

Correlation of chest radiography of confirmed COVID-19 patients with comorbid hypertension and diabetes mellitus



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ABSTRACT

Introduction: Several studies showed 324 severe cases of COVID-19 and 1234 mild cases with the highest comorbidities of Hypertension, Diabetes Mellitus, Chronic Obstructive Pulmonary Disease (COPD), and Cardiovascular disease. These comorbid factors lead to a poor prognosis in COVID-19. Chest radiography is an important modality as one of the parameters that can indicate the severity of COVID-19. This study aims to determine the relationship between Covid-19, comorbid Hypertension, and Diabetes Mellitus with chest radiography.

Method: This research is analytic observational with cross-sectional, relationship between Covid-19 patients with comorbid Hypertension and Diabetes Mellitus with chest radiography (type, location, and extent of lesions) that Modified Chest X-Ray Scoring System in Evaluating Severity of COVID-19 Patient in Dr. Soetomo General Hospital Surabaya, Indonesia in 2021, COVID-19 radiology category. The data from PKU Muhammadiyah Gamping Hospital, Yogyakarta retrospectively from the medical records of Covid-19 patients who met the inclusion and exclusion criteria. Chi-Square analyzed the results variables with unpaired categorization.

Result: Most of the respondents who had comorbid diseases had moderate chest radiological features (65.4%) and those who did not have comorbid diseases had mild chest radiological features (71.9%), the results of chi-square data analysis between variables were $p = 0.000$.

Conclusion: The results of data analysis showed that comorbid diseases had a significant relationship with chest radiography in patients with confirmed COVID-19. The novelty of this study is the importance of radiological modalities as one of the parameters that can indicate the severity of Covid-19 patients with comorbidities.

Keywords: chest radiography, comorbidities, COVID-19, diabetes mellitus, hypertension.

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INTRODUCTION

Corona Virus Diseases 2019 (COVID-19) is the latest infectious disease whose transmission can occur between humans and humans (human-to-human transmission). The disease was originally known as the 2019 novel coronavirus (2019nCoV). Then, on February 11, 2020, World Health Organization (WHO) announced a new name, namely Coronavirus disease (COVID-19), which is caused by the severe acute respiratory syndrome virus Coronavirus2 (SARSCOV2) which is an infectious disease and has similar properties to the SARS virus.^{1,2} Several factors that affect the severity of COVID-19 are decreased body resistance, increasing age, and comorbid disease factors such as Hypertension,

Diabetes Mellitus (DM), Chronic Obstructive Pulmonary Disease (COPD), and Cardiovascular disease. These comorbidities are a major risk factor in patients with COVID-19. Previous studies have found that patients with comorbid COVID-19 have a poor prognosis. Based on six studies, including 324 severe cases and 1234 non-severe cases, it was found that the highest comorbidities in COVID-19 patients were Hypertension (15.80%), DM (9.40%), COPD, and Cardiovascular Disease.^{3,4}

A person with a comorbid disease generally has a weak immune system so the COVID-19 virus can easily damage organs that can lead to death. Hypertension is a disease defined as a persistent increase in blood pressure.⁵ A person is considered to have hypertension or high blood

pressure if the blood pressure reaches 140/90 mmHg. Hypertension is one of the most common comorbidities in COVID-19 patients. There are about 15% of comorbid hypertension found in COVID-19 patients. As many as 2.3% of COVID-19 patients died because of their comorbidities. A meta-analysis of 8 trials covering 46,248 cases of COVID-19 found that the prevalence of mortality was also influenced by the presence of congenital disease in patients. The prevalence was 10.5% in cardiovascular patients, 7.3% in diabetic patients, 6.3% in COPD patients, 6% in hypertensive patients and 5.6% in cancer patients.⁶

Patients with COVID-19 are usually most commonly found on chest radiography or Chest X Ray (CXR) and Computed Tomography Scanning (CT-

Scan) with lung consolidation, followed by ground glass opacity. Patients with COVID-19 usually have bilateral ground-glass appearances or lung opacity in more than one lobe. Patients with severe clinical symptoms usually have opacity in two lobes of the lung, whereas patients with mild clinical symptoms usually have opacity in one lung lobe. Lesions in the lungs of COVID-19 patients tend to be bilateral, affecting 2 lung fields.⁷

The most common site of the lesion is the peripheral zone, the lower zone and the majority have bilateral lung involvement.⁸ This study aims to determine the relationship between comorbid hypertension and DM in COVID-19 patients with chest radiography. Based on the location, extent, and type of lesion. We need to know the characteristics of the chest radiography of COVID-19 patients to provide information on the severity of lung damage in COVID-19 patients with comorbid hypertension and DM, which often occur in the community. This study aims to determine the relationship between Covid-19, comorbid Hypertension, and Diabetes Mellitus with chest radiography.

METHOD

This research method is an observational quantitative analytic study with a cross-sectional method. The research data is secondary data from medical records of confirmed COVID-19 patients at PKU Muhammadiyah Gamping Hospital, Yogyakarta from January to May 2021. This research has passed the approval of the Ethics Committee No. 006/EC-EXEM-KEPK FKIK UMY/II/2021. The number of research subjects is 120 subjects. Inclusion criteria: (1). Patients aged >30 years who have comorbid hypertension with confirmed COVID-19 and have a chest radiograph, (2). Patients aged >30 years who have comorbid DM with confirmed COVID-19 and have a chest radiograph. The exclusion criteria were: (1) Chest radiography showed a mass, a picture of tuberculosis both active and passive, and the presence of diffuse abnormalities in the thorax such as massive pleural effusion. (2). Chest radiography results (expertise) were available, but no chest radiographs were available. The independent variables of this study were comorbid hypertension

and DM.

RESULT

The results of the recapitulation of age data can be classified as most aged 56-65 years, namely 37 people (30.9%), and at least 30-35 people, namely 10 people (8.3%). The research subjects were 63 men (52.5%) and 57 women (47.5%).

Table 1 shows that the research subjects who have comorbidities are 50% and those who do not have comorbidities are 50% and the radiological picture is in the mild category of 47.5%; moderate category of 45.33%, and with a severe category of 9.16%. These data indicate that based on the chest radiography results, COVID-19 patients have the highest degree of the radiographic lesion in the mild category.

Table 2 shows that COVID-19 patients with no comorbidities with chest radiography in the mild category are 68.3%, the moderate category is 30% and the mild category is 1.67%. COVID-19 patients with comorbid DM with a chest radiograph in the mild category are 11.7%, the moderate category is 28.3%, and the severe category is 6.7%. COVID-19 patients with comorbid hypertension with a chest radiograph in the mild category are 13.3%, the moderate category is 20% and the severe category is 5%. COVID-19 patients with comorbid DM and hypertension with a chest radiograph in

the mild category are 1.6%, the moderate category is 8.3% and the severe category is 5%.

Table 1 shows COVID-19 patients who have comorbidities with a mild chest radiograph of 28.1%, COVID-19 patients who do not have comorbidities with a mild chest radiograph of 71.9%. Comorbid COVID-19 patients with moderate chest radiographs were 65.4%, while COVID-19 patients who did not have comorbidities with moderate chest radiography were 34.6%. Comorbid COVID-19 patients with severe chest radiography were 90.1%, while COVID-19 patients who did not have comorbidities with severe chest radiography were 9.1%. The Chi-Square test results obtained a p-value of 0.000 ($P>0.05$), which means that comorbid disease has a significant relationship with chest radiography in COVID-19 patients at PKU Muhammadiyah Gamping Hospital.

DISCUSSION

Several references state that the risk factors for morbidity and mortality in COVID-19 patients are influenced by several factors, including age, male gender, comorbid factors such as hypertension, diabetes mellitus, kidney failure, clinical diagnosis of pneumonia, signs or symptoms of more than 3 (multiple). Patients with more than one comorbid disease have a six-fold risk

Table 1. Data classification of research subjects with comorbid hypertension and DM.

Variable	Category	Frequency	%
Comorbid	Comorbid	60	50%
	No Comorbid	60	50%
Total		120	100%
Chest Radiography future	Mild	57	47,5%
	Moderate	52	43,33%
	Severe	11	9,16%
Total		120	100%

Table 2. Distribution of comorbid and non-comorbid features on chest radiographs.

No.	Comorbid	Chest Radiography features			Total
		Mild	Moderate	Severe	
1	No Comorbid	41	18	1	60
2	With Comorbid				
	Diabetes Melitus	7	17	4	28
	Hypertension	8	12	3	23
	Diabetes-Hypertension	1	5	3	9

Table 3. The results of the Chi-square analysis of the relationship between comorbid diseases and chest radiography in COVID-19 patients.

Variable	Categori	Comorbid				Score p
		Y		Today		
		n	%	n	%	
CXR	Light	16	28,1%	41	71,9%	0,00
	Medium	34	65,4%	18	34,6%	
	Critical	10	90,1%	1	9,1%	

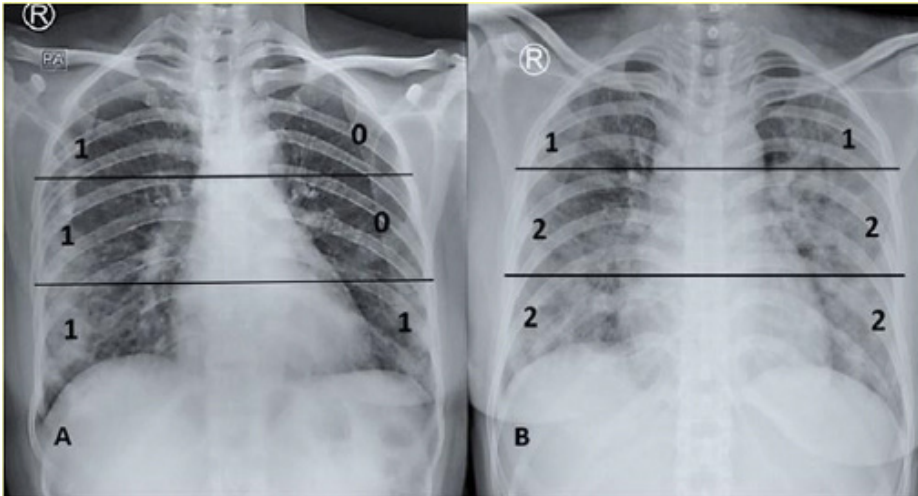
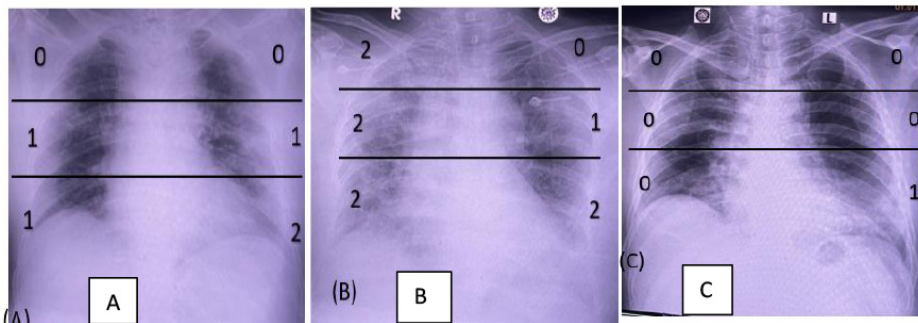


Figure 1. Illustration of two cases of implementing Chest X Ray Assesment System Dr. Soetomo on the AP projection (Modified Chest X-Ray Scoring System). (A) The total score calculated from the 6 chest divisions was 4, classified as a mild severity score. (b) The total score calculated from the 6 chest divisions was 9, classified as a severe severity score. Scoring Radiology Category Covid-19 System Dr Soetomo have 3 category for assessment the lesion of the lung, 0 : normal, 1: infiltrates or concolidation (< 50%), 2 : Infiltrates or concolidation (> 50%). Scoring this evaluate of chest are Mild : 1-4, Moderate : 5-8, and Severe : 9 -12.⁹



Source: Primary Data of Patient with Covid-19 at PKU Muhammadiyah Gamping Hospital, 2021

Figure 2. Three cases were obtained by Dr. Soetomo Modified Scoring System at the PKU Muhammadiyah Gamping Hospital patient. (A) The total score viewed from the 6 chest regions was 5, categorized as a moderate severity score in comorbid patients. (B) The total score viewed from the 6 chest regions was 9, categorized as a severe severity score in comorbid patients. (C) The total score viewed from the 6 chest regions was 1, categorized as a non-comorbid patient's mild severity score.⁹

of death compared to patients with one or no comorbid diseases.^{9,10} Ages that have a high risk for the incidence of COVID-19 are age > 50 years and age < 5 years. This age factor is related to the body's defense factors in old age and infants tend to be more susceptible to disease.¹⁰

The gender that tends to be at risk with the incidence of COVID-19 is male. because the mobilization of men is higher than that of women, it is easier to contract COVID-19. Another risk factor tends to be more COVID-19 patients in men (Relative Risk 1.86) or 1.86 times compared women.¹⁰ This is one of the reasons smokers have a higher risk factor for the incidence of COVID-19 than nonsmokers, while smokers are mostly male.^{11,12}

Table 1 shows that comorbid COVID-19 patients had a significantly higher chest radiographic severity score than patients without comorbidities. The results of the Chi-Square test evidence this obtained a p-value of 0.000 (P < 0.05). The study results are in line with studies that found that the severity of radiological features of COVID-19 patients with comorbid diseases was higher than that of patients without comorbidities. Patients with comorbidities had more GGO (Ground Glass Opacity) and consolidation than patients without comorbid.¹³

Table 3 shows that COVID-19 patients with comorbid diseases have more moderate chest radiographs (Scores of Severity 5-8), whereas COVID-19 patients without comorbid diseases have more mild chest radiographs (Severity Scores 1-4). People of all ages with a history of chronic health problems or serious comorbid illnesses are more susceptible to COVID-19. This is because these comorbidities will affect immunological disorders that can cause a cytokine storm that can damage lung tissue and fibrosis, causing functional disability.¹⁴

The research that has been carried out has found that COVID-19 patients who have comorbid diseases have more chest radiographs in the moderate category as much as 65.4% (there are infiltrates or consolidation of less than 50%). Meanwhile, COVID-19 patients without the comorbid disease had more mild chest radiographs than 71.9% (no involvement).

Diabetes Mellitus comorbid factors experienced by COVID-19 patients are serious risk factors and must be considered. This is to the meta-analysis research conducted, which found that the prevalence of DM patients hospitalized due to COVID-19 was 14.34%.¹⁶ COVID-19 patients with congenital diseases such as DM have a 2 times greater risk of developing more severe symptoms or critical illnesses that require treatment in special rooms or intensive care.^{17,18} Inpatients with congenital diseases such as DM risk dying three times from COVID-19. These results indicate an association between DM and poor prognosis and increased mortality. Therefore, intensive attention should be given to DM patients. The high morbidity and mortality in diabetic patients are caused by hyperglycemia, low immune function, and vascular complications. However, few studies have analyzed the effect of hyperglycemia on prognosis. In diabetes, the immune system is weakened, causing a cytokine storm that can damage lung tissue and fibrosis, causing functional disability.^{17,18}

A single-center retrospective study conducted in Korea reported that age was an independent risk factor for more severe outcomes in patients with diabetes. At the initial check of HbA1c and the administration of anti-diabetic drugs, it did not affect the results of COVID-19. Because baseline HbA1c does not account for fluctuations in blood glucose levels, glycemic variability is important for evaluating overall glycemic control. Due to the study's retrospective nature, it is impossible to determine whether intensive management of hyperglycemia improves COVID-19 severity or whether less severe COVID-19 states lead to good glycemic variability. Therefore, further analysis of the influence of clinical parameters such as duration of diabetes, degree of hyperglycemia, medication, and comorbid diabetes complications.¹⁹

Table 2 comorbid factors High blood pressure (hypertension) is one of the most severe comorbidities in COVID-19 patients. Several recent studies reported that among 3,017 hospitalized COVID-19 patients, 53% were diagnosed with hypertension.²⁰ Another study stated that ACEI/ARB drugs given to hypertensive

patients increased ACE2 expression in the lungs. The role of ACE2 is opposite to that of ACE. ACE2 can hydrolyze angiotensin I (Ang I) to produce the peptide angiotensin (1-7), resulting in vasodilation and lowering blood pressure. Thus, hypertensive patients who have taken ACEI/ARB may have increased levels of mRNA and ACE2 protein expression in the lungs, making them more susceptible to SARS-CoV-2 entry and the development of severe COVID-19 pneumonia. It was found that patients with acute respiratory distress syndrome (ARDS) treated with rhuACE2 injections had a rapid decrease in Ang II levels and an increase in Ang1-7 levels. Downregulation of ACE2 leads to an imbalance of ACE/Ang II and ACE2 and Ang II activity in the renin-angiotensin-aldosterone system (RAAS) is increased due to a lack of antagonism. Ang II mediates increased permeability of pulmonary vasculature by binding to AT1 receptors, and may also cause pulmonary vasculature to contract, resulting in elevation of hydrostatic pressure and pulmonary edema.^{20,21} The importance of this RAAS activation in developing pulmonary edema in COVID-19 remains unknown. First, the viral infection itself, including COVID-19, can directly cause the destruction of type I and type II alveolar epithelial cells, and the capillary-alveolar membrane may be insufficient. Second, an exaggerated inflammatory reaction due to infection can also directly impair the integrity of the pulmonary capillary endothelial barrier, resulting in a large increase in pulmonary vascular permeability and pulmonary edema that appears as a ground glass shadow on chest CT.²¹ If so, it is unknown whether the downregulation of ACE2 plays a key role in the impact of pulmonary edema and disease severity.²²

The age factor is a factor that must be considered for patients infected with COVID-19. The median age of patients who experience more COVID-19 is 56-65 years. Judging from the data, the highest number of patients experiencing COVID-19 are adults, namely 56-65 years, so old age can be said to be a risk factor for COVID-19 morbidity. The percentage of COVID-19 deaths is increasing with age, with the youngest patients being 5% to the

oldest at 55%.²³

Gender is a risk factor for mortality in COVID-19 patients, this is obtained because men are more infected with COVID-19 than women. The reason is that there are basic differences in the immunological system in men and women, in addition to lifestyle differences in men and women, and the prevalence of smoking there are also differences in men and women. Women have a higher prevalence of cure compared to men. Higher mortality rates are associated with higher chronic comorbidities in men, eg disease, hypertension, pulmonary disease, and smoking.²⁴

General features Chest radiography in COVID-19 is pneumonia with findings of ground-glass opacity (GGO), consolidation, or both, both focal and multifocal. Thus, although sometimes normal pulmonary features are found in patients with COVID-19, chest X-rays still have a special role in evaluating COVID-19. A retrospective study reported that the most common features of chest X-ray examination of COVID-19 patients were consolidation of 59% and ground-glass opacity (GGO) of 41%, with a peripheral or posterior distribution, especially in the lower lobes. In addition, GGO can also be found with inter/intra-lobular, peripheral, and basal septal thickening. Even in asymptomatic COVID-19 patients, disease progression from focal unilateral to diffuse ARF and consolidation was observed. Pleural effusions are rare and may be a predictor of poor prognosis if found.²⁵

Age and comorbidities are associated with increased opacities on chest X-rays. Increased cloudiness is associated with increased rate and acuity of care, manifesting as ETT or central line placement.²⁶ Chest radiography analysis in acute COVID-19 outbreaks showed that the severity of cloudiness was associated with advanced age, comorbidities, and acuity of care. A small series from the initial time point of the outbreak.

Italy demonstrated that chest radiography can inform the triage and management of COVID-19 patients and attempt to predict outcomes and prognosis based on clinical input, including imaging.²⁷

CONCLUSION

Based on the results of the analysis and discussion, it can be concluded that most of the respondents who have comorbid diseases have a Chest radiography feature in the moderate category (65.4%) and most of the respondents who do not have comorbid diseases have a Chest radiography feature in the mild category (71.9%). The results of data analysis showed that Comorbid Diseases had a significant relationship with Chest radiography in confirmed COVID-19 patients at PKU Muhammadiyah Gamping Hospital. This is evidenced by the results of the Chi-Square test obtained a p-value of 0.000 ($P < 0.05$).

FUNDING

No additional funding or third party sponsor involved during all phase of this study

CONFLICT OF INTEREST

The conflict of interest in this research is irrelevant because the research was conducted by making ethical clearance and with the permission of the hospital director. This study did not mention the patient's identity so that confidentiality is maintained. This study aims to see the comorbid factors of hypertension and DM that can aggravate the severity of radiological images based on available data, without being manipulated and without the author's personal interest.

ETHIC APPROVAL

The authors conducted this study after obtaining an ethics certificate with No. 006/EC-EXEM-KEPK FKIK UMY/II/2021 from the Ethics Commission of The Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta

AUTHOR CONTRIBUTION

AM and Annisa together conceptualize the study. AM and Annisa constructed the study design, conducted the literature search, collected and analyzed the data. AM prepared the manuscript, conducted editing and review. All authors agree for the final version before publication

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