

Conference Paper

Causes of Death in Patients with COVID-19 at Muhammadiyah University General Hospital of Malang

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Abstract.

The global death rate from COVID-19 is 2.1%, while it is 3.2% in Indonesia. There were 81 deaths (32%) out of the 244 total COVID-19 cases at Muhammadiyah University General Hospital of Malang in July 2021. This study examined the immediate causes and conditions leading to these deaths in COVID-19 patients. We aimed to describe several causes of death defined in the death certificate compared with the autopsy findings based on previous literature. This was a retrospective and analytical observational study. There was a death rate of 40.7% in the emergency department, 22.0% in the intensive care unit and 37.0% outside of the intensive care unit. Respiratory failure was the main immediate cause of death with 77 cases (95.06%). Covid-19 pneumonia was the main condition leading to death with 61 cases (75.31%). These data are expected to encourage clinicians to better understand and perceive the circumstances under which a patient may progress from severe infection towards death and manage such cases more efficiently.

Keywords: causes of death, COVID-19, immediate condition leading to causes of death, emergency room, non-ICU, ICU

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1. Introduction

The number of COVID-19 cases was increasing. Indonesia is ranked 13th with the most active cases in the world. Active cases COVID-19 who are receiving treatment and care at the hospital or are undergoing self-isolation. Based on BBC data on August 28, 2021, the number of COVID-19 cases worldwide was 216 million, with a death cases of 4.49 million (2.1%). The number of COVID-19 cases in Indonesia is 4.06 million, with a total death cases of 131,000 (3.2%). The number of COVID-19 cases in East Java is 372,388, with a total death cases of 26,862 (7.2%). The number of cases died with comorbid 19.2%.

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COVID-19 refers to a disease caused by the Novel Human Coronavirus (Severe Acute Respiratory Syndrome CoV-2) which is defined as a respiratory pathogen. In the human host, it causes symptoms that vary from Dry Cough and fever to ARDS-induced respiratory failure. The mortality of cases with COVID-19 was highly dependent on the underlying health conditions and the most common comorbidities include Hypertension, Diabetes, Heart Conditions, and Immunocompromised status. Fever and cough are not related to the cause of death, but in the course of the disease, dyspnea causes low survival, so intensive intervention is needed[1]. The clinical picture of the cause of death was influenced by the direct cause, the conditions that caused the death, the main cause, comorbidities and other risk factors. The cause of death is the disease that triggers the event that results in death. According to Elezkurtaj, 2020 based on autopsy findings, several causes of death in COVID-19 patients were found, namely hypoxia, sepsis, MODS sepsis, septic shock, respiratory failure, heart failure, pulmonary embolism. The conditions that led to death consisted of ARDS and COVID-19 pneumonia[2].

The increase in the number of COVID-19 deaths occurred in all referral hospitals including Muhammadiyah University General Hospital of Malang. The Hospital has been a COVID-19 referral hospital since April 9, 2020 based on the East Java Governor's Decree Number 188/157/KPTS/013/2020 concerning the Establishment of a COVID-19 Referral Hospital in East Java. The number of deaths due to COVID-19 from April 2020 to July 2021 at The Hospital was 251 (16.7%). The highest number of deaths in July 2021 was 81 deaths (32%). There are several risk factors and causes of death. The description of the causes of death for COVID-19 is influenced by many holistic and comprehensive factors. The factors that will be investigated in this study are the direct causes and conditions that cause death. This study aims to determine the cause of death at Muhammadiyah University General Hospital of Malang for the period of July 2021.

2. Material and Method

This study is an retrospective analytic observational research type, with secondary data. Secondary data was taken from the cause of death listed in the death certificate of a COVID-19 patient who died in the period in July 2021. Then did an analysis between the cause of death on the death certificate. This research was conducted at the University Muhammadiyah General Hospital of Malang from August to September 2021. The analysis without testing the hypothesis such as SPSS program. The analysis was carried out by comparing the causes of death listed on the death certificate with

the autopsy results based on the literature. The analysis carried out is about immediate dan condition leading to cause of death. Based on this analysis, it can be seen how far the doctor's level of knowledge about the causes of death for COVID-19 patients.

3. Results

In the July 2021, there were as many as 81 cases of death of COVID-19 patients at Muhammadiyah University General Hospital of Malang, the data was the total number of death cases with COVID-19, whether they were admitted to the treatment ward with a ventilator, non ventilator or in the emergency room. The characteristic data of this research are gender and age. Of the 81 cases of death there were female 35 cases (43.75%) and male 46 cases (56.25%). The age group consisted of 21-40 years 9 cases (11.11%), 40-60 years 33 cases (40.74%), and over 61 years 40 cases (49.38%).

The immediate causes of death consisted of Cardiovascular failure were 2 cases (2.47%), Respiratory failure were 77 cases (95.06%), and sepsis and sepsis shock with the same number of 1 case each (1.23%). The conditions leading to cause of death, there were only 2 conditions, namely ARDS 20 cases (24.69%) and Covid Pneumonia 61 cases (75.31%). There were 4 rooms where the decedent to place, namely the Emergency Room, Alamanda Ward, ICU Non Ventilator (Alamanda Room) and ICU Ventilator (Matahari Room). 33 cases (40.74%) were found in the Emergency Room, Alamanda Ward 26 cases (32.09%), and ICU Non Ventilator (Alamanda Room) 4 cases (4.94%), ICU Ventilator (Matahari Room) 18 cases (22.22%) listed in the table 1.

4. Discussion

Based on the data characteristics of gender, there were 35 cases (43.75%) female and 46 cases (56.25%) male, which is in accordance with previous studies both from Indonesia and globally have shown that the male had a greater risk[3], [4], [5]. The next characteristic is the age group, were the age over 61 years (49.38%) was the highest percentage. Some literature announce that the elderly group having a higher risk of death. [6].

The main immediate cause of death was Respiratory failure in 77 cases (95.06%), that was listed in the death certificate filled by the physician. It shows most of the physician had an authority to decide the cause of death among patients during July 2021 were respiratory failure. ARDS was the condition leading to respiratory failure in death case. In addition, there are 3 other types of immediate causes of death, Cardiovascular failure

TABLE 1: Table of Immediate and Conditions Leading to Cause of Death of COVID-19 Patients During July 2021 at the Muhammadiyah University General Hospital of Malang.

Case	Age	Gender	LOS (days)	Immediate cause	Condition Leading to cause of death
1	71	Female	0	Respiratory failure	Covid-19 pneumonia
2	39	Male	3	Respiratory failure	Covid-19 pneumonia
3	77	Female	1	Respiratory failure	ARDS
4	67	Male	3	Respiratory failure	Covid-19 pneumonia
5	75	Female	7	Respiratory failure	Covid-19 pneumonia
6	47	Female	1	Respiratory failure	ARDS
7	56	Male	0	Respiratory failure	ARDS
8	45	Female	4	Respiratory failure	Covid-19 pneumonia
9	85	Male	5	Respiratory failure	Covid-19 pneumonia
10	37	Female	3	Respiratory failure	Covid-19 pneumonia
11	63	Female	2	Respiratory failure	Covid-19 pneumonia
12	35	Female	16	Respiratory failure	Covid-19 pneumonia
13	44	Male	6	Respiratory failure	Covid-19 pneumonia
14	67	Male	3	Cardiovascular failure	Covid-19 pneumonia
15	26	Female	6	Respiratory failure	Covid-19 pneumonia
16	77	Female	8	Respiratory failure	Covid-19 pneumonia
17	49	Male	2	Respiratory failure	Covid-19 pneumonia
18	51	Male	10	septic shock	Covid-19 pneumonia
19	41	Female	2	Respiratory failure	ARDS
20	75	Female	0	Respiratory failure	ARDS
21	82	Male	5	Respiratory failure	Covid-19 pneumonia
22	64	Male	1	Respiratory failure	Covid-19 pneumonia
23	61	Female	9	Respiratory failure	Covid-19 pneumonia
24	73	Male	0	Respiratory failure	ARDS
25	71	Female	0	Respiratory failure	ARDS
26	56	Male	0	Respiratory failure	ARDS
27	84	Female	0	Respiratory failure	ARDS
28	29	Female	7	Respiratory failure	Covid-19 pneumonia
29	59	Female	1	Respiratory failure	Covid-19 pneumonia
30	59	Male	0	Respiratory failure	ARDS
31	58	Male	14	Respiratory failure	Covid-19 pneumonia
32	66	Male	2	Respiratory failure	ARDS
33	48	Male	3	Respiratory failure	ARDS
34	45	Female	2	Respiratory failure	Covid-19 pneumonia
35	53	Male	8	Respiratory failure	Covid-19 pneumonia
36	37	Male	1	Respiratory failure	Covid-19 pneumonia
37	68	Male	4	Respiratory failure	Covid-19 pneumonia
38	73	Female	1	Respiratory failure	Covid-19 pneumonia
39	62	Female	0	Respiratory failure	Covid-19 pneumonia

TABLE 1: (Continued).

Case	Age	Gender	LOS (days)	Immediate cause	Condition Leading to cause of death
40	57	Male	4	Respiratory failure	Covid-19 pneumonia
41	57	Male	0	Respiratory failure	ARDS
42	76	Male	1	Respiratory failure	Covid-19 pneumonia
43	52	Female	4	Respiratory failure	Covid-19 pneumonia
44	63	Male	11	Respiratory failure	Covid-19 pneumonia
45	29	Female	2	Respiratory failure	Covid-19 pneumonia
46	56	Male	3	Respiratory failure	Covid-19 pneumonia
47	65	Male	12	Respiratory failure	Covid-19 pneumonia
48	46	Male	6	Respiratory failure	Covid-19 pneumonia
49	54	Male	0	Respiratory failure	ARDS
50	49	Male	12	Respiratory failure	Covid-19 pneumonia
51	45	Male	0	Respiratory failure	Covid-19 pneumonia
52	39	Male	9	Cardiovascular failure	Covid-19 pneumonia
53	46	Male	0	Respiratory failure	Covid-19 pneumonia
54	65	Female	1	Respiratory failure	Covid-19 pneumonia
55	69	Male	17	Respiratory failure	Covid-19 pneumonia
56	62	Female	1	Respiratory failure	ARDS
57	84	Female	2	Respiratory failure	Covid-19 pneumonia
58	67	Female	5	Respiratory failure	Covid-19 pneumonia
59	57	Female	0	Respiratory failure	ARDS
60	86	Female	4	Respiratory failure	Covid-19 pneumonia
61	42	Male	14	Sepsis	Covid-19 pneumonia
62	73	Female	1	Respiratory failure	Covid-19 pneumonia
63	69	Female	5	Respiratory failure	Covid-19 pneumonia
64	57	Male	4	Respiratory failure	Covid-19 pneumonia
65	76	Male	0	Respiratory failure	Covid-19 pneumonia
66	50	Female	1	Respiratory failure	Covid-19 pneumonia
67	62	Female	8	Respiratory failure	Covid-19 pneumonia
68	61	Male	3	Respiratory failure	Covid-19 pneumonia
69	61	Male	0	Respiratory failure	ARDS
70	67	Female	2	Respiratory failure	Covid-19 pneumonia
71	40	Male	10	Respiratory failure	Covid-19 pneumonia
72	51	Male	0	Respiratory failure	Covid-19 pneumonia
73	77	Female	4	Respiratory failure	Covid-19 pneumonia
74	63	Male	12	Respiratory failure	Covid-19 pneumonia
75	58	Female	13	Respiratory failure	Covid-19 pneumonia
76	69	Male	1	Respiratory failure	ARDS
77	55	Male	14	Respiratory failure	Covid-19 pneumonia
78	74	Male	4	Respiratory failure	Covid-19 pneumonia
79	45	Male	2	Respiratory failure	ARDS
80	53	Male	1	Respiratory failure	Covid-19 pneumonia
81	73	Male	4	Respiratory failure	ARDS

2 cases (2.47%), sepsis and septic shock in 1 case (1.23%) respectively. The immediate

causes of death in COVID-19 consist in 4 types, while in several literature the immediate causes of death listed up to 11 types in 26 autopsy[7]. This was due to the pathophysiology of SARS-CoV-2 where this virus infects human cells by binding to the cell surface protein angiotensin-converting enzyme 2 (ACE2) through the Receptor Binding Domain (RBD) of its spike (S) protein, ACE2 itself has an important role in the Renin Angiotensin Aldosterone System (RAAS) disorders of this system could cause various other pathophysiological conditions such as atherosclerosis, heart failure, hypertension, diabetes, renovascular disorders, pulmonary hypertension, pneumonia, fibrosis, and sepsis[8]. Referring to this in terms of treating patients with COVID-19, collaboration between multidisciplinary sciences is needed so that in determining immediate cause of death which should be more specific and supported by direct autopsies, it still be a big obstacle in the learning process on cases of COVID-19 in Indonesia, especially at Muhammadiyah University General Hospital of Malang.

Profound suppression of the adaptive and hyperactivity of innate immune systems with macrofage activation was the main factor in Sars-CoV-2 infection. Immune dysregulation together with endothelitis and severe hypercoagulation results in thromboinflammation and microvascular thrombosis in the pulmonary vasculature leading to the severe respiratory distress[9]. These study was appropriate with microscopic results through post-mortem biopsy[1]. In the lungs of decedents, should an alveolar damage due to epithelial cell injury, hyaline membrane formation, edema, type II pneumocyte hyperplasia, multinucleated giant cell formation without hyaline membrane, and consolidation by fibroblastic proliferation extracellular membrane. and fibrin forming clusters. The intra-alveolar neutrophilic infiltration consists with superimposed bacterial bronchopneumonia[1], [8]. Sepsis was found due to lung infections and respiratory insufficiency were the most frequent immediate causes of death. However, the autopsy series included no single case of immediate deadly ischemic heart disease or stroke, these findings indicate that immediate causes of death were directly linked to lung damage initiated by SARS-CoV-2 infection and not related to preexisting health conditions and comorbidities in most cases[7].

The cardiovascular failure has a lot of mechanism which started a mild disease, and it can progress to severe symptoms characterized by hyperinflammatory syndrome, multiorgan dysfunction and even death. The pathophysiology that occurs in the lungs is that the viral glycoprotein SARS-CoV-2 interacts by the same mechanism of ACE reseptor. Vascular endothelial cell dysfunction, inflammation-myocardial depression, cardiomyopathy, direct viral heart infection and its blood vessels, or other matters related to heart failure, demand ischemia, and arrhythmias(10). In all 12 cases, the cause

of death was found in lungs or pulmonary vascular system. However, macroscopically distinguishing viral pneumonia from subsequent diffuse alveolar damage (histological diagnosis) from bacterial pneumonia is not always possible. Lung surface was often showed mild pleurisy and a distinct patchy pattern, with Alternating pale areas with slight prominence and firmness, The hypercapillary area is dark blue and the consistency of the lung tissue is hard but brittle(11).

Poeta (2020) there were 3 possible factors in the process of death in Covid-19 patient. The first was predominant terminal failure, such as terminal respiratory failure, septic shock, and cardiogenic shock. The second was proportion of care in the dying process, such as withholding and withdrawing life support, and full care with or without cardiopulmonary resuscitation. The third was the involvement of covid-19 in the dying process such as previous health, old age, frailty, advanced disease(12). Most patients who diagnosed with COVID-19 at the hospital were being created by the pulmonologist himself. Multidisciplinary in handling Covid-19 patients in a holistic manner was very important to be a better management. In the care of critically ill patients with COVID-19 pneumonia, a strategy for protection of vital organs should be emphasised to improve their survival. It should be noted that the elevation of cardiac troponin I in COVID-19 patients was indicative of myocardial injury leading to secondary severe hypoxaemia, that needed an appropriate respiratory support strategy to improve oxygenation and hoping for the recovery of the myocardial damage(13).

Furthermore, all patients admitted to the ICU on a ventilator (Matahari) experienced 100% of death 18 cases during July 2021. This was due to the high number of patients admitted to the ICU who were already in a severe condition(14). According to Hajjar et al (2021) the criteria for ICU admission in patients with severe symptoms are RR 30 times per minute, oxygen saturation 93%, and pulmonary infiltration >50%, but due to the limitations in the ICU Ventilator (Matahari room) causing the patient could not be treated from the beginning(15). Multidisciplinary involvement in the care of the pulmonologist, Cardiologists, Anesthetists and Internists were important to a better treatment, namely Hypoxia, Sepsis, Sepsis MOF, Septic Shock, Respiratory Failure, Cardiovascular Failure, Pulmonary Embolism, Bacterial Superinfection, Viral Pnemounia, ARDS, Staphylococcal Pnemounia is urgently needed[2]. ARDS was a non-cardiogenic inflammatory form of pulmonary edema, with a reduction in lung area resulting in decreased respiratory ability and a shunt effect(15). To determine the condition of ARDS, it is necessary to carry out laboratory examinations for blood gas analysis with results of degree of hypoxemia: mild ($200 \text{ mmHg} < \text{PaO}_2/\text{FIO}_2 \leq 300 \text{ mmHg}$), moderate ($100 \text{ mmHg} < \text{PaO}_2/\text{FIO}_2 \leq 200$

mmHg), and severe ($\text{PaO}_2/\text{FIO}_2 \leq 100$ mmHg). D-dimer and IL-6 were needed for a complete diagnosis to cardiovascular complication(16).

5. Conclusion

Respiratory failure was the main immediate cause of death with 77 cases (95,06%). COVID-19 pneumonia was the main condition leading to cause of death with 61 cases (75,31%). The cause of death listed on the death certificate must be evaluate carefully and so far the guidelines needed for amandment. These datas encouraged the clinicians to better understood and perceived the circumstances under which a patient may progress from severe infection towards death, and manage such cases in a more efficient manner.

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