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Clinical Features, Imaging, Laboratory Result, and Severity of COVID-19 Patients in Referral Hospital

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Abstract

BACKGROUND: COVID-19 pandemic became a global health problem due to the high number of cases and no specific treatment. Furthermore, the diagnosis was difficult due to limited publication data and diagnostic tests.

AIM: The aim of this study was to determine the demographics, clinical features, laboratory results, radiological results, and factors related to the severity of COVID-19 at a referral hospital.

METHODS: A descriptive analytic study of confirmed COVID-19 patients was conducted during March–October 2020. Data were collected from the medical records to determine the patient demographics, clinical symptoms, comorbidities, laboratory, chest X-ray, and first illness severity at 24 h of treatment.

RESULTS: There were 79 (59%) male and 55 (41%) female patients during the study. The clinical symptoms were fever 103 (77%), cough 100 (75%), shortness of breath 88 (66%), comorbidities of diabetes mellitus 18 (13%), hypertension 24 (18%), and heart disease 20 (15%). The patient's laboratory profiles were lymphopenia 85 (63%) and increased C-reactive protein 82 (61%). The radiology imaging of the patients was mostly atypical of COVID-19. Factors that influence the severity of COVID-19 are age, comorbid diabetes, and hypertension

CONCLUSION: Most cases with severe symptoms are old age, a history of comorbid diabetes mellitus and heart disease, and abnormal laboratory results.

Introduction

Novel coronavirus 2019 (COVID-19) was first detected in Wuhan, Hubei, China, at the end of 2019. The diseases are caused by the severe acute respiratory syndrome coronavirus 2 [1]. It was considered a pandemic by the WHO on March 11, 2020, since the confirmed cases of COVID-19 in 223 countries worldwide on October 1, 2021, amounted to 233,503,524 with 4,777,503 deaths [2]. The number of confirmed cases in Indonesia from January 3, 2020, to October 1, 2021, was 4,216,728, with 142,026 deaths, which became the highest number of cases in Southeast Asia [2], [3]. Indonesia was predicted to have more cases than what was recorded due to problems with the provision of diagnostic facilities and limited health facilities [4].

According to several studies, the characteristics of COVID-19 patients are primarily males (48.4% in China, 60.3% in New York, 82% in Italy, and 56.2% in California). These findings also happen in Jakarta; men are more affected mainly by COVID-19 than women with a percentage of 53.3% [4]. Another study also reported that the prevalence of COVID-19 in Southeast Asia was dominated by men, with a ratio of 3.95, especially household and industrial sector workers [5], [6]. The high number of confirmed cases in men is related to men's activities to leave work, and biologically, men are more susceptible to being infected with the virus [4]. The median age of patients with confirmed COVID-19 in Northern California and Italy is over 60 years [7], [8].

The most common clinical symptoms are dry cough, fever, shortness of breath, weakness, body aches, abdominal pain, vomiting, and loose stools [9], [10]. The clinical manifestations of COVID-19 vary and can be determined by the interaction between the agent factors or the cause of infection, the environment, and the host [11]. Other factors that cause the diversity of clinical manifestations are different viral variants in each patient [12], [13]. Enforcement of the diagnosis in addition to clinical symptoms also uses molecular examinations in the form of rapid polymerase chain reaction (PCR) tests, laboratories, and radiological examination in the form of a chest X-ray or computed tomography (CT) scan. Blood tests included leukocytes, lactate dehydrogenase, C-reactive protein, creatine kinase (CK MB and CK MM), SGOT, SGPT, D-dimer, and abnormalities of coagulation factors. The radiologic examination that is often done

is a chest X-ray, which is characterized by bilateral alveolar opacity [7]. A comprehensive examination can predict the patient's prognosis. One factor that influences the progression or severity of COVID-19 is comorbidity. Patients with hypertension, diabetes mellitus, cardiovascular, or cerebrovascular disease have worse symptoms or outcomes than those without comorbidities [1], [7], [8]. Based on the current literature searches, data on the characteristics of COVID-19 in Indonesia have not been widely reported, thus making this study necessary to be considered in the diagnosis and management of COVID-19 patients.

This study aimed to determine the demographics, clinical features, laboratory results, imaging, and factors related to the severity of COVID-19 at a referral hospital in Semarang.

Methods

A descriptive study was conducted at Sultan Agung Islamic Hospital on all patients diagnosed with COVID-19 based on real-time PCR results using nasopharyngeal swabs from March to October 2020. The data were collected from the patient's medical records review, books and reports of doctors who provide services, and case reports. The dependent variable in the study was the patient's status, including recovered and dead patients. While, the independent variables were patient demographics, comorbidities, clinical manifestations, laboratory results, and patient radiology results. Laboratory data and imaging were the results of patient examinations on the 1st day of treatment or the first 24 h of hospitalization.

Statistic analysis

Data analysis used IBM SPSS statistics (Version 26). Descriptive data analysis (frequency and standard deviation) and analytical statistics were used to analyze the data. The Kolmogorov-Smirnov normality test showed that the data were not normal. The homogeneity test showed that the data were not homogeneous. Logistic regression was used to determine the relationship between patient characteristics and the severity of the disease.

Ethical considerations

This research has been approved by the Health Research Ethics Committee of RSI Sultan Agung No. 29/EC/KEPK/2020.

Results

Baseline characteristics

One hundred and eighty-five patients with a COVID diagnosis underwent an examination at the RSISA from March to October 2020. A total of 51 samples were excluded due to incomplete data; hence, we got 134 samples of 96 inpatients and 38 outpatients. The characteristics of these patients are shown in Table 1.

Table 1: Characteristics of COVID-19 patients

Variable	Improvement (n = 110), n (%)	Death (n = 24), n (%)	p CI 95% (lower–upper)
Gender			
Male	61 (77.2)	18 (22.8)	0.194 (0.173–1.428)
Female	49 (89.1)	6 (10.9)	
Age			
20–29	19 (100)	0	0.021 (1.123–4.250)*
30–39	29 (93.5)	2 (6.5)	
40–49	19 (95.0)	1 (5.0)	
50–59	30 (81.1)	7 (18.9)	
≥ 60	13 (48.1)	14 (51.9)	
Comorbidities			
DM	5 (27.8)	13 (72.2)	0.000 (0.008–0.176)*
HT	16 (66.7)	8 (33.3)	0.943 (0.219–4.114)*
Heart disease	11 (55.0)	9 (45.0)	0.005 (0.028–0.536)*
Lymphocyte			
High	6 (85.7)	1 (14.3)	0.484 (0.072–3.481)
Normal	41 (97.6)	1 (2.4)	
Low	63 (74.1)	22 (25.9)	
Neutrophil			
High	46 (73.0)	17 (27.0)	0.743 (0.163–3.648)
Normal	55 (90.2)	6 (9.8)	
Low	9 (90.0)	1 (10.0)	
CRP			
High	61 (74.4)	21 (25.6)	0.306 (0.452–12.502)
Normal	49 (94.2)	3 (5.8)	
Imaging			
Typical	26 (19.4)	15 (11.2)	0.15 (1.652–111.545)
Atypical	53 (39.6)	7 (5.2)	0.295 (0.367–27.394)
Indeterminate	4 (3.0)	1 (0.7)	0.200 (0.356–139.081)
Negative	27 (20.1)	1 (0.7)	0.54 (0.17–1.037)
Patient's status, total (%)			
Improvement	110 (82)		-
Death	24 (18)		-

*Significant. DM: Diabetes mellitus, HT: Hypertension, CRP: C-reactive protein, p: Logistic regression value test, CI: Confidence interval.

Based on Table 1, the characteristics of COVID-19 patients, out of a total of 134 patients in this study, were dominated by 79 male patients, while 55 were female. Patients who came to health facilities were alert (97.8%), and only 0.7% of patients who came to health facilities were apathetic, asleep, or stuporous. The patients aged mostly 50–59 years (27.6%), followed by 30–39 years (23.1%), and the rest ranged in age from 20–29 years, 40–49 years to 60 years. The COVID-19 patients in this study had various comorbidities that accompanied them so that they could aggravate the patient's clinical condition. The most comorbid patients in this study were hypertension 17,9%, heart diseases such as coronary heart failure (CHF), ischemic heart disease (IHD), and hypertensive heart disease (HHD) 14,9%, and diabetes mellitus 13,4%.

The imaging characteristics of COVID-19 patients were divided into 4 categories: typical, atypical, indeterminate, and negative. The atypical category is marked when the patient has a typical radiological picture of COVID-19: ground-glass opacity and/or consolidation located at the periphery of both lung

Table 2: Laboratory result

Laboratory test	High (%)	Normal (%)	Low (%)
Hemoglobin	21 (15.7)	100 (74.6)	13 (9.7)
Hematocrit	30 (22.4)	97 (72.4)	7 (5.2)
Thrombocytes	7 (5.2)	126 (86.6)	11 (8.2)
Leukocytes	24 (17.9)	107 (79.9)	3 (2.2)
Basophil	-	134 (100)	-
Neutrophil	63 (47)	61 (45.5)	10 (7.5)
Lymphocyte	7 (5.2)	42 (31.3)	85 (63.4)
Monocyte	44 (32.8)	88 (65.7)	2 (1.5)
CRP	82 (61.2)	52 (38.8)	-

CRP: C-reactive protein.

fields and/or subpleural. In comparison, the atypical picture is marked when the radiological picture is lobar or segmental consolidation in only one lung field, with distribution in the middle similar to bacterial pneumonia. The indeterminate category is a radiological picture not specific to COVID-19 in both the form of ground-glass opacity/non-segmental consolidation in one lung or lobar or multifocal with a distribution not typical of COVID-19. The negative category is a radiological picture that does not indicate the presence of pneumonia in the lungs. This study had an atypical radiological picture category of 44.8% or 60 patients. Most of the study's patients (82%) recovered after being treated. Patients who died after treatment in health facilities were 18% or 24, and these patients had several comorbidities that could aggravate the patient's condition.

Several variables in this study, followed by logistic regression analysis, included gender, age, comorbid diabetes mellitus, comorbid hypertension, cardiac comorbidity, and laboratory results (lymphocyte levels, neutrophil levels, and C-reactive protein [CRP] levels). Of the variables, there were three predictive variables for the risk of mortality in patients with COVID-19 in this study, namely, age (95% confidence interval [CI]: 1.189–4.278, p = 0.013), comorbid diabetes mellitus (95% CI: 0.008–0.151, p = 0.000), and cardiac comorbidities like CHF/IHD/HHD (95% CI: 0.027–0.463, p = 0.003).

While the patient was in treatment, the common symptoms were fever, weakness, cough, painful swallowing, runny nose, shortness of breath, nausea, vomiting, diarrhea, anosmia, ageusia, and decreased appetite. The most symptoms that patients complained about were fever and cough, which were

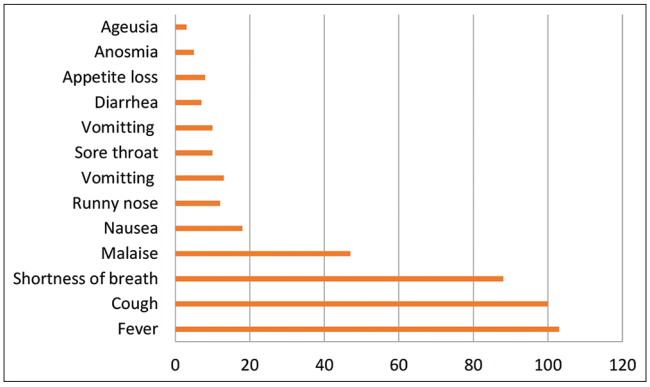

Figure 1: Clinical features.

76.8% and 74.6%, followed by shortness of breath at 65.7% (Figure 1).

Based on the hemoglobin level, 74.6% of treated patients had normal Hb levels (11.7–15.5g/dL), while patients who had low Hb (<11.7g/dL) were 9.7%, and patients who had Hb >15.5 g/dL by 15.7%. In the first 24 h of treatment, laboratory examinations showed that COVID-19 patients tended to have normal hematocrit, platelet, leukocyte, basophil, and monocyte levels. However, COVID-19 patients showed a decrease in lymphocyte levels by 63.4% and an increase in neutrophil and CRP levels (≤3mg/L) by 47% and 61.2%, respectively (Table 2).

Discussion

The results showed that a higher prevalence occurred in male patients than female. This is supported by several previous studies that state that the prevalence of COVID-19 is more prevalent in men than women [1], [8], [9]. This is because men have to go out to work; hence, the mobility of men is higher than women. According to the CDC's Morbidity and Mortality Weekly Report, the prevalence of COVID-19 patients from each age group is dominated by men. The results showed 74% of male deaths, while the number of female deaths was 26%. Differences related to sex affect the immunological response because women have an X chromosome, where the protein TLR7 is obtained. The female X chromosome 1 of 2 chromosomes is usually inactive; however, if the TLR7 gene is activated on both chromosomes, it makes the female immune response to COVID-19 stronger [10]. In addition, ACE2 expression factors related to testosterone are also the reason for the increase in the severity of the disease in men [14]. Understanding the basic mechanisms that cause women to be at lower risk of developing COVID-19 severity can be the basis for creating therapies that can modulate the male immune response to COVID-19.

The most clinical manifestations experienced by patients were fever, cough, shortness of breath, weakness, nausea, and vomiting. Other accompanying symptoms are painful swallowing, runny nose, diarrhea, and anosmia. The study results align with the previous research state that the typical symptoms of COVID-19 are fever, cough, and shortness of breath. Concomitant symptoms often experienced by patients, such as fever, muscle pain, sore throat, loss of smell, headache, myalgia, and diarrhea, have also been reported in several studies in China, India, Indonesia, and several literature [1], [9], [10], [14], [15], [16], [17], [18]. This study only recorded symptoms at the beginning of admission; hence, it could not identify the course of the disease. Whereas research evidence in China states

that COVID-19 has an incubation period of 1–14 days and usually begins with respiratory symptoms such as fever and cough [16]. The course of COVID-19 is often unpredictable because patients with severe symptoms initially only have mild symptoms such as fever and cough. Patients usually experience progressive deterioration such as shortness of breath, 7–10 days after onset of symptoms. Some cases lead to complications such as acute respiratory failure, sepsis, acute liver and kidney damage, metabolic acidosis, shock, cytokine storm, and coagulopathy [1], [9].

The patients' most common comorbidities in this study were hypertension, heart disease, and diabetes mellitus. These patients have a greater risk of disease severity than patients without comorbidities. It is explained in Table 1 that from a total of 27 patients who died, most of the patients had comorbid diabetes mellitus, hypertension, and heart disease. Research in China, California, and Indonesia states that people with comorbid hypertension and diabetes mellitus risk being infected with COVID-19 like the general population, but it more often cause severe symptoms and mortality [7], [9], [18]. The severity of COVID-19 symptoms is influenced by the affinity of the virus for ACE2, which is present in the lung, endothelial, cardiac, and renal pneumocytes [19]. The higher levels of ACE2 expression are proportional to the increased progression and mortality of COVID-19. It was reported in a study that children have a lower risk of death because they have a lower expression of ACE2 in the nasal epithelium [14], [20], more significant than other risk factors [9], [18], [21]. Patients with diabetes mellitus are mostly hypoxic and require intensive care with controlled ventilation[14], [20], [21]. The previous study stated that patients have a risk of severe symptoms if they were elderly with comorbidities such as COPD, diabetes, hypertension, and heart disease [9]. This study only identified a few comorbidities, namely, diabetes mellitus 18 (13%), hypertension 24 (18%), and heart disease 20 (15%); hence, it is not significant in the hypothesis test.

The radiological features of the patients in the study were mostly atypical. The radiological examination helps diagnose suspected COVID-19 patients and is also used to follow up on the patient's condition. The most common radiological examination is a chest X-ray. The chest X-ray examination showed a visual index related to COVID-19, which had a sensitivity of 44%, while the specificity was 100% [22], [23]. Another examination used in patients with suspected COVID-19 is the chest CT which has a higher sensitivity than the chest X-ray [22], [23], [24]. Radiological examination is recommended for patients with moderate to severe COVID-19 symptoms, abnormal breathing patterns, and patients with previous comorbidities that increase the risk of disease progression [24], [25]. Typical radiological features in COVID-19 patients are focal or multifocal ground-glass opacity and peripheral or subpleural consolidation, which can be unilateral or bilateral, in a minority of cases, may be accompanied by minimal pleural effusion. According to a previous study, unilateral lung involvement was more common in the right lung (58%) than the left lung (42%) [22]. The radiological features in the study mostly consisted of atypical features of COVID-19, which is thought to be related to the collection of radiological data in the first 24 h of patient care. This condition is also associated with the early stages of the disease in patients who can find normal chest radiographs at an early stage and advanced stage radiological features of pneumonia or acute respiratory distress syndrome. This finding is in line with previous studies, which stated that chest X-rays cannot be used as a reference in the early stages of the disease and may not show significant changes in radiological features [1].

Laboratory examination showed that most patients had normal hemoglobin, hematocrit, platelets, neutrophils, and monocytes, while the levels of lymphocytes and eosinophils decreased. These laboratory results align with previous studies, which reported a decrease in lymphocytes, eosinophils, and platelets and an increase in neutrophils, monocytes, and CRP [26], [27]. Another study stated that a decrease in platelet levels or thrombocytopenia increased the severity of COVID-19 in patients [28]. A decrease in the number of lymphocytes (<20%), leukocytosis, thrombocytopenia, and neutrophilia was essential to determine the prognosis of the COVID-19 patient's severity of illness and hospitalization. This finding is related to the coagulation process [26], [27], [29]. This study showed that some COVID-19 patients experienced increased neutrophils and monocytes. Other studies have shown an increase in neutrophil levels associated with disease severity; the mechanism may be related to hypoxia and prolonged COVID-19 infection leading to increased production of granulocytes consisting mainly of neutrophils by the bone marrow [30].

This study cannot explain the continuous course of the disease, especially the progression of COVID-19, because the data taken are data in the first 24 h of hospitalization. The main limitations have not been able to describe the course of COVID-19 disease in cases who experience asymptomatic symptoms at the beginning of treatment. This is a limitation of the data of this study, as well as an idea for future research.

Conclusion

This study identified symptoms of fever, cough, and shortness of breath as the main symptoms in patients with COVID-19. Most of the patient's laboratory results showed an increase in neutrophils, CRP, and a

decrease in lymphocyte levels, while the radiological results of the patients mostly had atypical radiological features. Variables related to the mortality rate of patients are comorbid diabetes mellitus, heart disease, and age; hence, these three variables require special vigilance and attention in the management and better prognosis of patients, especially to reduce mortality rates.

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