The Relationship of Risk Factors and Comorbidity with Chest Radiography Features of COVID-19 Confirmed Patients

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Abstract

Introduction: *COVID-19 is a worldwide health problem with a high mortality rate, especially in patients with risk factors. One type of examination to inspect the severity of COVID-19 patients is a chest radiograph. There is a lack of studies on chest radiography features in Indonesia. This study aims to observe the relationship between age, gender, and comorbid conditions with chest radiography features in COVID-19 confirmed.*
Method: *This study was conducted at dr. Soebandi General Hospital uses a cross-sectional design with medical records as the instrument. Chest radiography examination was performed using BSTI classification. Meanwhile, data were analyzed using Chi-Square and contingency coefficient C.*
Result: *The study included 173 patients: 52% were 40-59 years old, 36,4% were 20-39 years old, and 11,6% were ≥ 60 years old; 56,1% were female and 53,9% were male; 50,9% have comorbidities, with hypertension, diabetes, and COPD were the most type of comorbidities. About 48,6% sample had a normal chest radiograph, 27,7% had a mild severity, 17,3% had a moderate severity, and 6,4% had a severe severity. There was a correlation between age and comorbidity with chest radiography features. Otherwise, no correlation was found between sex and chest radiography features.*
Conclusion: *Age and comorbidity were found as significant risk factors for the severity of chest radiograph in COVID-19 with a moderate correlation. However, no correlation was found between sex and chest radiography features.*

Keywords: *chest radiograph, COVID-19, risk factor*

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Hubungan Faktor Risiko dan Kondisi Penyakit Penyerta dengan Gambaran Foto Toraks pada Pasien Terkonfirmasi COVID-19

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Abstrak

Pendahuluan: *COVID-19 merupakan masalah kesehatan di seluruh dunia dengan angka kematian cukup tinggi terutama pada pasien dengan faktor risiko. Salah satu jenis pemeriksaan untuk melihat keparahan pasien COVID-19 adalah foto toraks. Studi tentang gambaran foto toraks pasien COVID-19 di Indonesia sangat terbatas. Studi ini bertujuan untuk melihat hubungan antara umur, jenis kelamin, dan kondisi penyakit penyerta dengan gambaran foto toraks pada pasien terkonfirmasi COVID-19.*
Metode: *Studi ini dilakukan di RSD dr. Soebandi Jember menggunakan desain cross-sectional dengan instrumen rekam medis. Pemeriksaan foto toraks dilakukan dengan menggunakan klasifkasi BSTI. Sedangkan, data dianalisis menggunakan Chi-Square dan koefisien kontingensi C.*
Hasil: *Studi ini melibatkan 173 sampel: 52% berumur 40-59 tahun sisanya berumur 20-39 dan ≥ 60 tahun, 56,1% berjenis kelamin perempuan dan 53,9% laki-laki. 50,9% sampel memiliki penyakit penyerta dengan urutan terbanyak hipertensi, diabetes, dan PPOK. 48,6% sampel memiliki foto toraks normal, 27,7% keparahan ringan, 17,3% keparahan sedang, dan 6,4% keparahan berat. Hasil analisis menunjukkan ada hubungan antara umur dan penyakit penyerta terhadap gambaran foto toraks. Sebaliknya, tidak ada hubungan yang ditemukan antara jenis kelamin dan gambaran foto toraks.*
Kesimpulan: *Umur dan kondisi penyakit penyerta ditemukan sebagai faktor risiko yang signifikan untuk tingkat keparahan gambaran foto toraks pada COVID-19 dengan korelasi sedang. Namun, tidak ada korelasi yang ditemukan antara jenis kelamin dengan gambaran foto toraks.*

Kata kunci: *foto toraks, COVID-19, faktor risiko*

Introduction

Coronavirus Disease 2019 (COVID-19) is a respiratory tract disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] After spreading to various countries rapidly, COVID-19 had become a global problem and pandemic declared by WHO on 11 March 2020.[2] On 28 September 2020, there were 278,722 COVID-19 confirmed cases in Indonesia and 32,730,945 globally.[3] Then, a total of 805 positive cases of COVID-19 and 53 deaths in Jember Regency.[4] In Southeast Asia, India, Indonesia, and Bangladesh reported the highest COVID-19 confirmed cases. Until 28 September, the COVID-19 mortality level in Indonesia was 3.76%. Meanwhile, the global mortality level was 3.03%.[3]

There are various clinical manifestations of COVID-19, starting from no clinical symptoms (asymptomatic), a mild disease without complications, mild pneumonia, severe pneumonia, acute respiratory distress syndrome (ARDS), to death. Various clinical manifestations of COVID-19 patients are affected by several risk factors, namely age, race/ethnicity, sex, comorbidities, certain medicine usage, poverty and crowding, and certain occupations.[5]

COVID-19 diagnosis is confirmed through the Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) examination method.[1] Diagnostic examination of SARS-CoV-2 is supported by radiological examination such as chest radiograph. The British Society of Thoracic Imaging (BSTI) suggests chest radiograph utilization as the first-line imaging examination on patients with clinical suspicion of COVID-19 infection to differentiate between COVID-19 and non-COVID-19 infections. This result can help with triage for

patients waiting for the diagnosis of RT-PCR. It also helps to evaluate disease development, particularly in patients with risk factors.[6] Studies regarding chest radiographs of COVID-19 patients in Indonesia are limited. This study aimed to determine the relationship between age, sex, and comorbidities with chest radiography features in COVID-19 confirmed patients.

Methods

Study Design and Participants

This study was an observational study carried out in the medical record room and radiology laboratory of dr. Soebandi general hospital, Jember, Indonesia, using a cross-sectional design. The retrospective study was performed from 27 January to 11 May 2021. The research protocol has been approved by the Ethics Commission of the Faculty of Medicine, Universitas Jember (No. 1.454/H25.1.11/KE/2021). The inclusion criteria were patients who were confirmed positive for COVID-19 through the RT-PCR examination from March to November 2020, patients ≥ 20 years, and patients undergoing chest radiographs between 5-15 days after the symptom onset.

Data Collection

Patient data of age, sex, comorbidities, symptom onset, and chest radiograph were collected from the hospital's medical records. Chest radiograph was performed on the posteroanterior (PA) projection. All images were determined by local radiologists and classified into the following categories: normal and classic/probable COVID-19 following the British Society Thoracic Imaging (BSTI) classification. Then, they determined the severity of chest radiography features on the classic/probable COVID-19. The severity degree was reported as mild (radiolucent > radiopaque), moderate (radiolucent = radiopaque), and severe (radiolucent < radiopaque).[6]

Data Analysis

Data analysis was conducted by IBM SPSS version 26. Categorical data were presented using the frequency, percentage, chart, and tested by the Chi-Square. If the Chi-Square requirements were not met, cell merging was performed. A p-value < 0,05 was considered significant. Significant results in the Chi-Square were subjected to the association level

calculation using the contingency coefficient C, calculating the Cmax value and C/Cmax ratio by categories of very low (0.00-0.199), low (0.20-0.399), moderate (0.40-0.599), high (0.60-0.799), and very high (0.80-1.00).[7]

Results

Characteristics of Subject

From 223 patients, 173 patients fulfilled the inclusion criteria. Patients were excluded due to the following reasons: patients < 20 years (n = 23), more than 5-15 days after the symptom onset (n = 11), less than 5-15 days after the symptom onset (n = 4), and did not undergo chest radiograph (n = 12). The

Table 1. Clinical Characteristics of COVID-19 Confirmed

Clinical Characteristics	Amount (n)	Percentage (%)
Age group, years		
20-39	63	36,4
40-59	90	52
≥ 60	20	11,6
Sex		
Male	76	43,9
Female	97	56,1
Comorbidity presence		
Yes	88	50,9
No	85	49,1
Number of comorbidities		
1	70	79,6
2	14	15,9
> 2	4	4,5
Type of comorbidities		
Hypertension	32	28,6
Diabetes Mellitus	28	25
Cardiovascular Disease	8	7,1
COPD	12	10,7
Asthma	9	8
Kidney Failure	5	4,5
Hepatic Cirrhosis	1	0,9
Drug-Induced Hepatitis	1	0,9
Tuberculosis	10	8,9
Pregnant	6	5,4
The Severity of chest radiography features		
Normal	84	48,6
Mild	48	27,7
Moderate	30	17,3
Severe	11	6,4

subject characteristics collected were age, sex, comorbidity presence, the number of co-morbidities, comorbidity type, and severity of chest radiography features (Table 1). The average age was 43,55 years, ranging from 20-89 years.
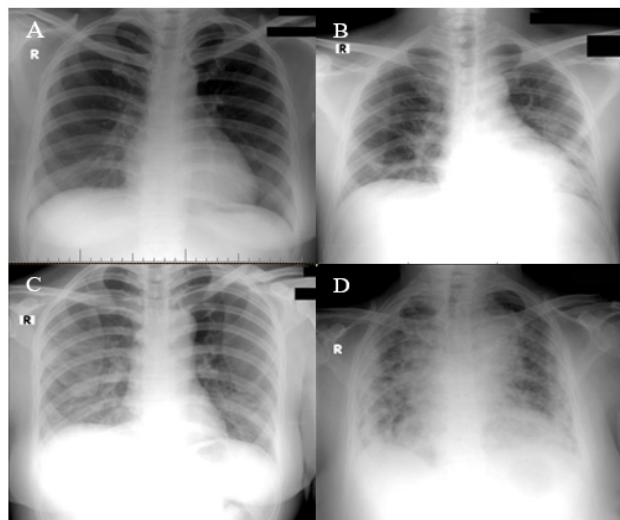

Figure 1. The severity of Chest Radiography Features. (A) 35-year-old female acquired seven days after symptom onset with a normal chest radio-graph. (B) 45-year-old female acquired 14 days the symptom onset, showing ground-glass opacity on peripheral of the lungs and consolidation with mild severity. (C) 45-year-old male acquired nine days after the symptom onset, showing ground-glass opacity on both lung fields, with moderate severity. (D) 66-year-old female acquired 14 days after symptom onset, showing diffused extensive consolidation on both lung fields, with severe severity.

Table 3. Distribution of Chest Radiography Features Based on the Type of Comorbidities

Type of Comorbidities	The Severity of Chest Radiography Features			
	Normal	Mild	Moderate	Severe
	n	n	n	n
None	51	25	8	1
1	28	17	18	7
2	4	6	2	2
>2	1	0	2	1

Relationship between Age and Chest Radiography Features

In the Chi-Square, obtained an expected count result of less than five, excessing 20%, which is 25%. It indicates that the Chi-Square requirement was not fulfilled. Therefore, another alternative test was performed in a 3x4 table that merges the cells into a 3x3 table. There was a significant relationship found between age and severity of chest radiography features in COVID-19 confirmed patients ($p < 0,001$) with a moderate level correlation (C/Cmax = 0,478). This result is shown in Table 4.

Relationship between Sex and Chest Radiography Features

In the Chi-Square, the relationship between sex and chest radiography features in COVID-19 confirmed patients at Dr. Soebandi General Hospital obtained an expected

Table 2. Distribution of Chest Radiography Features Based on the Number of Comorbidities

Type of Comorbidities	The Severity of Chest Radiography Features			
	Normal	Mild	Moderate	Severe
	n	n	n	n
None	51	25	8	1
Hypertension	11	9	7	5
Diabetes Mellitus	7	7	8	6
Cardiovascular Disease	2	1	4	1
COPD	6	4	1	1
Asthma	7	1	1	0
Kidney Failure	2	1	1	1
Hepatic Chirrhosis	0	1	0	0
Drug Induced Hepatitis	0	1	0	0
Tuberculosis	1	3	5	1
Pregnant	3	1	2	0

Table 4. Correlation between Age with Severity of Chest Radiography Features

Age (years)	The Severity of Chest Radiography Features			Total	P- value	C/Cmax
	Normal	Mild	Moderate-Severe			
20-39	47 (74,60%)	10 (15,87%)	6 (9,52%)	63(100%)	< 0,001	0,478
40-59	30 (33,33%)	34 (37,78%)	26 (28,89%)	90 (100%)		
≥ 60	7 (35,00%)	4 (20,00%)	9 (45,00%)	20 (100%)		
Total	**86**	**47**	**40**	**173**		

count less than five of 12.5%. It shows that the Chi-Square requirement was fulfilled. There was no significant relationship found between sex and severity of chest radiography features

old for females and 45 years old for males. There were 89/173 (51.4%) COVID-19 patients with pneumonia illustrated in the thorax image. To the best of our knowledge, this

Table 5. Correlation between Sex with Severity of Chest Radiography Features

Sex	The Severity of Chest Radiography Features				Total	P-value
	Normal	Mild	Moderate	Severe		
	n	n	n	n		
Male	35 (46,05%)	23 (30,26%)	11 (14,47%)	7 (9,21%)	76 (100%)	0,414
Female	49 (50,52%)	25 (25,77%)	19 (19,59%)	4 (4,21%)	97 (100%)	
Total	**84**	**48**	**30**	**11**	**173**	

in COVID-19 confirmed patients (p = 0,414), with details as shown in Table 5.

Relationship between Comorbidity and Chest Radiography Features

In the Chi-Square, the relationship between comorbidity and chest radiography features in COVID-19 confirmed patients at Dr. Soebandi General Hospital obtained an expected count result less than five of 0%. It shows that the Chi-Square requirement was fulfilled. There was a significant relationship found between comorbidity and severity of chest radiography features in COVID-19 con-

study is the first to examine the relationship between age and comorbidity with the severity of chest radiograph using the BSTI guideline in an Indonesian population with confirmed COVID-19.

The bivariate analysis shows that age and commodity were the risk factors highly related to the severity of chest radiography features. In line with various studies, the current study found that older age was correlated with higher severity of pulmonary disorders. A study by Borghesi et al.[8] obtained a p-value = 0.0001, showing a correlation between age groups based on sex with the severity of chest radiograph based on the Brixia score in

Table 6. Correlation between Comorbidity with Severity of Chest Radiography Features

Comorbidity Presence	The Severity of Chest Radiography Features				Total	P-value	C/Cmax
	Normal	Mild	Moderate	Severe			
	n	n	n	n			
Yes	33 (37,50%)	23 (26,14%)	22 (25,00%)	10 (11,36%)	88 (100%)	< 0,001	0,431
No	51 (60,00%)	25 (29,41%)	8 (9,41%)	1 (1,18%)	85 (100%)		
Total	**84**	**48**	**30**	**11**	**173**		

firmed patients (p < 0,001) with a moderate level correlation (C/Cmax = 0,431). This result is shown in Table 6.

Discussions

This study acquired an insignificant median result in each sex, namely 42.5 years

COVID-19 patients. This study reveals a positive linear correlation between age groups and severity of chest radiograph based on the Brixia score. The higher the age, the higher the Brixia score, which indicates the severity of chest radiography features in COVID-19 confirmed patients. Furthermore, a study

on 338 COVID-19 patients in New York by Toussie et al.[9] obtained a p-value = 0.004, indicating a relationship between age and severity score of chest radiograph based on three-zone classifications of each lung field. It is due to a decreased immune system, changes in the respiratory system, and a sedentary lifestyle that makes the resistance to the virus weaken so that the virus can attack other tissues. As a result, it will cause clinical symptoms and affect the chest radiography features and outcome.[10,11]

This study found that most of the sex confirmed for COVID-19 was female. Based on the theory, males are more susceptible to COVID-19 than females. This is because the amount of angiotensin-converting enzyme 2 (ACE2) is more in males, a disproportionate mortality ratio in males is associated with higher pre-existing comorbidities (ischemic heart disease, hypertension, diabetes, chronic kidney disease, chronic lung disease, and cancer), higher risk behaviors (smoking and alcohol use), and occupational exposure. Another behavioral and social difference is that females are more likely to follow hand hygiene practices and seek preventative care than males. Then, males may be worse at implementing medical advice and less punctual. In addition, females generally have stronger innate and adaptive immune responses than males because X chromosome is associated with immunity.[12,13] However, a study by Samudra and Setyonaluri[14] found that females in Indonesia have higher working mobility and use more public transportation than males. Hence, females are more susceptible to COVID-19 than males since they mostly do not have personal vehicles. The sex factor obtained an insignificant relationship based on the bivariate analysis. It follows a study by Reeves et al.[15] with a p-value = 0.245, indicating an insignificant relationship between sex and severity score of chest radiograph based on two-zone classifications of each lung field.

The most common comorbidities in the current study were hypertension, diabetes, and COPD. It strengthens a study by Rozaliyani et al.,[16] which asserted that hypertension and diabetes are the most common comorbidities in Jakarta. The comorbidity presence factor had a significant relationship with the severity of chest radiography features. There is no study correlating the comorbidity presence and the severity of chest radiograph. However, a study by Toussie et al.[9] stated a specific comorbidity relationship, namely Human Immunodeficiency Virus (HIV) with severity

score based on three-zone classifications of each lung field, obtained a p-value = 0,04. In older people with comorbid conditions, the number of MicroRNAs decreases. MicroRNA responses are specific to each virus. MicroRNA works to reduce viral replication inside host cells in COVID-19.[17]

This study has limitations. First, obesity was not included as comorbidity due to the incomplete height data, and therefore, the Body Mass Index (BMI) fails to be calculated. Second, this study used a cross-sectional design that only observed the risk factors and effects once. Thus, a cross-sectional design is the weakest study design since it cannot observe which variable occurs first. Last, the results were sourced from one hospital network, which may not be representative of patients from Jember or other regions. Further research with a cohort or case-control design is required to minimize biases during data collection.

Conclusion

Age and comorbidity were found to be significant risk factors for the severity of chest radiograph in COVID-19 with a moderate correlation. However, no correlation was found between sex and chest radiography features.

Conflicts of Interest

The authors confirmed no conflict of interest.

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