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Correlation Analysis of Bronchoscopy Visualization to Results of Fungal Cultures in Lung Cancer

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ABSTRACT

Background: Fungal colonization is common as a secondary infection in lung cancer; currently it is often neglected due to similar clinical characteristics. Pulmonary mycosis impacts patient survival and quality of life. Bronchoscopy provides diagnostic benefits by enabling the direct visualization of suspicious lesions. Damage to the bronchial epithelium caused by cancer results in long-lasting inflammation, which makes it easier for fungi to stick, invade, and worsen the infection.

Methods: This observational analytic study used a cross-sectional design with 52 lung cancer patients that had bronchoscopy at Arifin Achmad General Hospital, Pekanbaru, from August 2024 to January 2025. Samples were chosen by consecutive sampling methods. We assessed the correlation between bronchoscopic visual findings and positive fungal cultures in lung cancer cases.

Result: The positive rate of fungal cultures was 76.9% and was significantly correlated with a high Brinkman Index smoking status (p=0.000), a history of COPD (p=0.046), and the use of bronchodilators with/without ICS (p=0.046). Candida sp. (61.5%) and Aspergillus species (9.6%) are the primary fungal types identified in lung cancer. The finding of irregular mucosa and hyperemic and infiltrative stenosis (53.8%) is the main finding in bronchoscopy and is significantly associated with positive fungal cultures (p=0.000). Infiltrative stenosis shows positivity for all fungal species, especially Candida sp. and Aspergillus sp. (p=0.015). Candida sp. isolates tend to manifest in orifices obscured by mass, while Aspergillus sp. tends to show up in cases of decompression stenosis.

Conclusion: A significant correlation exists between bronchoscopy visualization and the positivity of fungal cultures in lung cancer. Irregular mucosa, hyperaemia, and infiltrative stenosis show a high incidence in bronchoscopy visualization and have a significant correlation with the presence of all types of fungal infections in lung cancer.

KEYWORDS: *Bronchoscopy Visualization, Fungal Culture, Lung Cancer, Positivity*

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1. INTRODUCTION

The global prevalence of pulmonary mycosis has yet to be comprehensively detailed. The burden of pulmonary mycosis cases appears to be rising annually, particularly in low- to middle-income countries.[1] The increase in pulmonary mycosis cases is often attributed to inadequate treatment of chronic lung infections, such as pulmonary tuberculosis (TB), chronic obstructive pulmonary disease (COPD), lung abscesses, and lung cancer. These persistent conditions significantly impact mortality and morbidity, with over 1.6 million deaths reported among 300 million people worldwide.[2,5]

Currently, reporting data on pulmonary mycosis in Indonesia remains challenging due to limited and uncertain information.[6] According to Wahyuningsih et al. (2021), pulmonary mycosis affects approximately 2.89% of the Indonesian population, or around 7.7 million individuals, each year.[5] The growth of fungal colonies is particularly likely in

immunocompromised individuals, including those with lung cancer, pulmonary TB, HIV, or autoimmune diseases, or those undergoing long-term corticosteroid treatment. Several studies have documented instances of pulmonary mycosis in patients with HIV (14.5%), multidrug-resistant TB (44.5%), persistent asthma (68.9%), and lung cancer (22.72%).[6,7]

The rise in pulmonary mycosis cases is primarily due to delays in diagnosis. The clinical symptoms of pulmonary mycosis often overlap with those of other chronic lung diseases.[2] This similarity, particularly in lung cancer patients, can lead to biased diagnostic results regarding sputum specimens. Rozaliyani et al. (2019) reported that 33.8% of patients with Non-Small Cell Lung Carcinoma (NSCLC) tested positive for *Aspergillus niger*, while 72.3% had *Candida albicans*. Additionally, Shin et al. (2020) identified 56 out of 3,430 NSCLC patients who developed Chronic Pulmonary Aspergillosis (CPA) following lung tumor resection.[8]

Lung cancer damages the bronchial epithelium down to the alveoli, creating pathways for fungi to form biofilms that colonize extensively. Disruption of the mucociliary system and malnutrition further contribute to fungal infections in lung cancer patients. The immunocompromised state caused by lung cancer leads to diminished macrophage function, which is crucial for eliminating fungal infections.[3,4] Utilizing bronchoscopy can assist healthcare professionals in identifying airway issues caused by fungal infections, thereby expediting the diagnosis of lung fungal diseases. Collecting specimens via bronchoscopy offers a more accurate positivity rate for fungal cultures compared to sputum specimens and avoids biased results.[7,9,10]

Bronchoscopy visualization serves not only as a diagnostic tool but also as a specific parameter to evaluate the potential for or occurrence of fungal infections in lung cancer patients. Obtaining specimens directly from the primary lesion area enhances the accuracy of positivity. This study aims to analyze the correlation between bronchoscopy visualization and fungal culture results in lung cancer patients.

2. METHODS

This study examines the relationship between bronchoscopy images and fungal culture results in lung cancer by observing a cohort of patients at a single point. The research was conducted at the Microbiology Laboratory of the Faculty of Medicine, University of Riau, and the Bronchoscopy Procedure Operating Room at Arifin Achmad General Hospital, located in Riau Province. The study commenced in August 2024 and is scheduled to conclude in January 2025, having received approval from the Ethics Committee of the Faculty of Medicine, Universitas Riau, under Ethical Clearance number B/III/UN19.5.1.1.8.UEPKK/2024.

The study population comprises all hospitalized patients diagnosed with lung cancer and scheduled to undergo diagnostic procedures. The sample was determined using consecutive sampling, which included lung cancer patients who met the specified inclusion and exclusion criteria without stratification or randomization, resulting in a total sample of 52 lung cancer patients. The inclusion criteria encompassed hospitalized patients with lung cancer who had an indication for and were eligible to undergo bronchoscopy procedures. The exclusion criteria involved patients already diagnosed with pulmonary mycosis or those currently undergoing antifungal treatment.

Specimen collection will involve two distinct actions during the bronchoscopy procedure. All samples will undergo bronchial washing, while tissue specimens will be obtained using bronchial brushing or biopsy forceps. Each patient will provide two test specimens, which will subsequently be processed for fungal culture examination. All specimens will be cultured on Sabouraud Dextrose Agar media and incubated at a temperature of 25°C. The incubation period will last for five days, during which growth will be observed both macroscopically and microscopically.

A positive culture result indicates the presence of fungus in one or both test specimens, which will be classified as pulmonary mycosis. Fungal cultures that show growth after five days of incubation will be regarded as non-pathogenic fungi and interpreted as negative cultures. If the two specimens identify two different types of fungi, a microbiologist will make the final determination. All data will be compiled, and data analysis will be performed. Univariate analysis will be presented in the form of a distribution table. The relationship between variables will be explored further through bivariate analysis using the chi-square test, with the Fisher test as an alternative, employing SPSS software for analysis.

3. RESULTS

Overall, there were 145 cases of thoracic cavity malignancies, which included 127 cases of lung cancer, 14 cases of mediastinal tumors, and four cases of metastatic tumors in the lungs. All patients were admitted to Arifin Achmad General Hospital in Pekanbaru from August 2024 to January 2025. According to the established inclusion and exclusion criteria, a total of 52 lung cancer patients underwent bronchoscopy procedures as part of this study (Figure 1).

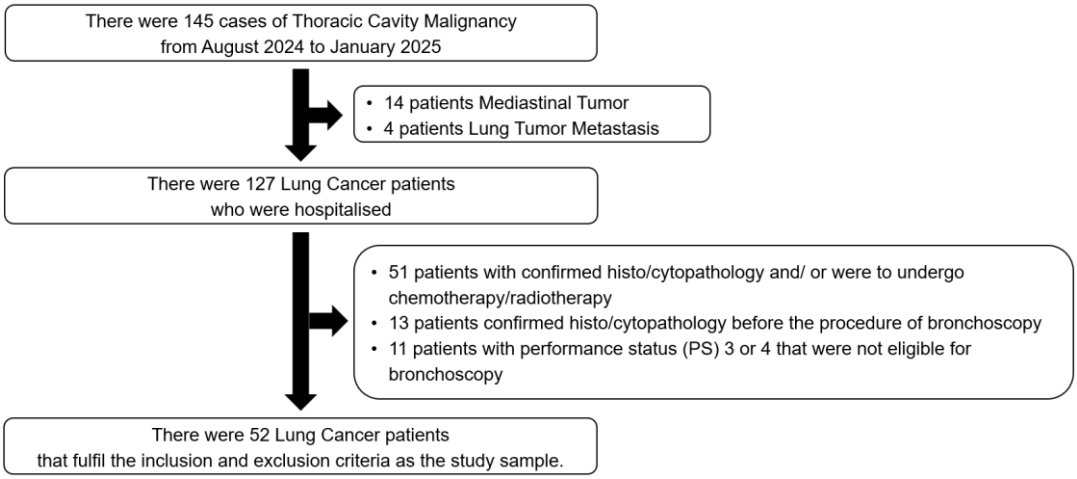

Figure 1. Research Sample Selection

Demographic and Clinical Characteristics

The research findings presented in Table 1 reveal that a substantial proportion of lung cancer patients are over 40 years of age (90.4%), with a predominance of males (71.2%). Additionally, a significant number of patients exhibit an underweight body mass index (BMI) (51.9%) and have a history of heavy smoking (55.8%). 44.2% of patients reported a history of chronic obstructive pulmonary disease (COPD), identifying it as the most prevalent comorbidity. The study also found that the most frequently reported medication was bronchodilators, either by themselves or in conjunction with inhaled corticosteroids. The left upper lobe was identified as the most frequently observed lesion location (34.6%). Specimen collection for fungal culture examination was mainly carried out using bronchial washing and biopsy forceps (67.3%) during bronchoscopy procedures.

Table 1. Demographic and Clinical Characteristics

Variable	N (52)	%
Age		
• ≤ 40 years	5	9.6
• > 40 years	47	90.4
Gender		
• Male	37	71.2
• Female	15	28.8
Body Mass Index		
• Underweight	27	51.9
• Normoweight	16	30.8
• Overweight	4	7.7
• Obesity Class I	4	7.7
• Obesity Class II	1	1.9
Smoking Status		
• Non-Smoker	15	28.8
• Mild Brinkman Index	2	3.8
• Medium Brinkman Index	6	11.5
• Severe Brinkman Index	29	55.8
History of Pulmonary Disease		
• None	15	28.8
• Former TB	5	9.6
• COPD	23	44.2
• Hypertension	11	21.2
• Diabetes Mellitus Type 2	4	7.7
• Heart Failure	3	5.7
• Stroke	1	1.9
• Autoimmune Disease	1	1.9

Drug History		
• None	15	28.8
• Bronchodilators with/without Inhaled Corticosteroids	23	44.2
• Anti Tuberculosis Drugs	5	9.6
• Anti Hypertensives	15	28.8
• Anti Diabetics	4	7.7
• Oral Corticosteroids	1	1.9
Location of Lesion		
• Upper Right Lobe	14	26.9
• Medial Lobe	5	9.6
• Lower Right Lobe	8	15.4
• Upper Left Lobe	18	34.6
• Lower Left Lobe	7	13.5
Specimen Collection		
• Bronchial Washing and Bronchial Brushing	17	32.7
• Bronchial Washing and Biopsy Forceps	35	67.3

Distribution of Culture Positivity and Fungal Identification

Figure 2 illustrates that out of 52 lung cancer patients, 40 (76.9%) showed positive results for fungal culture identification. Among these, *Candida sp*. was identified in 32 patients (61.5%), followed by *Aspergillus sp*. in 5 patients (9.6%), *Cryptococcus sp*. in 2 patients (3.8%), and *Epicoccum sp*. in 1 patient (1.9%).

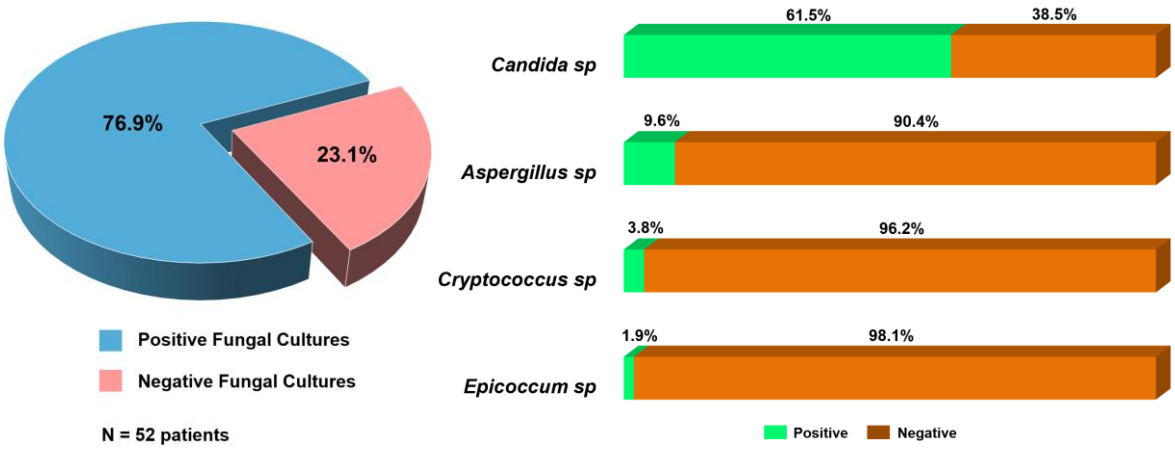

Figure 2. Distribution of Culture Positivity and Identification of Fungal Species

The Role of Demographic and Clinical Factors and the Positivity of Fungal Cultures

Table 2 shows that fungal cultures are more likely to be positive in males (55.8%), individuals over the age of 40 (69.2%), those with a low BMI (40.4%), and people with a history of heavy smoking (44.2%). When demographic factors are considered, there is a significant association between heavy smoking and positive fungal cultures (p=0.000). Furthermore, in the context of demographic factors, the positivity of fungal cultures significantly correlates with heavy smoking status (p=0.000).

Chronic Obstructive Pulmonary Disease (COPD), which affects 40.4% of patients, is the most prevalent comorbidity and is significantly associated with positive fungal cultures (p=0.046). This aligns with the history of bronchodilator use, whether alone or in conjunction with inhaled corticosteroids, which is the most prescribed long-term medication and is also significantly linked to positive fungal cultures (p=0.046).

Fungal cultures are mostly positive in the left upper lobe (26.9%), and adenocarcinoma (30.8%) is the most common type of lung cancer linked to this. The highest rates of positivity for fungal cultures were obtained via bronchial washing and biopsy forceps (50.0%). Overall, being a heavy smoker, having Chronic Obstructive Pulmonary Disease (COPD), and using bronchodilators—whether by themselves or with inhaled corticosteroids—greatly increase the chances of getting positive results from fungal cultures (Table 2).

Table 2. The Role of Demographic and Clinical Factors on the Positivity of Fungal Cultures

Variable	Fungal Culture Results (%)		p Value
	Positive	Negative	
Age			
• ≤ 40 years	4 (7.7)	1 (1.9)	1,000
• > 40 years	36 (69.2)	11 (21.2)	
Gender			
• Male	29 (55.8)	8 (15.4)	0,726
• Female	11 (21.2)	4 (7.s7)	
Body Mass Index			
• Underweight	21 (40.4)	6 (11.5)	0,178
• Normoweight	11 (21.2)	5 (9.6)	
• Overweight	4 (7.7)	0 (0)	
• Obesity Class I	3 (5.8)	1 (1.9)	
• Obesity Class II	1 (1.9)	0 (0)	
Smoking Status			
• Non-Smoker	9 (17.3)	6 (11.5)	**0,000***
• Mild Brinkman Index	2 (3.8)	0 (0)	
• Medium Brinkman Index	6 (11.5)	0 (0)	
• Severe Brinkman Index	23 (44.2)	6 (11.5)	
History of Pulmonary Disease			
• None	9 (17.3)	6 (11.5)	0,081
• Former TB	5 (9.6)	0 (0)	0,578
• COPD	21 (40.4)	2 (3.8)	0,046*
• Hypertension	7 (135)	4 (7.7)	0,253
• Diabetes Mellitus Type 2	3 (5.8)	1 (1.9)	1,000
• Heart Failure	4 (7.7)	0 (0)	0,562
• Stroke	0 (0)	1 (1.9)	0,231
• Autoimmune Disease	0 (0)	1 (1.9)	0,231
Drug History			
• None	9 (17.3)	6 (11.5)	0,081
• Bronchodilators with/without Inhaled Corticosteroids	21 (40.4)	2 (3.8)	**0,046***
• Anti Tuberculosis Drugs	5 (9.6)	0 (0)	0,316
• Anti Hypertensives	11 (21.2)	4 (7.7)	0,726
• Anti Diabetics	3 (5.8)	1 (1.9)	1,000
• Oral Corticosteroids	0 (0)	1 (1.9)	0,231
Location of Lesion			
• Upper Right Lobe	12 (23.1)	2 (3.8)	0,232
• Medial Lobe	4 (7.7)	1 (1.9)	
• Lower Right Lobe	7 (13.5)	1 (1.9)	
• Upper Left Lobe	14 (26.9)	4 (7.7)	
• Lower Left Lobe	3 (5.8)	4 (7.7)	
Specimen Collection			
• Bronchial Washing and Bronchial Brushing	14 (26.9)	3 (5.8)	0,729
• Bronchial Washing and Biopsy Forceps	26 (50.0)	9 (17.3)	

Distribution of Bronchoscopy Visualisation in Lung Cancer

Figure 3 illustrates the distribution of 52 samples from lung cancer patients who underwent bronchoscopy. Among these, 28 patients had uneven, hyperemic mucosa with narrowing of the airway (53.8%), making it the most common finding during bronchoscopy. Next, there were 13 patients with irregular, hyperemic mucosa that blocked the airway (25.0%); 6 patients had irregular, hyperemic mucosa with narrowed airways (11.5%); and 5 patients had smooth, non-hyperemic mucosa with a normal airway (9.6%) among all lung cancer cases.

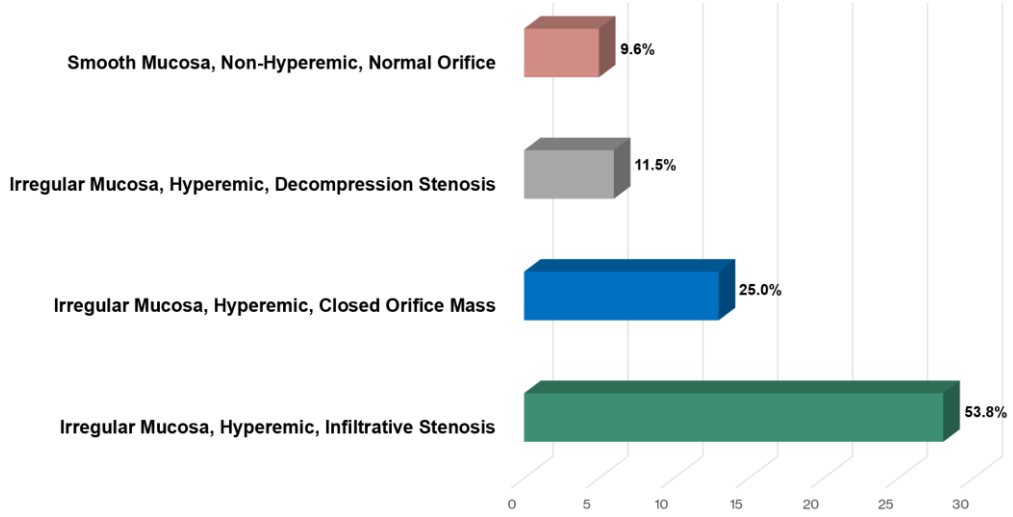

Figure 3. Distribution of Bronchoscopy Visualisation in Lung Cancer

Correlation of Bronchoscopy Visualisation to Fungal Culture Positivity

The research results in Figure 4 show the bivariate test of bronchoscopy visualization against the positivity of fungal cultures. These results indicate that out of 52 total lung cancer patient samples, 26 patients showed bronchoscopy visualization results with irregular, hyperemic mucosa and infiltrative stenosis (50.0%), which indicated the highest fungal culture positivity in lung cancer. Based on statistical results, these findings also showed a significant relationship (p=0.000). Bronchoscopy visualization with irregular, hyperemic mucosa and infiltrative stenosis is a variable that can be used as an indicator of suspicion for positive fungal culture in lung cancer cases and is categorized as a high-risk group for pulmonary mycosis.

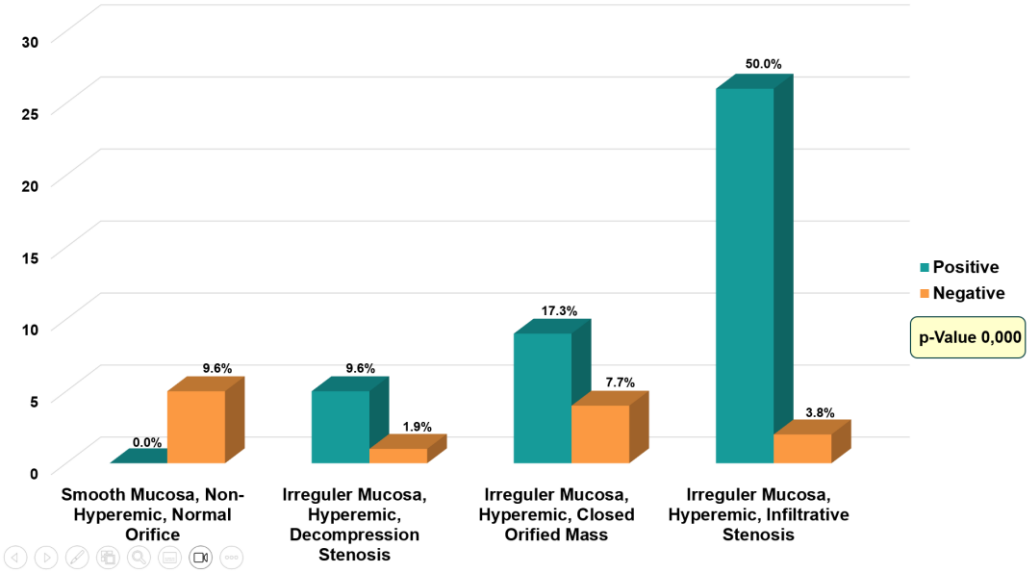

Figure 4. Correlation of Bronchoscopy Visualisation to Fungal Culture Positivity

Correlation of Bronchoscopy Visualisation to the Identification of Fungal Types

Figure 5 illustrates the results of a bivariate test conducted via bronchoscopy visualization to identify various types of fungi. The findings indicate that, among 26 lung cancer patients exhibiting irregular mucosal visualization and hyperemic infiltrative stenosis, four distinct types of fungi were identified. *Candida sp*. (38.4%) was the most prevalent, followed by *Aspergillus sp*. (5.8%), *Cryptococcus sp*. (3.8%), and *Epicoccum sp*. (1.9%). It can be generally concluded that infiltrative stenosis may act as a risk factor for the positivity of all types of fungi, particularly *Candida sp*., in lung cancer cases. Additionally, other bronchoscopy images showing a blockage caused by a mass are more likely to test positive for *Candida sp*. (17.3%), while decompression stenosis is more often linked to positive results for *Aspergillus sp*. (3.8%).

Based on statistical results, bronchoscopy visualization can establish a meaningful or significant relationship when identifying the type of fungus (p = 0.015). The irregular surface of the lung tissue, redness, and narrowing seen during bronchoscopy visualization might suggest a higher risk of fungal infections, even if various fungi are found in lung cancer patients. Also, the results from this visualization can be used to identify groups of fungal infections that occur as secondary infections in patients with lung cancer.

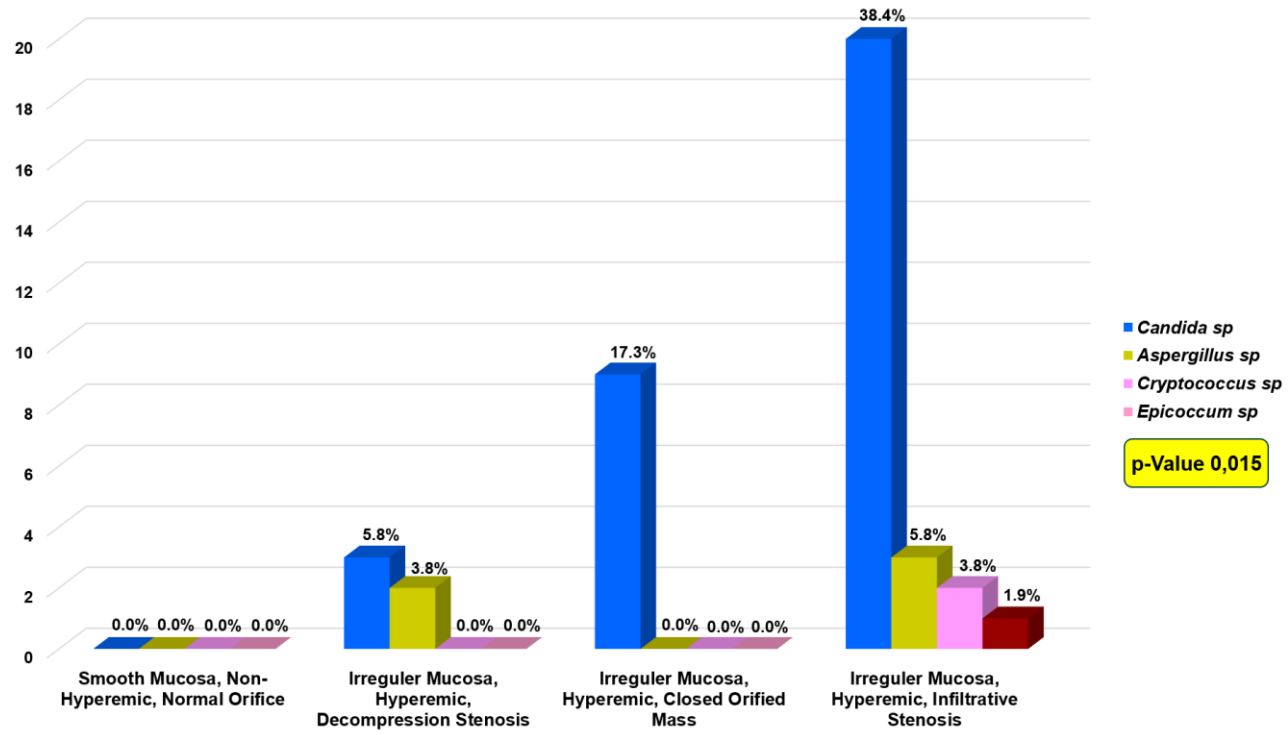

Figure 5. Correlation of Bronchoscopy Visualisation to the Identification of Fungal Types

4. DISCUSSION

The results of this study use several variables to assess the relationship between demographic and clinical factors and the general positivity of fungal cultures. These variables include age, gender, BMI, smoking history, comorbidities, history of long-term medication use, and lesion location. All these variables were examined using statistical tests to see if there is a meaningful connection with the positivity of fungal cultures in lung cancer.

Most subjects in this study were male patients (71.2%) over the age of 40 (90.4%) with an underweight nutritional status (51.9%). There was no significant relationship found between these three variables and the positivity of the fungal culture. The study by Alfarisa et al. (2021) indicated that lung cancer cases predominantly occurred in men (70.4%) aged over 40 years (95.4%).[11] Additionally, the study by Agung et al. (2020) noted that most lung cancer patients were men aged 50 to 69 years.[12] This male demographic is often linked to smoking habits, which are a significant source of carcinogens associated with lung cancer. Typically, the incidence of lung cancer is highest among individuals over 40 years of age.[11,12] Moreover, the study by Polanski et al. (2017) found that most lung cancer patients were in a state of malnutrition (51.1%). As the disease progresses, increased metabolism, systemic inflammatory responses, and reduced appetite contribute to this malnutrition. Conditions of malnutrition adversely affect prognosis and contribute to increased mortality rates.[14,15]

The results of this study show that many lung cancer patients (55.8%) have a history of heavy smoking, which is strongly linked to positive fungal cultures, as shown by a p-value of 0.000. Smoking habits are among the most critical factors associated with the formation of fungal colonies in the respiratory tract, with an incidence rate ranging from 60% to 85% in lung cancer patients.[16] The repeated exposure to nicotine in cigarettes leads to alterations in the structure of epithelial cells, resulting in ciliary dysfunction, hypersecretion, and impaired mucus clearance. This condition increases the likelihood of fungal cultures forming in active smokers, particularly those diagnosed with lung cancer.[17,18]

Cases of COPD (44.2%) represent the highest comorbidity among lung cancer patients and show a significant association with positive fungal cultures, evidenced by a p-value of 0.046. Research indicates that a history of COPD is prevalent in lung cancer cases and occurs in 50–90% of patients. The connection between COPD and thoracic malignancies is intricate, sharing common risk factors such as cigarette smoke, occupational exposures, and genetic predispositions.[19,20] Chronic inflammation, oxidative stress, and lung tissue remodeling associated with COPD contribute to cellular mutations that can lead to the development of malignant cells.[21] Smoking habits are closely linked to both COPD and lung cancer, with the potential to facilitate fungal colonization.[18] Alveolar macrophages in smokers exhibit a reduced capacity for phagocytosis and a diminished ability to eliminate pathogens. Cigarette smoke can directly damage the respiratory epithelium, affecting cilia, goblet cells, basal cells, and secretory glands. The buildup of secretions in the respiratory epithelium initiates the process of fungal colonization, particularly in lung cancer cases.[17,18]

Using bronchodilators, whether alone or with inhaled corticosteroids (44.2%), significantly correlates with a history of long-term medication use and the positivity of fungal cultures in lung cancer (p=0.046). According to a study by Lu and Mao (2024), 61.5% of COPD patients are at risk of fungal colonization if they have a history of bronchodilator use. Moreover, inhaled corticosteroids significantly increase the risk of fungal colonization in COPD patients with lung cancer.[22] The administration of inhaled corticosteroids results in vasodilation, increased capillary permeability, and reduced migration of leukocytes to injured tissues, exerting immunosuppressive effects via glucocorticoid receptors, which inhibit the transcriptional activity of pro-inflammatory genes, including NF-κB. Additionally, corticosteroids can lower the number of certain immune cells in the blood and prevent the joining of phagolysosomes in macrophages by keeping lysosomal membranes stable during the process of engulfing pathogens. Consequently, the use of high-dose glucocorticoids can significantly raise the risk of infection.[22,32]

The location of lesions in the left upper lobe (34.6%) is the most common site in lung cancer and does not have a significant relationship with the positivity of fungal cultures. The study by Kinsey et al. (2014) mentioned that most cancer lesions are in the upper lobe of the lungs, with the left upper lobe accounting for 31.6% and the right upper lobe for 30.8%. The location of lesions might be affected by how air and blood flow differently in the upper lobes compared to the lower lobes, which can lead to cancer cells getting stuck and forming lesions there. This phenomenon causes cancer cells to become trapped and form cancer lesions in that area. The anatomic distribution of blood circulation in the upper lobe also supports the acceleration of carcinogenesis. The influence of exposure to cigarette smoke or air pollution is distributed earlier in the upper lobe after the trachea, causing cancer cells to invade that area more frequently.[24]

Distribution of Culture Positivity and Fungal Identification

Positive fungal cultures were found in 76.9% of lung cancer patients, with four types of fungi identified in this study. The study by El-Badarawy et al. (2023) showed 68% positive fungal cultures from 100 lung cancer patients.[25] The study by Prasenohadi et al. (2021) also found 40% positive fungal cultures from 20 lung cancer patients.[7] This study identified four types of fungi: *Candida sp*. (61.5%), *Aspergillus sp*. (9.6%), *Cryptococcus sp*. (3.8%), and *Epicoccum sp*. (1.9%). The study by Laroumagne et al. (2013) identified *Candida sp*. (42.9%) as the most prevalent type of fungus, followed by *Aspergillus sp*. (6.2%) in lung cancer cases.[26] The study by El-Badarawy et al. (2023) also mentioned that *Aspergillus sp*. (36%) and *Candida sp*. (32%) were the most frequently identified types of fungi from 100 lung cancer patients.[25]

Structural damage to the lining of the lungs and lung tissue can create an environment conducive to fungal growth, potentially resulting in positive culture tests among lung cancer patients.[27] The common finding of *Candida sp*. in lung cancer patients might be due to the organism's ability to grow more widely in the upper respiratory tract and become a regular part of the body's normal bacteria.[9] Additionally, *Candida sp*. can change their shape from yeast to a more invasive form, which helps them enter the respiratory lining. Factors such as body temperature, pH changes, and nutritional deficiencies can influence these transformations. The necrotic conditions resulting from cancer invasion can lead to the formation of biofilms in Candida species, enabling them to spread to surrounding organs.[27,28]

Unlike *Candida sp*., *Aspergillus sp*. positivity is rarely identified in lung cancer cases. This difference can be caused by the type of test specimen collection used. This study shows that the use of bronchial washing is the primary modality used for fungal culture examination. The characteristics of Aspergillus sp. also contribute to its low positivity. *Aspergillus sp*. has a higher penetration and invasive power in the respiratory tract epithelium down to the lung parenchyma, resulting in more positive results from tissue specimens.[3,23] The most tissue samples were taken in this study using biopsy forceps, followed by bronchial brushing. This sampling process can also yield negative culture results due to the quality of the specimen used. Damage to the fungal cell structure or the integrity of fungal cell components during the procedure significantly affects the results of the fungal culture process.[29]

The fungal species *Cryptococcus sp*. and *Epicoccum sp*. are rarely reported as pathogenic fungi, particularly in cases of pulmonary mycosis or secondary infections related to lung cancer. Infections from *Cryptococcus sp*. are strongly linked to serious immune system problems, such as HIV, organ transplants, autoimmune diseases, and long-term use of

corticosteroids.[30] In contrast, *Epicoccum sp*. is primarily recognized as an environmental fungus and is often considered a contaminant of normal flora rather than a pulmonary pathogen.[31]

Distribution of Bronchoscopy Visualisation in Lung Cancer

Based on the bronchoscopy procedure, there are four groups of bronchoscopy visualization findings in lung cancer patients. The most common findings associated with lung cancer include irregular, hyperemic mucosa and infiltrative stenosis, observed in 53.8% of cases. These findings align with the study conducted by Aycicek et al. (2022), which reported irregular and infiltrative mucosa in 24.47% of lung cancer patients. The infiltrative appearance in the opening area indicates ongoing tissue damage, potentially facilitating fungal growth.[17,28] Additionally, several studies suggest that typical bronchoscopy findings such as tracheobronchial stenosis, mucosal edema, irregular mucosa, ulceration, infiltration, yellowish-white secretions, white patchy nodules, and blackish-gray pigmentation are often associated with pulmonary mycosis in patients with lung cancer.[7,28,33]

Correlation of Bronchoscopy Visualisation to Fungal Culture Positivity

The results of this study indicate that bronchoscopy visualization significantly influences the positivity of fungal cultures (p=0.000). Visualizations displaying irregular, hyperemic mucosa and infiltrative stenosis (50.0%) exhibited the highest distribution of positive cultures. These findings align with the research conducted by Aycicek et al. (2022), which highlighted a strong correlation between specific lung patterns and positive fungal cultures in lung cancer patients. Procedures such as bronchial washing and bronchoalveolar lavage (BAL) primarily identify the increased incidence of positive fungal cultures in these cases. Additionally, these results suggest that changes in anatomical structures seen during bronchoscopy visualization do not facilitate the specific identification of fungal infections.[28]

Infiltrative stenosis is a significant factor in the observation of bronchoscopy lung cancer and fungal growth. This infiltrative process indicates chronic damage to the bronchial epithelium, which becomes a site for carcinogenesis, ultimately leading to the development of lung cancer lesions.[33] Consequently, damage to the epithelium facilitates the adhesion of hyphae, promoting their colonization and invasion of the tissue. The location of the lesion in the upper lobe is associated with a more rapid invasion of hyphae due to the increased oxygen supply in that area. The inflammatory response in the affected region will demonstrate a pattern of repeated infiltration, which induces chronic inflammation and results in mucosal damage.[7,25,33]

Correlation of Bronchoscopy Visualisation to the Identification of Fungal Types

The results of this study indicate a significant influence of bronchoscopy visualization on the identified types of fungal (p=0.015). In general, the unusual look of the lung lining, increased redness, and narrowing of the airways helped grow positive fungal cultures for all types of fungi in this study. The importance of the bivariate analysis shows that the infiltrative condition makes it easier for fungi to grow, which can cause health problems in the lungs.

Isolate *Candida sp*. is the most frequently identified type of fungus in this study. This species shows a marked susceptibility to infection, characterized by an irregular and hyperemic appearance of the mucosa. Signs that might indicate a possible *Candida sp*. infection are more common when the opening is narrowed and blocked by a growth. This tendency is linked to how *Candida sp*. sticks strongly to damaged tissue, making it easier for the fungus to grow.[34] Also, the way cancer affects the epithelial tissue can cause tissue death, making it easier for *Candida sp*. to create biofilms and spread to nearby tissues. Furthermore, *Candida sp*. can change its shape from yeast to hyphae, which helps it invade the damaged areas of the epithelium more quickly.[27,28]

The low positivity rate for *Aspergillus sp*. in this study may be attributed to inadequate specimen collection. Positive cultures for *Aspergillus sp*. are seldom obtained from bronchial washing specimens and are more commonly identified in tissue specimens.[27] However, the methods used to obtain tissue specimens in this study, specifically bronchial brushing and biopsy forceps, may also contribute to the low positivity rate for *Aspergillus sp*. This reduced positivity rate can occur because the specimen collection process during bronchoscopy may damage the fungal components, making the fungal hyphae microscopically unidentifiable. *Aspergillus sp*. is the most prevalent pathogenic fungus responsible for pulmonary mycosis, yet it poses challenges for identification. This difficulty arises because *Aspergillus sp*. has greater penetration/invasiveness compared to other fungi and can even infect the circulatory system.[9,18,28]

Other types of fungi, *Cryptococcus sp*. and *Epicoccum sp*., are rarely recorded as causes of pulmonary mycosis. These two types of fungi tend to be identified as contaminants. *Cryptococcus sp*. is more likely to appear in severe immunocompromised conditions such as HIV/AIDS. Meanwhile, *Epicoccum sp*. is more often found through contamination with soil environments. However, the results of both fungi types in this study can be used as scientific references because they are relevant to bronchoscopy visualization and infiltrative stenosis lesions.[28,30,31]

5. CONCLUSION

The positivity of fungal cultures has the potential to be a secondary infection in lung cancer. A history of severe smoking, indicated by a high Brinkman index, comorbidity with COPD, and the use of bronchodilators are significantly related to the positivity of fungal cultures in lung cancer. The most common bronchoscopy findings in lung cancer are irregular, hyperemic mucosa and infiltrative stenosis. These results also show a significant correlation with the positivity of fungal cultures. Anatomical changes due to epithelial damage during the carcinogenesis process become the main pathway for hyphal adhesion and invasiveness to form fungal colonization in lung cancer.

Bronchoscopy visualization with findings of irregular, hyperemic mucosa and infiltrative stenosis has a significant relationship with the identification of the fungal types of *Candida sp*., *Aspergillus sp*., *Cryptococcus sp*., and *Epicoccum sp*. Isolates of *Candida sp*. were the most frequently cultured fungi in this study and were predominantly formed in orifices experiencing infiltration and mass occlusion based on bronchoscopy visualization. Meanwhile, *Aspergillus sp*. tends to be found in infiltrative and decompressed orifices, based on bronchoscopy visualization. The bronchoscopy visualization parameters in this study can be used as a reference diagnostic indicator in establishing pulmonary mycosis as a secondary infection in lung cancer.

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CONFLICT OF INTEREST
The authors declared there is no conflict of interest.

AUTHOR CONTRIBUTION
Idea and concept: SI, DA, ETMS. Design and manuscript writing: SII and ETMS. Data collection and processing: ETMS. Control and supervision: SII, DA, IY. Review and revision: SII, DA, IY. All authors contributed and approved the final version of the manuscript.

REFERENCES

[1] Shah A, Armstrong-James D, Chotirmall SH. Respiratory Mycoses: A Call to Action to Recognize, Educate and Invest. *Mycopathologia*. 2021;7:186(5):569–573. DOI:10.1007/s11046-021-00589-3
[2] Shankar P, Vijay B, Pendse N, Rahman M, Nampoothiri V. Ayurveda management of pulmonary mycosis: an integrative approach: a case report. *Journal of Medical Case Reports* 2023;17(1):48. DOI:10.1186/s13256-022-03736-6
[3] Amich J, Mokhtari Z, Strobel M, Vialetto E, Sheta D, Yu Y, et al. Three-dimensional light sheet fluorescence microscopy of lungs to dissect local host immune-aspergillus fumigatus interactions. *Mbio* 2020;11(1):10–1128. DOI:10.1128/mbio.02752-19
[4] Azim A, Ahmed A. Diagnosis and management of invasive fungal diseases in non-neutropenic ICU patients, with a focus on candidiasis and aspergillosis: a comprehensive review. *Frontiers in Cellular and Infection Microbiology* 2024;14:1256158. DOI: 10.3389/fcimb.2024.1256158
[5] Wahyuningsih R, Adawiyah R, Sjam R, Prihartono J, Ayu Tri Wulandari E, Rozaliyani A, et al. Serious fungal disease incidence and prevalence in Indonesia. *Mycoses* 2021;64(10):1203–1212. DOI:10.1111/myc.13304
[6] Rozaliyani A, Jusuf A, Priyanti, Burhan E, Handayani D, Widowati H. Infeksi jamur paru di Indonesia: Situasi saat ini dan tantangan di masa depan. *Jurnal Respirologi Indonesia* 2019;39(3)
[7] Prasenohadi, Hermansyah, Rozaliyani, Nurwidya. Profile of Fungal Culture from Bronchoalveolar Lavage (BAL) 2021. *PJCM* 2021;27(2):60-67
[8] Shin SH, Kim BG, Kang J, Um SW, Kim H, Kim HK, et al. Incidence and risk factors of chronic pulmonary aspergillosis development during long-term follow-up after lung cancer surgery. *Journal of Fungi* 2020;6(4):1–10. DOI:10.3390/jof6040271
[9] Sahara SA, Noorhamdani SK, Ruliatna EF. Perbedaan Profil Kolonisasi Candida sp Pada Sputum Pasien Kanker Paru Dan TB Paru. *Universitas Brawijaya* 2021
[10] Prakash P, Agarwal P, Gupta A, Gupta E, Dasgupta A. Comparison of Induced Sputum and Bronchoalveolar Lavage Fluid Examination in the Diagnosis of Sputum-Negative Pulmonary Tuberculosis. *The Indian Journal of Chest Diseases & Allied Sciences* 2016;58(3):173–175. DOI:30152650

[11] Alfarisa S, Mitra E, Wahyuni S. Karakteristik Pasien Kanker Paru di RSUP Dr. M. Djamil Padang Tahun 2021. *Scientific Journal* 2023;2(6):141–149. DOI: 10.56260/sciena.v2i6.116

[12] Agung I, Saputra H, Mahendra I, Sumadi D, Juli IW. Karakteristik Pasien Karsinoma Paru di RSUP Sanglah Denpasar Tahun 2017-2018. *J Med Udayana* 2020;9(11):43–50. DOI:10.24843/MU.2020.V09.i11.P07

[13] Polanski J, Jankowska-Polańska B, Uchmanowicz I, Chabowski M, Janczak D, Mazur G, et al. Malnutrition and quality of life in patients with non-small-cell lung cancer. *In Advances in Experimental Medicine and Biology* 2017;1021:15–26). DOI:10.1007/5584_2017_23.

[14] Aapro M, Arends J, Bozzetti F, Fearon K, Grunberg SM, Herrstedt J, et al. Early recognition of malnutrition and cachexia in the cancer patient: a position paper of a European School of Oncology Task Force. *Annals of Oncology* 2014;25(8):1492–1499. DOI:10.1093/annonc/mdu085.

[15] Hamaker ME, Oosterlaan F, van Huis LH, Thielen N, Vondeling A, van den Bos F. Nutritional status and interventions for patients with cancer–a systematic review. *Journal of Geriatric Oncology* 2021;12(1), 6–21. DOI:10.1016/j.jgo.2020.06.020

[16] Rahal Z, El Nemr S, Sinjab A, Chami H, Tfayli A, Kadara H. Smoking and Lung Cancer: A Geo-Regional Perspective. *Frontiers in Oncology* 2017;7. DOI:10.3389/fonc.2017.00194.

[17] Kanwal M, Ding XJ, Cao Y. Familial risk for lung cancer. *Oncology Letters* 2017;13(2):535–542. DOI:10.3892/ol.2016.5518

[18] Galev G, Nagoti S, Sansano I, Armstrong SM, Herman M, Mukhopadhyay S. Smoking and the lung: Landmark papers (1929–2023). *Journal of Diagnostic and Academic Pathology* 2024;1(1):3–12. DOI:10.4103/jdap.jdap_9_24

[19] Takiguchi Y, Sekine I, Iwasawa S, Kurimoto R, Tatsumi K. Chronic obstructive pulmonary disease as a risk factor for lung cancer. *World Journal of Clinical Oncology* 2014;5(4):660–666. DOI:10.5306/wjco.v5.i4.660

[20] Santos NC, Miravitlles M, Camelier AA, de Almeida VDC, Maciel RRBT, Camelier FWR. Prevalence and Impact of Comorbidities in Individuals with Chronic Obstructive Pulmonary Disease: A Systematic Review. *Tuberc Respir Dis* 2022;27;85(3):205–220. DOI:10.4046/trd.2021.0179

[21] Kuźnar-Kamińska B, Mikuła-Pietrasik J, Ksiażek K, Tykarski A, Batura-Gabryel H. Lung cancer in chronic obstructive pulmonary disease patients: importance of cellular senescence. *Polish Archives of Internal Medicine*, 2018;128(7–8), 462–468. DOI:10.20452/pamw.4297

[22] Lu C, Mao X. Risk of adverse reactions associated with inhaled corticosteroids for chronic obstructive pulmonary disease: A meta-analysis. *Medicine* 2024;03(3). DOI:10.1097/MD.0000000000036609.

[23] Akata K, van Eeden SF. Lung Macrophage Functional Properties in Chronic Obstructive Pulmonary Disease. *International Journal of Molecular Sciences* 2020; 21(3):853. DOI:10.3390/ijms21030853.

[24] Heo JW, Kang HS, Park CK, Kim SK, Kim JS, Kim JW, et al. Regional emphysema score is associated with tumor location and poor prognosis in completely resected NSCLC patients. *BMC Pulm Med* 2020:1:20(1):242. DOI:10.1186/s12890-020-01268-7

[25] El-Badrawy MK, Elsaied AR, Ibrahim AA. M, Eladl AE, Elmorsey RA. Prevalence and pattern of isolated fungi from bronchoalveolar lavage among patients with lung cancer: a prospective cross-sectional study. *The Egyptian Journal of Bronchology*, 2023;17(1):7. DOI:10.1186/s43168-023-00178-6

[26] Laroumagne S, Lepage B, Hermant C, Plat G, Phelippeau M, Bigay-Game L, Lozano S, et al. Bronchial colonisation in patients with lung cancer: a prospective study. *European Respiratory Journal*, 2013;42(1):220–229. DOI:10.1183/09031936.00062212

[27] Zhang D, Li X, Zhang J, Wu J, Sun X. Characteristics of invasive pulmonary fungal diseases diagnosed by pathological examination. *Canadian Journal of Infectious Diseases and Medical Microbiology*, 2021;(1):5944518. DOI:10.1155/2021/5944518

[28] Aycicek O, Küçük MP, Koç I, Mürtezaoğlu SA, Pehlivanlar A, Öztuna F, Bülbül, Y, et al. Fungal culture results and clinical effects of bronchoscopy specimens. *Tuberkuloz ve Toraks*, 2022;70(1):15–26. DOI:10.5578/tt.20229903

[29] Freeman Weiss Z, Leon A, Koo S. The evolving landscape of fungal diagnostics and current and emerging microbiological approaches. *Journal of Fungi* 2021;7(2):127. DOI:10.3390/jof7020127

[30] Yao K, Qiu X, Hu H, Han Y, Zhang W, Xia R, et al. Pulmonary cryptococcosis coexisting with central type lung cancer in an immuocompetent patient: a case report and literature review. *BMC Pulmonary Medicine* 2022;20:1–6. DOI:10.1186/s12890-020-01200-z.

[31] Abed RM. Exploring Fungal Biodiversity of Genus Epicoccum and Their Biotechnological Potential. In A. M. Abdel-Azeem, A. N. Yadav, N. Yadav, & Z. Usmani (Eds.), Industrially Important Fungi for Sustainable Development: Volume 1: Biodiversity and Ecological Perspectives (pp. 237–276). *Springer International Publishing* 2021. DOI:10.1007/978-3-030-67561-5_7

[32] Li Z, Denning DW. The impact of corticosteroids on the outcome of fungal disease: a systematic review and meta-analysis. *Current Fungal Infection Reports* 2023;17(1):54–70. DOI: 10.1007/s12281-023-00456-2

[33] Moçin ÖY, Karakurt Z, Aksoy F, Güngör G, Partal M, Adigüzel N, et al. Bronchoscopy as an indicator of tracheobronchial fungal infection in non-neutropenic intensive-care unit patients. *Clinical Microbiology and Infection* 2013;19(3):136-141. DOI: 10.1111/1469-0691.12112

[34] Nugratama KA, Raharjo AF, Mashuri YA. Risk Factors for Pulmonary Mycosis in Immunocompromised Patients in Surakarta, Indonesia. *Smart Medical Journal* 2024;7(1):20–28. DOI:10.13057/smj.v7i1.78386