

Literature Review : Risk of Death in COVID-19 Patients

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Literature Review : Risk of Death in COVID-19 Patients

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Abstract

COVID-19 is a contagious pulmonary infectious disease caused by a new type of coronavirus (SARS-COV-2). COVID-19 is a global pandemic that has infected millions of people and killed thousands of people in the world. Cases of death in COVID-19 patients were first discovered in China in December 2019. In Indonesia, since it was first discovered, cases of death of COVID-19 patients continue to increase and has become one of the countries with the highest fatality rate in the world reaching 9.11 percent. The purpose of this study is to determine factors for death in COVID-19 patients in China in order to get guidance in preventing death in COVID-19 patients in Indonesia. This type of research is a literature review. The results of the study found five risk factors for death in COVID-19 patients, namely age, COVID-19 complications, the immune system (immunity), concomitant disease (comorbidity), and treatment facilities. Suggestions of various risk factors for death in COVID-19 patients in China are expected to be a guide in efforts to prevent death in COVID-19 patients that occur in Indonesia.

INTRODUCTION

COVID-19 is an acute infectious disease that infects the respiratory system and kills humans in various parts of the world. COVID-19 became a global pandemic in 2020. This disease is caused by a new type of coronavirus called SARS-CoV-2. Coronavirus is a large family of viruses that cause respiratory system diseases such as SARS and MERS. The SARS-Cov-2 virus was first discovered in the city of Wuhan in China in December 2019. The rapid development and spread of the SARS-Cov-2 virus throughout the world made WHO determine the corona virus outbreak that causes COVID-19 as a global pandemic.

Since it first happened in December 2019 until April 2020, there have been 1,016,310 positive cases of COVID-19 worldwide with 53,236 fatal cases and 213,126 confirmed cases (worldometers. info/coronavirus/ updated April 03,2020. 05:27 GMT). COVID-19 has become an epidemic in various countries in the world including Indonesia. The positive case of COVID-19 in Indonesia was first discovered in DKI Jakarta Province on March 2, 2020. Since it was first discovered on March 2, 2020 until April 3, 2020 (1 month), the National Disaster Management Agency of the Republic of Indonesia (BNPB) announced that the number of COVID-19 positive cases in Indonesia have reached 1,986 cases

and are predicted to continue to increase. The number of deaths was 181 cases and cured cases were 134. The high number of deaths compared to cases recovered due to COVID-19 infection made Indonesia as one of the countries that had the highest fatality rate due to COVID-19 in the world reaching 9.11 percent.

COVID-19 is a type of acute infectious disease caused by a new type of coronavirus called SARS-Cov-2. COVID-19 is a type of acute infectious disease that attacks the respiratory system. In general the symptoms of COVID-19 are high fever (temperature ≥ 38 °C), cough, and difficulty in breathing. Other symptoms are complaints of shortness of breath that is getting heavy, fatigue, headaches and digestive system disorders (Perhimpunan Dokter Paru Indonesia, 2020). In some patients, symptoms that appear mild or even no symptoms. Patients positive for COVID-19 cases will be determined after undergoing various physical, laboratory and radiological examinations. The most important laboratory tests are PCR (Polymerase Chain Reaction) and genome sequencing (Ministry of Health of Republic of Indonesia, 2020). COVID-19 transmission occurs through close contact of infected patients, splashes of infected patient's airway droplets and virus-contaminated environment or objects (Perhimpunan Dokter Paru Indonesia, 2020). The dangerous complications of COVID-19 are ARDS (acute respiratory disease syndrome), such as sepsis, shock, organ failure, and death.

The first case of death of a COVID-19 patient occurred in China along with the emergence of an outbreak of the SARS-Cov-2 virus causing COVID-19 in the World. Cases of death for COVID-19 patients continue to increase throughout the world, including in Indonesia. Until now, the risk factors for the cause of death in COVID-19 patients in Indonesia have not been known with certainty. The purpose of this study is to determine the risk factors for death in COVID-19 patients that occur in China as the first country to have a case of death due to COVID-19. The benefits of the study provide an overview of the risk factors for death in COVID-19 patients so that efforts to prevent death can be done appropriately in Indonesia.

METHOD

This research method is literature review. Literature sources are international journals about COVID-19 in China. Data collection is done by searching international journals electronically on the Scopus and PubMed databases. The keywords used are "Death Covid in Chinese", "COVID-19 in Wuhan", "Death Covid in Wuhan". The journals selected as research material are those that meet the

inclusion criteria, namely journals with all types of research methods, related to mortality risk factors in COVID-19 patients, research in China, researched by Chinese health workers, publications in English, publications in December of the year 2019 and January - April 2020. Journal exclusion criteria do not describe risk factors for death in COVID-19 patients.

RESULTS AND DISCUSSION

The results of data collection found 14 international journals that met the inclusion criteria. Risk factors for death in COVID-19 patients in China can be grouped into five main factors, namely age, COVID-19 complications, immunity, comorbidities, and patient care facilities. The results of the study are illustrated in Table 1.

Age factor

The risk of death is known to be experienced by many elderly patients. Some of the results of the study were found to indicate that the risk of death in COVID-19 patients was higher in the majority of those aged ≥ 47 .

Increasing age causes humans to experience a decline in various bodily organs or degenerative processes. Decreased immune system can be the cause of susceptible elderly people infected with various microorganisms including coronavirus that causes COVID-19. Changes in the anatomy and physiology of respiratory organs; Lung elasticity and lung capacity put the elderly at risk of experiencing respiratory failure during an infection. This is in accordance with the results of research Wu, C. et al. (2020) found that old age is a risk factor for developing COVID-19 patients experiencing ARDS (acute respiratory syndrome). This condition is at risk of causing death in the elderly if not treated quickly and appropriately.

Old age is a risk factor for death in COVID-19 patients is also supported by various research results, namely Wang et al. (2020) found that the average age of COVID-19 patients who died was 75 years with a range of 48-89 years of age. The results of the study of Wu, J. T. et al. (2020) found those aged over 59 years had a risk of 5.1 times more likely to die from COVID-19 after experiencing symptoms. The results of research Liu et al. (2020) found that the main risk of death was related to old age. The results of the study of Guan et al. (2020) show that the average age of COVID-19 patients who were admitted to the ICU, underwent invasive mechanical ventilation, and who died was 47 years. Multivariable regression showing an increase in hospital deaths due to COVID-19 is associated with older age (Zhou, F. et al., 2020).

Table 1. Distribution of a description of risk factors for death in COVID-19 patients

Researchers (Publication)	Risk Factors of Death in COVID-19 Patients				
	Age	Complications COVID-19	Immunity	Comorbidity	Patient Care
Huang et al. (2020)	-	Acute respiratory distress syndrome	Lymphopenia	-	-
Wang et al. (2020)	Age > 75 years old (range 48-89)	-	-	-	25 average number of days from the first symptom to death tends to be shorter in people > 70 years, 11.5 (6-19 days) compared to patients < 70 years old, 20 (range 10-41 days)
Chen, N. et al. (2020)	-	Acute respiratory distress syndrome, organ failure	-	-	-
Liu et al. (2020)	-	-	Decreased white blood cells, lymphocytopenia	-	Early respiratory support to facilitate recovery of the disease and improve prognosis
Yang et al. (2020)	Old age > 64 years old	Damage to organ function; ARDS, acute kidney injury, heart injury, liver dysfunction	-	-	Patients need mechanical ventilation. The duration of treatment in the ICU to death is found to be around 7 days.
Ji et al. (2020)	-	-	-	-	The availability and accessibility of adequate health services reduces mortality
Zhou, F. et al. (2020)	Old age	Organ failure	-	19 Hypertension, diabetes mellitus, coronary heart disease	-

Researchers (Publication)	Risk Factors of Death in COVID-19 Patients				
	Age	Complications COVID-19	Immunity	Comorbidity	Patient Care
Fang et al. (2020)	-	-	-	Hypertension, diabetes mellitus	Intensive care of care unit
Wu, C. et al. (2020)	Older age, 51 years on aver- age	ARDS, Organ dysfunction and coagulation	Neutrofilia	-	Among ARDS patients, treat- ment with meth- ylprednisolone leads to death
Leung (2020)	≥ 60 years old	-	-	-	-
Wu, J. T. et al. (2020)	Age over 59 years old	-	-	-	-
Deng et al. (2020)	≥ 62 - 74 years old	Low oxygen saturation, ARDS compli- cations, shock, cardiac injury, kidney injury, disseminated intravascular coagulation	WBC and Low Lymphocytes	-	The risk of death is indicated by the lack of improve- ment during treatment
Du et al. (2020)	≥ 65 years old	-	CD3 + CD8 + T Cells ≤ 75	Previous car- diovascular and cerebrovascular diseases	-
Cao et al. (2020)	-	Acute res- piratory distress syndrome, organ failure	-	-	Patients need to be treated in the Intensive Care Unit because they tend to experi- ence respiratory failure and death

At a young age, COVID-19 positive patients generally show mild symptoms. Research from Wang et al. (2020) shows the average number of days of the first COVID-19 symptoms until death is shorter in the elderly compared with those who are young. Young people have a 1.1 times risk of death after experiencing symptoms (Wu, J. T. et al., 2020).

Complication Factor

COVID-19 is caused by a new type of corona virus called SARS-Cov-2. Pathogenesis of corona virus which causes COVID-19 is known to be very fast in damaging the function of the respiratory system. The corona virus enters the upper respiratory

tract and then replicates in the upper respiratory tract epithelial cells; do a life cycle. The virus subsequently spreads lower respiratory tract; lungs and interferes with the functioning of the respiratory system. The rate of COVID-19 infection is known to be higher than SARS infection in 2002 (Perhimpunan Dokter Paru Indonesia, 2020). Wang et al. (2020) say this disease might develop faster.

The rapid infection process causes COVID-19 patients who are not handled properly will experience complications due to damage to various vital organs. The results of the study by Wu, C. et al. (2020) found that the rapid reaction of COVID-19 infection resulted in organ dysfunction and coagulation. Most research shows that the first reaction to

the fastest infection occurs in the respiratory system. Yang et al. (2020) found that the process of COVID-19 infection that is not treated quickly causes acute respiratory distress syndrome (ARDS). Chen, W. et al. (2020) mentioned that coronavirus cov 2 causes pneumonia. Pneumonia is an infection of the lung alveolar tissue where the pulmonary alevolus is filled with pus with the main symptoms shown are shortness of breath and high fever. Alveoli is the main part of the human lungs as a place of exchange of oxygen and carbon dioxide. Damage to the pulmonary alveolar function of patients with severe COVID-19 positive results in the patient experiencing extensive tissue hypoxia. This is evidenced by the results of research from Deng et al. (2020) that patients will experience a decrease in oxygen saturation and risk of death if not treated quickly.

Widespread infections in COVID-19 patients are also found outside the lungs. Chen, W. et al. (2020) found that corona virus RNA that causes COVID-19 was detected in blood and anal swabs. There is a strong correlation between serum viral load and disease severity. Patients with a virus-positive annal swab are found to be in a severe clinical stage. The viral load concentration in anal swabs is higher than in the blood. This proves that the virus has replicated in the digestive tract. Overall, the results of the study confirm that the presence of viral RNA has occurred at the extra pulmonary site (Chen, W. et al., 2020).

The spread of the virus also occurs very quickly (Han et al., 2020). The speed of spread of the virus, the speed of viral replication, excessive inflammatory reactions, extra-pulmonary virus replication, and worsening of symptoms in COVID-19 patients are important factors that must be understood so that death can be avoided. The condition of COVID-19 patients can worsen in a short time and die due to failure of many organs (Chen, N. et al., 2020).

Immune Factor

COVID-19 patients are known to experience healing from the period of infection. Some cases of COVID-19 positive patients show no symptoms typical of COVID-19 (asymptomatic). There are COVID-19 patients who show severe symptoms until death. The immune system is the most influential indicator of this condition.

COVID-19 positive patients with low endurance have the potential to experience a worsening of the disease and risk of death if not handled properly. Liu et al. (2020) found that COVID-19 positive patients with major initial symptoms nearly 80% were those who had low white blood cell counts and 72.3% had lymphocytopenia. This condition if not treated properly will have an impact on the high risk

of worsening the disease and the risk of death in patients. This is evidenced by the results of the study of Guan et al. (2020) who found that lymphocytopenia was present in 83.2% of cases of COVID-19 patients who entered ICU care room to get intensive care. Research Deng et al. (2020) found that COVID-19 patients who died had decreased white blood cells (WBC) and lymphocytes. Research from Du et al. (2020) also found that the risk of death occurred in COVID-19 patients with a decrease in CD3 + CD8 + T cells ≤ 75 .

The immunity of the patient is very important in healing COVID-19 disease. An improved immune system will facilitate the development of antidote antibody feedback to suppress the corona virus infection that causes COVID-19 (Deng et al., 2020). Number of higher CD3 and CD4 T-cells in COVID-19 patients who have good endurance can protect patients from the dangers of complications from Acute Respiratory Distress Syndrome (ARDS). A gradual and gradual increase in lymphocyte response may be needed for effective immunity against SARS-CoV-2 infection (Wu, C. et al., 2020).

Concomitant Disease Factors

Enclosing disease is another disease that the patient experienced before COVID-19 infection. The results of research Zhou, F. et al. (2020) found that risk factors for death occur in COVID-19 patients with comorbidities or comorbidities of hypertension, diabetes mellitus, and coronary heart disease. Patients with comorbidities of heart disease, hypertension, or diabetes, who are treated are higher risk for severe COVID-19 infection (Fang et al., 2020). Death cases are found in patients with comorbid cardiovascular and cerebrovascular diseases (Du et al., 2020)

Cardiovascular diseases such as hypertension are diseases where systolic and diastolic blood pressure rises more than normal. Hypertension will result in impaired oxygen perfusion to all tissues of the body's organs. The danger of hypertension is the occurrence of ischemia of heart tissue (coronary heart disease) and rupture of cerebral blood vessels (Ganong & McPhee, 2010). Diabetes mellitus is a disease in which blood glucose levels increase more than normal (hyperglycemia). The danger of diabetes mellitus is an increase in viscosity / blood coagulation which results in blood flow retention which functions as oxygen and nutrient transport throughout the body's tissues. Coronary heart disease is a disease of heart arteries. The danger of coronary heart disease is extensive heart tissue hypoxia that results in ischemia or heart tissue death.

The SARS-Cov-2 virus that causes COVID-19 undergoes replication and lives infecting the res-

piratory system. COVID-19 becomes more severe when the infection process attacks the alveoli of the lungs (pneumonia). In the pathophysiology of the disease, the body will release various compounds, especially the immune system to fight the infection reaction, namely white blood cells and lymphocytes. It is understood that the immune system or the body's immune system can enter the area of injury or infection through the bloodstream. Patients with hypertension and diabetes mellitus are patients who have problems with the blood circulation system. Impaired blood circulation due to hypertension and diabetes mellitus causes white blood cells and lymphocytes difficult to reach the area of injury. This condition allows injury due to corona virus infection in the lung tissue to spread. On the other hand, the process of healing wounded lung tissue due to COVID-19 infection has been delayed because the supply of oxygen and nutrients for wound healing is hampered. This condition occurs because of tissue perfusion in patients with hypertension and diabetes mellitus experiencing problems. All of these conditions if not treated quickly, severe COVID-19 patients are at risk of expanding infections, organ failure and death.

Treatment Facility Factors

COVID-19 patients who have severe symptoms are in dire need of adequate treatment facilities. Wang et al. (2020) found that the average days from the first symptoms to death tended to be shorter in people > 70 years (11.5 days) than patients aged <70 years, 20 (range 10 -41 days). Patients need to be treated in the Intensive Care Unit because they tend to experience respiratory failure and death (Cao et al., 2020). The risk of mortality will be high in severe COVID-19 patients if facilities and care are inadequate. Research Guan et al. (2020) shows that severe COVID-19 patients require intensive care in the ICU and undergo invasive mechanical ventilation treatment.

Patients who are at risk of dying need special care in the intensive care unit (Cao et al., 2020). Patients need mechanical ventilation or ventilators (Yang et al., 2020). Early respiratory support facilitates recovery of the patient's disease and improves good prognosis (Liu et al., 2020). The risk of death is indicated by the lack of improvement during treatment (Deng et al., 2020)

The results of this study indicate that the availability of adequate care facilities largely determines the safety of COVID-19 patients. Care services must meet the requirements to meet the patient's oxygen needs, intensive care unit care, and mechanical ventilation equipment or ventilators. Limitations of adequate treatment facilities can be a risk factor for mortality in COVID-19 patients. This is supported

by the results of the study of Ji et al. (2020) who found that there was a significant positive correlation between death and health care burden. Ji et al. (2020) found that there are gaps in the availability and accessibility of health care service resources.

This gap explains the availability of complete facilities will result in a low death rate despite the high number of cases. The Chinese government is aware of the limitations of care facilities in the regions by increasing the delivery of care logistics, mobilizing medical forces for doctors and nurses, and quickly building new treatment facilities. These steps are very important in controlling the epidemic, protecting health workers in the front lines, and reducing the severity of patients (Ji et al., 2020).

The health condition of health workers is one of the factors that cannot be compared in patient care. The results of research Zhou, P. et al. (2020) show that health workers are at high risk when fighting COVID-19 outlined at the front. On February 11, 2020 it was recorded that around 3019 health workers might have been infected with COVID-19, 1716 cases of health workers were confirmed by nucleic acid testing, and at least 6 health workers died including the famous pioneer, doctor Li Wenliang.

CONCLUSION

Risk factors for mortality in COVID-19 patients in China that can be a reference in the prevention of death in COVID-19 patients in Indonesia are the age factor ≥ 47 years, COVID-19 complications namely ARDS, low oxygen saturation, and organ failure, immunity or power. The patient's low body resistance is characterized by low white blood cells (WBC), lymphocytopenia, and neutrophilia. Comorbidity or concomitant diseases of diabetes mellitus, hypertension, heart disease, cardiovascular disease, and differences in the availability of patient care facilities namely ICU, ventilator, logistics, and doctors and nurses' health workers. Various mortality risk factors that occur in COVID-19 patients in China are expected to be a guide in efforts to prevent death in COVID-19 patients in Indonesia quickly and accurately.

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