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Research Article

# Description of Covid-19 Patients with Comorbidity

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## Abstract

Coronavirus Disease-19 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2). At this point, COVID-19 remains the main health issue worldwide, including in Indonesia, with existing risk factors. Comorbidities, smoking, male sex, and the elderly are some of its biggest risk factors. Current data about COVID-19 patients with comorbidities in Indonesia were limited, so this study was made to present more data about the clinical profile of COVID-19 with comorbidities. The descriptive retrospective method was used in this study with secondary data obtained from Christian University of Indonesia General Hospital medical records from January 2020 to December 2020 and aimed to describe the clinical profile of COVID-19 patients with comorbidities. Among 156 samples of COVID-19 patients that were found in this study according to inclusion and exclusion criteria, 91 patients (58,3%) had at least one comorbidity. They were distributed based on sex, age group, clinical symptoms, type of comorbidity, and the number of comorbidities in each patient. Based on sex distribution, there were 46 male patients (50,5%) and 45 female patients (49,5%). The most prevalent age group was 50 – 54 years old, with 14 patients (15,4%). Fever with 88 patients (95,9%), cough with 86 patients (93,8%), and dyspnea with 55 patients (60,8%) were the most common clinical symptoms. The most common types of comorbidity were hypertension with 66 patients (72,5%), diabetes mellitus (DM) with 20 patients (22,0%), and obesity with 14 patients (15,4%). There were 58 patients (63,8%) with only one comorbidity and 33 patients (36,3%) with ≥ 2 comorbidities. Prompt identification of comorbidities, public enlightenment about comorbidities with other risk factors of COVID-19, and complying with health protocols are recommended to decrease the proportion of COVID-19 patients with comorbidities.

**Keywords:** COVID-19, SARS-CoV-2, Comorbidity.

## INTRODUCTION

Coronavirus Disease-19 (COVID-19) is an infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2) virus which belongs to the Betacoronavirus (βCoV) genus of the Coronavirus subfamily.[1] According to the World Health Organization (WHO), the first case of COVID-19 was reported in December 2019 in Wuhan, China.[2]

COVID-19 is still a significant health problem worldwide, including in Indonesia. The first two cases in Indonesia confirmed positive for COVID-19 were found on March 2, 2020, originating from Jakarta, then spreading to 34 provinces in Indonesia.[3] In October 2021, based on data from the official website of the COVID-19 task force in Indonesia, there were 4,219,284 confirmed cases of COVID-19 and 142,173 deaths. Until now, the prevalence of COVID-19 cases in Indonesia is dynamic, where new cases are found daily.[4]

COVID-19 has a very high transmission rate through droplets and aerosols from the respiratory tract. Infected people quickly spread the virus by coughing, sneezing, or talking to others.[1] Common symptoms in COVID-19 patients are fever, fatigue, dry cough, and shortness of breath. Other symptoms such as headache, muscle aches, anosmia, sore throat, chest pain, diarrhea, and nausea and vomiting were reported.[2,5,6,7] Symptoms may develop between 2 and 14 days after exposure to the virus, with a median of 5 days.[8] According to WHO, cases of COVID-19 patients can be divided based on the severity of symptoms and signs, namely asymptomatic, mild, moderate, severe, and critical.[9]

Until now, there is no specific treatment for COVID-19, but symptomatic treatment can be given and maintain typical vital signs.[10] The development of a vaccine against COVID-19 is underway to prevent the spread of the disease and reduce morbidity and mortality. According to WHO, as of March 2, 2021, there are 76 vaccine candidates in the preclinical trial phase and 182 currently in the clinical trial phase.[11]

Several risk factors for COVID-19 are often associated with a poor prognosis, such as advanced age (>65 years), male gender, smoking, and comorbidities.[2,6] Based on the literature review research by Ejaz H et al., the most frequent comorbidities or comorbidities in COVID-19 are hypertension, cardiovascular disease, and diabetes mellitus (DM), followed by obesity, chronic obstructive pulmonary disease (COPD), liver disease, heart disease, and stroke and kidney and malignancy. Individuals with comorbidities are also advised to vaccinate as a preventive measure during the COVID-19 pandemic.[12] It also follows the research results by Karyono DR et al., who took data from the official website of the COVID-19 task force in Indonesia.[4]

According to researcher Sanyaolu A et al., there is an increase in morbidity and mortality in COVID-19 patients with hypertension, DM, and COPD. Patients with chronic kidney disease and malignancies are at higher risk of viral infection and a higher risk of death.[13] According to epidemiological research by Rozaliyani A et al. in Indonesia, a history of hypertension, the most frequent comorbidity in COVID-19 patients, also has a risk of death twice as high as those without hypertension.[2]

Data regarding the comorbidities of COVID-19 patients in Indonesia are still in the form of estimates of the total cases due to limited data and the possibility of under-reporting in several regions in Indonesia.[4]

COVID-19 imposes a considerable health burden in Indonesia and throughout the world, with the heaviest cases being dominated by comorbidities in the disease course. With this study, researchers hope to provide valuable data on the description of COVID-19 patients with comorbidities and help the medical world in preventing and managing COVID-19 more quickly and precisely.

Based on the existing background, the research problem formulation is a) "What is the picture pattern of COVID-19 patients with comorbidities at the Indonesian Christian University (UKI) General Hospital (RSU) for the 2020 period?" and b) "What is the proportion of COVID-19 patients with comorbidities to all COVID-19 patients at UKI General Hospital for the period 2020?". The study aimed to determine the pattern of the description of COVID-19 patients with comorbidities at the General Hospital (RSU) of the Indonesian Christian University (UKI) for the 2020 period and to determine the proportion of COVID-19 patients with comorbidities in all COVID-19 patients at the UKI General Hospital for the 2020 period.

## LITERATURE REVIEW

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), previously known as 2019-nCoV. On December 31, 2019, the World Health Organization (WHO) reported a cluster of cases of pneumonia of unknown etiology in the city of Wuhan, Hubei, China.[14] Then in February 2020, WHO named the disease coronavirus disease-2019. COVID-19 quickly spread throughout the world and became a pandemic.[5] COVID-19 is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which belongs to the subfamily Orthocoronavirinae or is often called Coronavirus. Based on serotype and genotype characteristics, Coronaviruses can be divided into four genera: Alphacoronavirus, Betacoronavirus, Deltacoronavirus, and Gammacoronavirus. SARS-CoV-2 belongs to the genus Betacoronavirus.[1]

Based on genome sequence analysis, SARS-CoV-2 is closely related to the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), which caused the SARS epidemic in 2002. The virus was initially named 2019-nCoV by WHO, which later became SARS-CoV-2.[15]

SARS-CoV-2 has four main structural proteins, namely spike protein (S), membrane protein (M), an envelope protein (E), and nucleocapsid protein (N). There are 16 non-structural proteins (nsp1-16) that aid in the replication process and 5-8 accessory proteins. The structural protein of SARS-CoV-2 plays a role in shaping the structure and facilitating the viral replication cycle.[16]

The main transmission of SARS-CoV-2 is in the direct human-to-human form. Infected people can spread the virus through droplets by coughing, sneezing, or talking if there is close contact within a 1-meter range. Dispersed droplets can infect other people when they come into contact with mucous membranes, usually in the eyes, nose, or mouth. Droplets from the respiratory tract are 6-10 m in diameter, and if they are 5μm in diameter, they are referred to as droplet nuclei or aerosols that can last up to 3 hours.[17]

Before entering the cell, the SARS-CoV-2 S protein must be cleaved with protease enzymes available on the host cell membrane, such as cathepsin, Furin, and Transmembrane protease serine 2 (TMPRSS2) enzymes.[18] After cleavage, the S protein divides into S1 and S2 subunits. S1 will bind directly to the receptor in the form of Angiotensin Converting Enzyme 2 (ACE2) on the cell surface, and S2 will undergo structural changes that allow fusion or unification of the viral membrane with the cell membrane. After the fusion process occurs, the positive single-stranded Ribonucleic Acid (RNA) from SARS-CoV-2 will be released into the cell cytoplasm and translated into several polyproteins to form a transcription complex. With transcription, the complex will be the site of the formation of 2 types of RNA, genomic RNA, which is the genetic material of viruses, and subgenomic RNA, which forms structural proteins and accessories as protectors of genomic RNA.[1]

After the RNA transcription process, structural proteins S, E, and M will be translated and inserted into the endoplasmic reticulum of the host cell, forming the Golgi-reticulum compartment. The viral genetic material that has been replicated will fuse with other structural proteins to produce a mature virus. After the assembly process, the virus will be released to the cell surface through the membrane by exocytosis.[1,19]

Infection from SARS-CoV-2 in COVID-19 occurs when the viral S protein binds to ACE2 from the membrane of a host cell. ACE2 is a carboxypeptidase enzyme that is a negative regulator of the Renin-Angiotensin System (RAS) in humans. ACE2 can convert Angiotensin I (Ang I) to Angiotensin 1-9 and Angiotensin II (Ang II) to Angiotensin 1-7, thereby counteracting the vasoconstrictive, proliferative, and fibrotic effects of Ang II. ACE2 is widely expressed on various cells in different tissues, namely nasal epithelial cells, endothelium, pulmonary alveolar epithelium, heart, kidney, intestinal epithelium, conjunctival epithelium, and other cell types.[20]

ACE2 in the nasal cavity allows SARS-CoV-2 to infect and interfere with olfactory receptors, decreasing olfactory function and causing hyposmia/anosmia. The following process is the spread of SARS-CoV-2 to the trachea and the lungs' alveoli. Infected cells will secrete proinflammatory cytokines, cause respiratory tract irritation, and cause a cough reflex.[21]

In moderate to severe COVID-19 patients, SARS-CoV-2 can spread to type II alveolar epithelial cells in the lungs and then begin to replicate using ACE2. Under normal conditions, macrophages around alveolar epithelial cells assisted by surfactant proteins will fight viral invasion by phagocytosis.[10] When the phagocytic ability of macrophage cells has reached the limit, proinflammatory cytokines will initiate. Cells that have been infected with the virus will undergo lysis and produce several proinflammatory cytokines, namely Interleukin (IL)-1, IL-6 and IL-8, and Tumor Necrosis Factor (TNF-α). IL-1, IL-6, and TNF-α will stimulate fever, while IL-8 will stimulate neutrophil cells in the lungs and induce vasodilation in the capillaries in the alveoli. The process of vasodilation, if excessive, can cause increased capillary

permeability and leakage of plasma fluid into the alveolar cavity and lung tissue injury.[22]

Massive elevations of proinflammatory cytokines, known as a "cytokine storm," are common in COVID-19 patients with severe symptoms. Cytokine storm is a cascade of activation of cytokine production resulting from an unregulated immune response by various etiologies, such as infections, malignancies, and rheumatic disorders.[22] Cytokine storm will further aggravate lung tissue injury and the alveolar-capillary barrier cavity, thereby increasing the amount of exudate that collects in the alveolar cavity. Accumulation of exudate can reduce the surface area required for the oxygen diffusion process, causing manifestations of shortness of breath. These mechanisms can cause severe acute lung injury, namely Acute Respiratory Distress Syndrome (ARDS) in COVID-19 patients.[10] COVID-19 first spread to Thailand and has now spread to 215 countries, including Indonesia.[14] The first two cases in Indonesia came from West Java Province on March 2, 2020, then increased to 1,285 cases in 30 provinces on March 29, 2020.[23]

According to the official website of the COVID-19 task force in Indonesia, as of January 16, 2022, there were a total of 4,280,248 confirmed positive cases, with 14,119 active cases, 96.3% of cases recovered, and 3.4% of cases died. Provinces in Indonesia with the highest number of cases are DKI Jakarta, West Java, and Central Java. Based on gender distribution, women have a proportion of 51.3%, and men have a proportion of 48.7%. More males died than females (52.3%). The age group with the highest COVID-19 cases in Indonesia is 31 - 45 years (28.7%), but the age group with the highest mortality rate is > 60 years (46.8%). The most frequent clinical symptoms of confirmed patients in Indonesia were cough (64.9%), history of fever (44.6%), fever (39.2%), and runny nose (37.9%). The most common comorbid conditions or comorbidities of COVID-19 in Indonesia are hypertension (50.1%), DM (36.8%), and heart disease (16.8%).[24]

Positive data based on province, gender, age, symptoms, and comorbidities from the site comes from the Publication of Data and Information section of the Indonesian Ministry of Health, which is updated every specific period. The incubation period of COVID-19 ranges from 2 to 14 days, with an average of 5 days.[25] The clinical presentation of COVID-19 varies, from asymptomatic or asymptomatic patients to ARDS and sepsis.[26] The most common manifestation of COVID-19 occurs in the lungs. The most common initial symptoms of COVID-19 are dry cough, fever, fatigue, and myalgia or muscle pain in the first four days, followed by other symptoms, namely shortness of breath and productive cough until the sixth day.[25] Other symptoms are chills, sore throat, loss of taste and smell, headache, and gastrointestinal symptoms such as nausea and vomiting.[12]

According to WHO, cases of COVID-19 in adults can be distinguished based on the severity of clinical manifestations: a) Asymptomatic (Patients are asymptomatic or asymptomatic); b) Mild (Patients are symptomatic without viral pneumonia or hypoxia. Symptoms that appear are general symptoms of COVID-19, namely fever, anorexia, myalgia, and cough. Other symptoms that may appear are nausea, vomiting, diarrhea, anosmia, sore throat, and loss of taste); c) Moderate (Adult or adolescent patients with pneumonia symptoms such as cough, shortness of breath, and fever but no signs of severe pneumonia with Blood Oxygen Saturation (SpO2) 90%); d) Severe (Adult or adolescent patients with clinical signs and symptoms of pneumonia such as fever, cough, shortness of breath, and rapid breathing plus one of the following criteria: SpO2 < 90%; respiratory rate > 30x/minute; or severe respiratory distress); and e) Critical (ARDS patient, septic shock, and acute thrombosis).[9]

In addition to lung manifestations, COVID-19 can cause impaired function in various organs. Acute kidney injury has been reported to occur in severely symptomatic COVID-19 patients.30 Acute kidney injury is the most common extra-pulmonary manifestation in COVID-19 patients.[26]

Cardiac manifestations commonly occur are myocardial injury such as myocardial infarction and myocarditis, characterized by elevated cardiac enzymes.[7] Gastrointestinal manifestations such as nausea and vomiting have also been reported in 20% of COVID-19 patients. Liver function in COVID-19 may be impaired by elevated aspartate transaminase and alanine transaminase enzymes.[17] Other endocrine manifestations such as increased blood glucose have been reported in COVID-19 patients with comorbid DM. The most common neurologic manifestations are anosmia and ageusia. Headache, stroke, and impaired consciousness have also been reported.[6,9]

COVID-19 can cause hematological manifestations. Impaired hemostasis characterized by elevated levels of fibrinogen, prothrombin time, activated partial thromboplastin time, and fibrin degradation product is associated with higher mortality.[28] According to a meta-analysis of 8697 patients in China, 47.6% of COVID-19 patients had lymphopenia followed by elevated cardiac enzymes in 49.4%, and 20.4% had elevated D-dimer.[29] Several studies support these findings.

Risk factors for COVID-19 can be divided into non-modifiable ones, such as advanced age and male gender, and modifiable ones, such as smoking habits and comorbidities. Risk factors for COVID-19 can exacerbate symptoms and increase mortality. Comorbidities in COVID-19 consist of hypertension, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease, obesity, kidney disease, and other comorbidities.[30,31] The diagnosis of COVID-19 consists of anamnesis, physical examination, and supporting examinations. A positive result can only confirm the diagnosis of COVID-19 from the Polymerase Chain Reaction (PCR) examination with a sample in the form of a nasopharyngeal or oropharyngeal swab.[9]

With appropriate management, symptoms of COVID-19 patients will generally improve until they recover. However, high cytokine levels in the late phase of the disease have been reported to correlate with a poor prognosis.[32] Elderly patients and comorbidities also adversely affect the prognosis.

A computed tomography scan of the thorax can predict the prognosis of COVID-19. About 14 days after the onset of symptoms, outcomes generally improve. The presence of signs of pleural effusion and diffuse alveolar damage is rare but can suggest a poor prognosis.

## RESEARCH METHOD

This study uses a descriptive method with a cross-sectional retrospective approach. The data taken is secondary data from patient medical records at the hospital from January 2020 to December 2020. The measurement results are based on the data obtained as is, and the data analysis is guided by theory and literature. This research was conducted from October to December 2021 in the medical records section of the UKI General Hospital. The population in this study was COVID-19 patients at UKI General Hospital for the 2020 period, with the study sample consisting of 156 COVID-19 patients at UKI General Hospital for the period 2020. The study sample used a consecutive sampling technique. The population registered in the medical records section of the UKI General Hospital with a

diagnosis of "Coronavirus infection" was randomized through the Microsoft Excel program. The research instrument used in this study was the medical records of COVID-19 patients who entered the UKI RSU for 2020. The method of collecting data on the characteristics of COVID-19 patients was carried out by taking secondary data, namely the medical records of COVID-19 patients who entered the UKI RSU in 2020. The data that has been collected will be processed through a computer using Electronic Data Processing from the Statistical Package for the Social Sciences (SPSS) application and Microsoft Excel. Data analysis from the research was carried out through the accumulation of primary data in the form of a description without explaining the relationship between variables or testing hypotheses.

## RESULT AND DISCUSSION

Sampling was conducted at the Medical Records Unit at UKI RSU Jakarta from November 3, 2020, to November 15, 2020. The sampling technique was consecutive sampling. Researchers took samples from the general population according to predetermined inclusion and exclusion criteria. The population in this study amounted to 262 patients, and the samples obtained according to the inclusion and exclusion criteria were 156 patients.

**Table 1: The proportion of COVID-19 patients with comorbidities to all COVID-19 patients**

| Comorbidity | Frequency (n) | % |
|---|---|---|
| Yes | 91 | 58,3 |
| No | 65 | 41,7 |
| **Total** | 156 | 100 |

Based on Table 1, from 156 COVID-19 patients at UKI Hospital, 91 patients (58.3%) of all COVID-19 patients had comorbidities, and 65 patients (41.7%) did not have comorbidities, so the proportion of COVID-19 patients with comorbidities of all COVID-19 patients was 58.3%.

**Table 2: Distribution of COVID-19 patients with comorbidities by sex**

| Gender | Frequency (n) | % |
|---|---|---|
| Male | 46 | 50,5 |
| Female | 45 | 49,5 |
| **Total** | **91** | **100** |

Based on Table 2, the sex distribution in this study shows that the male sex of COVID-19 patients with comorbidities amounted to 46 patients (50.5%), more than the female sex, which amounted to 45 patients (49.5%). ).

**Table 3: Distribution of COVID-19 patients with comorbidities by age group**

| Age group | Frequency (n) | % |
|---|---|---|
| 20 – 24 years old | 3 | 3,3 |
| 25 – 29 years old | 4 | 4,4 |
| 30 – 34 years old | 6 | 6,6 |
| 35 – 39 years old | 7 | 7,7 |
| 40 – 44 years old | 8 | 8,8 |
| 45 – 49 years old | 13 | 14,3 |
| 50 – 54 years old | 14 | 15,4 |
| 55 – 59 years old | 10 | 11,0 |
| 60 – 64 years old | 8 | 8,8 |
| 65 – 69 years old | 8 | 8,8 |
| 70 – 74 years old | 4 | 4,4 |
| 75 – 79 years old | 5 | 5,5 |
| 80 – 84 years old | 1 | 1,1 |
| **Total** | 91 | 100 |

Based on Table 3, the distribution of age groups in this study shows that the age group 50-54 years is the most common age group of COVID-19 patients with comorbidities, namely 14 patients (15.4%), followed by the 45-49 year age group in as many as 13 patients (14.3%) and the age group 55 – 59 years as many as ten patients (11%). The age group with the minor distribution was the age group 80-84 years with one patient (1.1%), followed by the age group 20-24 years with three patients (3.3%). The youngest age of COVID-19 sufferers with comorbidities is 21, while the oldest age is 83 years.

**Table 4: Distribution of COVID-19 patients with comorbidities based on clinical symptoms**

| Clinical symptoms | Frequency (n) | % |
|---|---|---|
| Fever | 87 | 95,6 |
| Anorexia | 27 | 29,7 |
| Myalgia | 5 | 5,5 |
| Hard to breathe | 54 | 59,3 |
| Cough | 85 | 93,4 |
| Sore throat | 10 | 11,0 |
| Nauseous | 41 | 45,1 |
| Vomit | 10 | 11,0 |
| ageusia | 6 | 6,6 |
| Anosmia | 17 | 18,7 |
| **Total** | 342 | 375,9 |

Table 4 above is compiled in multiple responses by the SPSS program. Distribution based on clinical symptoms in this study showed that fever was the most complained clinical symptom by 87 patients (95.6%), followed by a cough which

was complained of by 85 patients (93.4%), and shortness of breath was complained of by 54 patients (59.3%), and nausea was complained by 41 patients (45.1%). The rarest clinical symptom was myalgia which was complained by five patients (5.5%), followed by ageusia, which was complained by six patients (6.6%).

**Table 5 Distribution of comorbid COVID-19 patients by type of comorbidity**

| Type of Comorbidity | Frequency (n) | % |
|---|---|---|
| Hypertension | 66 | 72,5 |
| Diabetes mellitus | 20 | 22,0 |
| Cardiovascular Disease | 8 | 8,8 |
| Chronic Obstructive Pulmonary Disease | 4 | 4,4 |
| Kidney illness | 5 | 5,5 |
| Obesity | 14 | 15,4 |
| Asthma | 3 | 3,3 |
| Malignancy | 2 | 2,2 |
| Pulmonary TB | 1 | 1,1 |
| Cerebrovascular Disease | 3 | 3,3 |
| Pregnancy | 3 | 3,3 |
| Hyperthyroid | 1 | 1,1 |
| Gouty Arthritis | 1 | 1,1 |
| Frailty | 1 | 1,1 |
| **Total** | 132 | 145,1 |

Table 5 above is compiled from multiple responses by the SPSS program. Distribution by type of comorbidity showed that hypertension was the most common type of comorbidity suffered in this study with a total of 66 patients (72.5%), followed by DM, which was suffered by 20 patients (22.0%), obesity suffered by 14 patients (15,4%) and cardiovascular disease suffered by eight patients (8.8%). The least COVID-19 comorbidities found were pulmonary TB, hyperthyroidism, gouty arthritis, and frailty in 1 patient (1.1%).

**Table 6: Distribution of COVID-19 patients with comorbidities based on the number of comorbidities per patient**

| Number of Comorbidities | Frequency (n) | % |
|---|---|---|
| 1 | 58 | 63,7 |
| 2 | 29 | 31,9 |
| 3 | 3 | 3,3 |
| 4 | 1 | 1,1 |
| **Total** | 91 | 100 |

Based on Table 6, the distribution of the number of comorbidities shows that COVID-19 patients who have one comorbidity are 58 patients (63.7%), two comorbidities are 29 patients (31.9%), three comorbidities are three patients (3.3%), and four comorbidities totaling one person (1.1%).

Based on the study results, most of the COVID-19 patients at the UKI General Hospital in the 2020 period had comorbidities, with 58.3%. These results align with the epidemiological investigation of Rozaliyani et al. in Indonesia, which found that the proportion of COVID-19 patients with comorbidities was 83.6% of all COVID-19 patients studied.[2] According to research by Surendra et al. in Jakarta, Indonesia, the proportion of comorbidities found was only 31%.[33] Other studies outside Indonesia, such as the Guan et al. study in China, had a comorbidity proportion of 33%, then the Gupta et al. study in India showed a comorbidity proportion of 41.5%.[34]

In this study, all samples of COVID-19 patients were recorded as hospitalized in medical records, and some patients who were not hospitalized at the time of data collection did not meet the inclusion and exclusion criteria, so they were not part of the sample of this study. The decision and indication of hospitalization in COVID-19 patients are strongly influenced by the symptoms and signs of the patient.[35] According to research by Guan et al. in China, Ramatillah et al. in Jakarta, Indonesia, and Wang et al. in China, comorbidities with COVID-19 can exacerbate symptoms.[30,31] Based on this basis, it can explain why this study's proportion of COVID-19 patients with comorbidities was more significant than those without comorbidities.

Based on the sex distribution in this study, male patients were more than female patients with the respective proportions of 50.5% and 49.5%. These results align with the research in China by Guan et al. and the study of Marik PE et al. in Virginia; In the United States, the proportion of male COVID-19 patients with comorbidities is more significant than that of women.[35]

Several studies show that there are more male COVID-19 patients overall, one of which is the study of Karyono et al. in Indonesia which examined the prevalence of COVID-19 in Indonesia until June 3, 2020, with the proportion of 54 males, 6%.[4] Epidemiological research by Rozaliyani et al. in Jakarta, Indonesia, showed that the proportion of men was 53.5%.[2]

The male gender is a risk factor for more severe symptoms and a higher risk of dying from COVID-19. Based on data by the CDC from China, males have a case fatality rate (CFR) of 2.8% and females of 1.7%.[25] The mechanism that can explain this is the lower estrogen levels in men than in women. Estrogen upregulates ACE2 in the RAS system, thereby providing a protective function in anti-inflammatory and vasodilating effects against SARS-CoV-2 infection and hypertension.[36] Compared to men, women also have a higher number and activity of T lymphocytes and a higher level of antibody production by B lymphocytes. T lymphocyte cells and B lymphocyte cells are part of the adaptive immune system that is very effective against viral infections, including infection by SARS-CoV-2.

Based on the distribution of age groups in this study, the largest age group in COVID-19 patients with comorbidities was the 50-54 year age group, namely 14 patients (15.4%), followed by the 45-49 year age group with 13 patients (14, 3%) and the age group 55 – 59 years as many as ten patients (11.0%). Based on Garg et al.'s study results, more comorbid COVID-19 patients were found in the age group 65 years.[37] Another study by O'Hare A et al. in the United States showed that the most age group in COVID-19 patients with comorbidities using the Charlson comorbidity index was 65 – 79 years (28.7%).[38] Hypertension, DM, obesity, and cardiovascular disease were the most common comorbidities

found in this study. Globally, DM and cardiovascular disease are more common in patients over 40. Progressive changes in blood vessels occur with age, which will decrease heart function and increase the risk of cardiovascular disease.

The influence of age also plays a role in the pathogenesis of DM. The mean age range of DM patients is 40 – 59 years. Glycemic control may decrease with age and increase the risk of developing DM.[24] Along with advancing age, the immune system is increasingly vulnerable to disruption. The aging process causes a decrease in the body's physiological reserves, one of which is a decrease in the optimal immune system, or what is called immunosenescence. This process is characterized by progressive dysfunction of the immune system and an increase in inflammatory reactions that can exacerbate the course of COVID-19, resulting in more severe manifestations.[6]

Based on the results of this study, fever and cough were the most common clinical symptoms complained of by comorbid COVID-19 patients, with 87 patients (95.6%) and 85 (93.4%). These results align with the research of Surendra et al. in Jakarta, Indonesia; Guan et al. in China; and Wang et al. in China.[28,44] As the most common symptom in this study, fever is a cardinal sign of an infectious process. Following the pathogenesis of COVID-19, pulmonary alveolar epithelial cells infected with SARS-CoV-2 will secrete proinflammatory cytokines to stimulate the immune system. IL-1 is one of the central proinflammatory cytokines that play a role in inducing the fever process when infection occurs.[10]

Cough was the most common symptom in this study after fever. Coughing is a protective reflex of the human body due to the stimulation of sensory nerve fibers that innervate the airways from the pharynx to the lung parenchyma. Epithelial cells along this pathway infected with SARS-CoV-2 will induce a cough reflex through direct inflammatory reactions from nerve cells and an activated immune system.[24,39]

Shortness of breath was the third most frequently complained symptom in this study after cough and fever. There were 54 patients (59.3%) who experienced symptoms of shortness of breath from a sample of COVID-19 patients with comorbidities. These results align with Guan et al.'s study in China, where the proportion of clinical symptoms of shortness of breath in patients with comorbidities is two times higher than in those without comorbidities. According to WHO, shortness of breath is also one of the clinical symptoms of moderate to severe COVID-19.[9] A study by Shoaib et al. in Pakistan showed that the proportion of severe symptoms in COVID-19 patients increased with the number of comorbidities suffered. 5% of patients without comorbidities experienced severe symptoms; with 1 type of comorbidity, 12% experienced severe symptoms, and with two types of comorbidity, 27% experienced severe symptoms. Collection of secretions due to SARS-CoV-2 infection in alveolar cells reduces the surface area of oxygen exchange, lowers oxygen levels in the blood, or is referred to as hypoxemia. Hypoxemia will activate Chemoreceptors in the carotid body, which in turn causes an increase in the work of breathing and the sensation of "shortness of breath".[24]

Other clinical symptoms researchers took in this study were nausea, anorexia, and vomiting. Each of these symptoms was suffered by 41 patients (45.1%), 27 patients (29.7%), and ten patients (11.0%). The proportion of nausea was very high compared to the proportion in several other studies by Guan et al. in China, Rozaliyani et al. in Indonesia, and Wang et al. Symptoms of anorexia, nausea, and vomiting in COVID-19 have not been fully elucidated.[2,28,44] Several theories have been proposed: direct infection of SARS-CoV-2 in the gastrointestinal tract epithelium rich in ACE2 and systemic inflammatory burden factors due to proinflammatory cytokines. Stress and anxiety factors experienced by patients when exposed to COVID-19 can also induce nausea and vomiting.[40] Diabetes mellitus, the second most common comorbidity in the study, may exacerbate the inflammatory burden caused by elevated IL-6, CRP, and D-dimer.

Anosmia or loss of smell and age or loss of taste in COVID-19 with comorbidities were complained by 17 patients (18.7%) and six (6.6%). SARS-CoV-2 is easily transmitted to the nasal and oral cavities rich in ACE2 receptors. Infection that then spreads to the area can damage the sensory nerve cells of the senses of taste and smell.[23]

Other symptoms such as sore throat in this study were complained by ten patients (11.0%) with COVID-19 with comorbidities. Another study by Guan et al. in China showed that the proportion of sore throat symptoms was 14.5%. Several other studies show that the proportion of sore throat symptoms is above 20%.[2,37] A sore throat can occur if there is inflammation in the oral cavity to the throat, precisely in the nasopharynx, oropharynx, and hypopharynx. SARS-CoV-2 can infect epithelial cells in the area and induce an inflammatory reaction. At the same time, it can also trigger the cough reflex.[10]

Myalgia or muscle pain in COVID-19 is a fairly common symptom. In a meta-analysis by Li et al., myalgia was present in 35.7% of patients and was the most common clinical symptom after cough and fever.[41] This study showed that myalgia suffered only in 5 patients (5.5%) and was the least experienced symptom. However, myalgia can also be caused by systemic inflammation with an etiology that is not specific to the infectious process alone, thus leading to inconsistent results from various studies due to its low specificity for COVID-19.

Based on the distribution of comorbidities in this study, hypertension was the comorbid type that had the highest proportion of comorbid COVID-19 patients (72.5%), followed by DM (22.0%), obesity (15.4%), and cardiovascular disease (8.8%). These results align with the literature review of Sanyaolu et al., the epidemiological research of Rozaliyani et al. in Indonesia; research by Surendra et al. in Jakarta, Indonesia; and research by Karyono et al. in Indonesia.[2,4,13]

Hypertension had the highest proportion of comorbidities in this study, with 66 patients (72.5%). The pathogenesis of hypertension is related to the life cycle of SARS-CoV-2, particularly in the RAS system. Under physiological conditions, the ACE2 enzyme of the RAS system can reduce the vasoconstrictive effect of Ang-II by cleaving Ang-II into Angiotensin (1-7). According to its life cycle, this study's cleavage of ACE2 by SARS-CoV-2 can potentially inhibit the Ang-II cleavage process that causes an increase in blood pressure in COVID-19 patients.[42]

In this study, data on previous medical history from patients were not taken because all patients did not share these variables with comorbidities, but the researchers took data on comorbidities based on secondary diagnoses from these patients. The results of Chen et al.'s research in China stated that hypertension could be a sequela or result of SARS-CoV-2 infection. In this study, it was found that several patients without a history of hypertension experienced an abnormal increase in blood pressure for several days while hospitalized. As time goes on and the inflammatory response decreases, the patient's blood pressure drops back to average.[42] On this basis, there is a possibility that a proportion of hypertension found

in this study is a transient increase in blood pressure caused by the inflammatory response of SARS-CoV-2 infection.

DM is this study's second most common comorbidity after hypertension, affecting 20 patients (22.0%). One mechanism that can explain this is the high level of Furin in COVID-19 patients with DM in this study. Furin can facilitate the fusion process of SARS-CoV-2 into the host cell, thereby facilitating the SARS-CoV-2 infection. According to a literature review study by Zhou et al., another mechanism that aggravates COVID-19 in DM is that COVID-19 patients have impaired viral clearance and insulin regulation and decreased glucose uptake. The cytokine storm in COVID-19 can also be exacerbated by oxidative stress that commonly occurs in DM patients. Simultaneously, COVID-19 can exacerbate DM by infecting pancreatic Langerhans cells and reducing insulin levels required to reduce hyperglycemia in DM patients.[7]

The most common comorbid COVID-19 in this study after hypertension and DM was obesity in 14 patients (15.4%). The proportion of obese patients in this study was relatively high because, during the data collection process, researchers determined obese patients only based on BMI values of 30 kg/m2 and did not assess waist circumference or blood fat levels. BMI as an anthropometric tool is not specific for assessing body fat levels.[43] High-fat content in obese patients causes immune system dysfunction, impaired lung physiology, and higher viral infectivity than in non-obese people.

Cardiovascular disease other than hypertension was this study's fourth most common comorbidity, affecting eight patients (8.8%). According to another study by Rozaliyani et al. and Karyono et al., cardiovascular disease is the most common comorbidity after hypertension and DM.[2,4] Hypertension, the most common type of comorbidity found in this study, can increase the risk of other cardiovascular diseases due to the close relationship between heart and blood vessel function.[24] The presence of hypertension may allow increased expression of ACE2 in cardiac myocytes, and patients with cardiovascular disease have been reported to have increased RAS system activity and facilitate the pathogenesis of SARS-CoV-2.[32]

All the comorbid COVID-19 patients in this study consisted of five patients (5.5%) with kidney disease and four (4.4%) with COPD. The proportion of kidney disease in some studies is not as high as hypertension and DM, but according to a study by Cheng et al. in China, COVID-19 patients with kidney injury had the highest risk of death compared to other comorbidities. COPD is associated with an increased risk of SARS-CoV-2 infection and severity of symptoms in COVID-19 patients due to decreased lung function.[25]

Other comorbidities in this study each had a proportion below 4% of all COVID-19 patients with comorbidities. The comorbidities are asthma, cerebrovascular disease, pregnancy, malignancy, pulmonary tuberculosis, hyperthyroidism, gouty arthritis, and frailty. Data for the above comorbidities are still limited. Malignancy and pulmonary TB have a proportion of 7% and 5%, respectively, in elderly COVID-19 patients, according to research by Azwar et al. in Indonesia.[6] High levels of eosinophils in asthma are thought to protect from viral infections that cause the very low prevalence of asthma in COVID-19 patients. Frailty, one of the most common geriatric syndromes, can cause immunosenescence in elderly patients susceptible to severe COVID-19 symptoms. This process will lead to progressive immune system dysfunction and exacerbate the clinical manifestations of COVID-19.[24]

According to the number of comorbidities suffered by each patient in this study, the most comorbid COVID-19 patients had one comorbidity or single comorbidity with a total of 58 patients (63.7%). The presence of 2 or more comorbidities was declared as Multi-morbidity. Multi-morbidity is associated with a poorer prognosis in COVID-19 patients. The results in this study where COVID-19 patients with one comorbidity were more than COVID-19 patients with multi-morbidity in line with studies by a cohort in Jakarta, Indonesia by Surendra et al., and studies in China by Guan et al.[33]

## CONCLUSION

Based on 156 samples of COVID-19 patients obtained from medical record data at UKI General Hospital for the period 2020, it can be concluded that: a) The proportion of COVID-19 patients with comorbidities (58.3%) is more than those without comorbidities (41.7%) ; b) Based on the sex distribution of comorbid COVID-19 patients, gender with the most significant proportion was male (50.5%) followed by female (49.5%); c) Based on the distribution of age groups in COVID-19 patients with comorbidities, the age group with the most significant proportion is the age group 50 – 54 years (15.4%), followed by the age group 45 – 49 years (14.3%), and the age group age 55 – 59 years (11.0%); d) The symptoms most frequently complained by COVID-19 patients with comorbidities were fever (95.6%), followed by cough (93.4%), and shortness of breath (59.3%); e) The most common types of comorbidity found were hypertension (72.5%), followed by DM (22.0%), and obesity (15.4%); and f) Comorbid COVID-19 patients who have single comorbidities (63.7%) are more than those who have multi-morbidities, namely with 2 comorbidities (31.9%), 3 comorbidities (3.3%), and 4 comorbidities. Comorbidity (1.1%).

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