



Pulmonary tuberculosis as a risk factor for lung cancer: A systematic review

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Abstract

Tuberculosis is a disease caused by infection with the bacterium *Mycobacterium tuberculosis*. Even if a person has been declared cured of tuberculosis (TB), this disease can still leave long-term effects on health, especially disorders in the lungs. This review aims to review the risk of lung cancer in people with pulmonary tuberculosis. The research method used was a systematic review. Literature was searched through Google Scholar, PubMed, and Mendeley databases in March-April 2025. A total of 1669 articles were obtained, then the articles were selected through the stages of titles, abstracts, keywords and continued with selection on full text and relevance. The results of the selection were obtained 5 articles that met the set criteria. Review reporting uses Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Based on the systematic review that has been carried out, the results are obtained that there is an increased risk of lung cancer in patients with pulmonary tuberculosis.

Keywords: Lung Cancer; Pulmonary Tuberculosis; Risk Factor; Tuberculosis

1. Introduction

Tuberculosis (TB) is a preventable and generally curable disease. However, by 2023, tuberculosis is expected to return to the leading cause of death from infection worldwide, having been replaced by COVID-19 for the previous three years [1]. Patients with pulmonary tuberculosis generally show symptoms such as cough, chest pain, fever, night sweats, and weight loss, accompanied by the findings of infiltrates or cavitates on chest imaging examinations that can also be seen in cases of lung cancer [2]. Therefore, the link between tuberculosis and lung cancer has been of particular concern [3].

Based on the WHO Global Tuberculosis Report 2023, there are 10.6 million people in the world who fall ill from tuberculosis and as many as 1.3 million people die from tuberculosis. Indonesia is among the eight countries that account for 2/3 of tuberculosis cases worldwide [4]. In 2022, the International Agency for Research on Cancer (IARC) reported that 2.48 million cases of lung cancer were newly diagnosed and 1.8 million people died from the disease [5]. Lung cancer tends to have a lower chance of cure than other types of cancer. Because the chances of cure depend so much on how early the cancer is discovered, it is crucial to detect lung cancer early [6].

Tuberculosis (TB) is caused by the bacterium *Mycobacterium tuberculosis*, which usually attacks the lungs or commonly called pulmonary tuberculosis. However, these bacteria can also spread to other parts of the body such as the intestines, bones, joints, and other organs, and are referred to as extrapulmonary tuberculosis [7]. Tuberculosis is known to be a disease that can affect various body systems, even though the lungs are the main organs it attacks [2]. When people with TB cough, sneeze, or spit, they spread TB germs into the air, and people who breathe air contaminated with TB germs can contract the disease. Active tuberculosis is a chronic inflammatory reaction in lung tissue that causes fibrosis and irreversible scarring, and is accompanied by a disturbance in the body's immune response. Chronic TB infection can lead to the accumulation of genetic changes, and exposure to growth factors can trigger gradual cell transformation, eventually leading to dysplasia and malignant squamous cell carcinoma. A person's susceptibility to tuberculosis is also

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associated with genetic variation (polymorphism) in several genes associated with the innate immune system and inflammatory responses, such as Toll-like receptors, tumor necrosis factor (TNF), and induced nitric oxide; These genes are also known to be associated with susceptibility to cancer [8].

Lung cancer is a condition in which abnormal malignant tissue grows in the lungs and develops uncontrollably and can spread to other parts of the body [9]. Lung cancer is a disease whose causes are quite complicated, because it involves several genes that work in different ways. If these genes interact with environmental factors, such as cigarette smoke or pollution, as well as age, then a person can develop lung cancer [10].

The link between tuberculosis and lung cancer can occur because tuberculosis creates conditions in the body that support tumor growth. This condition can stimulate the immune system and produce substances such as cytokines, which can then promote the growth of cancer cells [11]. In a study conducted by Kumar et al. (2022), it was found that the frequency of tuberculosis in patients with lung cancer is quite high. Tuberculosis can increase the risk of lung cancer through severe and prolonged lung inflammation, which leads to tissue damage, fibrosis (scar formation), scar formation, and genetic changes [13].

A study conducted by the National Cancer Institute showed that patients with tuberculosis have an increased risk of developing lung cancer, and another study estimated that men with tuberculosis have a twice as high risk of developing lung cancer [10]. The symptoms of these two diseases (tuberculosis and lung cancer) are sometimes similar, with common signs such as coughing, coughing up blood (hemoptysis), weight loss, fever, chest pain, shortness of breath, loss of appetite, as well as a similar radiological picture. These radiological features include enlargement of lymph nodes, pleural effusion (fluid in the pulmonary cavity), blurring of air space in the lungs, consolidation of the lungs with irregular edges, thick-walled cavities, and infiltration of the parenchyma with increased metabolic activity [13].

The purpose of this study is to provide an overview of the risk of lung cancer incidence in patients with pulmonary tuberculosis. The study thoroughly reviewed several high-quality studies, then analyzed the relationship between pulmonary tuberculosis and lung cancer, including looking at different groups in the study population to find out what factors might influence the relationship.

2. Method

The research method used was *systematic review* using the PRISMA (*Preferred Reporting Items for Systematic Review and Meta-Analysis*) reporting guidelines regarding pulmonary tuberculosis and lung cancer. The literature search was conducted in February – April 2025. Some of the steps taken in this study are: 1) defining eligibility criteria, 2) defining information sources, 3) study selection, 4) data collection process, 5) selecting data items.

The data used in this study came from the results of previous research, not from direct observation. To make it easier to find the right article or journal, article and journal searches use keywords to expand or specify the search.

2.1. Eligibility criteria

Eligibility criteria include inclusion criteria and exclusion criteria. The inclusion criteria are: 1) journals published in 2021-2025, 2) journals using English, 3) research discussing the incidence of lung cancer in patients with pulmonary tuberculosis, 4) full text is available. Meanwhile, the exclusion criteria in choosing this article are articles published before 2021.

2.2. Resources

The articles used in this study are sourced from online databases, namely Google Scholar, PubMed, and Mendeley. Authors will eliminate articles that do not have full text. The researcher also adapted the article to the research questions that had been made.

2.3. Study selection

2.3.1. There are four study selections, namely

- Keywords used in article search include: "Pulmonary Tuberculosis", "Lung Cancer", "Risk Factor", keyword search is expanded by adding the words "and", "or" and a combination of two keywords at the same time.
- Article selection using the year of publication filter, namely 2021-2025
- The selection of articles is based on the abstract content, title and keywords in the article.

- To determine whether an article should be included in the review or removed according to the established criteria, the article will be examined in full. The researcher conducted the stages of summarizing, comparing, summarizing, and synthesizing several studies on the incidence of lung cancer in patients with pulmonary tuberculosis. Ensure that each selected article on pulmonary tuberculosis as a risk factor and lung cancer as an outcome disease meets the inclusion and exclusion criteria of the article.

2.4. Data collection process

The type, title, year of publication, and method of collecting articles are collected manually. The researcher examined the collected articles to ensure their relevance.

3. Result

3.1. Study Selection

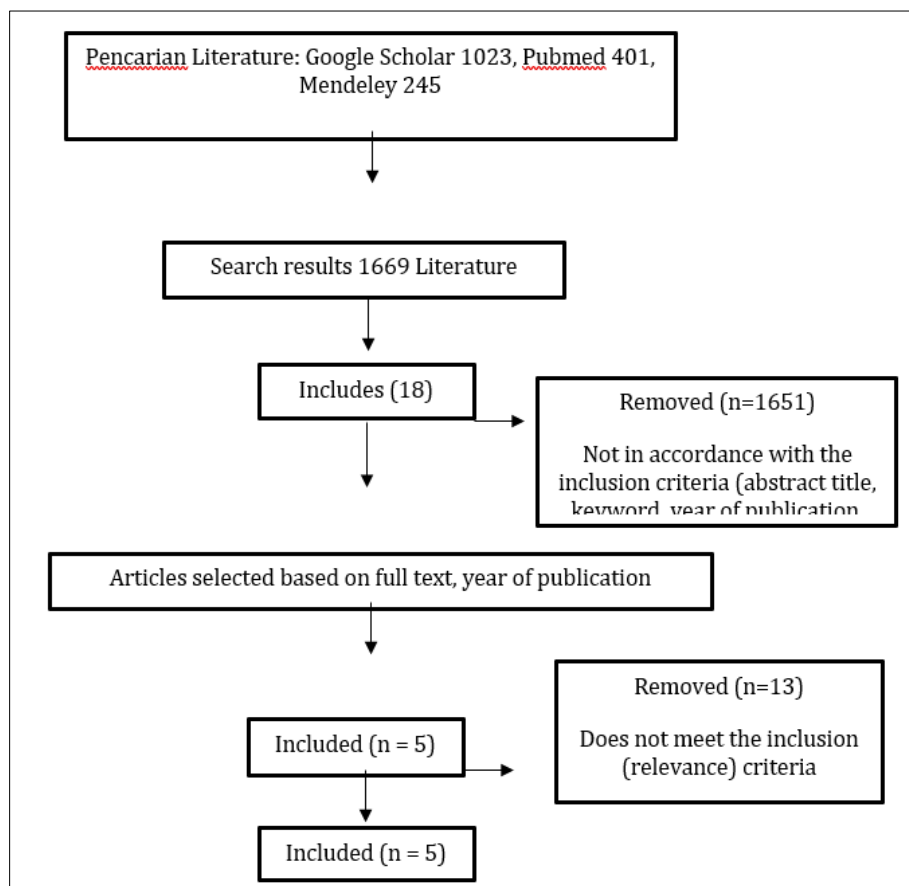


Figure 1 Systematic Review Results

The results of the article selection were obtained for a total of 5 relevant articles according to the criteria that have been set, namely 5 articles from 2021 to 2025. In the first stage, the author obtained 1669 articles obtained in accordance with the set criteria. After that, the researcher reviewed the search results by adjusting the title, abstract and keyword, and 18 articles that matched the criteria as many as 1651 articles did not meet the criteria. Of the 18 articles that have been reviewed, the author from the abstract then the author reviews by looking at the complete text and there are only 5 articles that are suitable and 13 articles that are not suitable. After the author conducted a review, the total number of articles used in the study was 5 articles.

3.2. Characteristic Study

The 5 articles obtained from several online databases are described in the following table

Table 1 Results of Research Data Analysis

No	Author, Research Location, Journal	Objectives, Research Design, and Variables	Data Source and Sample Count	Result
1	Ho et al., (2021) Taiwan PLoS ONE 16(5): e0250531. https://doi.org/10.1371/journal.pone.0250531	To evaluate the risk of secondary lung cancer in patients with or without a history of tuberculosis using national-based data. Cohort. Age, monthly income, comorbidities, urbanization rate, and hospital rate.	The data source comes from the International Classification of Disease (ICDp-CM) code 010–011 from 2000 to 2015. A total of 6394 lung cancer patients with tuberculosis infection and 13,686 lung cancer patients without tuberculosis infection.	During the monitoring period, as many as 761 patients (10.97%) who had a history of tuberculosis were diagnosed with secondary lung cancer, while in patients without a history of tuberculosis the number was 1263 people (9.11%). After considering other factors that may have influenced, it is known that the risk of developing secondary lung cancer in patients who have had tuberculosis is 1.67 times higher compared to patients who have never had tuberculosis.
2	Park et al., (2022) Korea Annals ATS Volume 19 Number 4 April 2022	To investigate whether a history of pulmonary tuberculosis (PTB) is associated with an increased risk of developing lung cancer in populations with COPD (Chronic Obstructive Pulmonary Disease). Cohort. Age, gender, smoking history, and pulmonary tuberculosis (PTB) status based on the results of initial health screening examinations from participants who had COPD (Chronic Obstructive Pulmonary Disease).	The data source comes from data from the Korean National Health Insurance Service – National Sample Cohort (NHIS-NSC) 2.0. The number of samples consisted of 13,165 people in the COPD group and 34,467 people in the non-COPD group.	History of pulmonary tuberculosis (PTB) identified by chest X-ray (CXR) examination was associated with a 1.23-fold higher increased risk of lung cancer in participants with COPD. History of pulmonary tuberculosis (PTB) is associated with an increased risk of lung cancer in COPD patients.
3	Moon et al., (2023) Korea. Clinical Infectious Diseases. CID 2023;77 (1 November)	Evaluate risk factors related to lung cancer and develop lung cancer prediction models for tuberculosis survivors. Cohort.	The data source comes from the National Health Insurance Service (NHIS) Korea. The population in this study was tuberculosis	During the 4.8-year follow-up period, tuberculosis survivors had a 1.72 times higher risk of lung cancer than controls. The highest risk was found in active smokers with ≥ 20 packs (hazard ratio 6.78) and survivors with COPD (2.43). The main risk factors include pulmonary tuberculosis, age >60 years, smoking,

		Body mass index (BMI), smoking history, alcohol consumption, regular exercise, and other comorbid conditions.	survivors (n = 75,467) between 2010 and 2017 and the control group was matched by age and sex with a ratio of 1:1.	COPD, and asthma. The lung cancer risk prediction model showed good accuracy (statistical concordance = 0.827).
4	Martarita et al., (2024) Indonesia. Respiratory Science. 2024; 4(2): 94-9.	To find out the relationship between tuberculosis (TB) and lung cancer (LC) at Arifin Achmad Regional General Hospital, Riau Province. Cross sectional – retrospektif. Gender, age, sputum smear, type of anti-TB drug, type of lung cancer, stage of lung cancer, long diagnosed TB before lung cancer.	The data source comes from the medical records of 2015-2018 at the Arifin Achmad Regional General Hospital, Riau Province. There are 24 medical record data that meet the inclusion criteria in this study.	Of the 203 patients, 24 patients (11.8%) had a history of TB. The age of the patient ranges from 41 to 60 years. The most frequent pathological finding was adenocarcinoma in 13 patients (54.0%). The most common stage of cancer was advanced stage IIIB in 7 patients (29.2%). Cases of TB infection are seen in lung cancer patients, which is about 11% of all lung cancer cases.
5	Hong et al., (2024) Korea. Journal of Cancer Prevention. 2024;29(4):157-164.	To examine the risk of lung cancer in people infected with tuberculosis (TB) compared to the general population as well as to evaluate factors associated with lung cancer in individuals infected with TB. Cohort. Gender, age, income, history of smoking, history of alcohol consumption, physical activity, BMI, comorbid diseases, treatment complications.	Data sources came from the Gyeonggi Infectious Disease Control Center (GIDCC) in 2010-2016 and the National Health Insurance Service (NHIS) from January 1, 2002 to April 30, 2022. This population is 35,140 patients with tuberculosis.	The results showed that 1.26% (n = 444) of 35,140 TB patients developed lung cancer. Compared to the incidence in the general population, the risk of lung cancer was higher in people with TB (SIR: 2.04, 95% CI: 1.85-2.23). TB patients have a higher risk of lung cancer compared to the average person. Factors that affect this risk include gender, age, and smoking habits.

4. Discussion

The selected articles are 5 articles that have gone through a review process regarding the risk of lung cancer that can be experienced by patients with pulmonary tuberculosis. The articles used are since the last 5 years. In the table, there are risks, risk factors, impacts/complications, and the relationship between pulmonary tuberculosis and lung cancer. The result is that pulmonary tuberculosis increases the risk of lung cancer.

Based on the results of the study conducted by Ho et al. (2021) [14], it was shown that secondary lung cancer was found in 761 patients who had had TB (about 11%) and in 1,263 patients without a history of TB (about 9%). After considering other factors that may have influenced, it is known that patients with a history of TB have a 1.67 times higher risk of developing secondary lung cancer compared to those without a history of TB. When the data were grouped by comorbidities (such as diabetes, high blood pressure, liver cirrhosis, heart failure, stroke, chronic kidney disease, and COPD), the results were significant in increasing the risk of secondary lung cancer in TB patients compared to non-TB patients.

Studies conducted by Hong et al. (2024) [18] show that individuals with a history of pulmonary TB have a significantly higher risk of lung cancer than the general population. One large-scale study of more than 35,000 TB patients showed that about 1.26% of these patients developed lung cancer within a certain period of time, with a Standardized Incidence Ratio (SIR) of 2.04. This means that the risk of lung cancer in TB survivors is twice as high as in individuals without a history of TB. Multivariate analysis showed that age, male gender, smoking habit, and number of daily cigarettes were significant risk factors. This study confirms the need to pay attention to lung cancer as a long-term complication of TB, even after TB treatment is declared complete.

From the study Martarita et al. (2024) [17] data from Arifin Achmad General Hospital in Riau noted that of 203 lung cancer patients, around 11.8% had a history of TB. The majority of these patients are diagnosed in advanced stages and have a histopathological type of adenocarcinoma. These findings reflect a global phenomenon in a local context: delayed diagnosis, lack of integrated screening programs, and high burden of TB in Indonesia are major challenges.

A study conducted by Hong et al. (2024) [18] the effect of smoking on the development of lung cancer (LC) in tuberculosis (TB) patients found that smokers had a higher increased incidence of lung cancer compared to non-smokers. The results of the study Moon et al. (2023) [16] also show that smoking habits, old age (>60 years), and the presence of asthma or COPD are strong predictors of lung cancer in TB survivors. This study highlights an individual prediction model based on risk factors with a high discriminative value (C-statistic 0.827), which indicates the potential for application in risk-based screening at the community level. However, a study conducted by Park et al. (2022) [15] reported that in COPD patients who had never smoked, the risk of lung cancer incidence was higher in participants with a history of pulmonary tuberculosis (PTB) compared to those without a history of PTB. Meanwhile, in COPD patients who are former or active smokers, the risk is not found (insignificant).

Biologically, the link between pulmonary TB and lung cancer can be explained through chronic inflammatory processes caused by *Mycobacterium tuberculosis* infection [11]. Pulmonary TB causes tissue damage and the formation of granulomas that can lead to fibrosis and pulmonary remodeling. Long-lasting inflammation triggers the occurrence of oxidative stress and the production of proinflammatory cytokines such as TNF- α and IL-6, which can contribute to the process of carcinogenesis [18]. In addition, scar tissue formed due to TB can also be a place for abnormal cells to develop. The concept of scar carcinoma is a cancer that develops from the area of scar tissue in the lungs [19].

In patients with a history of TB, the most common type of lung cancer is adenocarcinoma, which is a subtype of non-small cell lung cancer (NSCLC) [12]. This cancer is often diagnosed in advanced stages, such as stage IIIB or IV, because the symptoms are similar to active or residual TB, such as chronic cough, hemoptysis, and weight loss [13]. The clinical similarities between TB and lung cancer are a challenge in diagnosis. It is not uncommon for delayed lung cancer to be detected because it is considered a recurrence of TB or a residual effect of a previous infection [10].

The studies we reviewed as a whole showed that tuberculosis (TB) could increase a person's risk of developing lung cancer. Factors such as age, gender, smoking habits, and other accompanying illnesses also influence this relationship. Therefore, patients who have or are experiencing TB need to be monitored more intensively to detect the possibility of lung cancer. They should also be a priority in prevention programs. It is important for medical personnel to be more vigilant and quicker in handling cases like this, so that diseases can be recognized early and treated before they get worse. This step will be very helpful in reducing the number of illnesses and deaths due to lung cancer in the community.

5. Conclusion

Implications for Health Practice/Services

Special attention needs to be paid to these patients to recognize and treat the condition early, which will help reduce the rate of illness and death in the community. The authors found similarities between signs and symptoms in pulmonary tuberculosis and lung cancer so that precision and accuracy of proper diagnosis are needed to handle cases in patients.

Implications for Research

The authors analyzed the incidence of lung cancer experienced by tuberculosis patients with significant results. Therefore, it is hoped that future researchers can expand or develop more effectively and efficiently.

Compliance with ethical standards

Disclosure of conflict of interest

The author has no conflict of interest in this study.

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