Profile of Fungal Culture from Bronchoalveolar Lavage (BAL) and Bronchial washing in Bronchoscopy patients at Persahabatan Hospital, Jakarta

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P EH FN conceived idea, P FN AR drafted the study, P FN collected data, AR FN did statistical analysis and interpretation of data, P FN AR critical review manuscript, All approved final version to be published.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Abstract

Background: Pulmonary infection is a major health problem in Indonesia, including pulmonary mycosis caused by infection, fungal colonization and hypersensitivity reactions to fungi. Bronchoscopy is used as a diagnostic tool to observe endobronchial lesions and to obtain clinical specimens such as bronchoalveolar lavage (BAL) and bronchial washing. Fungal culture examination from clinical specimen of bronchoscopy could assist in diagnosing pulmonary mycosis.

Methodology: This was a cross-sectional descriptive study of patients underwent bronchoscopy who were examined for fungal culture from BAL and bronchial washing. Number of samples was the total sampling from January 2016 to December 2017. The study was conducted in Department of Pulmonology and Respiratory Medicine, Persahabatan Hospital, Jakarta.

Results: Clinical specimens from bronchoscopy in this study were 67 bronchial washing samples and 21 BAL samples. There were positive fungal growth in 35 samples and no fungal growth in 53 samples. All growing fungi originated from Candida sp. with most species found was Candida albicans in 30 isolates, followed by Candida parapsilosisin 3 isolates, Candida glabrata and Candida tropicalisin one isolate, respectively. Bronchoscopy samples of BAL and bronchial washing could be used for fungal culture examination.

Conclusion: This study concluded that fungal growth were observed in several specimens and the species were Candida albicans, Candida parapsilosis, and Candida glabrata and Candida tropicalis.

Key words: Fungal Culture: Bronchoscopy; Bronchoalveolar Lavage; Bronchial Washing

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Introduction

Pulmonary infection remains a major health problem in Indonesia. One of pulmonary infection rarely discussed is pulmonary mycosis. Pulmonary mycosis is a disruption in respiratory tractand lung parenchymacaused by fungal infection, colonization or hypersensitivity reactions to fungi. However, pulmonary mycosis is not only found in neutropenic immunosuppressed-patients, but also in patients without neutropenic condition. Candida sp., Aspergillus sp. and sometimes Zygomycetesare the most common fungi found in respiratory secretions. Candida isolation is found more often, specifically in 18-56% of intubated patients and in 57% of cases of bacterial pneumonia, these are higher than the Aspergillus.[1,2]

Bronchoscopy is an important diagnostic tool for pulmonologists. Through a bronchoscopy examination, pulmonologist could observe

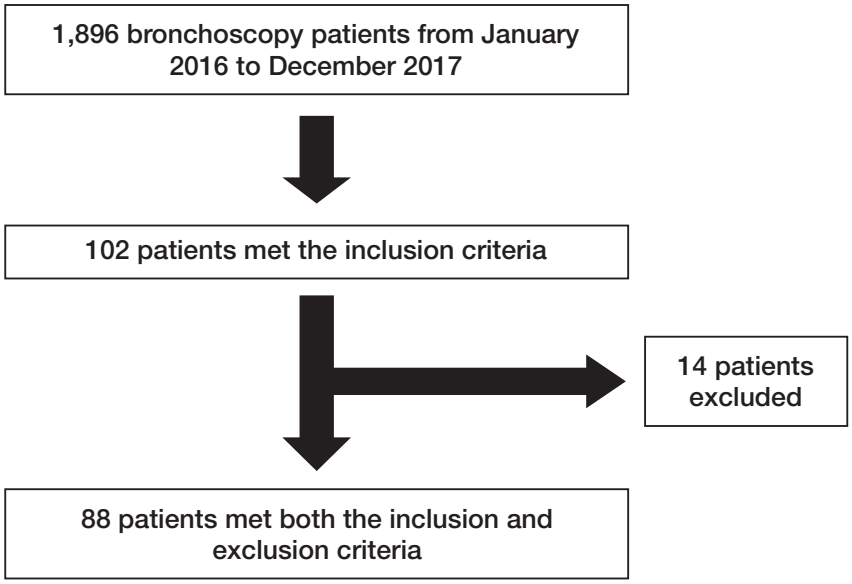

Figure 1: Study plot

endobronchial lesions and obtain the necessary laboratory examination specimens such as bronchoalveolar lavage (BAL), bronchial washing, brushing and biopsy. This examination is needed as a follow-up in patients with suspicious lesions from chest X-ray (CXR) or chest Computed Tomography (CT) scans.[1,3] Flexible bronchoscopy belongs to the treatments for pulmonary fungal infection or pulmonary mycosis. Fungal culture from BAL or bronchial washing could assist in diagnosing pulmonary mycosis.[4]

There have not been many studies conducted on the fungal cultures results from clinical specimens such as BAL or bronchial washing. One study by Sukamto was conducted in Department of Pulmonology at Adam Malik Hospital Medan which examined the fungal cultures results from bronchial washing in 40 former tuberculosis (TB) patients. The results showed that 11 patients (27.5%) had positive fungal culture results. Based on these considerations, we felt the need to understand the profile of fungal culture results from BAL and bronchial washing in patients underwent bronchoscopy at Persahabatan Hospital.The objective of this study was to understand the fungal culture profile of BAL and bronchial washing in patients underwent bronchoscopy with certain indications at Persahabatan Hospital.

Methodology

This was a cross-sectional descriptive study of bronchoscopy patients at Persahabatan Hospital, who were examined for fungal cultures in the Department of Parasitology, Faculty of Medicines Universitas Indonesia (FMUI). The sampling technique was total sampling of bronchoscopy patients started from January 2016 to December 2017. This study examined secondary data obtained from the medical records of Persahabatan Hospital and the Department of Parasitology, FMUI. The inclusion criteria were patients aged >18 years old (WHO) who were subjected to bronchoscopy to obtain BAL or bronchial washing specimens and were examined for fungal cultures from those BAL or bronchial washing specimens. The exclusion criteria was incomplete medical record data. This study has been granted an ethical approval from the Institutional Review Board (IRB) of the Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.

Results

Study plot is described in Figure 1. The age of subjects in this study ranged from 20 to 76 years with the median age was 54 years and the mean was 51.7 years. The largest age group was ≥50 years as many as 53 people (60.2%). The sex of the study subjects consisted of 60 males (68.2%) and 28 females (31.8%). The pulmonary underlying diseasesfound were 50 subjects (56.8%) with lung tumors, 14 subjects (15.9%) with former tuberculosis (TB), 11 subjects (12.5%) had pulmonary TB and 7 subjects (8%) had chronic obstructive pulmonary disease (COPD). The non-pulmonary underlying diseases found in this study were 4 subjects (4.6%) with diabetes mellitus (DM), 1 subject (1.1%) had HIV/AIDS and 1 subject (1.1%) with renal failure.

Clinical Characteristics of the Subjects

Bronchoscopic features most frequently obtained in

this study were hyperemic mucosa in 29 subjects, followed by normal features in 23 subjects, infiltrative mass in 19 subjects, compression stenosis in 10 subjects and cicatricial features in 7 subjects. The final diagnosis of the study subjects who underwent bronchoscopy were lung tumor in 58 subjects, pulmonary TB in 23 subjects, pneumonia in 4 subjects and pulmonary mycosis in 3 subjects.

Clinical Specimens and Fungal Culture Results

The clinical specimens obtained from the bronchoscopy were 67 bronchial washings and 21 BALs. From these clinical specimens of bronchoscopy, it was found that the fungal culture results were 35 specimens with fungal growth and 53 without fungal growth. The summary of profile of the study subjects and fungal culture results can be found on Table 1.

Fungal Species Characteristics

All growing fungi from the cultures originated from Candida sp. with the following details: Candida albicansin 30 isolates, Candida parapsilosisin 3 isolates, 1 isolate of each Candida glabrata and Candida tropicalis, respectively. The number of fungal colonies found the most was several colonies in 19 isolates. Nineteen isolates found several colonies, 8 isolates found plentiful colonies, whereas the last 8 isolates found full fungal colonies. The profile of fungal species based on the underlying diseases was reported in Table 2. Candida albicans grew on all bronchoscopic features and final diagnosis. Table 3 and Table 4 respectively represented the fungal species based on bronchoscopic features and final diagnosis, while Table 5 and Table 6 summarized the fungal colonies number based on the final diagnosis and the fungal species.

Discussion

Demographic Characteristics of the Study Subjects

Table 1. Profile of the study subjects and fungal culture results

Subject profiles	Fungal growth		No fungal growth	
	Patients number (n=35)	Percentage	Patients number (n=53)	Percentage
Age				
< 50 years	10	28.6%	25	71.4%
≥ 50 years	25	47.2%	28	52.8%
Sex				
Male	23	38.3%	37	61.7%
Female	12	42.9%	16	57.1%
Pulmonary underlying diseases				
Pulmonary TB	3	27.3%	8	72.7%
Former TB	4	28.6%	10	71.4%
Lung Tumor	20	40.0%	30	60.0%
COPD	5	71.4%	2	28.6%
Bronchoscopy Results				
Normal	5	21.7%	18	78.3%
Hyperemic	10	34.5%	19	65.5%
Infiltrative	9	47.4%	10	52.6%
Stenosis	6	60.0%	4	40.0%
Cicatricial	5	71.4%	2	28.6%
Final diagnosis				
TB	6	26.1%	17	73.9%
Lung tumor	25	43.1%	33	56.9%
Pneumonia	2	50.0%	2	50.0%
Mycosis	2	66.7%	1	33.3%
Clinical specimens				
Bronchial washing	25	37.3%	42	62.7%
BAL	10	47.6%	11	52.4%

Table 2. Profiles of fungal species based on the underlying diseases

Underlying diseases	C. albicans	C. parapsilosis	C. glabrata	C. tropicalis
Pulmonary TB	3	0	0	0
Former TB	3	1	0	0
Lung tumor	17	1	1	1
COPD	4	1	0	0
DM	1	0	0	0
HIV/AIDS	1	0	0	0
Renal failure	1	0	0	0

This study found that the age of the study subjects ranged from 20 to 76 years with the median value of 54 years and the mean of 51.7 years. The age group ≥ 50 years was found the most with as many as 53 subjects (60.2%). This result was in accordance with the 2013 National Basic Health Research or Riset Kesehatan Dasar (Riskesdas) data which stated that the prevalence of pulmonary patients was more common in the age group > 45 years. Study from Setiadi, et al. carried out indr. Moewardi Hospital Surakarta also revealed that the highest number of patients with lung disease who underwent bronchoscopy was in the > 40 years age group (84%). There were more groups of patients in the older age because patients in the study generally had underlying disease and their final diagnosis were chronic lung diseases, mainly lung tumor.[6]

Based on the sex, there were 60 male subjects (68.2%) and 28 female subjects (31.8%). This result was consistent with the 2013 Riskesdas data which expressed that there were more male patients with lung disease than the females in Indonesia.[5] The same result was also seen in the study of Setiadi, et al. which stated that most patients underwent bronchoscopy were male (64,84%). Male gender was correlated with higher risk factors for lung disease due to smoking.[6]

Based on the underlying disease of the study subjects, 11 subjects (12.5%) had pulmonary TB, 14 subjects (15.9%) with former TB, 50 subjects (56.8%) had lung tumor, 7 subjects (8%) had COPD, 4 people (4.5%) had DM, 1 subject (1.1%) with HIV/AIDS and 1 subject (1.1%) had renal failure. This result corresponded with the study by Mocin, et al. on ICU patients who were suspected of having pulmonary fungal infections. Among these patients, 66.3% had COPD as the underlying disease, 18.9% had DM and 12.6% had lung cancer. In addition, other study by Lin, et al. also observed DM, COPD, former TB and cancer as underlying diseases. This was due to decline on the immune system in lung tumor and DM as well as damage to the lung parenchyma in former TB and COPD; both could facilitate fungal infections.[8]

Clinical Characteristics of Study Subjects

The clinical characteristics of the study subjects consisted of the bronchoscopy results and final diagnosis. Based on bronchoscopic features, hyperemic mucosa was found the most in 29 subjects, followed by normal feature in 23 subjects, infiltrative mass feature in 19 subjects, compression stenosis feature in 10 subjectsand cicatricial feature in 7 subjects. These results were in accordance with a study by Sukamto, which obtained the hyperemic inflammation of the mucosa as the most common bronchoscopic feature in 28 out of 40 bronchoscopy patients, followed by normal feature, stenosis and infiltrative masses.[2]

Based on the final diagnosis, the results got lung tumors in 58 subjects, pulmonary TB in 23 subjects, pneumonia in 4 subjects and pulmonary mycosis in 3 subjects. This result was consimilar with the study from Gupta, et al. concerning the diagnosis of patients

Table 3. Profile of fungal species based on the bronchoscopy results

Bronchoscopy results	C. albicans	C. parapsilosis	C. glabrata	C. tropicalis
Normal	5	0	0	0
Hyperemic	10	0	0	0
Infiltrative	5	2	1	1
Stenosis	6	0	0	0
Cicatricial	4	1	0	0

who underwent bronchoscopy in tertiary hospitals in Indiafor 34 years. Final diagnosis of lung tumor was the most frequently observed (32.2%), continued with pulmonary infections (18.6%). This result developed because the patients were generally subjected to bronchoscopy due to suspicion of an initial diagnosis of a malignancy in the thoracic cavity which then evidenced by bronchoscopy.[9]

Fungal Culture Results of Study Subjects

The fungal culture results were obtained from medical record data and the results of fungal cultures from clinical specimens conducted at the Department of Parasitology, FKUI. Based on clinical specimens data taken by bronchoscopy, there were 67 bronchial washings and 21 BALs. From these bronchoscopy clinical specimens, it was observed that fungal culture had 35 results with fungal growth and 53 without fungal growth. The same results were also shown on study by Sukamto about former TB patients who were tested for fungal cultures from clinical bronchoscopy. Fungal growth was found in 11 out of 40 study subjects.[2] Another study by Baughman, et al. obtained positive fungal culture results from 85% BAL specimens. This was different possibly because the study by Baughman, et al. collected study subjects only with a diagnosis of pulmonary mycosis whereas our study included all subjects who underwent bronchoscopy.[10]

Fungal Species Characteristics of Study Subjects

It was found that 35 clinical specimens of the study subjects who underwent bronchoscopy gained fungal growth from the culture. The fungal specieswhich grew from all culture examinations originated from Candida sp. with the following details: 30 isolates of Candida albicans, 3 isolates of Candida parapsilosis, each 1 isolate of Candida glabrata and Candida tropicalis, respectively. Candida albicanswas the most common species obtained by 30 isolates out of the total 35 specimens. This was consistent with the study by Ratna, et al. in lung cancer patients on whom the bronchial washings were examined. The fungal culture results obtained Candida albicansas the most common species.[11]

Another study by Leon, et al. in non-neutropenic patients who were admitted to the ICU obtained similar results; the most common species obtained from fungal cultures were Candida albicans (69.7%), followed by Candida tropicalis, Candida parapsilosis and Candida glabrata. This was probably due to the fact that patients with chronic pulmonary disease experienced a decline in immune system thus facilitating Candida colonization and fungal infections. Moreover, Candida albicanswas included in the human respiratory tractnormal flora, so that in this study there was a risk of contamination which caused a large number of Candida albicans culture results.[4]

Profile of the Study Subjects and Fungal Culture Results

About 35 study subjects had fungal growth on the cultures and 53 subjects did not. Based on the age group, it was shown that among subjects <50 years, 10 (28.6%) had positive fungal culture results, while 25 subjects (47.2%) from those aged >50 years had positive fungal culture results. This result was similar to study by Leon, et al. which stated that positive fungal culture results were observed in patients with a mean age of 58.4 years. Age was one of the risk factors for fungal infection due to the decline in the immune system.[4] The male subjects showed more positive fungal culture results, namely in 23 subjects

Table 4. Profile of fungal species based on the final diagnosis

Final diagnosis	C. albicans	C. parapsilosis	C. glabrata	C. tropicalis
Pulmonary TB	5	1	0	0
Lung tumor	21	2	1	1
Pneumonia	2	0	0	0
Pulmonary mycosis	2	0	0	0

Table 5. Profile of fungal colonies number based on the final diagnosis

Final diagnosis	Several colonies	Plentiful colonies	Full colonies
Pulmonary TB	3	0	3
Lung tumor	15	6	4
Pneumonia	1	0	1
Pulmonary mycosis	0	2	0

Table 6. Profile of fungal colonies number based on the fungal species

Final diagnosis	Several colonies	Plentiful colonies	Full colonies
Candida albicans	3	0	3
Candida parapsilosis	15	6	4
Candida glabrata	1	0	1
Candida tropicalis	0	2	0

compared to 12 female subjects. This was in accordance with study by Sukamto which pointed out that 9 of 11 study subjects with positive fungal culture were males.[2]

The fungal culture results were predominantly found in patients with lung tumor as underlying disease, for as many as 20 subjects. This study found 1 HIV/AIDS patient and 1 patient with renal failure, all of whom showed positive fungal culture results. A study by Karnak, et al. which gathered a variety of literature on fungal infections of the respiratory tract also found that the risk factors for underlying diseases associated with fungal infections were tumors and immune system disorders.[12] Furthermore, it was thought that, in addition to lung tumor, HIV/AIDS and renal failure were diseases that could lead to a decline in the immune system.

Based on the bronchoscopy results, fungal growth in culture results were found as the most frequent in the feature of hyperemic mucosa, specifically in 10 subjects, followed by infiltrative mass feature of 9 subjects, stenosis feature of 6 subjects, normal feature and cicatricial feature of 5 subjects, respectively. A study by Sukamto obtained the similar result of positive fungal culture on the hyperemic mucosal inflammation in bronchoscopic feature, namely 9 out of 11 fungal growth cultures. This result was thought to occur because the tissue reaction to microorganisms infection was an inflammation which generated a hyperemic appearance.[2]

Based on the final diagnosis of study subjects, the lung tumor diagnosis group had the most fungal growth cultures, namely in 25 subjects. This was similar with Szymankiewicz, et al. who obtained positive fungal culture results in 60.78% of lung tumor patients. Lung tumors could induce immune system disorders which then facilitating fungal colonization and infections.[13]

From the clinical specimens, BALshowed the predominant fungal growth in cultures, specifically in 10 isolates (47.6%) from 21 BAL specimens, compared to 25 isolates (37.3%) from 67 bronchial washing specimens. Karnak, et al. collected various literatures on fungal infection in the respiratory tract and pointed out that as many as 36% of patients had positive fungal culture results on the bronchial washings, compared to BAL specimens with only 25%. However, these different results could be due to the circumstances that more bronchial washings were sent for fungal culture examination than BAL. In our study, BAL showed a higher number of positive results because the washing process was carried out more so that the clinical specimens obtained were more representative.[12]

Profile of Fungal Species Based on the Underlying Diseases

Candida albicans was the fungal type which grew in all underlying diseases groups. It was found mostly in the lung tumor group (17 isolates). This result was consistent with a study by Sukamto on former TB patients whose fungal cultures were positive for Candida albicans in 7 out of 11 bronchoscopy clinical specimens.[2] However, Lin, et al. obtained different results as Aspergillus sp. was considered to be the most prominent among the results. This difference was because Lin, et al. had distinct study subjects as the bronchoscopy was performed only on critically ill patients in the ICU.[8]

Profile of Fungal Species Based on the Bronchoscopy Results

Candida albicans was also the fungal type which grew in all bronchoscopic features groups. Hyperemic mucosa feature had the highest number of Candida albicans culture growth, specifically in 10 isolates. This result was in accordance to a study by Sukamto on former TB patients which also observed Candida albicans as the most common fungal species from culture and hyperemic mucosa as the most salient among the bronchoscopic features.[2] Isolates of Candida parapsilosis were seen in the infiltrative mass and cicatricial features while the isolates of Candida glabrata and Candida tropicalis were only found in the infiltrative mass feature group. Different results were visible in the study by Mocin, et al. who obtained mucosal plaque feature on the bronchoscopy results of patients with Candida sp. infection. This might be conditioned as Mocin, et al. selected only immunocompromised ICU patients as study subjects, so that not only had colonization occurred but there had been more severe fungal infections in

the respiratory tract.[7]

Profile of Fungal Species Based on the Final Diagnosis

The results of this study found that the fungal species which grew in all final diagnosis groups was Candida albicans. This species were seen mostly in the lung tumor group (21 isolates). Isolates of Candida parapsilosis was observed in the final diagnosis groups of pulmonary TB and lung tumor whilst Candida glabrata and Candida tropicalis isolates were only found in the lung tumor group. Karnak, et al. pointed out that the predisposing factors for diseases associated with Candida sp. Were tumors and immune system disorders that facilitated the fungal colonization in the respiratory tract and subsequently developed into fungal infections in the lungs.[12]

This study has several limitations. Our study used secondary data from patient medical records. This might cause the limitation of data collection if the medical record was incomplete so that researchers were difficult to analyze all the data obtained. In addition, researchers could not evaluate whether the acquired fungi were causing infection or only colonization because more comprehensive data were needed such as clinical conditions, laboratory results and periodic clinical monitoring of the patients. There was still a limited number of cases which were examined for fungal culture from bronchial washing or BAL specimes if compared to other pulmonary cases. This was considered to occur because fungal culture examination of bronchoscopy clinical specimens was quite expensive and required personal costs that were not guaranteed by the national health insurance.

Conclusion

The bronchoscopy results were hyperemic mucosa feature, normal feature, infiltrative mass feature, compression stenosis feature and cicatricial feature. Final diagnosis of the patients were lung tumor, pulmonary TB, pneumonia and pulmonary mycosis.The clinical specimens taken by bronchoscopy in this study were bronchial washings and BALs. From these specimens, fungal growth were observed in several specimens and the species were Candida albicans, Candida parapsilosis, and Candida glabrata and Candida tropicalis.

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