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Comorbidities of COVID-19 patients associated with mortality at the Baubau Regional Public Hospital, South East Sulawesi

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that cause coronavirus disease 2019 (COVID-19) has become a global pandemic. Until November 30th, 2020, World Health Organization (WHO) confirmed 61,869,330 positive cases with 1,448,896 deaths (CFR 2.3%). Some comorbidities are associated with the COVID-19 mortality. This study aimed to investigate risk factors of the COVID-19 mortality at the Baubau Regional Public Hospital, Sout East Sulawesi. It was a cross-sectional study with a retrospective analysis involving 81 COVID-19 patients. Purposive sampling was applied in this study. Chi-square analysis was conducted to calculate odd ratio (OR). The result showed that in the period from January to September 2021, 30 COVID-19 patients died consisting of 20 male and 10 female. Most of the patients died were >45 yo and only 4 patients died were <45 yo. Among the patients died, 11 patients had hypertension, 12 patients had type 2 diabetes mellitus (DM), 4 patients had pulmonary TB and 3 patients had dyspepsia. Further analysis showed that hypertension (OR=6.803; 95%CI: 1.925-24.038; p=0.002) and dyspepsia (OR=0.222; 95%CI: 0.059-0.838; p=0.016) were significantly associated with the COVID-19 mortality, whereas type 2 DM (OR=1.123; 95%CI: 0.445-2.832; p=0.495) and pulmonary TB (OR=0.559; 95%CI: 0.059-0.838; p=0.270) were not. In conclusion, hypertension is risk factor, whereas dyspepsia is protective factor of COVID-19 mortality.

ABSTRAK

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) yang menyebabkan penyakit *coronavirus disease 2019* (COVID-19) telah menjadi pandemi global. Hingga 30 November 2020, Organisasi Kesehatan Dunia (WHO) mengonfirmasi 61.869.330 kasus positif dengan 1.448.896 kematian (CFR 2,3%). Beberapa penyakit penyerta dikaitkan dengan kematian akibat COVID-19. Penelitian ini bertujuan untuk mengkaji faktor risiko kematian akibat COVID-19 di RSUD Baubau Sulawesi Tenggara. Penelitian ini merupakan penelitian potong lintang dengan analisis retrospektif yang melibatkan 81 pasien COVID-19. Sampling purposive dilakukan dalam penelitian ini. Analisis chi-kuadrat dilakukan untuk menghitung *odd ratio* (OR). Pada periode Januari hingga September 2021, pasien COVID-19 meninggal sebanyak 30 orang yang terdiri dari 20 laki-laki dan 10 perempuan. Pasien meninggal terbanyak berusia >45 tahun dan hanya 4 pasien meninggal berusia <45 tahun. Pasien meninggal tersebut terdiri dari 11 pasien menderita hipertensi, 12 pasien menderita diabetes melitus (DM) tipe 2, 4 pasien menderita TBC paru, dan 3 pasien menderita dispepsia. Analisis lebih lanjut menunjukkan bahwa hipertensi (OR=6,803; 95%CI: 1,925-24,038; p=0,002) dan dispepsia (OR=0,222; 95%CI: 0,059-0,838; p=0,016) berhubungan secara signifikan dengan kematian akibat COVID-19, sedangkan DM tipe 2 (OR=1,123; 95%CI: 0,445-2,832; p=0,495) dan TB paru (OR=0,559; 95%CI: 0,059-0,838; p=0,270) tidak. Kesimpulannya, hipertensi merupakan faktor risiko, sedangkan dispepsia merupakan faktor protektif terhadap kematian akibat COVID-19.

Keywords:
COVID-19;
dyspepsia;
hypertension;
mortality;
risk factor

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged in China in December 2019 and has since spread over the world. In severe patients with comorbidities, COVID-19 can cause death.[1,2] The World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of worldwide concern on January 30th, 2020, and a pandemic on March 11th, 2020.[3] It was reported around 20-51% of the patients had comorbidities such as hypertension, diabetes, cardiovascular, and other cerebrovascular.[4-6]

The first pathological findings of COVID-19 was obtained from a lung tissue biopsy sample of a patient died due to SARS-CoV-2 infection. The most common pathology of COVID-19 is pneumonia which may be accompanied by acute respiratory distress syndrome (ADRS) and can be fatal. COVID pneumonia is a potentially life-threatening complication that is most common in older patients, and patients with obesity, hypertension and diabetes.[6,7] These pathological findings can help physicians to identify a cause of death and formulate a therapeutic strategy to reduce mortality.[7]

In Indonesia, the first case of COVID-19 was reported on March 2nd, 2021 and then the cases are increasing and spreading rapidly throughout Indonesia. The Ministry of Health reported 70,736 confirmed cases of COVID-19 on July 9th, 2020, with 3,417 mortalities (CFR 4.8%). According to the National Task Force for COVID-19 Handling, the most positive confirmed cases (30.8%) were in the age range of 31-45 years, whereas the least occurred in the age range of 0-5 years (2.5%). Patients over 60 years of age would have the greatest fatality rate (43.3 percent). Males account for 56.7% of all death cases, while females account for 43.5%. Hypertension (11.8%), diabetes mellitus (10.6%), heart disease (6.9%), and renal disease (3%) are among the other causes of mortality.[8]

The Provincial Health Office of South East Sulawesi reported there were 6,502 confirmed cases on November 30th, 2020, with 106 deaths (CFR 1.63%). The Baubau Regional Public Hospital is one of the COVID-19 referral hospital in the province. This study aimed to investigate the risk factors of the COVID-19 mortality in the Baubau Regional Public Hospital. The risk factors included age, gender, and comorbidities were analyzed in this study.

SUBJECTS AND METHODS

Population and study design

This retrospective observation research used medical record from March to August 2021. Patients confirmed positive for COVID-19 who came to the Baubau Regional Public Hospital were gathered. The comorbidities of COVID-19 include hypertension, pulmonary TB, type 2 DM and dyspepsia were then listed.

Protocol of study

The diagnosis of COVID-19, type 2 DM, hypertension, and dyspepsia was taken from the medical records. The diagnosis of COVID-19 was carried out based on clinical examination using Swab Antigen and PCR in the hospital laboratory, then continued by reviewing the results. Patients with COVID-19 positive having comorbidities such as hypertension which had been diagnosed by a cardiologist, type 2 DM and dyspepsia by an internist, and co-morbidities with pulmonary TB by a pulmonologist were recruited as study sample. The protocol of the study was approved the Medical Research Ethic Board, Faculty of Medicine and Health Science, University of Bengkulu, Indonesia (ref. no. 2041N30.14.9 tLT 12022).

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows Version 20.0 (IBM Corp. Armonk, NY, USA). The univariate analysis was used to describe the characteristics of subjects. The bivariate analysis using the chi-square was used to calculate the odds ratio (OR) representing the association between potential risk factors of the COVID-19 mortality. If the OR value >1 indicates increased occurrences of a mortality and if OR value <1 indicates decreased occurrences of a mortality. A p value <0.05 was considered significant.

RESULTS

The characteristics of patients with COVID-19 at Baubau Regional Public Hospital are presented in TABLE 1. Male patients were higher than female patients. Patients aged >45 yr were higher than ≤45 yr. Most patients with COVID-19 did not have comorbidities.

Hypertension (p=0.002) and dyspepsia (p=0.016) were significantly associated with the COVID-19 mortality, whereas type 2 DM (p=0.495) and pulmonary TB (p=0.270) were not significantly associated with the COVID-19 mortality at the Babau Regional Public Hospital (TABLE 2). The COVID-19 patients with hypertension experienced approximately 6.8 times the risk of mortality (OR=6.803; 95%CI: 1.925-24.038), whereas the COVID-19 patients with dyspepsia experienced approximately 0.2 times the risk of mortality (OR=0.222; 95%CI: 0.059-0.838).

TABLE 1. The characteristic of patients with COVID-19 at Baubau Regional Public Hospital

Variable	n (%)
Gender	
• Male	51 (63.0)
• Female	30 (37.0)
Age (yr)	
• ≤ 45	19 (23.5)
• > 45	62 (76.5)
Hypertension	
• Yes	15 (18.5)
• No	66 (81.5)
Type-2 DM	
• Yes	31 (38.3)
• No	50 (61.7)
Pulmonary TB	
• Yes	15 (18.5)
• No	66 (81.5)
Dyspepsia	
• Yes	20 (24.7)
• No	61 (75.3)
Total	81 (100)

TABLE 2. Analysis of risk factors for COVID-19 mortality included hypertension, type 2 DM, pulmonary TB, and dyspepsia

Comorbid	Died	Survive	Total	OR (95% CI)	p
	n (%)	n (%)	n (%)		
Hypertension					
• Yes	11 (73.3)	4 (26.7)	15 (100)	6.803 (1.925–24.038)	0.002
• No	19 (28.8)	47 (71.2)	66 (100)		
Total	30 (37.0)	51 (63.0)	81 (100)		
Type 2 DM					
• Yes	12 (38.7)	19 (61.3)	31 (100)	1.123 (0.445–2.832)	0.495
• No	18 (36.0)	32 (64.0)	50 (100)		
Total	30 (37.0)	51 (63.0)	81 (100)		
Pulmonary TB					
• Yes	4 (26.7)	11 (73.3)	15 (100)	0.559 (0.161–1.946)	0.270
• No	26 (39.4)	40 (60.0)	66 (100)		
Total	30 (37.0)	51 (63.0)	81 (100)		
Dyspepsia					
• Yes	3 (15.0)	17 (85.0)	20 (100)	0.222 (0.059 – 0.838)	0.016
• No	27 (44.3)	34 (55.7)	61 (100)		
Total	30 (37.0)	51 (63.0)	81 (100)		

DISCUSSION

Among the risk factors investigated in this study, only hypertension was associated with the COVID-19 mortality (OR=6.803; 95%CI: 1.925-24.038; p=0.002). The COVID-19 patients with hypertension experienced approximately 6.8 times the risk of mortality compared to without hypertension or normotension. Previous studies reported that COVID-19 patients with hypertension are at higher risk of mortality and developing severe disease.[9-12] It was reported that hypertension is more prevalent in COVID-19 patients who lead to the primary endpoint and severe disease.[9] Moreover, COVID-19 patients with cardiovascular disease and hypertension had a higher mortality rate as compared to patients that without comorbid.[10] A meta-analysis included 24 observational studies reported that hypertension is associated with a significantly increased risk of COVID-19 mortality in hospital.[11] However, another meta-analysis reported that hypertension is not an independent risk factor for in-hospital mortality when adjusted for other comorbidities in hospitalized COVID-19 patients.[12]

Several hypotheses have been postulated to explain of the association between hypertension and COVID-19 mortality. Hypertension is more frequently experienced in elderly patients and it is often associated with other comorbidities such as cardiovascular disease, diabetes, and respiratory disorders. These comorbidities can contribute to COVID-19 severity and mortality.[9,12,13] Hypertension plays an important role in the regulation of renin-angiotensin-aldosterone system (RAAS), inflammation, immune responses, and the gastrointestinal tract which

partly explain in COVID-19 severity and mortality.[14]

The RAAS is key regulator of blood volume and vascular resistance in the body. Angiotensin-converting-enzyme 2 (ACE2) is an important component of the RAAS in the heart, kidney, and lung. In the other hand, ACE2 receptor is the main target of the SARS-CoV-2 virus to enter human cells.[15] Hypertension is associated with an increase in ACE2 receptor expression, potentially providing more entry points for the virus leading to promote viral interaction with host cells and exacerbating COVID-19.[15-17]

Hypertension activates the innate and adaptive immune systems, leading to cytokine release and enhanced inflammation. In hypertensive patients, the amounts of circulating monocytes, macrophages, CD8+ T cells, and CD4+ T cells are increased in the inflammatory environment.[18,19] High blood pressure promotes an acute cardiac inflammatory response and induces immune cell infiltration and activation in the myocardium that promote cardiac or other organ damage in patients with severe COVID-19.[14] SARS-CoV-2 infection also activates both innate and adaptive immune responses, triggers release of proinflammatory factors, and results in hyperinflammation or cytokine storms which can lead to ADRS and multiple organ failure (MOF).[14,20] The combination of pre-existing inflammation from hypertension and the hyperinflammation as well as immune responses to the SARS-CoV-2 infection can contribute to COVID-19 severity.

In contrast with hypertension, this study showed that dyspepsia was not the risk factor of COVID-19 mortality. The COVID-19 patients with dyspepsia only experienced approximately 0.2 times the risk of mortality (OR=0.222; 95%CI: 0.059-0.838) compared to without dyspepsia. With OR value < 1, it is indicated that dyspepsia is the protective factor of COVID-19 mortality. The protective factor of dyspepsia has been reported previously. Inversely, it was reported that COVID-19 pandemic negatively affected functional dyspepsia or irritable bowel syndrome. The COVID-19 is important independent factor associated with deterioration in gastrointestinal symptoms.[21] However, during COVID-19 quarantine an improvement of the majority of upper gastrointestinal symptoms was reported.[22] Further study is needed obtain conclusive evidence linking dyspepsia directly to COVID-19 mortality.

CONCLUSION

In conclusion, hypertension is risk factor of COVID-19 mortality at the Baubau Regional Public Hospital, South East Sulawesi. In contrast, dyspepsia is protective factor of COVID-19 mortality in this study. Further study should be conducted to obtain conclusive evidence linking dyspepsia directly to COVID-19 mortality.

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