

JURNAL

RESPIROLOGI

INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respiriology



Respiratory Emergency in Hospitalized patient with Intrathoracic Malignancy at H. Adam Malik General Hospital

Concordance of TST and QFT-Plus, Sensitivity and Specificity of TST and QFT-Plus in Detection of LTBI in MDR TB Contact

Analysis of Comorbidity and Its Association with Disease Severity and Mortality Rate in Hospitalized COVID-19 Patients

Correlation between N-Acetyltransferase 2 (NAT2) Polymorphism Genotype with Plasma Isoniazid (INH) Concentration in MDR TB Patients Receiving Short Regimen in West Sumatera

Impact of Pulmonary Rehabilitation on Hospitalization Duration, IL-6 Levels, and Respiratory Muscle Power in Hospitalized Community-Acquired Pneumonia Patients

The Effect of Inspiratory Breathing Muscle Exercise Using Spirometer on Changes in Lung Function and Dyspnea Severity in Tuberculosis Pleurisy Patients

Risk Factors of Prolonged QTc Interval in Patients with Drugs-Resistant Tuberculosis

The Correlations Between Measurement of Lung Diffusing Capacity for Carbon Monoxide and The Severity Group of Asthma Patients in Persahabatan Hospital Jakarta

Safety of Favipiravir for Treatment of COVID-19: Latest Systematic Review

The Efficacy of Remdesivir in Reducing SARS-CoV-2 Viral Load and Its Safety on COVID-19 Patients: A Systematic Review

JURNAL RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respiriology

Editorial Advisory Board

M. Arifin Nawas
Faisal Yunus
Agus Dwi Susanto

Editorial-in-Chief

Fanny Fachrucha

Editorial Board

Feni Fitriani Taufik
Noni Novisari Soeroso
Tutik Kusmiati
A. Farih Raharjo
Ginangjar Arum Desianti
Irandi Putra Pratomo
Jamal Zaini
Mia Elhidsi

International Editorial Board

Guido Vagheggini
Mayank Vats
Motoyasu Kato
Ira Paula Wardono

Secretariat

Shalzaviera Azniatinesa
Suwondo
SST : Surat Keputusan Menteri Penerangan RI
No.715/SK/DitjenPPG/SST/1980 Tanggal 9 Mei 1980

Editorial Office

PDPI Jl. Cipinang Bunder, No. 19, Cipinang Pulo Gadung
Jakarta Timur 13240 Telp: 02122474845
Email : editor@jurnalrespirologi.org
Website : <http://www.jurnalrespirologi.org>

Publisher

The Indonesia Society of Respiriology (ISR)
Published every 3 months (January, April, July & October)

Jurnal Respirologi Indonesia

2nd Rank Accreditation
According to the Decree of the Minister of Research and
Technology/Head of the National Research and Innovation
Agency of the Republic of Indonesia Number: 200/M/KPT/2020
December 23, 2020

JURNAL RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respiriology

VOLUME 42, NUMBER 1, January 2022

TABLE OF CONTENT

Original Article

- Respiratory Emergency in Hospitalized patient with Intrathoracic Malignancy at H. Adam Malik General Hospital* 1
Elizabeth Napitupulu, Noni Novisari Soeroso, Setia Putra Tarigan, Putri Eyoer
- Concordance of TST and QFT-Plus, Sensitivity and Specificity of TST and QFT-Plus in Detection of LTBI in MDR TB Contact* 9
Rullyano Hardian, Reviono, Harsini, Yusup Subagio Sutanto
- Analysis of Comorbidity and Its Association with Disease Severity and Mortality Rate in Hospitalized COVID-19 Patients* 18
Anthony Christanto, Aditya Sri Listyoko, Ngakan Putu Parsama Putra
- Correlation between N-Acetyltransferase 2 (NAT2) Polymorphism Genotype with Plasma Isoniazid (INH) Concentration in MDR TB Patients Receiving Short Regimen in West Sumatera* 26
Mega Senja, Masrul Basyar, Yessy Susanty Sabri, Afriani
- Impact of Pulmonary Rehabilitation on Hospitalization Duration, IL-6 Levels, and Respiratory Muscle Power in Hospitalized Community-Acquired Pneumonia Patients* 34
Santony, lin Noor Chozin, Teguh Rahayu Sartono, Rahmad, Harun Al Rasyid
- The Effect of Inspiratory Breathing Muscle Exercise Using Spirometer on Changes in Lung Function and Dyspnea Severity in Tuberculosis Pleurisy Patients* 43
Irmainsi, Herry Priyanto, Dewi Behtri Yanifitri
- Risk Factors of Prolonged QTc Interval in Patients with Drugs-Resistant Tuberculosis* 52
Andika Pradana, Katharine, Parluhutan Siagian
- The Correlations Between Measurement of Lung Diffusing Capacity for Carbon Monoxide and The Severity Group of Asthma Patients in Persahabatan Hospital Jakarta* 58
Bulkis Natsir, Faisal Yunus, Triya Damayanti
- ### Literature Review
- Safety of Favipiravir for Treatment of COVID-19: Latest Systematic Review* 67
Rizki Oktarini, Anna Rozaliyani, Ratika Rahmasari, Muhammad Alkaff, Rani Sauriasari
- The Efficacy of Remdesivir in Reducing SARS-CoV-2 Viral Load and Its Safety on COVID-19 Patients: A Systematic Review* 76
Afifah Fauziyyah, Ratika Rahmasari, Rani Sauriasari

Analysis of Comorbidity and Its Association with Disease Severity and Mortality Rate in Hospitalized COVID-19 Patients

Anthony Christanto, Aditya Sri Listyoko, Ngakan Putu Parsama Putra

Department of Pulmonology and Respiratory Medicine Faculty of Medicine, Universitas Brawijaya, RSUD Saiful Anwar, Malang

Abstract

Background: Comorbidity is a major factor in determining the outcome of COVID-19. However, existing studies regarding comorbidities and the disease severity and mortality of COVID-19 are mostly based on studies in the whole community, and not on those admitted to hospitals. This study aims to determine the demographic profile of comorbidities among COVID-19 patients hospitalized in tertiary care referral hospitals and its association with disease severity and mortality.

Methods: We analyzed the data from 60 laboratory-confirmed patients in our hospital in Malang City, East Java, Indonesia from March 12th, 2020 to June 5th, 2020. We describe the demographic profile of the patients and perform statistical analysis to determine its relationship to disease severity and mortality.

Results: The majority of the study samples (66.7%) were categorized as having a severe disease. Thirty-seven samples (61.7%) had at least one comorbidity. The mortality rate among the study population is 30.0%, and 37.8% among those with comorbidities. The most prevalent comorbidity was hypertension (40.0%), followed by heart failure (35.0%) and diabetes (25.0%). There is a statistically significant relationship between the presence of comorbidities and disease severity and between disease severity and mortality ($p < 0.05$). Diabetes was the only comorbidity with a significant relationship towards mortality in our study ($p < 0.05$, OR 4.0 95% CI 1.16-13.74).

Conclusion: Comorbidities are associated with worse disease severity and death in hospitalized COVID-19 patients. (*J Respirol Indones* 2022; 42(1): 18–25)

Keywords: Comorbidities; COVID-19; Disease Severity, Mortality Rate

Analisis Komorbiditas dan Hubungannya dengan Tingkat Severitas Penyakit dan Mortalitas pada Pasien COVID-19 yang Dirawat di Rumah Sakit

Abstrak

Latar Belakang: Komorbiditas merupakan faktor yang sangat penting dalam menentukan outcome dari COVID-19. Namun, studi yang telah ada terkait komorbiditas dan hubungannya dengan tingkat severitas COVID-19 dan mortalitas utamanya dibuat berdasarkan pengamatan pada komunitas, dan bukan pada mereka yang dirawat di rumah sakit. Studi ini bermaksud untuk mengamati dan menentukan profil demografik dari komorbiditas pada pasien-pasien COVID-19 yang dirawat di rumah sakit rujukan tersier dan hubungannya dengan tingkat severitas dan mortalitas.

Metode: Kami menganalisa data dari 60 pasien terkonfirmasi COVID-19 di rumah sakit kami di Kota Malang, Jawa Timur, dari Maret hingga Juni 2020. Kami menjabarkan profil demografik dari komorbiditas pada pasien kami dan melakukan analisa statistik untuk menentukan hubungannya dengan tingkat severitas penyakit dan mortalitas.

Hasil: Mayoritas dari sampel (66.7%) termasuk dalam kategori penyakit berat. 37 sampel (61.7%) mempunyai setidaknya satu komorbiditas. Tingkat mortalitas diantara sampel adalah 30% dan 37.8% pada kelompok sampel dengan komorbiditas. Komorbiditas dengan prevalensi tertinggi adalah hipertensi (40.0%), diikuti oleh gagal jantung (35.0%), dan diabetes (25.0%). Terdapat hubungan yang bermakna antara ada atau tidaknya komorbiditas dengan tingkat severitas penyakit dan antara tingkat severitas penyakit dan mortalitas ($p < 0.05$). Diabetes merupakan satu-satunya komorbiditas dengan hubungan bermakna terhadap mortalitas pada studi kami ($p < 0.05$; OR 4.0, 95% CI 1.16-13.74).

Kesimpulan: Pada pasien COVID-19 yang dirawat di rumah sakit, adanya komorbiditas berhubungan dengan tingkat severitas yang lebih berat dan mortalitas. (*J Respirol Indones* 2022; 42(1): 18-25)

Kata kunci: komorbiditas; COVID-19; Tingkat severitas; Angka mortalitas

INTRODUCTION

On December 31, 2019, China reported a mysterious case of pneumonia of unknown cause. Within three days, there were 44 patients with these cases, and the number continues to grow to this day, amounting to millions of cases. Isolates from patients were analyzed, and the findings revealed the presence of a new coronavirus infection, which was given the provisional name 2019 novel Coronavirus (2019-nCoV). On February 11, 2020, WHO named the new virus *Severe Acute Respiratory Syndrome Coronavirus-2* (SARS-CoV-2) and the name of the disease Coronavirus Disease 2019 (COVID-19).¹

In its development, WHO declared COVID-19 as a pandemic on March 11, 2020. This status determination was based on the fact that COVID-19 cases increased 13 times in two weeks, and the number of affected countries tripled. Despite the WHO recommendation that affected countries be "more aggressive", COVID-19 cases continued to increase as of June 9, 2020.² As a result, the number of COVID-19 cases worldwide has reached 7.222.353 and a mortality rate of 5.7%, much higher than the WHO's initial estimate of 2%.³

The COVID-19 Pandemic in Indonesia began on March 2, 2020, with the index case in Jakarta. The COVID-19 Pandemic expanded throughout Indonesia on April 9, 2020, with Jakarta, West Java, and East Java having the largest number of positive cases. Positive cases of COVID-19 in Indonesia totaled 33.076 as of June 9, 2020, with a mortality rate of 5.8%. East Java has eight regencies/cities identified as areas with local transmission (Kediri Regency, Malang Regency, Sidoarjo Regency, Magetan Regency, Gresik Regency, Malang City, Surabaya City, and Batu City).⁴

Previous studies have shown that COVID-19 patients with comorbidities have a poorer prognosis.⁵ Wang et al. found that in 138 cases of COVID-19, 64 (46.4%) of them had comorbidities. Patients admitted to the intensive care unit had a higher comorbidity rate (72.2% vs. 37.3%) than those who were not admitted to the intensive care unit. It suggests that

comorbidity may be an important risk factor for *outcome* in patients with COVID-19.⁶

This study aims to determine the distribution of comorbidities in patients treated in the PINERE treatment room, Dr. Saiful Anwar Malang Hospital and analyze its relationship with the level of severity and mortality.

METHODS

The design of this research is observational analytic with a cross-sectional approach. The research was conducted at Dr. Saiful Anwar Malang Hospital in April – June 2020. The inclusion criteria were all confirmed COVID-19 patients either through the SARS-CoV-2 Rapid Molecular Test (RMT) method using the GeneXpert® SARS-CoV-2 method or the real-time Polymerase Chain method Reaction (rt-PCR), which was treated in the PINERE Room, Dr. Saiful Anwar Malang Hospital from March 12 to June 5 2020. The research data is in the form of secondary data taken from medical records.

The patient's diagnosis determines comorbidity during treatment. In this study, eight types of comorbidities were investigated, namely "Age", defined as patients aged 60 years or older according to WHO criteria for the elderly; "COPD", defined as a patient with a clinical manifestations of COPD, radiological features supporting COPD, or a history of a previous diagnosis of COPD. "Diabetes Mellitus", defined as a patient with a history of the previous diagnosis of diabetes mellitus (type 1 and type 2), random blood glucose at admission >200 mg/dL with classic complaints, fasting blood sugar above 126 mg/dL, postprandial blood sugar 200 mg/dL, or HbA1C values above 6.5%. "Hypertension", defined as a patient with a blood pressure measurement above 130 mmHg for 2 consecutive times with a distance of at least 2 minutes and/or a history of a previous diagnosis of hypertension.

"Heart failure", defined as a patient with typical symptoms of heart failure (shortness of breath at rest or activity, fatigue, leg oedema) and typical signs of heart failure (tachycardia, tachypnea, pulmonary rales, pleural effusion, elevated jugular venous

pressure, peripheral oedema, hepatomegaly), as well as objective signs of structural or functional disturbances of the heart at rest, cardiomegaly, third heart sound, heart murmur, abnormalities in echocardiography, and increased concentrations of natriuretic peptides (according to the 2015 Guidelines for Management of Heart Failure of the Indonesian Cardiovascular Specialist Association (PERKI).

"Coronary artery disease", defined as a patient with classic symptoms of angina pectoris accompanied by other findings such as electrocardiography and cardiac enzymes suggestive of coronary artery disease according to the cardiologist's expertise. "Chronic Kidney Disease" or "CKD", defined as a patient with a clinical picture of CKD accompanied by decreased renal function or a history of a previous diagnosis of CKD; and "Cerebrovascular disease" is defined as the presence of clinical and/or radiological features suggestive of a cerebrovascular disorder or a sequela of cerebrovascular disease.

The severity of the disease is grouped into mild, moderate, and severe according to the division listed in the Guidelines for Prevention and Control of Coronavirus Disease-19 (COVID-19) published by the Director-General of P2P of the Ministry of Health of the Republic of Indonesia version 4, where "Mild" include fever $>38^{\circ}\text{C}$, cough, sore throat, nasal congestion, and malaise, without symptoms of pneumonia; "Moderate" include the above symptoms plus shortness of breath; and "Severe" include persistent fever $>38^{\circ}\text{C}$ plus symptoms of severe ARI or pneumonia (including respiratory rate >30 breaths/minute, severe respiratory distress, or oxygen saturation $< 90\%$ in room air).

We described the distribution of confirmed COVID-19 patients based on disease severity, comorbidities, and mortality (died/did not die). Then, statistical tests were carried out to see whether or not there was an association between the presence or absence of comorbidities with patient severity and mortality rates and whether there was an association between severity and patient mortality using IBM SPSS® 25 software.

RESULT

From a total of 60 research samples, the following results were obtained: According to the severity of the disease, 40 samples (66.7%) were categorized as severe symptoms, 14 samples (23.3%) were categorized as moderate symptoms, and six samples (10.0%) were categorized as mild symptoms. In addition, 37 samples (61.7%) had comorbidities, with details of 21 samples (56.8%) with two or more comorbidities (multiple comorbidities) and 16 samples (43.2%) with single comorbidities. The mortality rates were 18 samples (30.0%) in the total sample, 14 samples (37.8%) in the comorbid sample, six samples (37.5%) in the single comorbid sample, eight samples (38.1%) in the multiple comorbid samples, and four samples (17.4%) in samples without comorbidities.

According to comorbidity, a total of 20 samples (33.3%) had comorbid age or were 60 years or older. In addition to age comorbidity, the highest comorbidity rate was hypertension, which was 24 samples (40.0%), followed by heart failure in 21 samples (35.0%), diabetes mellitus in 15 samples (25.0%), COPD and coronary heart disease each with several four samples (6.7%). There were no samples with chronic kidney disease and cerebrovascular disease.

The statistical test that used is the Fischer's Exact test and found a significant relationship between the presence or absence of comorbidities and the severity level ($P<0.05$), a significant relationship between sample severity and mortality ($P<0.05$). Statistical analysis of comorbidities using logistic regression showed that there was no relationship between comorbidity and severity. Still, there was a relationship between comorbid diabetes mellitus and mortality ($P<0.05$; $\text{OR}=4.00$; 95% $\text{CI}=1.16\text{--}13.74$). The sample analysis with mortality (18 samples) found that 17 samples (94.4%) came with the category of severe symptoms. In addition, 14 samples (77.8%) had comorbidities, with details of six samples (33.3%) with single comorbidities and eight samples (44.4%) with multiple comorbidities (two or more comorbidities).

Table 1. Demographic Profile

	Variable	N (%)
Presence or no Comorbid (n=60)	At least one comorbid	37 (61.7%)
	No comorbid	23 (38.3%)
Number of comorbidities in samples with comorbidities (n=37)	Single	16 (43.2%)
	Multiple	21 (56.8%)
Age (n=60)	60 years or older	20 (33.3%)
	Less than 60 years old	40 (66.7%)
Mortality Rate		
On all samples (n=60)	Yes	18 (30.0%)
	No	42 (70.0%)
In samples with comorbidities (n=37)	Yes	14 (37.8%)
	No	23 (62.2%)
In samples with a single comorbid (n=16)	Yes	6 (37.5%)
	No	10 (62.5%)
In samples with multiple comorbidities (n=21)	Yes	8 (38.1%)
	No	13 (61.9%)
In samples without comorbid (n=23)	Yes	4 (17.4%)
	No	19 (82.6%)
In the sample aged 60 years or older (n=20)	Yes	9 (45.0%)
	No	11 (55.0%)
In the sample aged less than 60 years (n=40)	Yes	9 (22.5%)
	No	31 (77.5%)
Severity Level		
On all samples (n=60)	Mild	6 (10.0%)
	Moderate	14 (23.3%)
	Heavy	40 (66.7%)
In samples with comorbidities (n=37)	Mild	1 (2.7%)
	Moderate	8 (21.6%)
	Heavy	28 (75.7%)
In samples with a single comorbid (n=16)	Mild	0 (0.0%)
	Moderate	4 (25.0%)
	Heavy	12 (75.0%)
In samples with multiple comorbidities (n=21)	Mild	1 (4.8%)
	Moderate	4 (19.0%)
	Heavy	16 (76.2%)
In samples without comorbid (n=23)	Mild	5 (21.7%)
	Moderate	6 (26.1%)
	Heavy	12 (52.2%)
In the sample aged 60 years or older (n=20)	Mild	1 (5.0%)
	Moderate	3 (15.0%)
	Heavy	16 (80.0%)
In the sample aged less than 60 years (n=40)	Mild	5 (12.5%)
	Moderate	11 (27.5%)
	Heavy	24 (60.0%)
Comorbidities (other than age)		
Hypertension (n=60)	Yes	24 (40.0%)
	No	36 (60.0%)
Heart failure (n=60)	Yes	21 (35.0%)
	No	39 (65.0%)
Diabetes(n=60)	Yes	15 (25.0%)
	No	45 (75.0%)
COPD (n=60)	Yes	4 (6.7%)
	No	56 (93.3%)
Coronary artery disease (n=60)	Yes	4 (6.7%)
	No	56 (93.3%)
Chronic kidney disease (n=60)	Yes	0 (0.0%)
	No	60 (100.0%)
Cerebrovascular disease (n=60)	Yes	0 (0.0%)
	No	60 (100.0%)

The highest comorbidities in the sample group with mortality were age and hypertension, each with nine samples (50.0%), followed by diabetes mellitus

in eight samples (44.4%), heart failure in seven samples (38.9%) and COPD in two samples (11.1%).

Table 2. Table of contingency to the level of severity

	Variable	Severity Level			P
		Mild	Moderate	Heavy	
Presence of comorbid	Yes (n=37)	1 (2.7%)	8 (21.6%)	28 (75.7%)	0.037
	No (n=23)	5 (21.7%)	6 (26.1%)	12 (52.2%)	
Number of comorbids	Single (n=16)	0 (0.0%)	4 (25.0%)	12 (75.0%)	0.202
	Multiple (n=21)	1 (4.8%)	4 (19.0%)	16 (76.2%)	
Age	No comorbid (n=23)	5 (21.7%)	6 (26.1%)	12 (52.2%)	0.358
	60 years or older (n=20)	1 (5.0%)	3 (15.0%)	16 (80.0%)	
COPD	Less than 60 years old (n=40)	5 (12.5%)	11 (27.5%)	24 (60.0%)	1.000
	Yes (n=4)	0 (0.0%)	1 (25.0%)	3 (75.0%)	
Diabetes	No (n=56)	6 (10.7%)	13 (23.2%)	37 (66.1%)	0.904
	Yes (n=15)	1 (6.7%)	3 (20.0%)	11 (73.3%)	
Hypertension	No (n=45)	5 (11.1%)	11 (24.4%)	29 (64.4%)	0.468
	Yes (n=24)	1 (4.2%)	5 (20.8%)	18 (75.0%)	
Heart Failure	No (n=36)	5 (13.9%)	9 (25.0%)	22 (61.1%)	0.769
	Yes (n=21)	1 (4.8%)	5 (23.8%)	15 (71.4%)	
Coronary artery disease	No (n=39)	5 (12.8%)	9 (23.1%)	25 (64.1%)	1.000
	Yes (n=4)	0 (0.0%)	1 (25.0%)	3 (75.0%)	
Chronic kidney disease	No (n=56)	6 (10.7%)	13 (23.2%)	37 (66.1%)	-
	Yes (n=0)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Cerebrovascular disease	No (n=60)	6 (10.0%)	14 (23.3%)	40 (66.7%)	-
	Yes (n=0)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Table 3. Contingency Table on Mortality

	Variable	Mortality		P
		Yes	No	
Presence of comorbid	Yes (n=37)	14 (37.8%)	23 (62.2%)	0.147
	No (n=23)	4 (17.4%)	19 (82.6%)	
Number of comorbids	Single (n=16)	6 (37.5%)	10 (62.5%)	0.253
	Multiple (n=21)	8 (38.1%)	13 (61.9%)	
Severity level	No comorbid (n=23)	4 (17.4%)	19 (82.6%)	0.012
	Mild (n=6)	0 (0.0%)	6 (100.0%)	
Age	Moderate (n=14)	1 (7.1%)	13 (92.9%)	0.134
	Heavy (n=40)	17 (42.5%)	23 (57.5%)	
COPD	60 years or older (n=20)	9 (45.0%)	11 (55.0%)	0.576
	Less than 60 years old (n=40)	9 (22.5%)	31 (77.5%)	
Diabetes	Yes (n=4)	2 (50.0%)	2 (50.0%)	0.048
	No (n=56)	16 (28.6%)	40 (71.4%)	
Hypertension	Yes (n=15)	8 (53.3%)	7 (46.7%)	(OR 4.0 95% CI 1.16-13.74)
	No (n=45)	10 (22.2%)	35 (77.8%)	
Heart failure	Yes (n=24)	9 (37.5%)	15 (62.5%)	0.391
	No (n=36)	9 (25.0%)	27 (75.0%)	
Coronary artery disease	Yes (n=21)	7 (33.3%)	14 (66.7%)	0.771
	No (n=39)	11 (28.2%)	28 (71.8%)	
Chronic kidney disease	Yes (n=4)	0 (0.0%)	4 (100.0%)	0.306
	No (n=56)	18 (32.1%)	38 (67.9%)	
Cerebrovascular disease	Yes (n=0)	0 (0.0%)	0 (0.0%)	-
	No (n=60)	18 (30.0%)	42 (70.0%)	

DISCUSSION

Currently, COVID-19 has become a global pandemic. The number of cases worldwide continues to increase and currently has reached more than 7 million cases. In Indonesia, the number of COVID-19 cases has reached more than 30,000 in just 3 months since the first case was discovered, with a mortality rate of around 5.8%. This figure is not much different from the global mortality rate, which is around 5.7%.³

According to the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) report, approximately 80% of patients with confirmed COVID-19 exhibit only mild-moderate symptoms, with just about 14% developing severe symptoms.⁷ In contrast, data at our hospital showed that most of the samples (66.7%) had severe symptoms. This is natural considering that, as a tertiary referral hospital, the COVID-19 patients admitted to our hospital cannot be treated in other smaller satellite COVID-19 hospitals. It may also explain our sample's mortality rate, which is much higher than the national average (30.0% vs. 5.8%).

Comorbidity is a very important factor in determining the *outcome* of COVID-19. The studies conducted by Guan et al. and Wang et al. stated that comorbid COVID-19 patients had a poorer prognosis. Therefore, the presence and number of comorbidities could predict the clinical outcomes of COVID-19.^{5,6,8} A large-scale study of 1.590 patients in China put the comorbidity rate at 25.1%,⁸ and in Indonesia, provisional data from 2.171 cases showed the comorbidity rate was 30.68%.⁹

Our sample had a much higher comorbidity rate of 61.7%. This may be explained by the severity of the patient's condition when referred to our hospital, where we found an association in our sample between comorbidity and severity. This follows most studies showing that comorbidities will increase the risk of a person with COVID-19 having a more severe form of the disease and the possibility of mortality.^{5,7} Our study also showed that mortality rate in the sample with comorbidities was much higher than in the sample without comorbidities (37.8% vs. 17.4%).

Based on the comorbidity profile, excluding age, we found that the highest number of comorbidities was hypertension (40.0%), followed by heart failure (35.0%), diabetes mellitus (25.0%), and COPD and coronary heart disease (6.7% each). We did not find any samples with comorbid chronic kidney disease and cerebrovascular disease. This profile is similar to the comorbidity profile reported by Guan et al., namely hypertension as the most frequent comorbidity (16.9%), followed by diabetes mellitus (8.2%) and cardiovascular disease (3.7%). Cerebrovascular disease and chronic kidney disease account for only a small percentage of these comorbidities (1.9% and 1.5%).⁸

From the analysis of each comorbidity, only diabetes mellitus comorbidity has a significant relationship to mortality. People with diabetes mellitus tend to die four times more often than those without diabetes. This value is two times bigger than the hazard ratio of diabetes mellitus to mortality reported by Guan et al.⁸

Guan et al. also showed that patients with two or more comorbidities had a much more significant mortality risk.⁸ In our data, the mortality rate in the single comorbid sample was not significantly different from that of the multiple comorbid samples (37.5% vs. 38.1%). This was also seen in the sample with severe severity (75.0% in the single comorbid sample vs. 76.2% in the multiple comorbid samples). Djaharuddin et al. showed a hazard ratio of 1.79 (95% CI) in patients with two or more comorbidities compared with those at least two comorbidities.¹⁰

We also analyzed the samples with mortality and found that 94.4% of the samples who died were treated with severe symptoms, and most had comorbidities (77.8%). On the other hand, this shows that 22.2% of the sample died even though they did not have any comorbidities. Furthermore, half of those who died (50.0%) were 60 or older or had comorbid hypertension.

Existing studies show that the mortality rate increases significantly with age.^{6,11} In our sample, we found that the mortality rate in the sample aged 60 years or older was 45.0% and 22.5% in the sample aged less than 60 years. This is consistent with

existing studies showing that the risk of mortality from COVID-19 increases exponentially with age. In their study, Djaharuddin et al. showed that the mortality rate occurred most in the elderly group. This is thought to be caused by the tendency of the elderly to develop cytokine storms due to immunosenescence.¹⁰

Our data, therefore, is consistent with most studies that state either hypertension or diabetes as comorbidities that may have been the most impactful in increasing mortality rates in COVID-19 patients. It should be noted, however, that a significant amount of mortality occurs in those who have no comorbidities at all.^{12,13}

CONCLUSION

From the data we have obtained and its analysis, we conclude that the demographic profile of hospitalized COVID-19 patients (especially those in central referral hospitals) will be different from the demographic profile of COVID-19 sufferers in the community. Although the current demographic profile is drawn from most studies based on general community observations that include COVID-19 patients requiring treatment and those with mild disease, using this data as a basis for making clinical decisions in treating COVID-19 in the hospital would be irrelevant. For example, in our study, the number of comorbidities (single vs multiple) was less likely to have a significant association with the outcome than COVID-19. This indicates that the number of comorbidities that patients have may not be clinically significant in those hospitalized. This is undoubtedly in contrast to the findings of earlier research, which clearly demonstrated that the number of comorbidities had a significant impact on the outcome of COVID-19.

The presence of comorbidities remains a factor that influences the disease course of COVID-19, especially its severity and mortality, as the available data consistently show. However, we propose that when treating hospitalized COVID-19 patients, clinicians should consider that the absence of comorbidities is not directly associated with a better

prognosis. It was observed that some of the patients with mortality in our study had no comorbidities at all.

REFERENCES

1. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]. World Health Organization. 2020 [cited 2020 Aug 13]. Available from: [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it)
2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta bio-medica Atenei Parm.* 2020;91(1):157–60.
3. World Health Organization. Update on the situation regarding the new coronavirus [Internet]. World Health Organization. 2020 [cited 2020 Jan 29]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019?adgroupsurvey=%7Badgroupsurvey%7D&gclid=CjwKCAiA9aKQBhBREiwAyGP5lbJhBLYvL4aPp_BpK6NhpGHDIB0yNpbHI_X5KD1ySjS0RPfL2j3sGB0CQM5QAvD_BwE
4. Kementrian Kesehatan Republik Indonesia. Infeksi Emerging Kementerian Kesehatan RI [Internet]. Kementrian Kesehatan Republik Indonesia. 2020 [cited 2020 Jun 9]. Available from: <https://infeksiemerging.kemkes.go.id/>
5. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020;382(18):1708–20.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA.* 2020;323(11):1061–9.
7. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). World Health Organization. China; 2020.

8. Guan W-J, Liang W-H, Zhao Y, Liang H-R, Chen Z-S, Li Y-M, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020;55(5):2000547.
9. Kementerian Kesehatan Republik Indonesia. COVID-19 dalam Angka per 3 Juni 2020 [Internet]. Kementerian Kesehatan Republik Indonesia. 2020 [cited 2020 Jun 4]. Available from:
<https://www.kemkes.go.id/article/view/20060600001/covid-19-dalam-angka-per-6-juni-2020.html>
10. Djaharuddin I, Munawwarah S, Nurulita A, Ilyas M, Tabri NA, Lihawa N. Comorbidities and mortality in COVID-19 patients. *Gac Sanit*. 2021;35 Suppl 2:S530–2.
11. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ*. 2020 Mar;368:m1198.
12. Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. *J Infect Public Health*. 2020;13(12):1833–9.
13. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis*. 2020;94:91–5.