

LITERATURE REVIEW

COMORBIDITIES WITH THE HIGH RISK OF DEATH AMONG COVID-19 PATIENTS: LEARNING FOR INDONESIA

Komorbid Berisiko Kematian Tinggi pada Pasien COVID-19: Pembelajaran untuk Indonesia

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ABSTRACT

Background: In general, the entire population is vulnerable to COVID-19, but epidemiological research shows that the elderly and people with comorbid are more susceptible to COVID-19 and has a high risk of experiencing poor outcomes and death if infected with COVID-19. **Purpose:** This study aims to identify comorbidities with a high risk of death common among COVID-19 patients in China and the United States to provide learning for Indonesia in COVID-19 management. **Methods:** The literature review method was done by searching relevant articles through Google Scholar and ScienceDirect. Inclusion criteria are all original research and case series containing epidemiological information and comorbidities in COVID-19 patients aged >19 years with full text and open access. Exclusion criteria are study COVID-19 concerning children and adolescents (≤ 19 years) and study without comorbidities information. There is no language selection because all articles found are in English. **Results:** There are eight articles suitable for the criteria. Four articles were research conducted in China, and four articles were done in the United States. The articles use case series, cohort, and cross-sectional methods. **Conclusion:** Common comorbidities among COVID-19 patients are hypertension, diabetes, and cardiovascular disease in China and the United States. A more significant number of comorbidities also correlated with a higher risk of death.

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ABSTRAK

Latar Belakang: Secara umum, seluruh populasi rentan terhadap COVID-19 tetapi penelitian epidemiologi menunjukkan bahwa lansia

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dan penderita dengan penyakit penyerta (komorbid) lebih rentan terhadap COVID-19, serta memiliki risiko tinggi mengalami outcome yang buruk hingga kematian bila terinfeksi COVID-19. **Tujuan:** Penulisan ini bertujuan untuk mengidentifikasi komorbid dengan risiko kematian tinggi yang umum diderita pada pasien COVID-19 di Cina dan Amerika Serikat sehingga dapat memberikan pembelajaran bagi Indonesia untuk memberikan perhatian khusus dalam penanganan pasien COVID-19 yang disertai komorbid. **Metode:** Metode yang digunakan adalah literature review dengan mencari artikel yang relevan melalui Google Scholar dan ScienceDirect. Kriteria inklusi adalah semua penelitian original dan studi kasus yang berisi informasi epidemiologi, dan komorbid pada pasien COVID-19 berusia >19 tahun yang full text dan open access. Kriteria eksklusi adalah penelitian COVID-19 pada anak dan remaja (berusia ≤19 tahun) serta penelitian tanpa informasi mengenai komorbid. Tidak ada pemilihan bahasa karena artikel yang ditemukan telah berbahasa inggris. **Hasil:** Didapatkan delapan artikel yang sesuai dengan kriteria. Empat artikel berupa penelitian yang dilakukan di Cina dan empat artikel berupa penelitian di Amerika Serikat. Artikel menggunakan metode case series, kohort, dan cross sectional. **Kesimpulan:** Komorbid yang umum diderita pasien COVID-19 adalah hipertensi, diabetes, dan cardiovascular disease baik di Cina maupun di Amerika Serikat. Jumlah komorbid yang lebih banyak juga berkorelasi dengan risiko kematian yang lebih tinggi.

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INTRODUCTION

On December 30, 2019, the Wuhan Municipal Health Committee immediately notified pneumonia of unknown cause, which has now been identified as Coronavirus Disease 2019 (COVID-19). On January 30, 2020, the World Health Organization (WHO) declared the condition of COVID-19 as a Public Health Emergency of International Concern (PHEIC). COVID-19 quickly spread throughout the world, so that on March 11, 2020, the statement was declared a pandemic (World Health Organization, 2020b). Based on the Indonesian Ministry of Health, global data as of October 20, 2020, shows that 39,944,882 people from 216 infected countries and 179 local transmission countries have been confirmed with COVID-19 1,111,998 of them have died (Ministry of Health RI, 2020).

In general, the entire population is susceptible to COVID-19. Still, several epidemiological studies have shown that the elderly (> 65 years) and comorbid sufferers are more vulnerable to COVID-19 compared to young and non-comorbid age groups (Alkundi, Mahmoud, Musa, Naveed, & Alshawwaf, 2020; Zhou et al., 2020). Individuals with chronic diseases are primarily elderly and

have several comorbidities. These individuals have a high risk of experiencing outcomes poor and death if infected with COVID-19 (Du et al., 2020; D. Wang et al., 2020). Common co-morbidities include hypertension, diabetes mellitus, and cardiovascular disease (Arentz et al., 2020; Baradaran, Ebrahimzadeh, Baradaran, & Kachooei, 2020; Epidemiology Working Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention, 2020; Guan et al., 2020; Wang, Li, Lu, & Huang, 2020).

Guan et al. (2020) study in China found that 25.09% of patients had at least one comorbid. Most of the comorbidities were hypertension (16.92%), diabetes 8.18%), and cardiovascular disease (3.71%). A total of 6.23% of patients were referred to the ICU. The number of ICU referral patients with comorbidity was greater (13.53%) than patients without comorbidity (3.78%). Of the cases that died, 8.77% of the patients had comorbidities, i.e. 5.58% of patients had one comorbid, and 15.38% of patients had at least two comorbidities.

The country with the highest number of COVID-19 cases globally is the United States, with 6,662,003 people, with a death toll of 212,229 people (CFR = 2.79). This number is indeed the

largest, but the CFR is low compared to countries that have the lowest number of deaths such as Brazil 149,639 people (CFR = 2.59), Mexico 83,507 people (CFR = 10.31), and European countries such as the UK 42,760 people (CFR = 7.23), Italy 36,140 people (CFR = 10.34), France 32,449 people (CFR = 4.69), and Spain 32,929 people (CFR = 3.69) (World Health Organization, 2020a). The United States is still the country with the most cases globally as of November 2020, but only has a CFR of 2.58%. This figure is lower than Indonesia's CFR of 3.41% (John Hopkins Coronavirus Resource Center, 2020).

China had the highest CFR at the start of the pandemic, but China has continued to report a drop in cases since October. It is different from Indonesia, which continues to experience an increase in the number of cases. China's CFR has decreased to 5.19 (World Health Organization, 2020a). The two countries are intensively conducting a lot of research to know more about COVID-19. Based on the research that has been done, it is known that comorbidity is a risk factor for death in COVID-19 patients. Patients with comorbidities have a greater risk of experiencing more severe symptoms, so treatment and prognosis assessment need to be adjusted (Gupta et al., 2020; Richardson et al., 2020; Wang et al., 2020; Yu et al., 2020).

In connection with the ongoing research related to COVID-19 that has been carried out in both countries and the high risk of death in COVID-19 patients, this study aims to identify comorbidities with a high mortality risk. Moreover, it is common in COVID-19 patients in China and the United States. It can provide important lessons for Indonesia to pay special attention to handling COVID-19 patients who are accompanied by comorbid in Indonesia.

METHODS

Research Design

This study used a research design literature review by searching for relevant articles. The literature review design considered the most appropriate approach to achieving current goals. The design was a literature review used to obtain information about comorbidity with a high risk of death common to COVID-19 patients in two countries, namely China and the United States.

Data Sources

Articles are obtained through database providers of national and international journals, namely Google Scholar, ScienceDirect, and bibliography or other sources, until September 15, 2020. The keywords used are "COVID-19" AND "Diabetes" OR "hypertension" OR "cardiovascular disease" AND China OR United States. This keyword was chosen because it is included in the three comorbidities commonly suffered by COVID-19 patients. The articles obtained can be specific and follow the purpose of writing. The author only takes the original research design and case series to identify comorbidities commonly suffered and have a high risk of causing death in COVID-19 patients in two countries, namely China and the United States. The author did not choose the language because the articles found were in English. The inclusion criteria for this writing are research containing epidemiological and comorbid information on COVID-19 patients aged >19 years with full text that is open access. The exclusion criteria were COVID-19 research that focused on children and adolescents (aged ≤19 years) without information about comorbidities. The age of 19 years is the criterion limit because the mortality rate at ≤19 years is very low, or there are even no death cases (Bialek et al., 2020; Epidemiology Working Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention, 2020).

RESULTS

Article search through the database of international journal providers found 115 articles from Google Scholar, 12 articles from ScienceDirect and five articles from a bibliography or other sources. In total, 132 articles were obtained, then they were selected based on duplication and obtained 128 articles. The articles were then selected based on abstracts, so that 110 articles were excluded because they did not meet criteria such as not being done in China or the United States and not full text with open access until 18 articles were obtained. Among the search results, ten articles were excluded because they did not match the criteria. Those are three articles without comorbid information and seven articles with a systematic review or meta-analysis method so that 8 articles that fit the criteria were obtained (see Figure 1 and Table 1).

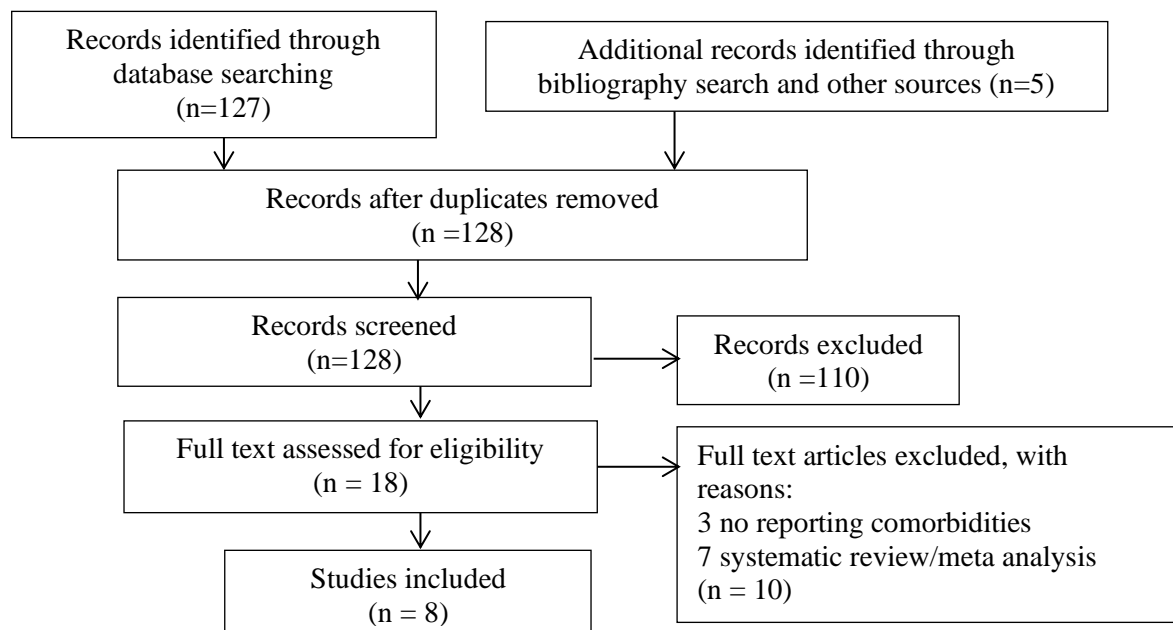


Figure 1. Flowchart of the Search and Article Selection Process for Literature Review

DISCUSSION

Older patients (> 65 years) are more vulnerable and have a higher risk of dying. It is found in the study of Liu, Chen, Lin, & Han (2020), which compared the clinical characteristics of COVID-19 patients aged (≥ 60 years) with young (<60 years). The study results stated that the mortality rate in COVID-19 patients aged ≥ 60 years was higher than those aged <60 years. Patients aged ≥ 60 years are more likely to develop severe disease. This is similar to the study of Zhou et al. (2020) and dan Du et al. (2020), which states that old age is a risk factor for COVID-19 patients.

Based on the research results by the Epidemiology Working Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention (2020) in China, the highest number of cases is in the ≥ 50 year age group. The Case Fatality Rate (CFR) continues to increase with age. It is also in line with research from Bialek et al. (2020) in the United States that the highest number of deaths was in patients aged ≥ 65 years, patients with the outcomes were most bandaged ≥ 85 years and the percentage of cases fatality increases with age. Both studies state that the highest CFR is old, and the lowest is at ≤ 19 years of age (Bialek et al., 2020; Epidemiology Working Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention, 2020).

Older individuals are closely related to comorbidities, risk factors for poor outcomes and death in COVID-19 patients. The results of research conducted by the Epidemiology Working

Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention (2020) stated that there is a difference in Case Fatality Rate (CFR) between COVID-19 patients with and without comorbidities. The Case Fatality Rate (CFR) of patients with comorbidities would be higher, namely 10.54% for cardiovascular disease, 7.26% for diabetes, 6.26% for chronic lung disease, 6% for hypertension, and 5.61% for cancer. It is also under Chen et al (2020) study, which stated that elderly patients with comorbidities have a high mortality rate of 34.54%. In Guan et al (2020) study, patients with comorbid blood circulation disorders such as hypertension and cardiovascular diseases are the most common comorbidities. Endocrine diseases such as diabetes are also common in COVID-19 patients.

Respiratory diseases such as Chronic Obstructive Pulmonary Disease (COPD) are rarely found in COVID-19 patients (Guan et al., 2020). This was also found in Imam et al. (2020) research that hypertension was the most common comorbidity, followed by diabetes. Respiratory-related comorbidities were found in less than 10%. The study of Guan et al (2020) also stated that patients with comorbidities had a higher risk of outcomes adverse than those who did not. A higher number of comorbidities correlates with the risk of outcomes adverse to death from COVID-19. It is also similar to Imam et al (2020) research, which stated that the more comorbidities you suffer, the greater the severity of COVID-19.

Table 1.

Matrix Literature Review

Author, Year, Country	Design, Respondent	Purpose	Results
Liu et al (2020), Cina	Retrospective Study Study of COVID-19 Patients admitted to Hainan Provincial Hospital from 15 January to 18 February 2020	Comparing the clinical characteristics of COVID-19 patients who are elderly (≥ 60 years) with young (< 60 years)	<ul style="list-style-type: none"> a. There are 56 patients, 18 (32.14%) are elderly patients and 38 (67.86%) are young . b. There were 12 elderly patients with chronic diseases, especially cardiovascular and cerebrovascular diseases and diabetes (7 more people than young patients) c. 1 elderly patient died (5.56%) and two young patients died (5.26%). The results state that COVID-19 is more susceptible to infecting adults with comorbidities due to weaker immune function
Guan et al (2020), Cina	Retrospective cohort Data from 1590 patients confirmed positive for COVID-19 from 575 hospitals in 31 provinces in China. From 11 December 2019 to 31 January 2020.	Assess the risk of outcomes adversely COVID-19 patients based on the level of comorbid status.	<ul style="list-style-type: none"> a. Based on 1590 cases, 16% of respondents are considered severe cases. 131 (8.24%) patients had a known outcome at the end of the study. b. 399 (25.09%) patients had at least one comorbid. The most common comorbidities were hypertension (16.92%) diabetes (8.18%). 130 (8.18%) patients had two or more comorbidities. COPD (HR (95% CI) 2,681 (1,424–5,048)), diabetes (1.59 (1.03–245)), hypertension (1.58 (1.07–2.32)) and malignancy (3.50 (1.60–7.64)) were associated risk factors. with the outcome at the end of the study. c. HR (hazard ratio) (95% CI) for patients with one comorbid was 1.79 (1.16–2.77) and 2.59 (1.61–4.17) in patients with two or more comorbidities.
Epidemiology Working Group for NCIP Epidemic Response Chinese Center for Disease Control and Prevention (2020), Cina	Cross-sectional All COVID-19 cases in China were reported up to 11 February 2020.	Provide descriptive and explanatory explanations regarding all COVID-19 cases until February 11, 2020.	<ul style="list-style-type: none"> a. Based on 72,314 reported cases, 44,672 (61.78%) were confirmed positive. 0.93% of cases occurred at age 0-9 years 1.23% at 10-19 years, 8.10% at 20-29 years, 17.01% at 30-39 years old, 19.19% at age 40-49 years, 22.40% at age 50 -59 years, 19.21% at 60-69 years old, 8.77% at 70-79 years old, and 3.15% aged > 79 years. b. There were 1,023 cases of death confirmed positive with a Case-fatality rate an overall(CFR) of 2.29%. There was no death in the age group <9 years, CFR increased with age with the highest CFR in the age group ≥ 80 years at 14.77%. c. CFR in patients without comorbidities was 0.86%, while in patients with comorbidities, 10.54% for cardiovascular disease, 7.26% for diabetes, 6.26% for chronic respiratory disease, 6% for hypertension, and 5.61% for cancer.

Continued

Tabel 1
Continued

Author, Year, Country	Design, Respondent	Purpose	Results
Yu et al (2020), China	Case series 1,663 patients admitted to Tongji Hospital with COVID-19 from 14 January to 28 February 2020	Describe the epidemiology and clinical characteristics of 1663 COVID-19 patients who were treated and knew the association of risk factors with the severity of COVID-19.	a. Respondents aged <30 years were 2.28%, 18.70% aged 30-49 years, 49.67% aged 50-69 years, and 29.34% aged > 69 years. b. More than a third of respondents had at least one comorbid. Based on laboratory results, respondents observed that most respondents had C-reactive protein (80.39%) and d-dimer (64.42%), which increased. c. 26% at the end of the study were declared cured, 10.16% died, and 63.80% were still treated.
Bialek et al (2020). United States	Case series COVID-19 patients in the United States from February 12 to March 16, 2020. There were 4,226 cases from 49 states, districts of Colombia, and 3 regions of the United States that were reported on the CDC.	Describing the epidemiology of COVID-19 in the United States with data. preliminary	a. There were 4,226 cases reported to the CDC, but only 2,449 patients were known for their age. 6% are aged ≥85 years, 25% are aged 65–84 years, 18% are aged 55–64 years and 45–54 years, and 29% are aged 20–44 years. Only 5% of cases occur in patients aged 0–19 years. b. A total of 508 (12%) patients were known to have been treated where the percentage of patients treated increased with age, from 2% - 3% in the ≤19 years age group to > 31% for the ≤85 years age group. A total of 121 patients were referred to the ICU with the lowest percentage in the 20–44 years age group (2% – 4%) and the highest in the 75–84 years age group (11% –31%). c. The highest mortality rate was found in the age group ≥85, amounting to 10% to 27%, followed by 3% -11% in the 65–84 years age group, 1% - 3% in the 55-64 years age group, <1% in patients aged 20-54 years, and there were no deaths in the ≤19 years age group.
Marcello et al (2020). United States	Case series Patients at New York Hospital who tested for COVID-19 between March 5 to April 9 2020, with follow-up until April 16, 2020	Describe the characteristics and outcomes of patients who tested and were hospitalized due to COVID-19	a. A total of 22,254 patients of those who were tested for COVID-19, 13,442 (61%) were positive for COVID-19. 46% had at least one comorbid (30% hypertension, 27% diabetes, 21% cardiovascular disease (CVD)). b. 6,248 (46%) of these positive patients were hospitalized, with 53% of them having at least one comorbid (37% hypertension, 33% diabetes, 24% CVD, 11% chronic kidney disease (CKD)) A total of 1,724 (28%) of these treated patients died. In those patients who died, the common comorbidities were 35% diabetes, 37% hypertension, 28% CVD, 15 % CKD.

Continued

Tabel 1
Continued

Author, Year, Country	Design, Respondent	Purpose	Results
Fried et al (2020). United States	Cohort Adult patient data with COVID-19 totalled 245 hospitals in 38 states between 15 February and 20 April 2020.	Assessing patient characteristics associated with morbidity and mortality of hospitalized in the United States.	a. Based on 11 721 patients, 10.80% were aged 18-40 years, 41-60 years old 29.31%, and 59.88% are aged > 60 years. b. Comorbidities found were hypertension (46.72%), diabetes (27.76%), cardiovascular disease (18.62%), obesity (16.13%), and chronic kidney disease (12.17%). c. A total of 1,967 (16.78%) patients required mechanical ventilation where the mortality rate of these patients was higher than patients without mechanical ventilation, namely 21.45%, increasing to 70.46%.
Richardson et al (2020). United States	Case series COVID-19 patients admitted to 12 hospitals in New York City, Long Island, and Westchester Country New York are included in the Northwell Health system. Data were obtained from March 1 to April 4, 2020.	Describing clinical characteristics and outcomes of COVID-19 patients are treated in the US health care system.	a. There were 5,700 patients, with the mean age being 63 years. b. 4,991 (88%) patients had more than one comorbid, 359 (6.29%) had one comorbid. The most common co-morbidities were hypertension (3026; 56.56%), obesity (1737; 41.70%), and diabetes (1808; 33.79%). 5,350 c. During treatment, 373 patients (14.16%) were referred to the ICU, 320 (12.15%) received mechanical ventilation, 81 (3.08%) received renal replacement therapy, and 553 (20.99%) died. In patients who received mechanical ventilation, the mortality rates in the 18-65 years age group and over 65 years were 76% and 97%, respectively. This figure is far above the mortality rate for patients who do not receive mechanical ventilation in the same age group, namely 1.98% and 26%.

Marcello et al (2020), showed an association between certain comorbidities and hospitalization and mortality in their study. More than half of the patients hospitalized had at least one comorbid. Commonly found in these patients are diabetes, hypertension, and cardiovascular disease. 28% of the patients admitted to the hospital were declared dead. Patients confirmed positive for COVID-19 with comorbidities had a significant association with intensive hospital care, such as patients with comorbid hypertension, diabetes, cardiovascular disease, congestive heart failure and chronic kidney disease. Several comorbidities are also associated with mortality, such as diabetes, cardiovascular disease, congestive heart failure and chronic kidney disease, whereas hypertension is not. This matter is slightly different from Gupta et al (2020) study, which stated that hypertension and diabetes are not associated with the death of

COVID-19 patients in the United States. It is in line with the results of a study conducted by Fried et al (2020), which stated that the three most common comorbidities suffered are hypertension, diabetes, and cardiovascular disease. This study showed that death in COVID-19 patients hospitalized was closely related to mechanical ventilation during treatment. During treatment, risk factors associated with mechanical ventilation include old age, obesity, chronic kidney disease, diabetes, and cardiovascular disease. The risk factors for death during treatment were almost the same, except for obesity.

Richardson et al (2020) describe the clinical characteristics and outcomes of COVID-19 patients admitted to US health facilities. Similar to the study in China, it was common to find COVID-19 patients with old age and the presence of comorbidities, especially hypertension and or

diabetes. Of the 5,700 COVID-19 patients, 88% of them had more than one comorbid. Commonly suffered from comorbidities are hypertension, obesity and diabetes. The study showed that patients who died with comorbid diabetes were more likely to receive invasive mechanical ventilation or treatment in the ICU. Patients with diabetes had a higher percentage of developing acute kidney injury than those without the condition. Patients with hypertension are less likely to receive invasive mechanical ventilation or treatment in the ICU.

Comorbidities with a high risk of death common in COVID-19 patients is also described in the study of Yu et al (2020). These researchers stated that among COVID-19 patients who were treated, more than a third had at least one comorbid where hypertension, diabetes, and coronary heart disease were the most common. Compared with patients whose clinical manifestations were not severe, severe patients mainly were elderly and had comorbidities as previously described. It is slightly different from Chow et al (2020), who stated that the comorbidities that are often found in the United States are diabetes, chronic lung disease, and cardiovascular disease. These three comorbidities increase the risk of COVID-19 severity.

CONCLUSION

Most of the deaths of COVID-19 patients are old and have comorbidities. Commonly suffered from comorbidities are hypertension, diabetes, and cardiovascular disease in China and in the United States. Patients with comorbidities have a higher risk of outcomes adverse than those who do not. The more comorbid suffered, the higher the risk of death. Therefore, the lessons can be drawn for handling COVID-19 in Indonesia is the need to look at the history of the disease so that it is easy to identify the possibility of progression into a serious outcome to death from COVID-19.

CONFLICT OF INTERESTS

There is no conflict of interest as of this writing.

AUTHOR CONTRIBUTION

MHN: Concept and Methodology. MAI: Editing and Supervision.

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