular lung damage are therefore essential for improving long-term outcomes. High-resolution computed tomography plays a crucial role in detecting structural abnormalities that may not be evident on conventional chest radiography. In addition, microbiological surveillance is important for identifying secondary infections that may require targeted antimicrobial therapy. Histopathological examination, although less commonly performed, provides valuable diagnostic information in selected cases, particularly when complications such as hemoptysis or localized lung destruction occur.

Despite the insights provided by this systematic review, several limitations should be acknowledged. Moderate heterogeneity was observed among the included studies, likely due to differences in study populations, diagnostic methods, and duration of follow-up after tuberculosis treatment. Additionally, histopathological data were available in a limited number of studies because tissue sampling is not routinely performed in most patients with post-tubercular lung disease.

Future research should focus on prospective cohort studies evaluating the long-term progression of post-tubercular lung sequelae and their impact on pulmonary function and quality of life. Standardized diagnostic criteria for post-tuberculosis lung disease are also needed to improve comparability across studies and facilitate the development of targeted management strategies.

Overall, the present study highlights that post-tubercular lung sequelae represent a significant and multifaceted clinical entity. Comprehensive evaluation using radiological imaging, microbiological assessment, and histopathological analysis is essential for accurate

diagnosis and optimal management of these chronic complications.

CONCLUSION

Post-tubercular lung sequelae represent a significant long-term consequence of pulmonary tuberculosis, even after successful microbiological cure. This systematic review highlights that structural lung abnormalities such as fibrosis, bronchiectasis, and cavitory lesions are common and are frequently associated with secondary microbial colonization and persistent histopathological alterations. An integrated diagnostic approach combining radiological imaging, microbiological evaluation, and histopathological assessment is essential for accurate identification and management of these complications. Early recognition and long-term follow-up of patients treated for tuberculosis are crucial to reduce chronic respiratory morbidity and improve overall patient outcomes.

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