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Original Article

Clinical Identifiers, Comorbidities, and Outcomes among COVID-19 Confirmed Patients in Banda Aceh, Indonesia

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a highly contagious disease with an increasing number of infections in Indonesia. However, hypertension and diabetes are chronic diseases with high incidence in Aceh, there is still limited information regarding the demographics and clinical data of COVID-19 patients. This study aims to explain the clinical characteristics, comorbidities, and outcomes of COVID-19 patients. A retrospective method was used to locate data from the medical record of COVID-19 patients that were admitted to the hospital between June–October 2020. The characteristics demographics, clinical data on admission, and outcomes were extracted from the medical record. In order to determine the comorbid relationship, the chi-square test was used for the laboratory tests and clinical outcomes. A total of 120 patients were included, and more than half were male 80 (60%) with 41–60 years of age at most (51.2%). Most of the patients had comorbid diabetes mellitus (40.5%), hypertension (28.9%), and chronic lung disease (8.3%). Furthermore, most COVID-19 was severe degrees 56 (46.3%). The patients with recovery are 92 (76.0%) and only 29 (24.0%) died. The neutrophilia, and comorbid had no relationship with the clinical outcome of COVID-19 ($p > 0.05$). The Lymphopenia and degree of severity had relationship with clinical outcome ($p > 0.05$). Diabetes melitus and hypertension are the most common comorbid reported in the COVID-19 patients. The Inflammation markers, such as lymphocytes, can be used as an early warning to increase awareness in treating patients with severe disease.

Keywords: clinical identifier; comorbidities; COVID19; outcomes

ABSTRAK

Coronavirus disease 2019 (COVID-19) merupakan penyakit yang sangat menular dengan jumlah infeksi yang terus meningkat di Indonesia. Hipertensi dan diabetes merupakan penyakit kronis dengan insiden yang tinggi di Aceh, masih terbatasnya informasi mengenai demografi dan data klinis pasien COVID-19. Penelitian ini bertujuan untuk menjelaskan karakteristik klinis, penyakit penyerta, dan outcome pasien COVID-19. Metode retrospektif digunakan untuk mencari data dari rekam medis pasien COVID-19 yang dirawat di rumah sakit antara Juni–Oktober 2020. Karakteristik demografi, data klinis saat masuk, dan hasil diambil dari rekam medis. Untuk menentukan hubungan komorbiditas, uji chi-square digunakan untuk uji laboratorium dan hasil klinis. Sebanyak 120 pasien dilibatkan, dan lebih dari setengahnya adalah laki-laki 80 (60%) dengan usia paling banyak 41–60 tahun (51,2%). Sebagian besar pasien memiliki penyakit penyerta diabetes mellitus (40,5%), hipertensi (28,9%), dan penyakit paru kronis (8,3%). Selanjutnya, sebagian besar COVID-19 adalah derajat berat 56 (46,3%). Pasien yang sembuh sebanyak 92 (76,0%) dan yang meninggal hanya 29 (24,0%). Neutrofilia, dan komorbiditas tidak memiliki hubungan dengan hasil klinis COVID-19 ($p > 0,05$).

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Limfopenia dan derajat keparahan memiliki hubungan dengan luaran klinis ($p>0,05$). Diabetes mellitus dan hipertensi adalah penyakit penyerta yang paling umum dilaporkan pada pasien COVID-19. Penanda peradangan, seperti limfosit, dapat digunakan sebagai peringatan dini untuk meningkatkan kesadaran dalam merawat pasien dengan penyakit parah.

Kata kunci: COVID19; komorbiditas; outcome; penanda klinis

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by SARS CoV2 with increasing morbidity and mortality.¹ Indonesia is one of the countries affected by SARS CoV2.² Clinical symptoms appear varied, asymptotically, mild and very severe symptoms. These trigger the difficulty of disease control in the community.³ Due to the large variety of clinical manifestations of COVID-19, and the Real-Time Reverse-Transcription Polymerase Chain Reaction (RRT-PCR) examination as the gold standard for COVID-19 is not always available in various places. Therefore, several studies are needed to describe the results of laboratory tests as a guide to determine the severity of the disease, prognosis, and clinical outcome. So, the laboratory examination results are valuable knowledge during the COVID-19 pandemic.⁴

COVID-19 patients with comorbidities such as hypertension and diabetes have a poorer prognosis, higher morbidity and mortality, and longer ICU stay.⁵ Diabetes mellitus was discovered to be higher in people with obesity, and hypertension was strongly associated with diabetes mellitus in Indonesia.⁶ And even the prevalence of smoking, high blood pressure, and obesity in men are increasing in Indonesia.⁷ Although there have been many studies describing the clinical characteristics of patients in China and other countries,^{8,9,10} a little description of the clinical characteristics of COVID-19 patients in Indonesia is very significant. A retrospective study in China showed that men with a mean age of 56 were mostly infected, while men in Italy with a mean age of 67.5

years were more infected.¹¹ Subsequently, there is significant differences between Indonesia and other countries based on population demographics, comorbid and clinical outcomes of patients. Therefore, this study aims to report on the clinical characteristics, comorbidities, and outcomes of COVID-19 patients in Banda Aceh, Indonesia.

MATERIALS AND METHODS

Setting Study

This is an observational analytical study with a retrospective method using medical data from the medical records of confirmed COVID-19 patients. Furthermore, this study was conducted at the dr. Zainoel Abidin General Hospital Banda Aceh from October 2021. This study was admitted by Institutional Review Board of the School of Medicine, Universitas Syiah Kuala, Banda Aceh (377/EA/FK-RSUDZA/2021) and National Ethics Commission the Ministry of Health of the Republic of Indonesia (#1171012P. Data were collected from the medical records of patients diagnosed with COVID-19 confirmed by positive reverse transcriptase PCR examination from nasal swabs, which were analyzed molecularly in the hospital virology unit according to WHO.¹²

Variable Definitions

This study collected demographic data (gender, age, and occupation), and clinical data (clinical symptoms, comorbidities, chest X-rays, laboratory tests). Basic demographic, comorbid and clinical symptoms are fully

documented in the medical record. The definition of clinical outcome is a patient that has completed his treatment in the hospital, either recovered or died. The severity of the disease is divided only into four categories based on the WHO guidelines, namely mild, moderate, and severe, and critically ill or very severe.¹³

Statistic Analysis

Exploratory statistical analysis was performed to determine characteristic variables of potential patients, clinical symptoms, laboratory results, and clinical outcomes. The association between comorbid, laboratory results and clinical outcomes was assessed using the Chi-square test. For statistical analysis, lymphopenia when the lymphocyte percentage is < 20, Absolute Lymphocyte Count (ALC) decreases when < 1500, Neutrophil Lymphocyte Ratio (NLR) decreases when < 13.5, and increases > 13.5. Neutrophils percentage decrease when the neutrophil percentage is < 55 and increases > 70. The significance for all data analyzed was $\alpha = 0.05$. All statistical analyzes were performed using SPSS (Statistical Package for Social Sciences) for Windows version 25.0 (IBM SPSS Inc., USA).

RESULTS AND DISCUSSION

This study collected medical record data for 120 confirmed COVID-19 patients that received diagnostic examinations and treatment. The majority were male 80 (66%) with the age of 41-60 years at most (51.2%) and 31.4% of the patients were over 60 years old. Most of the patients had comorbid diabetes mellitus (40.5%) and hypertension (28.9%), only 8.3% patient had chronic lung disease. Immunodeficiency cases such as Human Immunodeficiency Virus (HIV), Systemic Lupus Erythematosus (SLE), and congenital abnormalities like Congenital pulmonary anomaly and cardiac malformation were absent. Fever is the most

common clinical symptom found in treated 89 patients (73.6%). Almost all chest X-rays have bilateral pneumonia (95.9%). Moderate COVID-19 was mostly reported in 32 patients (26.4%) and severe degrees in 56 (46.3%) patients. All patients were well treated, and most of the patients treated out of the hospital in stable condition (recovery) were 209 (87.1%) and only 31 (12.9%) patients died. (Table 1).

Table 1. Baseline Characteristics

Characteristic Demographic	n	%
Age		
< 20 years	0	0.0
20 - 40 years	21	17.4
41 - 60 years	62	51.2
>60 years	38	31.4
Gender		
Male	80	66
Female	41	34
Comorbid		
Hypertension		
Yes	35	28.9
No	86	71.1
Diabetes mellitus		
Yes	49	40.5
No	72	59.5
Chronic Lung Disease		
Yes	10	8.3
No	111	91.7
Fever		
Yes	89	73.6
No	32	26.4
Cough		
Yes	96	79.3
No	25	20.7
Shortness of Breath		
Yes	79	65.3
No	42	34.7
Anosmia		
Yes	15	12.4
No	106	87.6
Chest Radiograph		
Pneumonia Bilateral	116	95.9
Without Pneumonia	5	4.1
Sore Throat		
Yes	30	24.8
No	91	75.2
Headache		
Yes	8	6.6
No	113	93.4
Anorexia		
Yes	76	62.8
No	45	37.2
Degree of Severity		
Mild	5	4.1
Moderate	32	26.4
Severe	56	46.3
Very Severe	28	23.2
Outcome	28	23.1
Recover	92	76.0
Died	29	24.0
Absolute Lymphocyte Count (ALC)		
Normal	39	32.2
Decrease	82	67.8
Neutrophyl Lymphocyte Ratio (NLR)		
High	24	19.8
Low	97	80.2
Total	121	100.0

A number of studies showed that the incidence of SARS-CoV and SARS-CoV-2 infection is higher in men than in women.^{14,15} Based on the history of the influenza epidemic, there is a variable risk of gender, where men are more susceptible to infection than women.¹⁶ Men generally had worse clinical outcomes and higher mortality rates in the SARS and MERS epidemics.¹⁴ Likewise, a number of studies showed that they are at greater risk of being infected with COVID-19 and most are hospitalized.¹⁷ Some of the mechanisms that put men at a higher risk of contracting the disease than women are gender hormones and gene X-related activity, which play a role in modulating innate and adaptive immune responses to viral infections.¹⁸ The main route of SARS-CoV-2 infection is via the ACE2 receptor, and therefore the biological differences in the angiotensin-converting enzyme 2 (ACE2) receptor also play a role, with men shown to have more ACE2 expression in the circulation and lungs than women.¹⁷ This is consistent with the findings that most men infected with COVID-19 received treatment in the hospital.

Diabetes is one of the top causes of morbidity and mortality, and relationship with infection has long been allowed. Infections such as pneumonia are generally seen in type 2 diabetes mellitus (T2DM) people. China and Italy reported that older patients with diabetes were at higher risk for more serious COVID-19 and mortality.^{19,20} Patients with comorbid cardiovascular disease are at higher risk of severe symptoms when infected with SARS-CoV-2. Hypertension is a major risk factor related

with poor clinical outcomes in COVID-19.²¹ According to this study, it was shown that Diabetes mellitus and hypertension was the most common comorbid disease but it was not significantly related to the clinical outcome ($p < 0.05$). This happens because the prevalence of diabetes mellitus and hypertension is quite high in Indonesia and half of the hypertensive patient are unaware of the dangers of this comorbid.⁷ It is not unexpected that immunity and metabolism have coevolved in such proximity. Cellular stressors in diabetes mellitus, such as endoplasmic reticulum stress, oxidative stress, and others, might exacerbate inflammatory responses.

In COVID-19, When SARS-CoV-2 infects diabetic patients with the aforementioned cellular stressors, the decreased immune response may result in significant lung and other pathology and frequently results in mortality.²² The worse outcomes in COVID-19 patients can be partially attributed to hypertension, which plays a significant role in the control of RAAS, inflammation, immunological responses, and the gastrointestinal tract. Because of this, patients who have both hypertension and SARS-CoV-2 infection may suffer a double blow.²³

Most patients admitted to the hospital had a complaints of, coughing 96 (79.3%), and Shortness of breath 79 (65.3%), and only 8 patients had a headache. The laboratory examinations results at the hospital showed that the mean levels of leukocytes were $11.276 \times 10^3/uL$, lymphocytes percentage 14.6, neutrophils percentage 81.2, NLR 6.7, and ALC 1375 (Table 2).

Table 2. Clinical and Laboratory Findings on Admission

Parameter	Min.	Max.	Mean	SD
Systolic (mmHg)	14.00	194.00	130.4628	22.32974
Diastolic (mmHg)	48.00	275.00	79.9669	20.60014
Heart Rate (x/i)	71	130	95.13	11.272
Respiratory Rate (x/i)	18	40	25.51	4.384
SaO2 Without O2 (%)	40	99	87.69	9.930
Leukocytes x 10 ³ /uL (normal range 4.0-10.0)	1100	34400	11276.03	6576.904
Lymphocyte percentage, normal range 25-40	2	47	14.60	12.128
Neutrophyl Lymphocyte Ratio (NLR)	.00	47.50	6.7660	9.58457
Neutrofil percentage, normal range 50-70	26.00	126.00	81.2231	15.17591
Absolute Lymphocyte Count (ALC)	77.00	7082.00	1375.4380	1109.49531
Systolic (mmHg)	14.00	194.00	130.4628	22.32974
Diastolic (mmHg)	48.00	275.00	79.9669	20.60014

A meta-analysis of patients with COVID-19 had a fever as the most common initial symptom (88.8%), dry cough (68%), and fatigue (33%). Other symptoms reported were productive cough (28.5%), shortness of breath (17%), muscle aches (14.4%), sore throat (11.4%), and headache (10.2%). During the first week of the virus phase when the body becomes infected, fever is a manifestation of the body's immune response to virus replication.²⁴ In line with the findings, it shows that cough and fever are the clinical symptoms most complained of by COVID-19 patients.

The results show that most cases of COVID-19 are hospitalized in severe cases and the majority return to home in stable condition. This is most likely due to increased health worker awareness about signs, symptoms, early diagnosis, and identification of disease more quickly to reduce the severity of the disease that may occur.²⁵ Therefore, this had an impact on the clinical outcome as most of the patients treated were able to return home in a stable condition.

Neutrophilia and Comorbid had no significant relationship with the clinical outcome of patients ($p > 0.05$), and there is a significant relationship between Lymphocyte and the degree of severity with clinical outcome ($p < 0.05$). (Table 3).

Table 3. The Relationship of Clinical Characteristics and Outcomes

		Clinical Outcome		Total	p	
		Died	Recover			
Hypertension	No	17	19.8%	69	80.2%	0,09
	Yes	12	34.3%	23	65.7%	
Diabetes Mellitus	No	13	18.1%	59	81.9%	0,065
	Yes	16	32.7%	33	67.3%	
PPOK	No	28	25.2%	83	74.8%	0,280
	Yes	1	10.0%	9	90.0%	
ALC	Decreased	23	28.0%	59	72.0%	0,127
	Normal	6	15.4%	33	84.6%	
NLR	Low	22	22.7%	75	77.3%	0,505
	High	7	29.2%	17	70.8%	
Degree Of Severity	Mild	0	0.0%	5	100.0%	0,000
	Moderete	0	0.0%	32	100.0%	
	Severe	12	21.4%	44	78.6%	
	Very Severe	17	60.7%	11	39.3%	
Neutrofil	Decrease	0	0.0%	9	100.0%	0,101
	Normal	1	10.0%	9	90.0%	
	Increase	28	27.5%	74	72.5%	
Limfosit	Decrease	28	30.8%	63	69.2%	0,002
	Normal	1	3.3%	29	96.7%	
Total		29	24,0%	92	76,0%	121

Based on the laboratory tests in this study, Sars CoV2 infection affected the mean level of leukocytes, lymphocytes, and neutrophils (Table 2). Therefore, there is a significant relationship between the decrease in lymphocyte levels and the patient's clinical outcome. Our findings confirm the potential use of lymphocytes in disease severity in COVID-19. As is well known, Sars CoV2 primarily acts on T lymphocytes and further disrupts the stability of neutrophils in the immune system.²⁶ A meta-analysis showed that lymphopenia and neutropenia are associated with poor clinical outcomes in COVID-19.

Lymphopenia can cause interference with adaptive immunity and cytokine storms that trigger Acute Respiratory Distress Syndrome (ARDS).²⁷ Furthermore, low absolute lymphocyte levels can be used as a characteristic marker of diagnosis and describe the prognosis of the disease.¹¹

Lymphopenia and Neutrophilia observed can be the cause of the poor clinical outcome in COVID-19 because there is a disruption in the balance of the immune system in response to viral infection, leading to hyperinflammation and death. Because of the defensins and neutrophil elastase (NE) that are generated after excessive neutrophil activation during Sars CoV2 infection, blood arteries may become more permeable. Additionally, NET formation may actively harm vascular tissue or significantly contribute to the activation of endothelial cells aggravating the inflammatory circuit and activating alveolar macrophages for clearance.²⁸

CONCLUSIONS

Diabetes melitus and hypertension are the most common comorbid reported in the COVID-19 patients. Furthermore, lymphocyte can be used as markers of disease severity that influence the clinical profile of patients with COVID-19. Majority of the patients return home with a stable condition, most likely because health worker awareness is quite good regarding this disease.

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CONFLICT OF INTEREST

This research has no conflict of interest.

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