Correlation Between Chest X-Ray with Fungal Pneumonia in Immunocompromised Patients

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Abstract

Fungal infections are the most severe infections in immunocompromised individuals, and pulmonary involvement is the most common form of invasive tissue infection in immunocompromised hosts. Early and accurate diagnosis is essential given their high morbidity and mortality rates, reaching 50-100%. This study aims to analyse the correlation between chest x-rays and fungal pneumonia in immunocompromised patients to help diagnose and alleviate the morbidity and mortality burdens. This study is a retrospective analytic study conducted at Dr Soetomo General Academic Hospital Surabaya, entailing 201 samples in the form of chest x-rays, sputum cultures and blood laboratories obtained from medical records from a period from January 2019 - December 2021. Among patients with a fungal infection, males predominated the group with 62.5%, and the most frequent age group was between 50 and 59. The most common underlying condition of the patients was diabetes mellitus, and the most pathogen discovered was *Candida sp*. Most patients presented with mild diseases (41.79%), with the majority of chest x-rays featuring consolidations and ground-glass opacity. There is a poor correlation between ground glass opacity/infiltrate in the left paracardial and reticulonodular pattern with fungal pneumonia in immunocompromised patients, with a poor negative correlation between lymphocyte count and NLR (neutrophil-lymphocyte ratio) value with fungal infection and severity degree of chest radiographs. Chest x-ray images along with clinical information such as age and laboratory tests can assist radiologists in making a differential diagnosis of fungal pneumonia.

Keywords: pneumonia; chest x-ray; fungal; immunocompromised; fungal pneumonia

1. Introduction

Fungal pneumonia is inflammation in lung parenchyma following one or more endemic or opportunistic fungi (Mandanas RA, 2018). Being the most severe infection in individuals with immunocompromised, it frequently invades the pulmonary tissue of immunocompromised patients (Torres P et al., 2018).

The statistics on mycosis disease in Indonesia are still limited due to various challenges. A study conducted in a hospital in Jakarta demonstrated a prevalence of Pneumocystis pneumonia of 14.5% (eight out of 55 patients) among HIV/AIDS cases (Rozaliyani A, 2019; Singh, 2018). Meanwhile, the incidence of fungal lung infection in Indonesia, particularly in Dr Soetomo General Hospital Surabaya, remains unveiled (Arini AD, 2019).

Pneumonia affects roughly 75% of all pulmonary complication cases in immunocompromised patients; therefore, timely and accurate detection is imperative given its high morbidity and mortality rate of up to 50 – 100% (Yu WO, 2000; Peck KR et al., 2018). Early diagnosis is able to repress the mortality rate to 33 – 50% (Von EM et al., 1995).

Based on the aforementioned brief overview, the authors are keen to investigate the correlation between chest x-ray imaging and fungal pneumonia in immunocompromised patients from January 2019 to December 2021. This project's results are supposed to aid the radiologist in assisting clinicians in narrowing down the differential diagnosis and alleviating the morbidity and mortality burden in immunocompromised patients.

2. Material and Methods

This research is an analytic study in a retrospective manner, conducted in the Diagnostic Radiology Centre in Dr Soetomo General Academic Hospital Surabaya between January 2019 and December 2021. We gathered the samples by reviewing the medical records of immunocompromised patients diagnosed with pneumonia who met the inclusion criteria in an agreed period.

The observed variables included the spectrum of disease, in which the pattern of lung parenchymal and pleural abnormalities was perceived, and the proportion of chest radiographs according to demographic data, comprising age and genre, distribution of lesions (upper, middle, and lower lobe), severity (mild, moderate, severe), rated using the modified scoring system adopted from Radiologic Assessment of Lung Oedema (RALE) and Radiologic Severity Index (RSI), along with blood samples, involving leukocyte counts and NLR.

The collected data were processed using Statistical Programme for Social Sciences (SPSS) version 26 software and illustrated in tables with percentages and graphs. The correlation analysis between variables was done by applying the Spearman formula, with a p-value of less than 0.05 indicating significance.

3. Results

The results were mustered by scrutinising the patients' radiographs and compared to the microbiology reports. The study entailed 201 chest radiographs of immunocompromised patients with pneumonia; 125 patients (62,19) yielded positive results in their microbiology examination, and the remaining 76 (37,81%) were negative for fungi. Based on the genre, our sample comprised 128 male (63,7%) and 73 female (36,3%) patients. The correlation analysis between genre and microbiology reports is illustrated in table 1. A p-value of more than 0.05 indicates no significant correlation between genre and fungal infection.

Table 1. Correlation analysis between genre and microbiology reports

Genre	Fungi detected		p-value
	Yes	No	
Male	80 (64%)	48 (63,2%)	
Female	45 (36%)	28 (36,8%)	0,905

Our samples ranged from 19 to 86-year-old, with a median of 53 and an average of 51. Patients aged 50-59 constituted a significant proportion of our subjects, involving 58 patients (28.9%), which also made up the notable percentage among patients with positive microbiology examination for 36 patients (28.8%). Statistically, there is no significant correlation between age and fungi detection, as in table 2.

Table 2. Correlation analysis between age and fungi detection

Age (years)	Fungi detected		p-value
	Yes	No	
<20	0 (0%)	1 (163%)	
20-29	10 (8%)	5 (6,6%)	
30-39	24 (19,2%)	12 (15,8%)	
40-49	21 (16,8%)	13 (17,1%)	
50-59	36 (28,8%)	22 (28,9%)	
60-69	23 (18,4%)	19 (25%)	
70-79	9 (7,6%)	2 (2,6%)	
80-89	2 (1,6%)	2 (2,6%)	0,691

Our immunocompromised patients included malignancy, diabetes mellitus, autoimmune, and HIV/AIDS, with diabetes representing the majority of samples for 114 patients (56.7%). There is no statistically significant correlation between the underlying diseases and microbiology reports.

Table 3. Correlation analysis between primary diseases and microbiology results

Underlying disease	Fungi detected		p-value
	Yes	No	
Malignancy	21 (16,8%)	12 (15,8%)	
Diabetes mellitus	70 (56%)	44 (57,9%)	
Autoimmune	18 (14,4%)	6 (7,9%)	
HIV/AIDS	16 (12,8%)	14 (18,4%)	0,829

The most frequently discovered fungi in the immunocompromised patient's lung are *Candida albicans* and *Candida tropicalis*. Non-*candida* pathogens involved *Cryptococcus*, *Aspergillus*, and *Trichosporon*.

Radiology features of pneumonia patients with immunocompromised comprise ground-glass opacity (GGO)/infiltrate, consolidation, nodule, bronchopneumonia, cavity, fibrosis, reticular pattern, reticulogranular pattern, bronchiectasis, atelectasis, pleural effusion, pleural thickening, and pneumothorax. In this study, we did not find the miliary, calcifications, or nodular patterns. Most radiographs of infected patients exhibited consolidation, ground-glass opacity/infiltrate, fibrosis, reticular, and reticulogranular patterns, similar to patients with negative microbiology examination. The correlation between chest radiographs and microbiology reports is described below in table 4.

Table 4. Correlation analysis between chest radiographs and microbiology results in immunocompromised patients

Radiograph features	Fungi detected		p-value
	Yes	No	
Ground-glass opacity (GGO)			
Yes	98 (78,4%)	58 (76,3%)	

No	27 (21,6%)	18 (23,7%)	0,733
Left paracardial GGO			
Yes	30 (24%)	8 (10,5%)	
No	95 (76%)	68 (89,5%)	**0,018 (r = 0,167)**
Consolidation			
Yes	118 (94,4%)	67 (88,2%)	
No	7 (5,6%)	9 (11,8%)	0,114
Nodule			
Yes	0	1 (1,3%)	
No	125 (100%)	75 (98,7%)	0,200
Parabronchial nodule			
Yes	1 (0,8%)	0	
No	124 (99,2%)	76 (100%)	0,200
Cavity			
Yes	10 (8%)	6 (7,9%)	
No	115 (92%)	70 (92,1%)	0,979
Fibrosis			
Yes	60 (48%)	28 (36,8%)	
No	65 (52%)	48 (63,2%)	0,123
Reticular pattern			
Yes	29 (23,2%)	14 (18,4%)	
No	96 (76,8%)	62 (81,6)	0,426
Reticulonodular pattern			
Yes	22 (17,6%)	23 (30,3%)	**0,037**
No	103 (82,4%)	53 (69,7%)	**(r = 0,147)**
Bronchiectasis			
Yes	2 (1,6%)	4 (5,3%)	
No	123 (98,4%)	72 (94,7%)	0,140
Atelectasis			
Yes	3 (2,4%)	1 (1,3%)	
No	122 (97,5%)	75 (98,7%)	0,596
Pleural effusion			
Yes	21 (16,8%)	10 (13,2%)	
No	104 (83,2%)	66 (86,8%)	0,491
Pleural thickening			
Yes	3 (2,4%)	4 (5,3%)	
No	122 (97,6%)	72 (94,7%)	0,285
Pneumothorax			
Yes	5 (4%)	0	
No	120 (96%)	76 (100%)	0,078

The severity of chest radiographs in immunocompromised patients with pneumonia is divided into mild, moderate, and severe. The degree of severity in our samples was dominated by mild disease for 84 patients (41.79%), followed by moderate for 79 patients (39.3%), and severe for 38 patients (18.91%).

In regards to laboratory tests, the correlation coefficient yielded a poor negative association, implying that patients with lymphocytopenia were linked to fungal pneumonia with severe disease. Poor correlation refers to patients with high NLR values related to fungal pneumonia and severe degree. There is no significant correlation between leukocytes and neutrophils with fungal pneumonia and severe disease (Table 5).

Table 4. Correlation analysis between chest radiographs and microbiology results in immunocompromised patients

Laboratory results	Microbiology		Severity of chest radiograph
Leukocyte	p = 0,569	p = 0,555	Leukocyte
Neutrophil	p = 0,551	p = 0,204	Neutrophil
Lymphocyte	**p = 0,037 (r = -0,147)**	**p = 0,017 (r = -168)**	Lymphocyte
NLR	**p = 0,096 (r = 0,118)**	**p = 0,003 (r = 209)**	NLR

4. Discussion

Our samples in this study consisted of 201 immunocompromised patients diagnosed with pneumonia, which did not improve after antibiotic treatments, and therefore were tested for sputum culture. Male patients predominated the proportion of patients with positive results for microbiology tests, aligning with reports by Makhnevich et al. in 2019 and Mandanas et al. in 2016, in which they stipulated that men are more often to suffer from pneumonia as opposed to their female counterparts (Mandanas RA, 2018).

The age group of 50-59 predominated our pneumonia patients. Similarly, a study by Ramirez et al. in 2018 reported that the median age of adult pneumonia was around 58. Another author also stated that most immunocompromised patients were between 50 to 59 years old (Aleem et al., 2021).

Diabetes mellitus comprised a significant part of the immunocompromised in our study; therefore, they are susceptible to infections, with pneumonia ranking first among diabetes mellitus (Vishwakarma et al., 2021).

In our study, *Candida* was the most discovered fungal species, whereas other species only made up a minor proportion, such as *Cryptococcus*, *Aspergillus*, and *Trichosporon*. *Candida* and *Aspergillus* are the two opportunistic pathogens that frequently affect people with immunosuppression (Ahmed et al., 2019).

The chest radiography features that repeatedly occurred in immunocompromised patients with fungal pneumonia included the consolidation and ground-glass opacity/infiltrate. This finding aligns with a previous report in which the dominating patterns involved consolidation, infiltration, and multiple nodules (Sharma et al., 2018).

Ground-glass opacity/infiltrate was found in 98 patients (78.4%) in a significant distribution of the middle lobe and paracardial. Statistically, there was a poor correlation between the left paracardial distribution of ground-glass opacities and fungal detection in immunocompromised patients. A prior study by Sharma et al. in 2018 also outlined a recurrent lower zone distribution in fungal pneumonia, particularly in the left lobe; however, both lungs may be affected.

Among 125 patients with positive microbiology tests, 118 (94.4%) yielded a consolidation pattern in their chest radiograph. There was no significant correlation between consolidation with fungal discovery in our patients. Reynolds et al., 2010 and Mandanas et al., 2018 also found that consolidations in pneumonia of fungal infection may develop in all lobes with lung base and lower zone predomination.

The nodule and parabronchial nodule in pneumonia patients with immunocompromised were only found in one patient with a negative microbiology test. This result disagrees with another study in which fungal pneumonia often presents with consolidation and nodules (Peck KR et al., 2018).

There was no significant correlation between either cavities or fibrosis with fungal pneumonia in immunocompromised patients. The cavity may be found in fungal pneumonia caused by *Candida* and *Aspergillus*. Moreover, the fibrosis in fungal pneumonia represents a chronic course and often occurs in the lower zone of the left lung (Gerg et al., 2019).

In this study, reticular patterns were recurring in the middle lobe and paracardial zone of the right lung. No significant correlation was established between reticular patterns with fungal pneumonia in immunocompromised patients. The reticular pattern is often seen in the upper zone (Torres et al., 2012).

The reticulonodular pattern in immunocompromised pneumonia patients with positive fungal detection was evident in 22 patients (17.6%), repeatedly occurring in the right and left paracardial zones. There was a scanty correlation between reticulonodular patterns and the evidence of fungal infections, similar to a previous study reporting that reticulonodular patterns can be found in fungal pneumonia due to *Cryptococcus* and *Pneumocystis jiroveci* in bilateral diffuse distribution (Garg et al., 2012).

Our study did not find a significant correlation between either bronchiectasis, atelectasis, pleural effusion, pleural thickening, or pneumothorax with fungal pneumonia in immunocompromised patients. Atelectasis scarcely appears in fungal pneumonia and is an atypical finding (Garg et al., 2012). Pleural effusion was only found in 22.9% of patients with fungal pneumonia, with a similar incidence to bacterial pneumonia (Sharma et al., 2018). Aspergillosis infection may lead to pleural thickening; nevertheless, the incidence is relatively low (Downer et al., 2013). Pneumothorax is also infrequent in fungal pneumonia (Pereira et al., 2010).

A poor negative correlation was established between lymphocyte count and fungal discovery with chest radiograph severity in immunocompromised patients, referring to an association between low lymphocyte count (lymphocytopenia) and a higher susceptibility to fungal infection with severe disease. There was a poor relationship between NLR value with fungal findings and severity of chest x-rays in immunocompromised patients, meaning that a higher NLR value is linked to a greater chance of fungal infection and severe ailment.

The lymphocyte may be a first-line consideration for fungal pneumonia investigation in immunocompromised patients (Garg et al., 2012). NLR is connected to the systemic inflammatory response in immunosuppressed patients and, therefore, can be a predictor in several cases corresponding to microinflammation, such as pneumonia (Man et al., 2021).

5. Discussion

The most common radiological findings in fungal pneumonia in immunocompromised patients were consolidations and ground-glass opacity/infiltrate. A poor correlation was established between ground-glass opacity/infiltrate in the left paracardial and reticulonodular pattern with fungal infections. Moreover, there was a slight negative association between lymphocyte count with fungal infection and severity degree on chest x-rays.

The radiological features of chest x-rays accompanying patients' clinical information, for instance, age, immunology status, and laboratory data can assist a radiologist in interpreting and making a differential diagnosis of fungal pneumonia.

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