Original Article

Analysis of Clinical Manifestation at Admission and Comorbidity on Clinical Outcome of COVID-19 Patients In RSUDZA Banda Aceh

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Abstract

Background: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus and has become a pandemic until now. Clinical outcomes in patients vary depending on many factors, such as demographics, vital signs, laboratory results, and comorbidities.

Methods: This study aims to analyze clinical outcomes in COVID-19 patients associated with the patient's general information (age, sex), demographic factors, admission vital signs, degree of symptoms at admission, blood laboratory results at admission, and comorbidities. This study is an analytic observational study with a cross-sectional design. All variables were examined based on medical records at the time of admission to the hospital. A multivariate analysis was conducted to determine what factors most influence clinical outcomes in treated COVID-19 patients.

Results: There were 183 COVID-19 patients included in this study with moderate to critical degrees. Factors that influence the clinical outcome of COVID-19 patients are the presence of comorbidities, old age, high blood pressure and heart rate, anemia, leukocytosis, and increased blood sugar and creatinine at admission. Multivariate analysis showed that clinical symptoms of severe COVID-19 were a factor that influenced poor clinical outcomes in COVID-19 patients, with OR=5.6 (95% CI=2.223-13.90).

Conclusion: Age, comorbidity, blood pressure, heart rate, hemoglobin, random blood glucose, and creatinine at admission influence the clinical outcome of admitted COVID-19 patients.

Keywords: Clinical outcome, comorbidity, COVID-19, degree of symptoms, demographic, laboratory result, vital signs

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on March 11th 2020. This disease impacts high morbidity and mortality rates in at-risk populations. Based on the WHO report as of 27th October 2021, the incidence was 243,561,596 confirmed cases, with a recorded number of deaths of 4,947,777.[1]

The clinical manifestations of COVID-19 vary widely. At the time of admission, 20–51% of patients have at least one comorbidity, the most common being diabetes mellitus (10-20%), hypertension (10-15%), and other cardiovascular and cerebrovascular diseases (7-40%).[2] Patients with chronic obstructive pulmonary disease (COPD) have a 4-fold risk of clinically adverse events during COVID-19 infection.[3]

Epidemiological research shows that the severity of comorbidities affects the prognosis of COVID-19. Systematic data from 69 research results show the severity of COVID-19 and comorbidities worsen the prognosis of COVID-19.[3] The American Center for Disease Prevention and Control (CDC) states that the risk of symptom severity due to COVID-19 is increasing in the elderly group clinical manifestations in men tend to be more severe than women. Based on vital signs, a poor prognosis for COVID-19 occurs with high blood pressure and an increased respiratory rate. Several studies have shown that increased blood glucose levels and leukopenia will have a worse prognosis.[3]

Published epidemiology data showed that the severity of the disease was correlated to comorbidity and influenced the prognosis. Data from a systematic evaluation of 69 publications showed that the severity of COVID-19 and comorbidity affected the terminal prognosis of COVID-19. Based on data by the Centers for Disease Control and Prevention

(CDC), the severe degree of disease was enhanced in the group of older age and male rather than younger female. Based on the vital sign, a lower prognosis of COVID-19 were influenced by higher blood pressure and tachypnea. Based on the laboratory parameter, several studies showed that higher blood glucose and leucopenia were correlated to a worse prognosis.[3]

The increasing incidence and mortality rate of COVID-19 and no current study to prove those prognosis parameters, specifically in Rumah Sakit Umum Daerah Zainoel Abidin (RSUDZA), the center of several COVID-19 cases in Aceh, encourage us to research "Analysis of Demographic Factor, Vital Sign, Degree of Symptom, Laboratorium Result and Comorbidity to Clinical Outcome of COVID-19 Patients in RSUDZA Banda Aceh".

METHODS

This study is an analytic observational study with a cross-sectional design. The research was conducted from April to June 2021 by collecting all medical record data for COVID-19 patients admitted at the PINERE and RICU RSUDZA from April to June 2021 using a total sampling technique. Medical records used as research samples met the inclusion criteria, namely COVID-19 patients confirmed by RT PCR, aged ≥18 years with or without comorbidities (COPD, DM, CKD, Hypertension). Exclusion criteria were COVID-19 patients who returned home at their request or incomplete medical records.

Descriptive data will be presented as mean and standard deviation, whereas the nominal data will be given as percentages. Bivariate analyses were performed to compare several variables between the two outcome groups (good and bad outcomes) with Chi-square and Fisher-exact test. Clinical outcomes were considered good if the patient was discharged (declared cured and allowed to go home with negative repeat RT PCR results), while those were declared bad if the patient died while in treatment. Multiple logistic regression analysis was done to obtain odds ratio (OR) and a 95% confidence interval. Data analysis was performed using Statistical Program for Social Sciences (SPSS) for Windows, version 24.

The study protocol was approved by the Ethics Committee, Faculty of Medicine Syiah Kuala University, and dr. Zainoel Abidin Hospital Banda Aceh, June 21st, 2022, with ethical clearance number 127/EA/FK-RSUDZA/2021.

RESULTS

This study collected 183 data from the medical records of COVID-19 patients; no medical records were excluded. The severity of COVID-19 in this study consisted of 80 (43.72%) patients with moderate symptoms, 77 (42.08%) patients with severe symptoms, and 26 (14.21%) patients with acute symptoms. There were 80 (43,72%) patients at all degrees who did not have comorbidities patients with severe symptoms more accompanied by hypertension (66.67%) and DM (51.35%) compared to other symptoms, CKD, COPD and other comorbidities accompanied the rest.

Table 1. Relationship between demographic factors and clinical outcome of COVID-19

Variable	Clinical Outcome		Total (N=183)	*P*
	Good (N=126)	Bad (N=57)		
Sex				
Men	73 (65%)	39 (35%)	112 (100%)	0.178
Woman	53 (75%)	18 (25%)	71 (100%)	
Age (years)				
17–25	9 (82%)	2 (18%)	11 (100%)	0.0001
26–35	24 (96%)	1 (4%)	25 (100%)	
36–45	45 (87%)	7 (13%)	52 (100%)	
46–55	25 (64%)	14 (36%)	39 (100%)	
56–65	20 (51%)	19 (49%)	39 (100%)	
>65	3 (18%)	14 (82%)	17 (100%)	

Bivariate analysis using chi-square showed no significant relationship between sex and clinical outcome (*P*=0,178). However, age differences were significantly correlated to the clinical outcome (*P*<0,001). Samples with younger ages had a better clinical outcome rather than older ones. Patients with younger ages had a better clinical outcome than older ones (Table 1).

Relations of vital signs to clinical outcome saturation were displayed in Table 2 with a component of the parameter; only blood pressure

(*P*=0,020) and vital sign were blood pressure, heart rate, heart rate (*P*<0,001) who were correlated to respiratory rate, temperature, and oxygen clinical outcome.

Table 2. Vital signs and clinical outcomes in COVID-19

Vital Sign	Clinical Outcome		Total (N=183)	*P*
	Good (N=126)	Bad (N=57)		
Blood Pressure				
Normal	51 (80%)	13 (20%)	64 (100%)	0,020
Pre HT	48 (71%)	20 (29%)	68 (100%)	
HT 1	13 (57%)	10 (43%)	23 (100%)	
HT 2	14 (50%)	14 (50%)	28 (100%)	
Heart Rate				
Normal	101 (84%)	19 (16%)	120 (100%)	0,0001
Tachycardia	25 (40 %)	38 (60%)	63 (100%)	
Respiratory Rate				
Normal	2 (67%)	1 (33%)	3 (100%)	0,934
Tachypneu	124 (69%)	56 (31%)	180 (100%)	
Temperature				
Hypothermia	1 (50%)	1 (50%)	2 (100%)	
Normal	93 (68%)	44 (32%)	137 (100%)	0,705
Febrile	32 (73%)	12 (27%)	44 (100%)	
Oxygen Saturation				
Normal	2 (100 %)	0 (0%)	2 (100%)	0,339
Desaturated	124 (69%)	57 (31%)	181 (100%)	

There is a statistically significant relationship between the degree of symptoms of COVID-19 and the clinical outcome of COVID-19 patients (*P*<0.001). Subjects with moderate symptoms tend to have an excellent clinical outcome, while patients with acute symptoms tend to have poor clinical outcomes (Table 3).

Table 3. Relationship between vital Relationship between degree of disease and the clinical outcome of COVID-19

Degree of Disease	Clinical Outcome		Total (N=183)	*P*
	Good (N=126)	Bad (N=57)		
Moderate	75 (94%)	5 (6%)	80 (100%)	0,0001
Severe	48 (62%)	29 (38%)	77 (100%)	
Critical	3 (12%)	23 (88%)	26 (100%)	

The results of blood laboratory tests showed that hemoglobin (*P*=0.025), leukocytes (*P*=0.001), random blood glucose (*P*=0.0001), and serum creatinine (*P*=0.0001) were significantly related to clinical outcomes in COVID-19 patients (Table 4).

Analysis of comorbidity and clinical outcome of COVID-19 were displayed in Table 5**,** indicating the significant relations between comorbidity and clinical outcome of COVID-19 (*P*<0,001). Samples without comorbidity were likely to have better outcomes than comorbidity ones.

Table 4. Relationship between blood laboratory results and the clinical outcome of COVID-19

Laboratorium result	Clinical Outcome		Total (N=183)	*P*
	Good (N=126)	Bad (N=57)		
Hemoglobin				
Normal	113 (72%)	44 (28%)	157 (100%)	0,025[1]
Anemia	13 (50%)	13 (50%)	26 (100%)	
Leukocyte				
Normal	81 (79%)	21 (21%)	102 (100%)	0,001[1]
Leukocytosis	45 (56%)	36 (44%)	81 (100%)	
Thrombocyte				
Thrombocytopenia	30 (67%)	15 (33%)	45 (100%)	
Normal	92 (71%)	38 (29%)	130 (100%)	0,439[1]
Thrombocytosis	4 (50%)	4 (50%)	8 (100%)	
Random Blood Glucose				
Normal	107 (75%)	35 (25%)	142 (100%)	0,0001[1]
High	19 (46%)	22 (54%)	41 (100%)	
Ureum				
Low	5 (83%)	1 (17%)	6 (100%)	
Normal	49 (71%)	20 (29%)	69 (100%)	0,725[2]
High	72 (67%)	36 (33%)	108 (100%)	
Creatinine				
Low	90 (84%)	17 (16%)	107 (100%)	
Normal	27 (64%)	15 (36%)	42 (100%)	0,0001[1]
High	9 (26%)	25 (73%)	34 (100%)	

Note=[1]Chi-Square test; [2]Fisher's exact test

Table 5. Relationship between comorbidity and the clinical outcome of COVID-19

Comorbidities	Clinical Outcome		Total (N=183)	*P*
	Good (N=126)	Bad (N=57)		
No comorbidity	76 (95%)	4 (5%)	80 (100%)	0,0001
Hypertension	22 (56%)	17 (44%)	39 (100%)	
Diabetes Mellitus	19 (51%)	18 (49%)	37 (100%)	
CKD	1 (8%)	12 (92%)	13 (100%)	
COPD	1 (33%)	2 (66%)	3 (100%)	
Others	7 (64%)	4 (36%)	11 (100%)	

Multivariate analysis of all variables (Table 6) was tested by logistic regression. It showed that age, the severity of the disease, comorbidity, and heart rate were correlated to the clinical outcome of COVID-19 patients with the *P*<0,05 and severity of disease with the *P*=0.0001 (OR=5.568; 95% CI=2.229–13.908). It means that severe disease would worsen clinical outcomes 5.6 times higher rather than another variable.

Table 6. Multivariate analysis of factors that affected the clinical outcome of COVID-19

Variable	*P*	OR	95% CI	
			Lower	Upper
Age	0,001	20,429	3,548	117,623
COVID-19 symptom	0,0001	5,568	2,229	13,908
Comorbidities	0,002	1,681	1,212	2,332
Blood Pressure	0,486	1,175	0,746	1,852
Heart Rate	0,032	2,86	1,092	7,492
Leucocyte	0,657	1,244	0,474	3,267
Random Blood glucose	0,102	2,283	0,85	6,134
Constanta	0,000	0,000	-	-

DISCUSSION

Based on gender, there are more people with COVID-19 males, with a proportion of 61.2%. This is supported by Karyono et al, which shows that more male suffers from COVID-19 than females.[4] This is thought to be due to the higher expression of angiotensin-converting enzyme-2 (ACE2), which male sex hormones may regulate.[5] The results of this study showed that there was no significant difference between gender and clinical outcome (p=0.178); this is following Zhang et al, which stated that there was no difference in the ratio of male to female sex in the outcome and severity of COVID-19 symptoms.[6]

There was a significant age difference in this study, with the highest incidence at the age of 36–45 years, but worse clinical outcomes were higher in the elderly in the age group of 56–45 years. This is under research by Karyono et al, which stated that almost a third of COVID-19 infections were in the young age group, but the highest mortality rate occurred in the elderly.[4] Older patients, especially those aged 65 and over with comorbidities, have an increased rate of intensive care unit (ICU) admission and death from COVID-19.[3]

In the vital signs variable, blood pressure (*P*=0.020) and heart rate (*P*=0.0001) showed significant differences in this study. The results of this study follow Karyono et al and Zhang et al which showed that cardiovascular disorders and high blood pressure were a greater risk for mortality.[4,6] Respiratory rate did not have a significant relationship (*P*=0.394) between the two groups, but 98.4% of subjects had an increased respiratory rate. This is different from Chatterjee et al, who stated that when oxygen saturation monitoring is not available, a respiratory rate of more than 22 times per minute is a marker of worsening COVID-19.[7]

In this study, the patient's temperature at admission had no significant relationship with clinical outcomes. This is under a study by Tharakan et al, which stated that higher body temperature at the initial clinical symptoms did not show a significant relationship with mortality, even though an increase in temperature was a predictor of the severity of viral infections in general.[8]

In this study, the oxygen saturation variable showed no significant relationship with clinical outcome (*P*=0.339), in contrast to the study by Mejia et al, which stated that oxygen saturation below 90% on admission was a predictor of death in hospitals in COVID-19 patients. Acute hypoxemia enhances various cytotoxic functions of neutrophils and triggers hyperinflammation. This is closely related to the occurrence of progressive lung tissue damage after the formation of the initial injury.[9]

This study found a statistically significant relationship between the degree of symptoms and the clinical outcome of COVID-19 patients (*P*=0.0001). It is the most dominant in multivariate analysis with OR=5.568 (95% CI=2.229–13.908). Based on a meta-analysis by Chidambaram et al, it

is shown that the severity of symptoms is closely related to COVID-19 mortality. The risk of death is higher in patients with increasing age, male, dyspnea, diabetes, hypertension, congestive heart failure, and the disease's severity.[10]

This study found that leukocyte levels were associated with clinical outcomes in COVID-19 patients (*P*=0.001). Study of Zhang et al showed that the leukocyte count was higher in patients with severe symptoms and became a more prominent marker of inflammation, a high risk of mortality, and a marker of secondary bacterial infection.[6]

Examination of blood glucose while also significantly related in this study. This was supported by Wang et al that blood glucose levels were a significant risk factor for death. Low serum hemoglobin and creatinine levels are also associated with the clinical outcome of COVID-19. Patients with high blood glucose levels are 58% more likely to develop more severe symptoms and 3.22 times more likely to die from COVID-19.[11]

In this study, comorbidities were associated with the clinical outcomes of COVID-19 patients. The most common comorbid disease was hypertension (21.3%), followed by diabetes mellitus (20.2%). The study by Karyono et al stated that COVID-19 patients had higher rates of hypertension, diabetes, and cardiovascular disease. Patients with comorbidities should avoid infection with SARS-CoV-2 because they are prone to poor prognoses.[4] Hyperglycemia and diabetes mellitus trigger the acceleration of viral replication by forming reactive oxygen species (ROS) in cellular mitochondria, mainly monocytes, which will activate factor 1α, which triggers hypoxia.[12]

Most of the population of Banda Aceh City has risk factors for diabetes and obesity due to the habit of high fat and high sugar intake and lack of physical activity. Data from the Banda Aceh City Health Office in 2018 showed 619 people with general obesity and 839 people with central obesity.[13] Another comorbid is CKD which is related to immune function dysregulation, which increases the risk of death in COVID-19 patients. ACE2 receptors are overexpressed in tubular cells, increasing serum creatinine as a marker of impaired kidney function.[5]

Cardiovascular disease is exacerbated by de novo COVID-19 infection. The SARS-CoV-2 agent that causes COVID-19 will migrate to the heart muscle through alveolar-capillary diffusion transport, which will eventually cause myocarditis. Conditions exacerbated by hypertension and coronary heart disease will increase the incidence of heart injury. Irregular regulation of the heart and blood vessels due to inflammation causes heart failure. The condition of old atherosclerotic formations can also cause the fragments to rupture, thus blocking the coronary arteries and eventually triggering a heart attack due to myocardial infarction.[14]

LIMITATION

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CONCLUSION

There is a relationship between age and the clinical outcome of COVID-19 patients, young people are more susceptible to infection, but old age has a higher mortality. Increased blood pressure and heart rate are related to clinical deterioration in COVID-19 patients. Subjects with moderate symptoms tend to have good clinical outcomes, while those with acute symptoms tend to have poor clinical outcomes. The degree of symptoms of COVID-19 is the most dominant and statistically influential factor. Leukocyte and blood sugar levels during and with comorbidities significantly correlate with the clinical outcomes of COVID-19 patients. The most common comorbidities are hypertension, diabetes mellitus, and CKD, so they must be treated more intensively to prevent mortality.

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CONFLICT OF INTEREST

None.

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