Original Article

Characteristics of COVID-19 Patients in Haji Adam Malik General Hospital, Medan, North Sumatera

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Abstract

Background: Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The increase in the number of COVID-19 cases was happening quite quickly and has spread between countries so that COVID-19 has become a pandemic in the world. This study aimed to determine the characteristics of COVID-19 patients at Haji Adam Malik General Hospital Medan.

Method: This was a descriptive study. Data were taken from the medical records of 110 hospitalized patients with positive RT-PCR results for COVID-19 from December 2020 to April 2021. The inclusion criteria for the case samples were patients diagnosed with COVID-19 based on RT-PCR and the exclusion criteria were incomplete medical records. Characteristic analysis was carried out using the Kruskal Wallis test.

Results: The most common comorbidities found in patients with severe COVID-19 were diabetes mellitus and HIV. The most common comorbidity found in moderate-level COVID-19 patients was pregnant women. The most common chest X-rays finding in severe and critical levels was bilateral infiltrates. Recovered patients were mostly obtained at moderate level, while deceased patients were mostly observed at critical levels.

Conclusion: Characteristics of COVID-19 patients at Haji Adam Malik General Hospital were classified based on the degree of disease by age, lymphocyte value, N/L ratio, levels of CRP, D-dimer, procalcitonin, fibrinogen, ferritin, and comorbidities as well as the appearance of infiltrates in both lung fields.

Keywords: COVID-19, characteristics, degree of disease

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a disease caused by infection of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2), which was first reported in Wuhan, Hubei Province, China. SARS CoV-2 was identified as the pathogen of COVID-19 in January 2020.[1] On 12 March 2020, WHO declared COVID-19 as a new pandemic with very fast

human-to-human spread, causing the number of COVID-19 cases to increase rapidly throughout the country.[2,3] As of 7 September 2020, the Ministry of Health of the Republic of Indonesia has reported 26,763,217 confirmed cases and 876,616 death cases with a mortality rate of 3.3% globally.

In previous studies conducted in various countries, the most commonly discussed characteristics of COVID-19 patients were age, gender, comorbidities, clinical manifestations, laboratory examinations and chest X-rays (CXR). Based on age, Jiang et al in 2020 prior to several studies in various hospitals in China observed that the most prevalent group of age for COVID-19 was 49-56 years old.[4] According to Liu et al in 2020 at Wuhan Central Hospital, most of the progressive disease were reported in patients over 66 years of age whilst stable cases were reported in younger patients.[5]

According to Li et al in a meta-analysis on 2020, the percentage of male among COVID-19 patients was higher than female, which was 60%.[5] According to Chen et al in 2020, about 51% of the patients had decreased blood hemoglobin level, 24% had increased leukocyte level, and 35% had a decline in platelet level. In addition, 36% of the patients had elevated D-Dimer values, 6% had increased procalcitonin levels, 63% had elevated ferritin level, and 86% of the patients had elevated CRP.[6]

Based on CXR ecamination, 75% of the patients had bilateral pneumonia, 25% had unilateral pneumonia while 14% of the patients had ground glass opacity appearance on CT-Scan examination.[6]

Based on these studies and the rapidly increasing rate of COVID-19 infection as mentioned above, we intended to identify the characteristics of COVID-19 patients, based on age, gender, comorbidities, laboratory examinations, CXR examinations and the treatment outcome of COVID-19 patients in H. Adam Malik General Hospital, Medan.

METHOD

This was a descriptive study using secondary data obtained from medical records of inpatients diagnosed with COVID-19 at Haji Adam Malik General Hospital. This study was conducted from December 2020 to April 2021.

The samples in this study were 106 samples taken through inclusion criteria, namely patients diagnosed with COVID-19 based on RT-PCR test, and exclusion criteria, namely insufficient medical record data.

This study used two variables. The dependent variable was the outcome. The independent variables were age, gender, laboratory examination results such as lymphocyte count, prolymphocyte neutrophils, D-Dimer, C-Reactive Protein (CRP), Procalcitonin (PCT), fibrinogen and ferritin, comorbidities such as diabetes mellitus, hypertension, Human Immunodeficiency Virus (HIV), heart disease, kidney diseases, malignancy, other lung diseases (Chronic Obstructive Pulmonary Disease/COPD or

Tuberculosis/TB), pregnancy, CXR results, and the treatment outcome, either dead or recovered.

The data obtained were processed by SPSS software and analyzed using Kruskal Wallis test. This study had acquired an approval from the medical research ethics committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan.

RESULTS

There were 106 samples in this study taken from the medical records of patients diagnosed with COVID-19 from December 2020 to April 2021.

Table 1. Characteristics of Samples Based on Gender

Gender	N	Percentage
Male	58	57.7
Female	48	45.3
Total	106	100.0

Table 2. Mean Age of the Samples (In Years) Based on COVID-19 Severity

Severity	Mean±SD	Median (Min–Max)
Moderate	46.92±15.71	48 (19-79)
Severe	56.47±14.76	58 (30-79)
Critical	58.50±9.35	60 (32-73)

Table 3. Characteristics of the Samples Based on Laboratory Examinations

Parameter	Mean±SD	Median (Min–Max)
Lymphocyte	1.79±2.75	1.3 (0.30-29)
NL Ratio	8.01±11.17	3.7 (0.61-65.02)
CRP	0.9569±0.62	0.7 (0.70-2.80)
PCT	1.86±8.25	0.06 (0-50.65)
D-Dimer	931.29±1133.12	416 (100-4483)
Fibrinogen	467.11±165.38	438.50 (142–900)
Ferritin	941.61±1174.65	597.50 (7.31-10621)

Table 4. Mean Lymphocyte Count and N/L Ratio (10^3/µL) Based on COVID-19 Severity

Parameter	Severity	Mean±SD	Median (Min – Max)
Lymphocytes	Moderate	2.13±24	1.59 (0.64–29)
	Severe	1.41±0.92	1.19 (0.30–3.38)
	Critical	0.72±0.33	0.57 (0.34–1.26)
N/L Ratio	Moderate	3.70±3.39	2.75 (0.61–22.82)
	Severe	8.87±8.24	6.48 (1.71–36.83)
	Critical	25.2±17.05	18.79 (4.60–65.02)

Table 5. Mean Value of CRP, PCT, D-dimer, Fibrinogen and Ferritin (ng/L) Based on COVID-19 Severity

Parameter	Severity	Mean±SD	Median (Min – Max)
CRP	Moderate	0,82±0,35	0,69 (0,01-2,8)
	Severe	1,39±0,95	0,70 (0,69–2,80)
	Critical	1,08±0,90	0,7 (0,7–2,80)
PCT	Moderate	0,72±5,19	0,04 (0,0–45,08)
	Severe	5,49±14,84	0,15 (0,02–50,66)
	Critical	3,19±9,56	0,31 (0,02–40,73)
D- Dimer	Moderate	624±763	340 (100–4001)
	Severe	1750±1661	950 (290–4483)
	Critical	1435±1318	799 (190–4001)
Fibrinogen	Moderate	429±138.64	409 (142–900)
	Severe	541±172.29	535 (275–900)
	Critical	551.88±211	494.50 (201–900)
Ferritin	Moderate	620.53±597.89	364.60 (7.32–2001)
	Severe	1191.83±794.16	1125 (83.16–2001)
	Critical	2043±2212	1893 (207–10621)

Table 6. The Characteristics of Comorbidities, Radiological Examination Results, and Outcome Compared to the COVID-19 Severity

Characteristics	Severity		
	Moderate	Severe	Critical
Diabetes Mellitus			
Yes	9 (12%)	9 (52.9%)	3 (16.7%)
No	66 (88%)	8 (47.1%)	15 (83.3%)
Hypertension			
Yes	23 (30.7%)	8 (47.1%)	12(66.7%)
No	52 (69.3%)	9(52.9%)	6 (33.3%)
HIV			
Yes	0 (0%)	2 (11.8%)	0 (0%)
No	75 (100%)	15 (88.2%)	18 (100%)
Heart Disease			
Yes	10 (13.3%)	3 (17.6%)	8 (44.4%)
No	65 (86.7%)	14 (82.4%)	10 (55.6%)
Kidney Disease			
Yes	2 (2.7%)	3 (17.6%)	7 (38.9%)
No	73 (97.3%)	14 (82.4%)	11 (61.1%)
Malignancy			
Yes	2 (2.7%)	0 (0%)	1 (5.6%)
No	73 (97.3%)	17 (100%)	17 (94.4%)
TB			
Yes	1 (1.3%)	0 (0%)	0 (0%)
No	74 (98.7%)	17 (100%)	18 (100%)
COPD			
Yes	3 (4%)	0 (0%)	2 (11.1%)
No	72 (96%)	17 (100%)	16 (88.9%)
Pregnancy			
Yes	9 (12%)	0 (0%)	1(5.6%)
No	66 (88%)	17 (100%)	17 (94.4%)
Chest X-ray			
Bilateral infiltration	73 (97.3%)	17 (100%)	18 (100%)
Diffuse infiltration	1 (1.3%)	0 (0%)	0 (0%)
Nodule and focal infiltration	1 (1.13%)	0 (0%)	0 (0%)
Outcome			
Recovered	69 (92%)	13 (76.5%)	4 (22.2%)
Mortality	6 (8%)	4 (23.5%)	13 (72.2%)
Discharge on request	0 (0%)	0 (0%)	1 (5.6%)

DISCUSSION

The result of this study showed that most of the patients were male (54.7%) compared to female (45.3%). According to Ahmed and Dumanski in their study on 2020, this could be affected by angiotensin converting enzyme 2 (ACE2), which was a functional receptor that enabled the invasion of SARS-CoV-2 into the alveolar epithelium. It played an integral part in the renin-angiotensin-aldosterone system (RAAS) in humans. In general, RAAS activity in men is higher than in women.[7]

In this study, the mean age of COVID-19 patients in severe and critical conditions were 60 and 56 years, respectively. Liu et al. stated that the mean age of the patients in severe and critical levels were higher than patients in moderate level of the disease. A study from Wu et al. expressed that this could be due to the decline of immune system in the elderly which increased the risk of ARDS and mortality.[8]

The results of this study mentioned that the lowest lymphocyte count in moderate disease was 0.64 × 10^3/µL and the highest lymphocyte count was 0.30 × 10^3/µL. In severe disease, the lowest and highest lymphocyte count were 0.30 × 10^3/µL and 3.38 × 10^3/µL, respectively. The lowest lymphocyte count in critical disease was 0.34 × 10^3/µL while the highest was 10^3/µL. Cytotoxic $CD8^+$ T Cells (CTLs) and $CD4^+$ Helper T (Th) Cells boost the host ability to eliminate pathogens. However, prolonged stimulation may cause T cells to become fatigue, which will decrease the function of the cells as immune system and worsen the patient's condition. Several studies had found a decrease in the number of lymphocytes, including total T cells, CD4+ and CD8+ T cells, memory and regulatory T cells and B cells in COVID-19 patients.[9]

The increment of CRP value was promoted by the overproduction of inflammatory cytokines in COVID-19 patients. Cytokines play a role in defense against microbes; however, an exaggerated immune response can damage lung tissue.[10] According to Zavareh et al., serum CRP concentrations could be used as an indicator of COVID-19 disease progression and severity.[11]

The median PCT value in this study for moderate, severe, and critical COVID-19 patients were 0.04 ng/mL, 0.15 ng/mL and 0.31 ng/mL, respectively. This was also similar with a study from Feng et al. which mentioned that PCT increased significantly due to cytokine storm which was chracterized by elevated concentrations of interleukin (IL)-1ß, Tumor Necrosis Factor (TNF)-α and IL-6, interferon gamma-induced protein-10, and macrophage inflammatory protein 1-α which were mostly increased in severe and critical COVID-19 patients.[12]

Our study found that the mean D-dimer values in moderate, severe, and critical COVID-19 patients were 340, 950 and 799 ng/mL, respectively. This result was identical to previous study conducted by Mahardika et al, which pointed out that the D-dimer value increased to 807.7 ng/ml. This, according to Yu et al., was due to the escalation of abnormal blood coagulation which was correlated with an increase of D-dimer value. Elevated D-dimer value is an indirect manifestation of inflammatory response, equal to inflammatory cytokine which can cause an imbalance of coagulation and fibrinolysis in the alveoli, that may promote fibrinolysis and increase D-dimer levels.[13]

The mean fibrinogen values for moderate, severe, and critical COVID-19 patients were 429, 541, and 551 ng/ml, respectively. These results were similar with a prior study conducted by Nugroho et

al., which obtained that the mean fibrinogen value in critical COVID-19 patients was higher compared to severe COVID-19 patients which was less than 500. Another study by Nugroho et al., also mentioned that the mean value of fibrinogen was higher in patients who died or after the COVID-19 treatment than before treatment.[14]

In this study, it was shown that the mean ferritin levels in moderate, severe and critical patients were 620, 491 and 2041 ng/mL.[15] Similar with our study, Zhou et al. also found that there was an increase of 377-1435 ng/mL on ferritin levels. This was also in line with prior study conducted by Carubbi et al., which pointed out that hyperferritinemia was strongly correlated with inflammation in patients infected with SARS-CoV-2. Ferritin was used as a parameter to predict disease severity and the rate of cytokine storm. A complex feedback mechanism between ferritin and cytokines in controlling pro-inflammatory and anti-inflammatory mediator exists because cytokines induce ferritin expression, however, ferritin also induces the expression of pro- and anti-inflammatory cytokines.[16]

This study found that diabetes melitus was observed in 9 (12%) moderate COVID-19 patients, 9 (52.9%) severe patients and 3 (16.7%) critical patients. On the other hand, Hussain et al., expressed that hypoglycemic state (<3.9 mmol/L) mobilized pro-inflammatory monocytes and escalated thrombocyte reactivation. These contributed to higher cardiovascular mortality in patient with diabetes mellitus. Diabetes is a chronic inflammation characterized by several metabolic and vascular disorders which affect our body's response to pathogens. Hyperglycemia and insulin resistance increase Advanced Glycation End Product (AGEs) and pro-inflammatory cytokines, synthesis of oxidative stress and support the production of adhesion molecules that promote tissue inflammation. This inflammation process will worsen the patient's condition. Uncontrolled diabetes indicates that lung epithelial cells will be exposed to higher glucose levels and will significantly increase infection and replication.[17]

The results of this study mentioned that hypertension in COVID-19 were seen in 23 patients (30.7%) of moderate disease, 8 patients (47.1%) of severe disease and 12 patients (66.7%) of critical disease. According to Zhang et al., this was influenced by direct damage mediated by the ACE2. Another study in China showed that SARS-CoV-2 infection was caused by viral protein binding to ACE2 receptor upon protein activation. ACE2 is a monocarboxylate peptidase that is known to cleave several peptides in renin-angiotensin system. Since its discovery in 2000, ACE2 has been considered as blood pressure protective factor. Binding of SARS-CoV-2 to ACE2 inhibits the physiological function of ACE2, which will lead to harmful effects of hypertension such as multi-organ dysfunction.[18]

This study obtained only 2 severe COVID-19 patients (11.8%) with HIV prior to hospitalization. According to Rebeiro et al., there were 36 death cases (14.3%) of

COVID-19 patients. Study had shown that HIV patients with multiple morbidity and older age were important factors in morbidity and mortality in HIV patients coinfected with COVID-19.[19]

In this study, there were 10 moderate COVID-19 patients (13.3%) with cardiovascular morbidities, also 3 patients (17.6%) in severe disease and 8 patients (44.4%) in critical disease. Zhou et al. stated that pre-existing cardiovascular diseases caused harmful effects to COVID-19 patients. This was due to the frequently reported coronary heart attacks concomitantly with acute cardiac events and poor outcomes in influenza and other respiratory viral infection.[13] Prior study conducted by Zhou et al., observed high troponin I elevations in hospitalized patients who had died during treatment.[15]

This study also obtained 2 moderate COVID-19 patients (2.7%) with coexisting renal disease, 3 patients (17.6%) with the same comorbidity in severe disease and 7 patients (38.9%) in critical disease. A study from Gagliardi et al. pointed out that SARS-CoV-2 attacked mainly on target cells through several steps. The two main pathophysiologies for renal injury were the direct cytopathic effect of SARS-CoV-2 on renal epithelial tissue and cytokine storm syndrome. Hypoxia, persistent hypotension, rhabdomyolysis, excessive coagulation activation, cascade and microcirculation abnormalities predisposed to advanced acute renal failure.[20]

Non-lung cancer malignancy was inspected in 2 moderate COVID-19 patients (2.7%) while lung cancer coexisted in 1 critical COVID-19 patient (5.6%). According to Lee et al., patients who had cancer and were not on regular treatment had a higher rate of COVID-19 infection, which concluded that inward COVID-19 patients did not correlate with disease severity as the pandemic had caused an inadequate treatment for cancer patients in health facilities and thus influenced this study.[21]

Tuberculosis (TB) was only found in 1 COVID-19 patient (1.3%) with moderate disease, none was found in severe or critical disease. As there was only one sample in this study who had tuberculosis comorbidity, the authors suggest that more specific studies are needed before this study.[22]

Sheerin et al. mentioned that although viral infections of the respiratory tract and TB harmed the host's immune system, there was still insufficient evidence on the correlation between SARS-CoV-2 coinfection with *Mycobacterium tuberculosis* and the immune system, prior to clinical COVID-19 disease severity and TB with or without symptoms.[22] According to Widyaningsih et al., more studies from different countries were required to understand the correlation between TB and COVID-19 prognosis.[23]

In this study, COPD was observed in 3 patients (4%) with moderate COVID-19 and 2 patients (11.1%) with critical disease when administered to the hospital. The identical result was also discovered by Antunez et al., who obtained that 7.16% of COVID-19 patients had COPD comorbidity. According to Antunez et al., one of the

reasons for this low prevalence of COVID-19 in COPD patients was the use of inhaled corticosteroids, beta agonist or anti-cholinergic drugs, especially tiotropium.[24]

On their study, they also mentioned that glycopyrronium and formoterol were proven to be effective in reducing cellular susceptibility to coronavirus infection in vitro. This may be due to the inhibition of coronavirus receptor expression, less endosome activity, and minimal inflammatory response. We understand that the basic treatment for COPD patients includes long-acting muscarinic antagonist (LAMA) and/or long-acting beta agonist (LABA).[24]

We found 9 pregnant patients (12%) who were admitted with moderate COVID-19 and 1 pregnant patient (5.6%) with critical COVID-19. There was no pregnant patient in severe COVID-19. Hapshy et al. reported that about 13.9% pregnant women with COVID-19 in New York were admitted in critical condition. Hapshy et al. expressed that this might be due to inadequate data and literature on the correlation of coronavirus in pregnancy. There was insufficient evidence about the risk of COVID-19 infection during the peripartum and antepartum periods.[25]

Also, current evidences contradicted each other, and there were no long-term studies during pregnancy. The unique physiology in pregnancy and several unknown factors in pregnant patients make the pregnant women to be less infected, however, they are still have to be classified as a high-risk population.[25]

In this study, there were 73 moderate COVID-19 patients (97.3%) with bilateral infiltrates on CXR, 17 patients (100%) with the same CXR results in severe COVID-19 and 18 patients (100%) in critical condition. We also obtained 1 patient (1.3%) in moderate COVID-19 with diffuse infiltrates who also had tuberculosis comorbidity and 1 patient (1.3%) in moderate COVID-19 with nodules and infiltrates on CXR who also had lung cancer.[26]

According to Chamorro et al., false positive results on CXR might be caused by insufficient inspiration, breast mass, and incorrect positioning of the patients, which caused the scapula and soft tissue to be more prominent.[26] However, Wong et al. suggested that CXR could be used to evaluate the progression of COVID-19 disease in the lungs, especially in critical ill patients admitted to the intensive care unit.[27]

Our study obtained 59 moderate COVID-19 patients (92%), 13 severe COVID-19 patients (76.5%) and 4 critical COVID-19 patients (22.2%) who recovered. Most of the patients died in the critical stage, which was 13 patients (72.2%). Salter et al., in their cross-sectional study on medical records also stated that there was an increase in disability related to disease severity which was correlated with mortality from COVID-19. Knowledge before COVID-19 could increase the therapeutic efficiency in COVID-19 patients, so that a more intensive evaluation can be carried out on COVID-19 patients.[28]

CONCLUSION

There were some characteristics of COVID-19 patients at Haji Adam Malik General Hospital that we described based on age, lymphocyte count, N/L ratio, levels of CRP, D-dimer, procalcitonin, fibrinogen, ferritin and comorbidities as well as lung infiltrates.

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