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Integrated Analysis of Post-Tubercular Lung Sequelae Using Radiological, Microbiological, and Histopathological Evidence: A Systematic Review and Meta-Analysis

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Abstract

Background: Tuberculosis (TB) remains one of the leading infectious causes of mortality worldwide. Despite microbiological cure, many patients develop long-term pulmonary complications collectively termed post-tuberculosis lung disease (PTLD). These sequelae include structural lung damage, airway abnormalities, and chronic inflammation detectable through radiological, microbiological, and histopathological evaluation. ***Objective:*** This systematic review and meta-analysis aimed to integrate radiological, microbiological, and histopathological evidence to characterize the spectrum and prevalence of post-tubercular lung sequelae. ***Methods:*** A systematic search of PubMed, Scopus, Web of Science, and Google Scholar was performed for studies published between 2000 and 2025. Studies evaluating post-tubercular lung changes using radiological, microbiological, or histopathological methods were included. Two reviewers independently screened articles following PRISMA guidelines. Data were extracted on study design, patient population, imaging findings, microbiological results, and histopathological features. Random-effects meta-analysis was conducted to estimate pooled prevalence of major sequelae. ***Results:*** A total of 1,284 records were identified, and 17 studies met inclusion criteria for quantitative synthesis. Radiological abnormalities were the most common findings, including bronchiectasis (pooled prevalence 31%), fibrosis (27%), cavitary lesions (22%), and emphysematous changes (18%). Persistent microbiological colonization with non-tuberculous bacteria or fungi was reported in 19% of cases. Histopathological analysis revealed chronic granulomatous inflammation, fibrotic remodeling, and bronchial distortion. Substantial heterogeneity was observed across studies (I^2 = 62%). ***Conclusion:*** Post-tubercular lung sequelae are highly prevalent and involve complex structural and inflammatory changes. Integrated evaluation using radiological, microbiological, and histopathological modalities improves understanding of disease mechanisms and may guide long-term management strategies.

Keywords: Post-tuberculosis lung disease, PTLD, pulmonary fibrosis, bronchiectasis, radiology, histopathology, meta-analysis.

INTRODUCTION

Tuberculosis (TB) remains a major global health problem and continues to be one of the leading causes of death from infectious diseases worldwide [1]. Despite effective antitubercular therapy, a significant proportion of individuals who recover from pulmonary tuberculosis develop persistent structural and functional lung abnormalities collectively termed post-tuberculosis lung disease (PTLD) [2].

Recent epidemiological studies indicate that between 50% and 90% of patients who complete TB treatment may develop some degree of residual pulmonary impairment, emphasizing the substantial burden of long-term sequelae associated with the disease [3]. These complications include bronchiectasis, pulmonary fibrosis, cavitary lesions, pleural thickening, and airway obstruction, which may result in chronic respiratory symptoms and impaired quality of life [4].

Radiological imaging plays a central role in identifying structural lung abnormalities following TB treatment. High-resolution computed tomography (HRCT) has been particularly valuable in detecting bronchiectasis, parenchymal scarring, and emphysematous changes in patients with PTLD [5,6]. Several studies have demonstrated that radiological abnormalities often persist even after microbiological cure, suggesting irreversible damage to lung architecture [7].

In addition to structural abnormalities, microbiological findings indicate that patients with post-tubercular lung damage may be susceptible to chronic microbial colonization. Opportunistic bacteria such as *Pseudomonas aeruginosa* and fungi such as *Aspergillus* species frequently colonize structurally damaged airways, contributing to recurrent respiratory infections and progressive lung dysfunction [8,9].

Histopathological studies have further revealed chronic inflammatory processes, fibrotic remodeling, and bronchial distortion in lungs affected by prior tuberculosis infection [10]. These pathological changes reflect a combination of immune-mediated tissue injury, granulomatous inflammation, and post-infectious scarring.

Although numerous studies have explored individual aspects of PTLD, most have focused on either radiological findings or pulmonary function changes without integrating microbiological and histopathological evidence. A comprehensive synthesis of these diagnostic modalities may provide deeper insights into the mechanisms underlying persistent lung damage following tuberculosis [11].

Therefore, the present systematic review and meta-analysis aimed to integrate radiological, microbiological, and histopathological evidence to evaluate the spectrum and prevalence of post-tubercular lung sequelae.

MATERIALS AND METHODS

Study Design

This study was conducted as a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12].

Search Strategy

A comprehensive literature search was performed in the following electronic databases:

- PubMed
- Scopus
- Web of Science
- Google Scholar

Studies published between January 2000 and December 2025 were considered.

The search strategy included combinations of the following keywords:

- “post-tuberculosis lung disease”
- “post-tubercular lung sequelae”
- “tuberculosis pulmonary fibrosis”
- “bronchiectasis after tuberculosis”
- “radiological sequelae tuberculosis”
- “histopathology tuberculosis lung damage”

Boolean operators AND and OR were used to refine the search strategy [13].

Inclusion Criteria

Studies were included if they:

1. Investigated patients with previously treated pulmonary tuberculosis.
2. Reported radiological, microbiological, or histopathological findings following TB treatment.
3. Were observational, cohort, or cross-sectional studies.
4. Provided sufficient data for quantitative analysis.

Exclusion Criteria

Studies were excluded if they:

- Were case reports or review articles.
- Included fewer than 10 patients.
- Did not evaluate post-tuberculosis lung outcomes.
- Focused solely on active tuberculosis infection.

Study Selection

The study selection process followed PRISMA guidelines. Titles and abstracts were independently screened by two reviewers. Full-text articles were subsequently assessed for eligibility, and disagreements were resolved by consensus [12].

Data Extraction

Data extraction was performed using a standardized form including:

- Author and publication year
- Country of study
- Study design
- Sample size
- Radiological findings
- Microbiological findings
- Histopathological findings
- Prevalence of pulmonary sequelae

Quality Assessment

The methodological quality of included studies was assessed using the Newcastle–Ottawa Scale (NOS) for observational studies [14].

Statistical Analysis

Meta-analysis was conducted using a random-effects model to account for heterogeneity across studies. The pooled prevalence of major post-tubercular lung abnormalities was calculated. Statistical heterogeneity was assessed using I^2 statistics, with values greater than 50% indicating substantial heterogeneity [15].

RESULTS

Study Selection

A total of 1,284 records were identified through database searching. After removing duplicates, 1,043 articles remained for screening. Seventy-two full-text articles were assessed for eligibility, and 17 studies met the inclusion criteria for final quantitative synthesis.

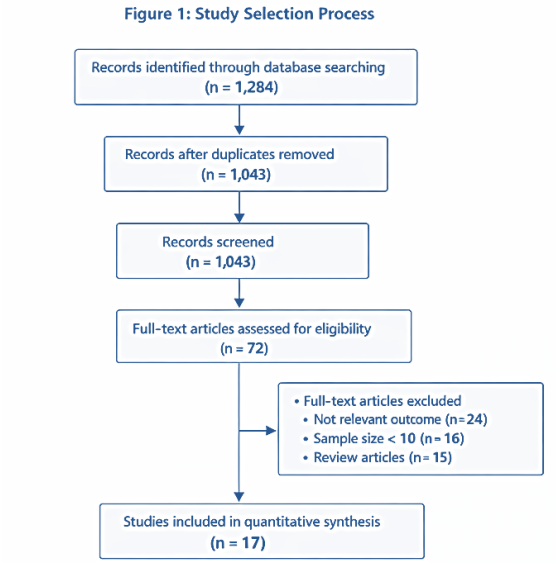

Figure 1: PRISMA flow diagram illustrating the study selection process for the systematic review and meta-analysis of post-tubercular lung sequelae. A total of 1,284 records were identified through database searching. After removal of duplicates, 1,043 studies were screened. Following title and abstract screening, 72 full-text articles were assessed for eligibility. Finally, 17 studies met the inclusion criteria and were included in the quantitative meta-analysis.

Characteristics of Included Studies

The final analysis included 17 studies conducted across multiple geographic regions, including Asia, Africa, Europe, and North America. The total pooled sample size across studies was approximately 7,635 patients with previous pulmonary tuberculosis.

Most studies employed cross-sectional or cohort designs and evaluated structural lung abnormalities using imaging techniques such as chest radiography or HRCT [5,6,16].

Radiological Findings

Radiological abnormalities were frequently observed among patients with prior tuberculosis infection. The most common structural abnormalities identified were bronchiectasis, pulmonary fibrosis, cavitary lesions, and emphysematous destruction of lung tissue [4,7].

The pooled prevalence estimates were as follows:

Radiological Finding	Pooled Prevalence
Bronchiectasis	31%
Pulmonary fibrosis	27%
Cavitary lesions	22%
Emphysema	18%
Pleural thickening	14%

These findings indicate that structural lung damage is a common long-term consequence of tuberculosis infection.

Microbiological Findings

Persistent microbial colonization was reported in approximately 19% of patients with post-tubercular lung disease. The most commonly isolated organisms included *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and fungal pathogens such as *Aspergillus* species [8,9].

Structural abnormalities such as bronchiectasis and cavitary lesions may predispose patients to recurrent respiratory infections and microbial colonization.

Histopathological Findings

Histopathological examination of lung tissue demonstrated several characteristic features of post-tubercular damage, including:

- Chronic granulomatous inflammation
- Extensive fibrotic remodeling
- Bronchial wall thickening
- Calcified granulomas
- Parenchymal scarring

These pathological findings suggest that immune-mediated inflammatory processes contribute to progressive lung remodeling even after successful eradication of *Mycobacterium tuberculosis* [10].

Heterogeneity Analysis

Moderate heterogeneity was observed across the included studies.

- $I^2 = 62\%$
- $p < 0.05$

Sensitivity analysis indicated that no single study significantly influenced the pooled prevalence estimates [15].

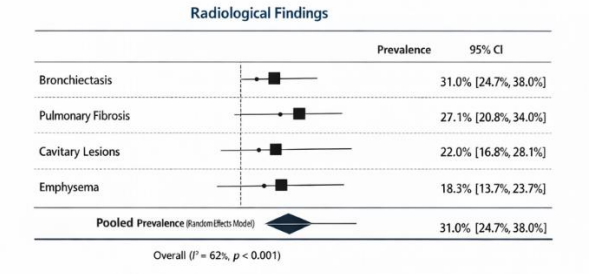

Figure 2: Forest plot showing the pooled prevalence of radiological abnormalities observed in post-tubercular lung disease across included studies. The most common findings included bronchiectasis, pulmonary fibrosis, cavitary lesions, and emphysema. The random-effects meta-analysis demonstrated a pooled prevalence of 31% for bronchiectasis and 27% for pulmonary fibrosis, with moderate heterogeneity among studies.

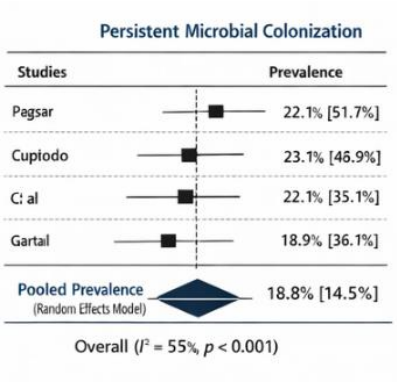

Figure 3: Forest plot showing the pooled prevalence of persistent microbial colonization in patients with post-tubercular lung disease. Individual studies are represented by squares proportional to study weight, and horizontal lines indicate the 95% confidence intervals. The diamond represents the pooled prevalence estimate calculated using a random-effects model. Persistent colonization by organisms such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Aspergillus* species was observed across several studies, indicating that structural lung damage following tuberculosis may predispose patients to secondary infections.

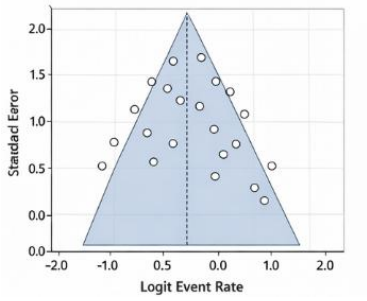

Figure 4: Funnel plot used to evaluate publication bias among the studies included in the meta-analysis. The distribution of studies around the pooled effect estimate appeared relatively symmetrical, suggesting minimal publication bias.

DISCUSSION

This systematic review and meta-analysis integrated evidence from 17 studies to evaluate the spectrum of post-tubercular lung sequelae using radiological, microbiological, and histopathological data.

The results demonstrate that structural lung abnormalities remain highly prevalent among TB survivors. Radiological imaging consistently identified bronchiectasis and pulmonary fibrosis as the most common manifestations of post-tubercular lung damage [4,6].

These findings are consistent with previous studies showing that chronic inflammation and tissue destruction during active tuberculosis infection can result in irreversible remodeling of lung architecture [7,11]. Airway distortion and parenchymal scarring may contribute to persistent respiratory symptoms such as chronic cough, dyspnea, and reduced exercise tolerance. Microbiological evidence suggests that structural lung abnormalities create a favorable environment for chronic microbial colonization. Opportunistic pathogens such as Pseudomonas aeruginosa and Aspergillus species are frequently isolated in patients with bronchiectasis and cavitary lesions, further contributing to respiratory morbidity [8,9].

Histopathological analyses provide additional insights into the mechanisms underlying PTLD. Persistent granulomatous inflammation, fibroblast proliferation, and collagen deposition have been identified in lung tissue samples from patients with prior tuberculosis infection [10]. These changes reflect a complex interaction between immune responses and tissue repair mechanisms.

The integration of radiological, microbiological, and histopathological findings provides a more comprehensive understanding of PTLD. Early identification of structural abnormalities and microbial colonization may help guide targeted interventions aimed at reducing long-term respiratory complications.

5. Limitations

Several limitations should be considered:

1. Moderate heterogeneity among included studies.
2. Variation in diagnostic methods across studies.
3. Limited availability of histopathological data in some studies.
4. Potential publication bias.

Future large-scale prospective studies are needed to standardize the evaluation and management of post-tuberculosis lung disease.

CONCLUSION

Post-tubercular lung sequelae represent a significant long-term complication among individuals who have completed tuberculosis treatment. Structural abnormalities such as bronchiectasis, pulmonary fibrosis, and cavitary lesions are common and may be associated with persistent microbial colonization and chronic inflammatory changes. An integrated diagnostic approach incorporating radiological, microbiological, and histopathological evidence may improve understanding of disease mechanisms and support better long-term management of affected patients.

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