Clinical Characteristics and Severity Profile of COVID-19 Patient with Hypertension in Palu, Central Sulawesi

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Info Article	ABSTRACT
	Until this year, coronavirus infection (COVID-19) is still an unsolved problem in Indonesia. Apart from Java, other islands, including Sulawesi, were also severely affected. The very high mortality rate in Central Sulawesi (3.36%) poses a challenge for health workers; therefore, they should be well informed and with up-to-date information about correct therapeutic decisions. One of the most common comorbidities that often occurs with the severity and mortality of COVID-19 is hypertension. This study aims to determine the clinical characteristics and severity profile and their relationship with the mortality rate of COVID-19 patients with hypertension in Palu, Central Sulawesi. A total of 185 data on COVID-19 patients undergoing treatment at the Palu City Hospital during 2021 and meeting the criteria were recruited as research samples. Patients were divided into hypertensive (43%) and non-hypertensive (57%). The results showed that the age group, comorbid diabetes mellitus, cardiovascular, blood pressure, and blood glucose levels showed a significant relationship between the two groups ($p < 0.05$). The median length of stay was 12 days, with conditions leading to discharge (83%) and death (17%); patients who died were hospitalized in moderate and severe clinical conditions. Age group, liver function, and kidney function were positively correlated with severity and mortality. However, hypertension did not show a significant relationship with the severity and mortality of COVID-19 patients. **Keywords:** Severe acute respiratory syndrome coronavirus 2, Hypertension, COVID-19 Severity, Central Sulawesi

INTRODUCTION

Covid-19 is a new type of coronavirus that infects humans and causes respiratory problems or sudden death. WHO declared Covid-19 a pandemic in March 2020. Until August 2021, Covid-19 cases in Indonesia reached 162 million patients with a total death of 3.2% ("Peta Sebaran COVID-19 | Covid19.go.id," 2021). Central Sulawesi ranks 20th by contributing 1% of Covid-19 cases in Indonesia. In August 2021, Central Sulawesi is included in 5 regions with the highest number of Covid-19 cases outside Java-Bali, with a total depth of 3.11%.

Twenty percent (8,042 cases) of them occurred in Palu City ("Covid-19 Archives - DINKES PROV SULTENG," n.d.). ("WHO Coronavirus Disease (COVID-19) Dashboard | WHO Coronavirus Disease (COVID-19) Dashboard," n.d.). Based on data from the COVID-19 distribution map in Indonesia, it is known that 50.3% of people who are confirmed positive for COVID-19 have comorbid hypertension (Karyono and Wicaksana, 2020).

Hypertension is one of the non-communicable diseases (NCDs), which is a significant health problem because it causes ~70%

of the causes of death in the world (Shibata *et al.*, 2020). In 2019, around 30% of the people in Central Sulawesi suffered from hypertension, and 25% did not receive treatment (Sulteng, 2019).

Several chronic diseases such as hypertension, diabetes, coronary heart disease, and chronic obstructive pulmonary disease are often severe, and patients do not survive Covid-19 (Chen *et al.*, 2020). The study involved 487 COVID-19 hospitalized patients in China; hypertension is related to the severity found on admission (Shi *et al.*, 2020). It was also found in the Wuhan population that 48% of Covid-19 patients with comorbid hypertension did not survive hospitalization (Zhou *et al.*, 2020). However, different things were shown in the French population; namely, from multivariate analysis, hypertension was not significantly associated with the development of COVID-19 (Simonnet *et al.*, 2020).

In the RAS pathway, ACE and ACE2 work synergistically to maintain hemodynamic stability of blood pressure. When the SARS-CoV-2 virus binds to the ACE2 receptor, the infected organ has a decrease in ACE2 activity (Li *et al.*, 2020). This decrease alters the balance of ACE and ACE2, causing an excess of Angiotensin-II, resulting in vasoconstriction and an increase in blood pressure. High ACE2 expression in hypertensive patients is thought to have the potential to increase the risk of COVID-19 severity (Gemmati and Tisato, 2020). The difference results warrant further studies into the interactions between SARS-CoV-2, ACE2, and ACE and the findings in the pathogenesis of hypertension related to the severity of COVID-19 in other populations.

Data shows that the number of people with hypertension and the number of Covid-19 cases in Palu is relatively high, but research involving this population has never been reported. Until now, there is also no clear evidence whether blood pressure affects the severe profile in Covid-19, assuming that high blood pressure will result in high severity and normal blood pressure will cause mild severity. However, it is also known that various other diseases usually accompany hypertension, so hypertension with complications may aggravate the severity profile of Covid-19 patients. Therefore, health workers must always get the latest information to conclude the correct therapeutic decision. This study aims to determine the relationship between clinical characteristics and disease severity profiles of patients with hypertension in the population in Central Sulawesi.

MATERIAL AND METHODS
Ethics Statement
This research has been approved by the Health Research Ethics Committee, Faculty of Medicine, Tadulako University, with number 7916/UN.28.1.30/KL/2020. Written informed consent was obtained before the investigation.

Participant and Data Sources
This study used a cross-sectional design by collecting clinical data from 185 patients diagnosed with COVID-19 at the Palu City Hospital, Central Sulawesi, from February to July 2021. In the first part, all patients were divided into two groups based on whether they had comorbid hypertension or not. We recorded the entire course of the disease and the clinical examination results at the initial admission for each person. Data sources include demographic, clinical features, disease severity, laboratory tests obtained from the medical record system. All patients with COVID-19 met the inclusion criteria, namely: (1) Age 18 years, (2) Having a fever or other respiratory symptoms, (3) Positive SARS-CoV-2 test by RT-PCR. Exclusion criteria: (1) went home at their request, (2) incomplete medicalrecords.

The clinical classification of patients is based on the COVID-19 treatment guideline, namely: (1) mild type: only mild clinical symptoms without signs of pneumonia on imaging features; (2) common type: complicated by fever, respiratory symptoms, and imaging features of pneumonia; (3) severe type: complicated by any of the following: (a) respiratory distress, respiratory rate 30 breaths/min; (b) mean oxygen saturation <93% at rest; or (4) critical type: complicated by any of the following: (a) respiratory failure and required mechanical ventilation; (b) shock; or (c) organ dysfunction and intensive care unit admission required. Our study combined severe and critical type patients into the severe group (Health, 2020).

Statistical Analysis
Using SPSS21.0 software (IBM, Inc., Chicago, IL, USA), categorical variables were expressed as frequency (percent), and continuous variables were defined as mean ± standard deviation or median quartile interval.

Table I. Baseline characteristics of COVID-19 Patients with Hypertension

Variable	Total (n =185)	Hypertension (n=79)	Non-hypertension (n = 106)	p Value
Age group (y)				0.000[b]
18-39	65 (35%)	12 (15%)	53 (50%)	
40-59	77 (42%)	40 (51%)	37 (35%)	
≥60	43 (23%)	27 (34%)	16 (15%)	
Sex				0.752[a]
Male	83 (45%)	37 (47%)	46 (43%)	
Female	102 (55%)	42 (53%)	60 (57%)	
Comorbidities				0.000[a]
Non comorbidities	69 (37%)	22 (28%)	69 (65%)	
With comorbidities	116 (63%)	57 (72%)	37 (35%)	
Comorbidities Type				
CPD	6 (3%)	2 (3%)	4 (4%)	1.000[c]
Diabetes mellitus	20 (22%)	29 (37%)	11 (10%)	0.000[a]
CVD (Other than Hipertension)	34 (18%)	26 (33%)	8 (8%)	0.000[a]
CKD	15 (8%)	8 (10%)	7 (7%)	0.551[a]
Sign and Symptoms				
Fever History	96 (52%)	34 (43%)	62 (58%)	0.053[a]
Cough	128 (69%)	51 (64%)	77 (73%)	0.309[a]
Mucus	27 (15%)	14 (18%)	13 (12%)	0.407[a]
Fatigue	67 (36%)	39 (49%)	28 (26%)	0.002[a]
Anosmia	20 (11%)	9 (11%)	11 (10%)	1.000[a]
Nausea	70 (38%)	28 (35%)	42 (39%)	0.670[a]
Dyspnea	95 (51%)	41 (52%)	54 (51%)	1.000[a]
Vomiting	31 (17%)	9 11%)	22 (21%)	0.137[a]
Diarrhea	13 (7%)	6 (7%)	7 (6%)	1.000[a]
Headache	20 (11%)	9 (11%)	11 (10%)	1.000[a]
Myalgia	76 (41%)	31 (39%)	45 (42%)	0.773[a]
Vital Sign				
Temperature (°C)	36.5±0.68	36.5±0.59	36.6±0,75	0.254[d]
Oxygen saturation (%)	94±7.34	93±7.33	95±7,4	0.294[d]
Respiration rate (bpm)	25±5.56	25±5.6	25±5,54	0.408[d]
Pulse (bpm)	87±14.36	87±12.2	88±15,8	0.873[d]
SBP (mmHg)	125±23.5	149±24.1	114±15	0.000[d]
DBP (mmHg)	79±13.7	85±14.6	75±11,2	0.000[d]
Disease Severity				0.566[b]
Mild	27 (14%)	9 (12%)	18 (35%)	
Moderate	129 (70%)	57 (72%)	72 (65%)	
Severe	29 (16%)	13 (16%)	16 (15%)	
Hospitalization time (days)	12±4.9	12 ±4	13±5.4	0.624[d]
Post-treatment				0.743[a]
Discharged	153 (83%)	64 (81%)	89 (84%)	
Death	32 (17%)	15 (19%)	17 (16%)	

CPD (Constructive pulmonary disease), CVD (Cardiovascular disease), CKD (Chronic Kidney Disease), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure)
[a]Continuity Correction, [b]Pearson Chi-Square, [c]Fisher's Exact test, [d]Mann Whitney test

RESULT AND DISCUSSION

A total of 185 patients were hospitalized for confirmed COVID-19 and met the sample criteria; they were all included in this study. Forty-three percent (79 of 185) samples carried hypertension comorbid while 57% (106 of 185) did not. The baseline characteristics, including clinical and demographic factors (Table I).

Baseline Characteristics of COVID-19 Patients with Hypertension

COVID-19 patients are predominantly female, mostly aged between 40-59 years. One hundred and sixteen (63%) COVID-19 patients carried comorbidities. In addition to hypertension, other comorbidities are diabetes mellitus (22%) and cardiovascular (other than hypertension) (18%). The most common symptoms in all patients were cough (69%) and dyspnea (61%). A total of 129 (70%) patients were admitted to treatment with moderate disease severity. The number of deaths in the hospital was 17% (Table I).

Compared with non-hypertensive patients, hypertensive patients tend to be middle to elderly. Most of them had comorbidities such as diabetes mellitus and cardiovascular disease. The most common symptom in the hypertension group was fatigue, and this group also had higher systolic and diastolic blood pressures (p = 0.000). Based on the severity of COVID-19 patients, the hypertension group had a higher proportion of patients with moderate to severe severity with a higher percentage of cases of death than the non-hypertensive group. However, the two did not show a significant difference (Table I).

Laboratory Parameters of COVID-19 Patients with Hypertension

The average laboratory parameters of all COVID-19 patients showed abnormal neutrophils, lymphocytes, basophils, NLR, AST, ALT, and creatinine. In addition, the hypertension group showed significant differences in the mean values of ALT, creatinine, blood glucose, and urea compared to the non-hypertensive group (p < 0,05) (Table II). These data suggest that COVID-19 patients with hypertension tend to exhibit more severe inflammation and organ damage symptoms than non-hypertensive COVID-19 patients, which may lead to a poor prognosis.

Clinical Characteristics on the Severity of COVID-19

Based on the baseline characteristics analysis with the severity profile as the dependent variable, it is known that comorbidities, symptoms of shortness of breath, and vital signs in the form of oxygen saturation and respiratory rate show a significant relationship with weak correlation strength. Furthermore, based on the analysis of laboratory parameters with severity profiles, it was found that several hematological parameters and AST showed a significant association with weak correlation strength (p<0.05; r=0.20–0.399) (Table III).

Association of Clinical Characteristics with Post-treatment Conditions of COVID-19 Patients

The cure rate for COVID-19 sufferers is relatively high (83%). However, the patient's clinical condition at the time of admission affected the post-treatment condition. Table 4 shows that comorbid diseases (CKD, CVD), low oxygen saturation, NLR values > 3.13, and AST values were associated with post-treatment patient mortality, with the strength of the correlation being weak. Urea levels showed a moderate correlation strength with post-treatment conditions. The average length of stay for discharged patients was 13 days (Table IV).

This study provides information about clinical characteristics and disease severity profiles of COVID-19 patients with hypertension in Palu, Central Sulawesi. It presents the latest status of SARS-CoV-2 infection in Indonesia, especially in Central Sulawesi. Hypertension was identified as a significant factor in the transmission of COVID-19. Association with the inhibition of the renin-angiotensin-aldosterone system (RAAS), ACE-2, confirmed study increased susceptibility to COVID-19. Our study shows that the dominant COVID-19 patients have hypertension in the middle age group. A study in South Korea showed that 50-59 was the highest group who received hospital treatment due to COVID-19, and 30% of hospitalized patients carry comorbid hypertension (Park *et al.*, 2020). The study in Wuhan also showed that the average age of COVID-19 patients was 56 years, with the highest comorbidity being hypertension (30%) (Zhou *et al.*, 2020). The higher number of age groups may explain our study's higher prevalence of hypertension.

Table II Laboratory parameters of COVID-19 patients with Hypertension

Variable	Normal range	Total (n = 185)	Hypertension (n = 79)	Non-hypertension (n = 106)	p Value
Hematology					
WBC (10^9/L)	4–11	8.7±4.74	7.96±3.7	9.19±5.34	0.124[a]
RBC (10^{12}/L)	4.1-6.1	4.5±0.87	4.57±0.92	4.45±0.84	0.581[a]
Hemoglobin (g/dL)	14-18	12.6±2.54	12.85±2.43	12.47±2.6	0.337[a]
Hematocrit (%)	36-47	36.9±7.15	37.19±7.1	36.7±7.2	0.546[a]
Platelets (10^9/L)	150-450	233±95.24	225.6±92.7	238.4±97.1	0.330[a]
Neutrophil (%)	50-70	39.9±33.2	66.6±31.7	70.5±29.6	0.266[a]
Lymphocyte (%)	20-40	12.1±22.4	16.6±12.2	19.3±26.6	0.960[a]
Monocyte (%)	2-8	5±5.6	4.9±5.2	5.1±5.8	0.988[a]
Eosinophil (%)	0-1	0.13±0.34	0.16±0.47	0.11±0.21	0.890[a]
Basophil (%)	1-3	0.53±0.78	0.5±0.67	0.53±0.86	0.715[a]
NLR ≥ 3,13		129 (70%)	52 (66%)	77 (73%)	0.403[b]
Electrolyte					
Sodium (mEq/L)	136-146	136±9.83	135.4±13	136.5 ±6.6	0.772[a]
Potassium (mEq/L)	3.5-5	3.9±0.91	3.97±0.71	3.99±1.03	0.409[a]
Chloride (mEq/L)	98-106	98.1±5.1	97.9±5.52	98.2±4.78	0.589[a]
Blood Chemistry					
AST (U/L)	<45	46.7±37	48.8±93.4	40±46.4	0.168[a]
ALT (U/L)	<35	43.8±70.3	51.04±40.3	43.4±34.9	**0.047[a]**
Creatinine (U/L)	0.6-1.1	1.77±2.98	1.8±2.51	1.74±3.3	0.083[a]
Urea (U/L)	<50	47±76	46.63±51.9	47.26±90	**0.003[a]**
Blood Glucose (mg/dL)	70-200	153±100.3	186±123	128±70.5	**0.000[a]**

WBC (White Blood Cell), RBC (Red Blood Cell), MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Hemoglobin), MCHC (Mean Corpuscular Hemoglobin Concentration), RDW-CV (Red Blood Cell Distribution Width Coefficient of Variation), MPV (Mean Platelet Volume), NLR (Neutrophil to lymphocyte ratio), AST (Aspartate Amino Transferase, ALT (Alanine Amino Transferase). [a]Mann Whitney test

In addition, our study found that the risk of death of COVID-19 patients was more significant in the elderly group (30%). Previously, older age has been reported as a significant independent predictor of mortality in SARS and MERS. Another study in macaques inoculated with SARS-CoV found that more aged macaques had a more robust response to viral infection than younger adults because of increased differential expression of genes associated with inflammation and reduced expression of type I interferon (Smits *et al.*, 2010).

Our study found more female than male patients with hypertension in COVID-19 infection. The reduced susceptibility of women to viral infections may occur with protection from the X chromosome and sex hormones, which play essential roles in innate and adaptive immunity (Giefing-Kröll *et al.*, 2015). However, it is suspected that the susceptibility of 55-year-old women to develop hypertension is caused by decreased levels of estrogen and progesterone, which affect the balance of the renin-angiotensin system in the kidneys, which functions to maintain blood pressure stability. Estrogen receptors also protect the body and assist the immune system, including T cells, B cells, macrophages, neutrophils, dendritic cells, and natural killer cells. (Channappanavar *et al.*, 2017).

In our study, the most common symptoms were cough, dyspnea, and fever history. In the hypertension group, 49% of patients felt fatigued, but only 43% had a history of fever. This symptom is the same as the results of many studies (Karyono and Wicaksana, 2020; Niu *et al.*, 2020; Park *et al.*, 2020). Fever, fatigue, and dry cough are the main manifestations. Nasal obstruction, runny nose, and other upper respiratory symptoms are rare. About half of patients develop dyspnea, and severe cases progress rapidly to acute respiratory distress syndrome (ARDS), septic shock, irreversible metabolic acidosis, coagulation dysfunction, and even death (Deng and Peng, 2020; Fuk-Woo Chan, *et al.*, 2020).

Table III. Correlation of Clinical Characteristics with the Severity of COVID-19 Patients

Variable	Severity Disease			p Value	r Value
	Mild (n = 27)	Moderate (n = 129)	Severe (n = 29)		
Age group (y)				0.045[a]	0.140[a]
18-39	11 (41%)	48 (37%)	6 (21%)		
40-59	12 (44%)	55 (43%)	10 (34%)		
≥60	4 (15%)	26 (20%)	13 (45%)		
Sex				0.048[a]	0.114[a]
Female	12 (44%)	52 (40%)	19 (65%)		
Male	15 (56%)	77 (60%)	10 (55%)		
Comorbidities Type					
CVD (Other than Hipertension)	2 (7%)	21 (16%)	11 (38%)	0.007[a]	0.265[a]
Sign and Symptoms					
Dyspnea	2 (7)	74 (57%)	19 (66%)	0.000[a]	0.292[a]
Vital Sign					
Oxygen saturation (%)	96±1.5	95±4.5	86±13	0.000[b]	-0.314[b]
Respiration rate (bpm)	22±2.7	25±5.4	29±6	0.000[b]	0.397[b]
Hematology					
Hematocrit (%)	33.9±5.3	37.4±7.1	37.6±8.1	0.009[b]	0.207[b]
Neutrophil (%)	52±33	70±32	77±9.6	0.000[b]	0.327[b]
NLR ≥ 3,13	18 (67%)	84 (65%)	27 (93%)	0.012[a]	0.166[a]
Blood Chemistry					
AST (U/L)	21.4±10.9	44.6±77	61±66	0.021[b]	0.321[b]
ALT (U/L)	29.9±11	46.6±36.7	62.3±49	0.000[b]	0.198[b]
Urea (U/L)	31.7±28	40.35±55.5	89.8±144	0.006[b]	0.152[b]
Hospitalization time (days)	13±3.9	12±4.4	8±6	0.001[b]	-0.223[b]

CVD (Cardiovascular disease), MCV (Mean Corpuscular Volume), MCHC (Mean Corpuscular Hemoglobin Concentration), RDW-CV (Red Blood Cell Distribution Width Coefficient of Variation), MPV (Mean Platelet Volume), NLR (Neutrophil to lymphocyte ratio), AST (Aspartate Amino Transferase, ALT (Alanine Amino Transferase). [a]Somers'd test, [b]Spearman Test

Patients who do not have a fever or a low-grade fever can increase the difficulty of identifying and diagnosing COVID-19 in clinical practice. In this study, it was found that oxygen saturation and respiration rate had a relationship with the mortality rate of COVID-19 patients. COVID-19 patients who experience decreased oxygen saturation or increased respiratory rate upon hospital admission significantly increase the risk of death (Zhou *et al*., 2020). COVID-19 patients often experience hypoxia without apparent symptoms, so the opportunity to start treatment early tends to be too late.

In addition, 63% of patients infected by COVID-19 undergoing treatment have underlying chronic diseases, mainly cardiovascular and diabetes. The hypertension group tends to have other comorbidities, namely diabetes mellitus, cardiovascular disease (other than hypertension). Our study found that the hypertensive group had higher glucose levels than the non-hypertension group. Comorbid hypertension, like diabetes and chronic kidney disease, is associated with severe COVID-19 and poor outcomes (Park *et al*., 2020). Researchers have identified that poor glycemic control is related to the prognosis of severe COVID-19 patients in the hypertension group. COVID-19 patients with diabetes have a higher risk of hospital stay and more extended periods (Hill, *et al.,* 2020; Wicaksana, *et al.*, 2020).

Comorbid diseases such as hypertension, diabetes, and chronic kidney disease, are associated with severe COVID-19 and poor outcomes. In this study, we did not find a relationship between hypertension and blood pressure with the severity and mortality of Covid-19 patients.

Table 4. Correlation of Clinical Characteristics with Post-treatment Conditions of COVID-19 Patients

Variable	Post-treatment		p Value	r Value
	Discharged (n = 153)	Death (n = 32)		
Age group (y)			0.008 [a]	0.198[a]
18-39	62 (40%)	3 (9%)		
40-59	64 (42%)	13 (41%)		
≥60	27 (18%)	16 (50%)		
Comorbidities Type				
CKD	9 (6%)	6 (19%)	0.027[a]	0.247[a]
CVD (Other than Hipertension)	22 (14%)	12 (38%)	0.005[a]	0.220[a]
Vital Sign				
Temperature (°C)	37 ±0.63	36 ±0.88	0.027[b]	-0.163 [b]
Oxygen saturation (%)	96 ±3.37	86 ±13.64	0.000 [b]	-0.323 [b]
Respiration rate (bpm)	24 ±4.23	30 ± 7.8	0.000 [b]	-0.114 [b]
Severity Disease			0.000[a]	0.281 [a]
Mild	27 (18%)	0 (0%)		
Moderate	116 (76%)	13 41%)		
Severe	10 (6%)	9 (28%)		
Hematology				
Platelets (10^9/L)	241.1 ±95.5	193.96 ±85	0.015[b]	-0.179 [b]
Neutrophil (%)	66.8 ±29.6	78.6 ±33.5	0,008 [b]	0.195 [b]
Lymphocyte (%)	19.9 ±23.3	9,5 ±5.38	0,000 [b]	-0.318 [b]
Eosinophil (%)	0.15 ±0.37	0.05 ±0.09	0.033 [b]	-0.157 [b]
NLR > 3,13	97 (63%)	32 (100%)	0,000[a]	0.248[a]
Blood Chemistry				
AST (U/L)	40.22 ±71.3	60.68 ±63.5	0.012 [b]	0.277 [b]
ALT (U/L)	43.39 ±35	62.29 ±44.7	0.000 [b]	0.186 [b]
Creatinine (U/L)	1.54 ±2.43	2.88 ±4.7	0.033 [b]	0.157 [b]
Urea (U/L)	34 ±46.8	108.9 ±136.7	0.000 [b]	0.435 [b]
Hospitalization time (days)	13 ±3.23	7 ±7.45	0.000[c]	

CKD (Chronic Kidney Disease), CVD (Cardiovascular disease), MCV (Mean Corpuscular Volume), RDW-CV (Red Blood Cell Distribution Width Coefficient of Variation), NLR (Neutrophil to lymphocyte ratio), AST (Aspartate Amino Transferase, ALT (Alanine Amino Transferase). [a]Lambda test, [b]Spearman Test, [c]Mann Whitney test

This result is in line with the research conducted by de Terwangne (2020), which found that although the percentage of patients experiencing hypertension admitted with a critical condition was higher than severe and moderate, there was no significant relationship between hypertension and blood pressure with the severity of Covid-19 (de Terwangne *et al.*, 2020). Another study involving the population of Surabaya showed no significant relationship between hypertension and blood pressure with the severity of Covid-19 (Tsany, 2021). In contrast to the research reported by Park (2020) showed that hypertension had a significant relationship with the severity of Covid-19 patients, where 73.1% of hypertensive patients experienced a critical illness or death during hospitalization or isolation due to Covid-19 (Park *et al.*, 2020). We

think that the use of antihypertensive groups may play a role in RAS influencing the severity of Covid-19. De Terwangne (2020) found that chronic treatment using ACE inhibitors in hypertensive patients had a significant relationship with the severity of Covid-19 patients (de Terwangne *et al.*, 2020). Fang (2020) revealed that patients with heart disease, hypertension, or diabetes, treated with drugs that increase ACE2 are at higher risk for severe COVID-19 infection. Therefore, it should be monitored for the use of drugs that modulate ACE2, such as ACE inhibitors or ARBs (Lei and Karakiulakis, 2020).

We found that CVD comorbidity was associated with the severity of COVID-19. Another study concluded that patients with comorbid had a nearly three times higher risk for ICU admission

(OR 2.79; 95% CI: 1.85-4.22) and death (OR 3.21; 95% CI: 1.82-5,64) (Roncon, *et al.*, 2020). Most cases were discharged as asymptomatic patients, but 17% died. It is related to the severity of the patient at the time of admission to the hospital, namely moderate-severe. For the hypertension group, moderate and severe severity was directly proportional to the percentage of mortality in this group. A previous study found that more than 50% of COVID-19 patients had sepsis (Zhou *et al.*, 2020). Viral infection is the only reason for sepsis. Sepsis is a common complication directly caused by infection with SARS-CoV-2. Therefore, sepsis is expected to experience these critically ill COVID-19 patients (Beltrán-García *et al.*, 2020). However, further research is needed on the pathogenesis of sepsis in COVID-19.

Based on laboratory tests, most patients have increased neutrophils and decreased lymphocytes, but this is not associated with comorbid hypertension. Instead, increased neutrophils, NLR values, and decreased lymphocytes are related to the severity of disease and mortality rate of COVID-19. These results indicate that SARS-CoV-2 acts on lymphocytes, especially T lymphocytes. Virus particles spread through the respiratory mucosa and infect other cells, induce a cytokine storm in the body, generate a series of immune responses, and cause changes in peripheral white blood cells and immune cells such as lymphocytes (Chen *et al.*, 2020).

In this study, the hypertension group showed an abnormal liver and kidney function tests pattern. An increase in Ureum, creatinine, ALT, and AST values were also associated with the severity and mortality rate of COVID-19. Several mechanisms related to renal impairment in COVID-19, such as the comorbid CKD, SARS-CoV-2 induces renal resident cell cytotoxic, and symptoms such as fever and shock can cause renal hypoperfusion (Liu *et al.*, 2021). The theory about the relationship between increased AST and ALT values when admission to SARS-CoV-2 infection is unclear. The ACE2 receptor for viral entry is more expressed in cholangiocytes than in hepatocytes (Moon and Barritt, 2021; Sharma *et al.*, 2021). We, therefore, assumed that the direct cytopathic effect of SARS-CoV-2 might not be the primary mechanism of COVID-19-associated liver damage. Liver dysfunction in COVID-19 can be associated with an uncontrolled immune reaction, sepsis, or drug-induced liver injury, in addition to the direct cytopathic effect of the virus, but further monitoring is needed (Xu, *et al.*, 2021).

CONCLUSION

Hypertension is associated with clinical characteristics but is not a poor prognostic factor for the severity profile and mortality rate. It appeared that age group, liver function, and kidney function were positively correlated with severity and mortality in COVID-19 patients in Palu, Central Sulawesi.

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ADDITIONAL INFORMATION

Part of the results described in this study has been presented at the International Teleconference on Technology and Policy for Supporting Implementation of Covid-19 Response and Recovery Plan in Southeast Asia (ITTP-Covid19), 6th-8th August 2021

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