Profile of Underdiagnosis Lung Cancer with Pulmonary Tuberculosis at Arifin Achmad General Hospital, Pekanbaru

Sri Melati Munir, Ananda Febriani Aulia, Elvando Tunggul Mauliate Simatupang*, Veghasanah Tanlie

Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Riau University - Arifin Achmad General Hospital, Pekanbaru, Riau

*Corresponding Author:

Elvando Tunggul Mauliate Simatupang

Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Riau, Arifin Achmad Hospital, Pekanbaru, Indonesia
elvando56@gmail.com

ABSTRACT

Background: Lung cancer and pulmonary tuberculosis are respiratory issues that collectively account for the world's leading cause of mortality. Indonesia, being a nation endemic for Pulmonary Tuberculosis, frequently encounters instances of diagnosis overlap with lung cancer. Delays in the diagnosis of both pulmonary tuberculosis and lung cancer have a global impact on morbidity and mortality. Based on this, this study aims to determine the profile of Lung Cancer patients who were previously diagnosed as pulmonary tuberculosis as an initial diagnosis that can provide new criteria in establishing a diagnosis between pulmonary tuberculosis and lung cancer.

Method: This study is a descriptive cross-sectional study using total sampling collected over 1 year. The inclusion criteria were lung cancer patients previously diagnosed with clinical pulmonary tuberculosis, with or without anti-tuberculosis drugs obtained from medical record data. All results are presented in the form of a distribution table.

Results: Twenty seven patients diagnosed with adenocarcinoma, with the highest prevalence among males (77.78%). The duration of delay was less than 6 months (62.96%), being the highest rate in this study. Due to the delay in diagnosis, all patients diagnosed with lung cancer were at stage IV.

Discussion: Adenocarcinoma is the most common form of lung cancer in men and individuals over 40 years old. Lung cancer with a latency duration of 6 months is typically diagnosed at stage IV. Clinical pulmonary tuberculosis must be investigated further if no clinical improvement is observed after one month of anti-tuberculosis drug treatment.

Conclusion: Diagnostic delays of lung cancer significantly impact patient survival. Screening for suspected lung cancer in clinical pulmonary tuberculosis is crucial to reduce morbidity and mortality. Sputum cytology and low-dose CT scan may be utilized as screening modalities.

INTRODUCTION

Cancer is one of the leading causes of death globally. According to the World Health Organization (WHO), in 2020, there were approximately 1.3 million cancer-related fatalities in China and 106 thousand in Indonesia. In 2020, lung cancer was the second leading cause of mortality. Lung cancer is the leading cause of death for men and the second leading cause of death for women. It is estimated that there were more than 2,2 million new cases of lung cancer in 2020, and this trend is expected to persist [1,2].

Pulmonary tuberculosis is a contagious disease that continues to be a public health concern. Based on data from the World Health Organization, the global incidence of pulmonary tuberculosis is projected to reach 10.6 million cases in 2021, with approximately 1.6 million deaths from pulmonary tuberculosis. Tuberculosis is the primary infectious disease cause of death worldwide.

In 2022, Indonesia had the second-highest prevalence of pulmonary tuberculosis after India. The incidence of pulmonary tuberculosis in Indonesia is estimated to be 970,000 pulmonary tuberculosis will be the infectious disease with the second-greatest mortality rate worldwide in 2020, after COVID-19 [1,2].

Patients with lung cancer are often misdiagnosed with pulmonary tuberculosis, resulting in a delay in diagnosis and inappropriate use of drugs. A study conducted by Chen et al. [3] in China showed that there were 5.46% of treated lung cancer cases previously diagnosed as pulmonary tuberculosis. The study also explained that lung cancer cases after pulmonary tuberculosis treatment tend to increase, ranging from 7.2 to 11.6% in regions with a high incidence of pulmonary tuberculosis. Both diseases share comparable symptoms and have a high incidence of lung parenchyma involvement. While data in Indonesia related to this condition is still limited. However, there are many distinctions in their causes, including the fact that pulmonary tuberculosis is an infectious disease and lung cancer is not. These two diseases are treated differently, resulting in diagnostic and treatment delays, a poor prognosis, and low survival rates [4,5]. Based on the above background, the article aims to determine the profile of lung cancer patients diagnosed as pulmonary tuberculosis as an initial diagnosis by examining several other supporting variables such as demographic data, history of anti-tuberculosis drugs consumption, duration of diagnostic delay, type, and stage of lung cancer experienced.

METHODS

This study is a descriptive study using a cross-sectional design. The data collection technique was carried out by total sampling, namely by collecting all data on lung cancer patients who had a diagnosis of pulmonary tuberculosis. The study was conducted from August 2022 to July 2023, with data acquired from hospital medical records. The inclusion criteria in this study were taking data on lung cancer patients who had been diagnosed with clinical pulmonary tuberculosis, with/without prior anti-tuberculosis drugs treatment. Selection and recapitulation of data followed by statistical analysis presented in the form of distribution tables. Lung cancer patients with a history of or currently on anti-tuberculosis drug treatment were not included in the study sample because this is referred to as a co-infection condition of pulmonary tuberculosis in lung cancer. In addition, other exclusion criteria included data on lung cancer patients who were treated more than once.

The independent variables in this study include demographic data, history of anti-tuberculosis drugs consumption, duration of diagnostic delay, and type and stage of lung cancer experienced. Age is grouped into 2 categories based on the risk factors for lung cancer, with the age group above 40 years. Body mass index and history of smoking are grouped using a categorical scale. Body mass index is classified based on WHO criteria, divided into 4 groups. The history of smoking is categorized according to the Brinkman index, which is calculated by multiplying the number of cigarettes consumed per day by the duration of smoking.

The history of anti-tuberculosis drugs consumption is divided based on the mean value from this study data, which is 12,03 months (1 year) of a total of 325 months of anti-tuberculosis drugs use across all samples. The type and stage of lung cancer are categorized using a categorical scale based on the lung cancer guidelines in Indonesia. Staging was determined when the patient was diagnosed with lung cancer, and all samples were stage IV at the time of treatment.

The duration of diagnostic delay is defined by calculating the time interval between the patient's diagnosis of clinical pulmonary tuberculosis to when the patient was diagnosed with lung cancer. The measurement used for the duration of diagnostic delay is based on the mean value from the entire sample data, which is 6.18 months (6 months) out of a total of 167 months across all patient durations. All data were analyzed using SPSS version 28.0 and presented in the form of a distribution table, including prevalence of lung cancer with a history of pulmonary tuberculosis, demographic data, and distribution of lung cancer Patients with delayed diagnosis due to pulmonary tuberculosis.

RESULTS

From August 2022 to July 2023, 253 patients were diagnosed with lung cancer from the total population. **Table 1** shows that 10.42% of the sample collected based on the inclusion criteria had a history of being diagnosed with clinical pulmonary tuberculosis prior to receiving a follow-up examination. The study's findings are then presented in the form of a distribution table based on demographic variables and diagnostic delay criteria distribution.

According to the study's demographic data, 77% of the participants in the research were male, according to the study's demographic data, and all samples were over 40 years old. In addition, samples with underweight BMI had the highest rate of 59.25%, followed by a history of smoking in the study with Severe IB at 70.37% **(Table 2)**.

Regarding diagnostic delay criteria, this study revealed that 62.97% of samples had a history of consuming ATD for more than a year. In the range of less than six months, 62.94% of diagnostic delays occurred. Based on anatomical pathology examination, adenocarcinoma was found with a prevalence of 77.78% and was found to be stage IV in all samples **(Table 3)**.

Table 1. Prevalence of lung cancer with a history of pulmonary tuberculosis

Population	N (%)
Lung cancer with a history of pulmonary tuberculosis	27 (10.42)
Lung cancer without a history of pulmonary tuberculosis	226 (89.58)
Total	253 (100)

Table 2. Demographic data of the sample

Variable	N (%)
Gender	
Male	21 (77.78)
Female	6 (22.22)
Age (years)	
≥ 40	27 (100)
< 40	-
Body mass index	
Underweight (< 18,5)	16 (59.25)
Normoweight (18.5–22.9)	8 (29.62)
Overweight (23–24.9)	3 (11.13)
Obese I (25–29.9)	-
Obese II (≥ 30)	-
History of smoking	
No smoking (< 200)	7 (25.92%)
Mild of BI (200–599)	-
Moderate of BI	1 (3.71%)
Severe of BI (> 600)	19 (70.37%)

BI: Brinkman Index

Table 3. Distribution of lung cancer patients with delayed diagnosis as pulmonary tuberculosis

Variable	n (%)
History of ATD consumption	
< 1 year	10 (37.03)
≥ 1 year	17 (62.97)
Duration of diagnostic delay	
< 6 months	17 (62.96)
≥ 6 months	10 (37.04)
Types of lung cancer	
Adenocarcinoma	21 (77.78)
Squamous cell carcinoma	6 (22.22)
Stage	
I	-
II	-
III	-
IV	27 (100)

ATD: Anti-Tuberculosis Drugs

DISCUSSION

Patients with lung cancer treated at Arifin Achmad General Hospital, Pekanbaru, between August 2022 and July 2023 numbered 253, with 199 men (78.65%) and 54 women (21.35%). In this study, 109 patients (43.08%) with lung cancer confirmed by anatomical pathology results and 27 patients (10.67%) with a history of clinical pulmonary tuberculosis diagnosis who were or had undergone anti-tuberculosis drugs treatment prior to examination and management at Arifin Achmad General Hospital, Pekanbaru were identified.

Based on age and gender variables, all 27 patients in the study were over 40 years old, constituting 100% of the sample. Among them, 77.78% were male. These results align with the Indonesian Collegium of Pulmonologists in the guideline, which mentions that men over 40 years of age have a higher risk of lung cancer [6,7]. The results of this study are also in accordance with research conducted by Aviani et al. [8], which explains that male patients have the highest percentage in prevalence of lung cancer. In addition, several other studies have also mentioned that the male patient group and the age of more than 40 years are the most common factors that occur in lung cancer cases [9,10]. The higher prevalence among men can be attributed to their increased exposure to cigarette smoke and pollutants because of their jobs, prolonged outdoor activities, and smoking habits, in comparison to women [11]. A cohort study used to study the prevalence of tuberculosis revealed that the rate of incidence of lung cancer was higher in the age group over 40 [12]. The age-related variable facing lung cancer with a diagnosed history is still uncertain and requires further research and clinical trials.

The frequency of lung cancer had delays in diagnosis, with the highest percentage of underweight nutritional status at 59.25%, according to the variable distribution of body mass index. The severity of the illness, connected to the prognosis of the patient, may be the reason for these delays. This study found a correlation between the length of time taken to diagnose lung cancer and nutritional status [13]. The study revealed that 62.96% of patients experienced diagnostic delays, with most of these delays occurring within the first six months of the delay. Clinical similarities between lung cancer and pulmonary tuberculosis are one of the factors leading to delays in diagnosis, which in turn reduces the concern about waiting time. These two factors support the disease's prognostic value and are correlated with how the progression of the illness [14].

According to the smoking history in this study, the biggest risk factor for lung cancer incidence among individuals with a history of pulmonary tuberculosis as an initial diagnosis was a severe Brinkman index (BI), accounting for 70.37%. The same findings were also

observed in a 2020 Korean study, which demonstrated that non-smokers had a lower risk of lung cancer than pulmonary tuberculosis patients with a history of smoking. Smoking history is one of the risk variables in anamnesis for lung cancer and pulmonary tuberculosis diagnosis [15,16]. Smoking can have negative effects on mucociliary function and increase the number of carcinogens in cigarettes, which start the carcinogenesis process. Lung cancer development is largely influenced by smoking habits [12].

In this study, adenocarcinoma was the most prevalent form of lung cancer, accounting for 77.78%, followed by squamous cell carcinoma at 22.22%. No additional types of lung cancer were detected in these patients. According to conducted in 2016 in Japan, 55.6% of lung cancer types with a history of clinical pulmonary tuberculosis were adenocarcinoma varieties [17]. This study's findings are consistent with research conducted in 2017 by Aviani et al. [8], which revealed that adenocarcinoma was the most prevalent form of cancer in patients who encountered diagnostic delays for pulmonary tuberculosis [7,8]. The finding of fibrosis or cavities in pulmonary tuberculosis radiologically can support the development of cancer cells. This will make cells surrounding the damaged tissue susceptible to DNA mutation and abnormal cell growth, such as cancer cells [9].

All samples in this study were diagnosed with stage IV of lung cancer, which indicates that there has been a metastatic process in the lungs or extrapulmonary. This condition will have an impact on clinical symptoms that are getting worse. These results are in line with a study conducted by Aviani et al. [8], which showed that there were 88.3% of lung cancer patients with stage IV who were previously diagnosed as clinical pulmonary tuberculosis. The similarity of clinical symptoms between lung cancer and pulmonary tuberculosis is the background for this problem, especially in countries with a high pulmonary tuberculosis burden [8,18]. In accordance with the findings of a second study conducted in Japan, 50% of patients with stage IV of lung cancer had a history of pulmonary tuberculosis. In patients with a history of pulmonary tuberculosis, the diagnosis of lung cancer in its earliest phases is extremely rare. Early diagnosis of lung cancer is very important, particularly with a history of clinical pulmonary tuberculosis as the initial diagnosis [12].

This study's discussion also highlights the absence of an evaluation of pulmonary tuberculosis management in previous health facilities. Clinical pulmonary tuberculosis management requires intensive monitoring and follow-up. The most important thing to evaluate is the patient's clinical response after receiving anti-tuberculosis drugs. The clinical evaluation considers drug compliance, dose accuracy, adverse drug effects, and comorbidities. If the 5 criteria are not met, the veracity of the diagnosis of pulmonary tuberculosis or lung cancer must be reconsidered. Chest X-ray evaluation should also be done every month during anti-tuberculosis drug treatment. If both parameters show a worsening condition, then a low-dose CT scan of the thorax and sputum cytology can be considered for further examination to identify the diagnosis of lung cancer earlier [19,20].

Overall through the results of this study, the underdiagnosis of lung cancer needs to be considered in patients with clinical pulmonary tuberculosis who do not respond to anti-tuberculosis drugs treatment which is also supported by several factors such as male gender, over 40 years of age, smoking history, and drastic weight loss [6]. In addition, a clinical evaluation of anti-tuberculosis drug treatment must be considered if there is no clinical improvement within two months of anti-tuberculosis treatment. Upon initial suspicion of Lung Cancer, a low-dose CT scan and sputum cytology examination may be recommended as follow-up examinations [20].

However, through this study, the researcher hypothesizes that the high incidence of lung cancer based on the origin of respondents from outside Pekanbaru is due to the lack of health facilities owned by regional hospitals [7,8,21]. Screening for lung cancer in patients with clinical pulmonary tuberculosis as part of the initial diagnosis is crucial for reducing morbidity and mortality rates. In cases of clinical pulmonary tuberculosis without clinical improvement, low-dose CT scan and sputum cytology may be considered as screening modalities.

The limitations of this study are that the number of samples is too small, with a fairly short time, and the research location is only in one hospital, so further research is needed with a larger number of samples and a longer duration to enable a better validity test.

CONCLUSION

Adenocarcinoma is the most common form of lung cancer in men aged more than 40 years, and with severe IB. Lung Cancer with a latency duration of 6 months is typically diagnosed at stage IV. If there is no clinical improvement after 1 month of anti-tuberculosis drug treatment in patients with clinical pulmonary tuberculosis and lung cancer, further evaluation with more extensive tests is required. Low-dose CT scans and sputum cytology examinations can be considered as further tests if clinical and radiological evaluations in patients with clinical pulmonary tuberculosis are conducted, so that the delay in cancer diagnosis can be prevented earlier.

DECLARATIONS

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