

ASSOCIATIONS BETWEEN CLINICAL MANIFESTATIONS AND THE FINAL STATUS COVID- 19 SUFFERER IN PALEMBANG, INDONESIA

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1 ASSOCIATIONS BETWEEN CLINICAL MANIFESTATIONS AND THE FINAL STATUS COVID-19 SUFFERER IN PALEMBANG, INDONESIA

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ABSTRACT

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The clinical manifestations of COVID-19 are the developments and impacts caused by COVID-19. Each person's clinical manifestations vary, such as mild and severe stages. The elderly and pre-elderly as a risk group usually experience severe clinical manifestations. As a result, they have a higher fatality rate than other groups with the highest mortality cases in Palembang City. This study aims to determine the associations between clinical manifestations and final status in the elderly and pre-elderly aged 50 with COVID-19 in Palembang City. This study uses a descriptive-analytic, cross-sectional research design by analyzing secondary data Epidemiological Surveillance Information System (SISUGI) COVID-19. The research sample was 278 data on elderly and pre-elderly with COVID-19 aged 50 in Palembang City who met the inclusion criteria. Data analysis techniques were univariate, bivariate, and multivariate. Univariate results were that 14.7% of elderly and pre-elderly died, and 37.4% experienced severe clinical manifestations. Bivariate analysis showed significant associations ($p < 0.0001$) between clinical manifestations and the last level of the elderly and pre-elderly with COVID-19 in Palembang City (OR: 3.982; CI 95%: 1.977-8.024). There are associations between clinical manifestations and final status after controlling for variables of occupation, age, and history of comorbidities. The comorbid history variable was found as the confounding variable. The research hopes to become the basis for categorizing the clinical manifestations of COVID-19 to prevent poor final status, especially in the elderly and pre-elderly groups.

Keywords: clinical manifestations, final status, elderly, pre-elderly

ABSTRAK

Manifestasi klinis COVID-19 merupakan perkembangan dan dampak yang ditimbulkan oleh COVID-19. Manifestasi klinis setiap orang berbeda-beda, seperti stadium ringan dan berat. Lansia dan pra-lansia sebagai kelompok risiko biasanya mengalami manifestasi klinis yang parah. Mereka memiliki tingkat kematian yang lebih tinggi dibandingkan kelompok lain dengan kasus kematian tertinggi di Kota Palembang. Penelitian ini bertujuan untuk mengetahui hubungan antara manifestasi klinis dengan status akhir pada lansia dan pra-lansia usia 50 tahun dengan COVID-19 di Kota Palembang. Penelitian ini menggunakan desain penelitian deskriptif-analitik, *cross sectional* dengan menganalisis data sekunder Sistem Informasi Surveilans Epidemiologi (SISUGI) COVID-19. Sampel penelitian sebanyak 278 data lansia dan pralansia penderita COVID-19 usia 50 tahun di Kota Palembang yang memenuhi kriteria inklusi. Teknik analisis data adalah univariat, bivariat, dan multivariat. Hasil univariat adalah 14,7% lansia dan pra-lansia dengan status akhir meninggal, dan 37,4% mengalami manifestasi klinis berat. Analisis bivariat menunjukkan adanya hubungan yang bermakna ($p < 0,0001$) antara manifestasi klinis dengan derajat terakhir lansia dan pralansia dengan COVID-19 di Kota Palembang (OR: 3.982; CI 95%: 1.977-8.024). Ada hubungan antara manifestasi klinis dan status akhir setelah dikontrol dengan variabel pekerjaan, umur dan riwayat komorbid. Variabel riwayat komorbiditas ditemukan sebagai variabel pengganggu. penelitian harapannya menjadi landasan untuk mengkategorikan manifestasi klinis COVID-19 untuk mencegah status akhir yang buruk terutama pada kelompok lansia dan pra lansia.

Kata kunci: manifestasi klinis, status akhir, lansia, pra-lansia

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Introduction

The clinical manifestations of COVID-19 are a series of developments and impacts from a person infected with COVID-19. Everyone's clinical manifestations are different, and there are several stages of clinical manifestations with three levels, namely mild, moderate, and severe clinical manifestations. Clinical manifestations often encountered and caused by this virus are cough, fever > 38°C, fatigue, shortness of breath, dizziness, sore throat, headache and vomiting, fatigue, and muscle aches until some cases are experiencing digestive disorders.¹⁻⁴ In addition, some patients have other symptoms that are pretty severe.^{1,3}

On September 3, 2021, globally, COVID-19 cases occurred in 79 countries with a Case Fatality Rate (CFR) rate of 2.4% per 100 cases.⁵ From January 3, 2020, to September 3, 2021, Indonesia's CFR figure is 3.3% per 100 population. On September 2, 2021, South Sumatra COVID-19 data with a CFR rate of 5.1% per 100 cases, and Palembang City with the highest number of other districts in South Sumatra with a CFR rate of 3.8% per 100 cases.⁶⁻⁷ From this data, it turns out that among them are elderly and pre-elderly patients. Besides that, this elderly age tends to have a history of comorbidities, worsening the situation of COVID-19 sufferers. Death from COVID-19, according to research, is due to its associations with clinical manifestations experienced by the elderly and *pre-elderly*. On the other hand, the elderly and *pre-elderly* are a range group and tend to have a history of comorbidities.⁸

The clinical manifestations that occur in the elderly are classified as mild and severe. The elderly who experience mild manifestations if they have a fever, respiratory symptoms, and radiographs result in pneumonia. In contrast, severe manifestations said the elderly who experience mild manifestations, fever, and respiratory symptoms are proven to be pneumonia and occur. Dyspnea or respiratory failure or what is often called shortness of breath. In a previous study, a person with severe clinical manifestations had a higher risk of death than those with mild clinical manifestations.^{9,21}

In contrast, someone with mild clinical manifestations tended to recover from COVID-19.⁹ Then, it will be more difficult if an older adult has a comorbid disease. The most common comorbid disorders are diabetes mellitus, cardiovascular disease, and hypertension. In previous studies that have analyzed logistic regression, the elderly have more than three clinical manifestations and experience pneumonia. These comorbidities will increase mortality.¹⁰⁻¹¹ Clinical manifestations of COVID-19 in the elderly can cause lung infections, increasing the heart's workload. At the same time, it will increase blood sugar so that controlling the disease experienced is more complicated. As with previous studies, elderly and pre-elderly with comorbidities increase the severity of the clinical manifestations of COVID-19. Even those who have symptoms and are

declared cured six months later experience advanced symptoms such as muscle pain and fatigue.^{2,9} Previous research stated that if a person's age increases, symptoms and chances of death will increase (AOR=1.07). Then, older people tend to experience a decline in the immune system. In mild clinical manifestations, the body's immune response to an elderly and elderly will be different. The body of the elderly and elderly with low immunity will work harder to fight the virus, so there will be increased inflammation which will increase clinical manifestations towards severe. Severe clinical manifestations will result in damage to the body to death.^{10,11}

Other studies show that increasing age by ten will increase the risk of advanced symptoms and disorders.¹²⁻¹³ In clinical manifestations that occur in the elderly, there will be a need for more attention in treatment and further identification of clinical manifestations so that they can prioritize clinical manifestations that will require more intensive care and services, in a study conducted in Hainan recommended in the elderly and prioritized.² This study aims to determine the associations between clinical manifestations and final status 19 in the elderly and *pre-elderly* with COVID-19 in Palembang City.

Methods

This type of research uses descriptive analysis with a cross-sectional study design. The location of this research is the entire area of Palembang City which consists of 18 districts. The site includes SeberangUlu I, SeberangUlu II, Kertapati, Jakabaring, Ilir Timur I, Ilir Timur II, IlirTimur III, Gandus, Plaju, Ilir Barat I, Bukit Kecil, Kemuning, Kalidoni, Sako, SematangBorang, Sukarami, Alang-AlangLebar, and Sukarami. This study uses secondary data from the COVID-19 Epidemiological Surveillance Information System application from March 1, 2020, to April 7, 2021, with a data request process at the Palembang City Health Office.

According to WHO and the Indonesian Ministry of Health (2013), the elderly are parents who have entered the age of 50 years and over or in the age group of 50-64 years and 65 years and over.²²⁻²³ The SISUGI data obtained as many as 428 elderly and *pre-elderly* with COVID-19 who were in the Palembang City area. This data went through a data cleaning process so that 150 data were released based on inclusion and exclusion criteria to obtain 150 elderly and elderly and 128 *pre-elderly* with a total of 278 who met the requirements. The inclusion criteria consisted of the age group of 50-64 years and 65 years and over with confirmed final status, cured or died status; the exclusion criteria consisted of missing data, and the elderly status was still sick.

The variables used include age, gender, occupation, clinical manifestations, travel history and contacts, and history of comorbid variables. Data analysis used univariate analysis, which distributed the frequencies of all variables. Then bivariate analysis determined whether the independent and dependent variables have an alleged associations. in this study, the independent variables consisted of clinical manifestations, age, gender, occupation, and history of comorbidities.

Variable clinical manifestations, age, gender, and occupation will use chi-square analysis. Then, for the history of comorbid variables, they use logistic regression analysis to see the magnitude of the risk that occurs. Moreover, lastly, multivariate analysis using multiple logistic regression risk factor model. The risk factor model is used to determine whether the study has confounding variables. To identification will be that sees a change in PR. Suppose the change in PR is $> 10\%$. In that case, the variable is a confounding variable. In contrast, if the difference is $< 10\%$, the variable is not confounding. The research significance level (α) is 5%. This research has obtained approval from the Research Ethics Committee, Faculty of Public Health, Sriwijaya University Number: 304/UN9.FKM/TU.KKE/2021.

Results

1. Univariate analysis

Table 1. Frequency Distribution of Characteristics of the Elderly and Pre-elderly (≥ 50 years old) with COVID-19 Patients in Palembang City

Variable	Sum (n)	Median	Mean	SD	Min	Max
Age (≥ 50 years old)	278	60	61.18	8.267	50	85
Variable	Frequency		Percentage (%)			
Age (≥ 50 years old)						
≥ 60 (elderly)	150		54			
50-59 (Pre-elderly)	128		46			
Gender						
Male	159		57.2			
Female	119		42.8			
Employment Status						
Not working	114		41			
Working	164		59			
Type of work						
Not working	114		41			
Health workers	10		3.6			
Teacher	1		0.4			
Private	15		5.4			
Self-employed	47		16.9			
Other	91		32.7			
Final Status						
Death	41		14.7			
Healed	237		85.3			
Total	278		100			

Univariate table analysis shows that in this study in Palembang City, the majority experienced COVID-19 over 60 years, with as many as 150 people. This study also found that patients with COVID-19 were higher among male patients, as much as 159 (57.2%). The research results in the city of Palembang, most are still working and have the most jobs, namely other types of work, followed by entrepreneurs. And the private sector. Furthermore, the majority of COVID-19 sufferers in the elderly and pre-elderly (≥ 50 years old) in Palembang City experience a final recovered status, which is higher by 85.3% compared to the final status of death.

Table 2. Frequency Distribution of Travel History and Contacts for Elderly and Pre-elderly (≥ 50 years old) with COVID-19 patients in Palembang City

Variable	Frequency	Percentage (%)
Overseas Travel History		
No	275	98.9
Yes	2	0.7
Do not know	1	0.4
Local Transmission History		
No	257	92.4
Yes	19	6.8
Do not know	2	0.7
Animal Market Visit History		
No	271	97.5
Do not know	7	2.5
Suspect Contact History		
No	241	86.7
Yes	9	3.2
Do not know	28	10.1
Contact History Confirm		
No	226	81.3
Yes	23	29
Do not know	29	10.4
Epidemiological Case Status		
Contact Confirmation	70	25.2
Travel confirmation	12	4.3
Confirm without history	78	28.1
Confirmation is not clear	35	12.6
Probable	8	2.9
Suspect	71	25.5
The suspect is not clear	4	1.4
Close Contact		
No	160	57.6
Yes	118	42.4
Close Contact		
Not having close contact	160	57.6
1-5 Close Contact	107	38.5
6 Close Contact	11	4
Total	287	100

Most elderly and pre-elderly (≥ 50 years old) in the city of Palembang have no history of travel abroad and local transmission and do not have a history of animal markets. Then, the majority did not have a history of suspected and confirmed contacts. However, the majority of the elderly had the status of suspected epidemiological cases. The majority had close connections with close contacts, one to five close contacts. The findings is similar with COVID-19 data from the Province of South Sumatra, including data local travel history, confirmed contact history, suspect contact history, and data closest contacts did not have and did not have contact.¹⁶

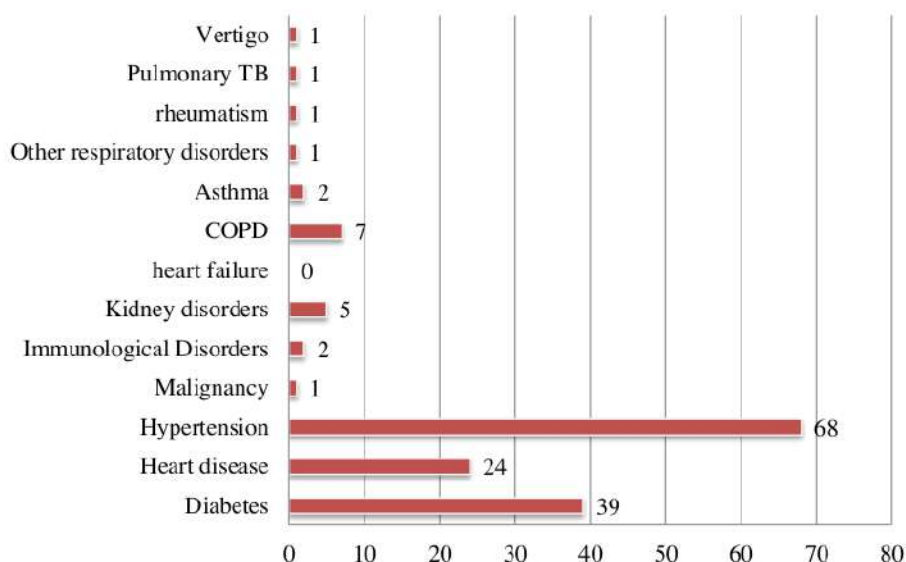


Figure 1. Distribution of the Frequency of Comorbidities in the Elderly and Pre-elderly (≥ 50 years old) with COVID-19 Patients in Palembang City

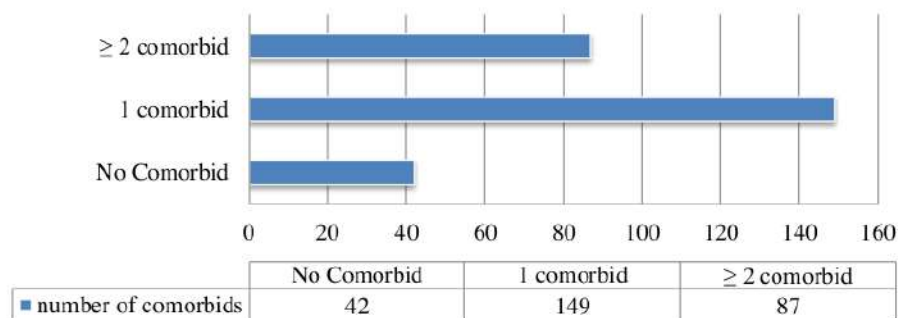


Figure 2. Distribution of the Frequency of the number of Comorbidity in the Elderly and Pre-elderly (≥ 50 years old) with COVID-19 Patients in Palembang City

From the diagram of the results of the study of the elderly and pre-elderly (≥ 50 years) in the city of Palembang, 149 (53.6%) people have one comorbidity and 87 (31.3%) with over two comorbidity. This comorbidity was the highest in the comorbid type, hypertension, in as many as 68 people, followed by diabetes, 39 among patients.

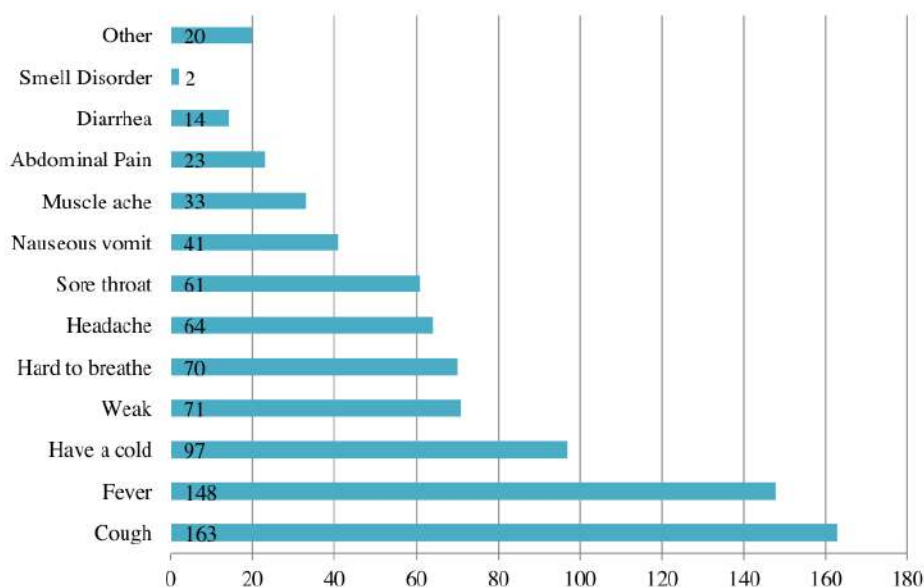


Figure 3. Distribution of the Frequency of Clinical Manifestations for the Elderly and Pre-elderly (≥ 50 years old) with COVID-19 Patients in Palembang City

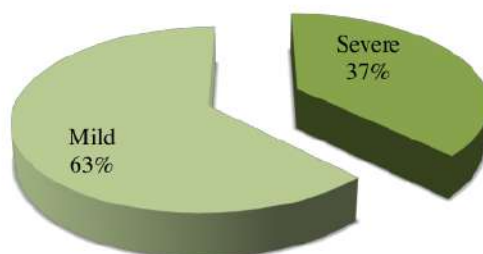


Figure 4. Distribution of the Frequency of Classification of Clinical Manifestations for the Elderly and Pre-elderly (≥ 50 years old) with COVID-19 Patients in Palembang City

Elderly and pre-elderly (≥ 50 year old) experienced the most clinical manifestations, namely mild, with the most common clinical manifestations of cough, fever, and runny nose. This study's participants with mild clinical manifestations suffered from several clinical manifestations, including fever, cough, runny nose, sore throat, headache, muscle aches, nausea/vomiting, and diarrhoea.⁶

2. Bivariate analysis

Table 3. Associations between Clinical Manifestations, Age, Gender, Occupation, and Comorbid History with the Late Status of Elderly and Pre-Elderly Patients with COVID-19

Variable	Final Status of COVID-19 Patients		Total	P value	PR (95% CI)
	Death	Healed			
Clinical Manifestations					
Severe	27 (26%)	77 (74%)	104 (100%)	<0.0001	3.208 (1.764-5.833)
mild	14 (14.8%)	160 (85.2%)	174 (100%)		
Age					
≥ 60	25 (16.7%)	125 (83.3%)	150 (100%)	0.420	1.333 (0.745-2.385)
50-59	16 (12.5%)	112 (87.5%)	128 (100%)		
Gender					
Male	25 (15.7%)	134 (84.3%)	159 (100%)	0.720	1.169 (0.654-2.090)
Female	16 (13.4%)	103 (86.6%)	119 (100%)		
Employment Status					
Not working	23 (14%)	141 (86%)	164 (100%)	0.813	0.888 (0.503-1.568)
Working	18 (15.8%)	96 (84.2%)	114 (100%)		
Comorbid history					
≥ 2 comorbid	6 (14.3%)	36 (85.7%)	42 (100%)	0.202	1.909 (0.707-5.159)
1 comorbid	14 (9.4%)	135 (90.6%)	149 (100%)	0.003	3.068 (1.469-6.415)
No comorbid	21 (24.1%)	66 (75.9%)	87 (100%)	0.011	Ref

The bivariate analysis showed a significant associations between clinical manifestations and final status in the elderly and the elderly (≥ 50 years). They would increase the risk factor by 3.208, and the researchers believe that a 95% CI of severe clinical manifestations in the population will increase the risk by 1.764 to 5.833, compared to mild clinical manifestations. Furthermore, there is a associations between the history of disease variables and the incidence of final status in the elderly and pre-elderly (≥ 50 years). At 2, a history of comorbidity would increase the risk factor by 1.909 times. The investigators believed a 95% CI that a history of comorbidity would decrease the risk factor by 0.707 to 5.159 times in the general population. The elderly and pre-elderly with one history of comorbid will increase the risk factor by 3.068, and researchers believe 95% CI that one history of comorbid will increase the risk factor by 1.469 to 6.415 in the general population. Meanwhile, age, gender, and occupation did not show a meaningful associations with the final status of the elderly and pre-elderly (≥ 50 years).

3. Multivariate Analysis

Table 4. Final Modeling of the Associations of Clinical Manifestations with Final Status of Elderly and Pre-elderly Patients with COVID-19

Variable	P-value	OR	95% CI
Clinical manifestations	0.001	3.441	1.676-7.064
Comorbid history ≥ 2	0.465	1.468	0.524-4.110
One comorbid	0.028	2.359	1.097-5.071
No comorbid	0.089	Ref	Ref

Multivariate analysis will use multiple logistic regression with a risk factor model. There are several processes: initial modelling (full model), confusion, and how to see changes in the Prevalence ratio value. If the change variable is more than 10%, it will remain in the analysis and is a confounding variable. If the difference is less than 10%, it will not be in the modelling. Moreover, it is not a confounding variable. The last stage of the risk factor model is the final modelling. From the final modelling results, the table shows that there is a significant **associations between clinical manifestations and final status in the elderly and pre-elderly** who have COVID-19. Then, the elderly and pre-elderly (≥ 50 years) after being controlled with a history of comorbidities. The OR value shows that the elderly and pre-elderly who experience severe manifestations have a chance of 3.441 to share the final status of death. Compared with the elderly and pre-elderly with mild clinical manifestations. It means that clinical manifestations will increase risk factors. Researchers also believe that a 95% CI will increase risk factors by 1,676 to 7,064 times in the general population.

Discussion

Everyone's clinical manifestations are different, and this happens due to differences in demographic characteristics, immunity, and a person's sociocultural circumstances. The average course of COVID-19 is with an incubation period of 4 to 14 days. This incubation period depends on a person's age and immunity, especially in **the elderly and pre-elderly as a vulnerable group** with low immunity.¹⁶⁻¹⁹ Clinical manifestations that occur have a classification of levels. Mild clinical manifestations, such as fever, cough, and runny nose, are often found. In addition, there are signs of headache, sore throat, and experience nausea/vomiting, abdominal pain, and muscle aches. Generally, mild clinical manifestations will experience a final recovery status. Suppose in one to two weeks; there has not been a recovery. In that case, it will usually increase to severe clinical manifestations with excessive fatigue and disturbances in smell. In addition, it will experience shortness of breath.^{2,6,18,20} Thus, mild clinical manifestations are cough, fever, sore throat, runny nose, headache, muscle aches, diarrhoea, and nausea/vomiting.

Meanwhile, severe manifestations are patients with COVID-19 who experience clinical manifestations of weakness, shortness of breath, and difficulty smelling.⁹ The results showed that clinical manifestations were related to the final status of the elderly and the pre-elderly. These results also suggest that clinical manifestations will increase the risk factors. This study is similar to the research conducted by Jang and Deng et al. in 2021, which described clinical manifestations as having a significant associations with final status.⁹ His research said that the clinical manifestations of high severity with the final status of death would have a risk of 1.7 times compared to someone with mild clinical manifestations. Mild to late death status with a 95% CI in the general population of 1.1 to 2.6 will increase the risk.^{6,9,21}

In a person infected with COVID-19, the immune response in the body will increase and activate T cells. In a person infected with COVID-19, the immune response in the body will increase and activate T cells. Clinical manifestations will appear on days 7 to 9. On that day, proinflammatory cytokine and chemokine molecules increase. Proinflammatory cytokines are protein molecules that form and regulate the immune system. At this time, the immune system will play a role in fighting viruses that enter the body. Proinflammatory cytokines will create an inflammatory reaction, which functions as an effort to eliminate pathogens or viruses that enter the body as a form of defence. It is at this stage that clinical manifestations occur. Clinical manifestations, body conditions, and the response that each person's body will experience will be different. In mild clinical manifestations, the performance of cytokines in the body will automatically stop working if it has succeeded in fighting viruses or infections.^{13-14,18,22,20}

Moreover, this stopped cytokine production will cause inflammation in the body to improve so that the condition of the elderly and *pre-elderly* will cause recovery. The human body's leukocyte and neutrophil molecules against body molecules such as lymphocytes, monocytes, eosinophils, and basophils will be lower in severe clinical manifestations. Moreover, proinflammatory cytokine molecules, procalcitonin, ferritin, and C-reactive protein will be abundant in the human body.^{18,20,22,25} Elderly and *pre-elderly* with severe clinical manifestations will die due to the rise in a systemic inflammatory response, or cells and tissues in the body are not controlled. The multiplicity of the inflammatory response is called a cytokine storm. Because, in severe clinical manifestations, the cytokines in the body will not stop working. So that immune cells will continue to be produced to fight disease. Inflammation is one of the body's ways of fighting infection in the event of a cytokine storm. It will cause excessive inflammation.^{1,12,13}

The immune response in the body will cause lung damage and fibrosis, and a functional disability will occur.²⁵⁻²⁶ In this case, it will cause Acute respiratory distress syndrome (ARDS) or respiratory disorders and respiratory failure in the body. Suppose the elderly and the *pre-elderly* have experienced this and have shown danger signs. In that case, further action is necessary so that complications do not occur and even death status appears.^{22,28-29}

The risk of severe clinical manifestations experiencing death is higher than mild clinical manifestations. However, the risk of death may occur if the mild clinical manifestations have a history of comorbidities. The elderly and *pre-elderly* tend to have comorbidity with vulnerable age. Therefore, this study's confounding variable is comorbid, meaning that someone with mild clinical manifestations died from comorbidities, not COVID-19.

Abdullah Abdi's research said aspects affecting the level of clinical manifestations and prognosis of COVID-19 were not only epidemiological factors but also comorbid history. These comorbidities can be 1 or 2 found in the elderly and *pre-elderly*. However, the comorbidities that contribute most to aggravating clinical manifestations and end in the final status of death are

hypertension, diabetes, and chronic respiratory and cardiovascular diseases (Abdullah Abdi, 2021).³⁰

A study by Putra (2021) showed that the severity of the outcome for COVID-19 sufferers was more at risk for two comorbidities than for one comorbid. However, this study explains that the groups and combinations studied show that these COVID-19 sufferers have a history of high cardiovascular comorbidities, diabetes, and hypertension simultaneously. So the risk and relationship between comorbid histories such as diabetes, hypertension, heart disease, and cardiovascular disease simultaneously will be at higher risk.²²⁻³¹ Because of all of this, prevention relevancy to overcome the clinical manifestations and history of comorbidities that occur.

Conclusion

Elderly and pre-elderly with severe clinical manifestations tend to experience the final status of death. The elderly and pre-elderly have low immunity, which will cause the immune response system in the body of the elderly who are affected by the COVID-19 virus to experience a cytokine storm. Cytokine storm will aggravate clinical manifestations so that it will cause complications and even death. For those with more than ≥ 2 comorbid histories, the risk is higher compared to having one comorbid only. A history of high-risk comorbidities includes diabetes, hypertension, and heart disease. These diseases combine to help COVID-19 sufferers get severe manifestations and experience the final status of death.

In clinical complaints of the elderly and pre-elderly, health workers and families pay attention to the elderly and pre-elderly. The way is by consulting a doctor every three days for 14 days being tested positive for a COVID-19 PCR test. This communication is through online media, such as WhatsApp or telemedicine media platforms. Then the elderly and pre-elderly with a history of comorbidities are advised to consult and visit health services six times a year. In addition, it provides specialist psychological support and mental health initiatives for sufferers.

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Conflict of Interest

There is no conflict of interest for this research.

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