



# Risk Factors for Mortality in Indonesian COVID-19 Patients

Ardi Pramono\*, Yosy Budi Setiawan, Nova Maryani

Department of Anesthesia and Intensive Care, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Kasihan, Indonesia

## Abstract

**Edited by:** Ksenija Bogoeva-Kostovska  
**Citation:** Pramono A, Setiawan YB, Maryani N. Risk Factors for Mortality in Indonesian COVID-19 Patients. Open Access Maced J Med Sci. 2022 Jan 02; 9(T5):181-184. <https://doi.org/10.3889/oamjms.2022.7826>  
**Keywords:** COVID-19; Cytokine storm; Indonesian; Mortality; Risk factors  
**\*Correspondence:** Ardi Pramono, Department of Anesthesia and Intensive Care, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Kasihan, Indonesia. E-mail: [ardipramono@umy.ac.id](mailto:ardipramono@umy.ac.id)  
**Received:** 05-Nov-2021  
**Revised:** 02-Dec-2021  
**Accepted:** 06-Dec-2021  
**Copyright:** © 2022 Ardi Pramono, Yosy Budi Setiawan, Nova Maryani  
**Funding:** This study was supported by Universitas Muhammadiyah Yogyakarta  
**Competing Interests:** The authors have declared that no competing interests exist  
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**BACKGROUND:** The coronavirus or COVID-19 was originally discovered in the Chinese city of Wuhan in December 2019 which quickly spread to various countries and caused a global pandemic. According to the WHO, this coronavirus is called SARS-CoV-2 or severe acute respiratory syndrome coronavirus 2, it attacks the respiratory tract suddenly and can be fatal or cause the sufferer's mortality in a short time.

**AIM:** This study aims to find predictors of risk factors for the mortality of people infected with COVID-19; thus, it can help medical personnel make decisions quickly whether the patient has a good or bad prognosis. Faster and more precise decision-making can increase the efficiency of the needs of limited resources.

**METHODOLOGY:** This research used a cross-sectional design of data collection of patients who died and returned home with a diagnosis of COVID-19 from medical records data of PKU Muhammadiyah Gamping Yogyakarta Educational Hospital. Logistic regression test was counted with a level of significance ( $p < 0.05$ ) using SPSS v.21 software

**RESULTS:** Subjects who died were 63 people or 48.8%, while subjects who were alive were 66 people or 51.2%. Female subjects were 61 people or 47.3%, while male subjects were 68 people or 52.7%. The logistic regression analysis results showed that the variables determining the risk factors for death ( $p < 0.05$ ) included age, impaired lung function, impaired kidney function, and increased D-dimer.

**CONCLUSION:** Four risk factors for patients with COVID-19 determined whether the patient dies or lives, namely, age, lung disorders, impaired kidney function, and increased d-dimer.

## Introduction

The coronavirus was originally discovered in December 2019 in Wuhan city, China, and causes severe and life-threatening acute respiratory tract attacks. Within a few weeks, this disease has spread to various countries and caused a global pandemic [1]. The virus can spread from person to person [2], and the number of those infected rose sharply from 1 million cases to 1.5 million cases in a week in 184 countries ("COVID-19 Map," n.d.) [3]. The increase in the number of patients is not proportional to adequate treatment facilities, including medical personnel who are increasingly exposed to the disease. The data show that 100 doctors died in Indonesia [4]. A good health system is currently needed to deal with the problems of the COVID-19 outbreak, such as personal protective equipment, diagnosis, and therapy, including risk factors for disease aggravation [4], [5].

The patient who died from COVID-19 and whose health condition worsens is caused by an excessive systemic inflammatory or immune reaction or cytokine storm [6]. This cytokine storm causes respiratory failure and damage other organs such as heart, kidneys, and liver [7]. Shang *et al.* [8] stated that

patients who died had a previous disease (comorbid). Incidence of death in COVID-19 patients related to old age, increased d-dimer value, the percentage of lymphocyte count, and coronary heart disease [8]. Patients with diabetes mellitus also have risk factors for worsening the disease [9]. Another study stated that male patients with cancer were more prone to suffer from critical COVID-19. Moreover, patients who received chemotherapy 4 weeks before being exposed to COVID-19 have a higher risk of death [10].

This research attempts to identify risk factors for worsening the disease to estimate the emergence of cytokine storms that worsen the patient's condition. If risk factors are identified early, medical officers will be able to treat patients better [11], such as prioritizing severe and potential patients to improve, recommending hospitalization at home or self-isolation for asymptomatic patients, and those who have no risk factors.

## Methods

This research has obtained research ethics feasibility with the number 025/EC-EXEM\_KEPK FKIK

UMY/III/2021. This research used a cross-sectional design of data collection of patients who died and returned home with a diagnosis of COVID-19 from PKU Muhammadiyah Gamping Yogyakarta Educational Hospital's medical records. The patient data were taken from medical records from 2020 to 2021 with the inclusion criteria of all patients with PCR test positive for a diagnosis of COVID-19 and the dead or alive final results. Subject variables were then grouped based on final conditions of the patients, gender, and age, comorbid diseases such as diabetes mellitus (DM), heart disease, lung disorders, cancer, impaired kidney function, liver function, hypertension, nervous disorders, and sepsis. The laboratory values were grouped into the variable numbers of leukocytes, platelets, hemoglobin (anemia), and the value of D-dimer. The data obtained were then processed using SPSS v.21 software. Categorical data are presented in the form of numbers and percentages, while the statistical test of the relationship between two variables (bivariable) was carried out using the Chi-Square or Fisher exact test based on the significance limit of  $p < 0.5$ . Multivariable analysis with logistic regression was performed on variables with a significance of  $p < 0.5$  to determine the statistical significance ( $p < 0.05$ ) of risk factors for all predictor variables.

## Results

The subjects who died were 63 people or 48.8%, while the living subjects were 66 people or 51.2%. The female subjects were 61 people or 47.3%, while the male subjects were 68 people or 52.7%. The subject characteristics are shown in Table 1.

### *Karakteristik subjek penelitian*

The results of the bivariable test showed that in addition to the anemia variable, the other variables showed a significant relationship with  $p$  values each lower than 0.5 (Table 2).

Furthermore, variables with  $p < 0.5$  were included in the multivariate analysis, with the results in Table 3.

## Discussion

COVID-19 disease or SARS-Cov-2 can be spread between humans through air. It can also spread through the patient's feces [12] by close contact [13]. People infected with COVID-19 and are symptomatic who are the most frequent source of disease

**Table 1: Subjects' characters**

| Variable            | Category | Description (%)    |
|---------------------|----------|--------------------|
| Patient's condition | Alive    | 66 (51.2)          |
|                     | Dead     | 63 (48.8)          |
| Age*                |          | 50.4219 ± 18.81054 |
| Gender              | Female   | 61 (47.3)          |
|                     | Male     | 68 (52.7)          |
| Diabetes mellitus   | No       | 93 (72.1)          |
|                     | Yes      | 36 (27.9)          |
| Heart disease       | No       | 117 (90.7)         |
|                     | Yes      | 12 (9.3)           |
| Lung disorder       | No       | 107 (82.9)         |
|                     | Yes      | 22 (17.1)          |
| Cancer              | No       | 128 (99.2)         |
|                     | Yes      | 1 (0.8)            |
| Impaired kidney     | No       | 107 (82.9)         |
|                     | Yes      | 22 (17.1)          |
| Liver disorder      | No       | 125 (96.9)         |
|                     | Yes      | 4 (3.1)            |
| Leucocyte           | No       | 99 (76.7)          |
|                     | Yes      | 30 (23.3)          |
| D-dimer high        | No       | 79 (61.2)          |
|                     | Yes      | 50 (38.8)          |
| Thrombocytopenia    | No       | 117 (90.7)         |
|                     | Yes      | 12 (9.3)           |
| ICU                 | No       | 108 (83.7)         |
|                     | Yes      | 21 (16.3)          |
| Hypertension        | No       | 99 (76.7)          |
|                     | Yes      | 30 (23.3)          |
| Neurology problem   | No       | 120 (93.0)         |
|                     | Yes      | 9 (7.0)            |
| Anemia              | No       | 125 (96.9)         |
|                     | Yes      | 4 (3.1)            |
| Sepsis              | No       | 124 (96.1)         |
|                     | Yes      | 5 (3.9)            |

\*Variable with no category, mean value ± SD. SD: Standard deviation, ICU: Intensive care unit.

transmission through droplets of saliva when sneezing or coughing [14]. Infected people may continue to recover or experience worsening symptoms due to a cytokine storm [7], [15], [16].

**Table 2: Variable relationship with patient outcome**

| Serial number | Variable          | Category | Alive, n (%) | Dead, n (%) | P     |
|---------------|-------------------|----------|--------------|-------------|-------|
| 1             | Gender            | Female   | 38 (62.3)    | 23 (37.7)   | 0.017 |
|               |                   | Male     | 28 (41.2)    | 40 (58.8)   |       |
| 2             | Age*              |          | 65 (50.8)    | 63 (49.2)   | 0.001 |
|               |                   |          | 58 (62.4)    | 35 (37.6)   |       |
| 3             | Diabetes mellitus | No       | 8 (22.2)     | 28 (77.8)   | 0.000 |
|               |                   | Yes      | 64 (54.7)    | 53 (45.3)   |       |
| 4             | Heart disease     | No       | 2 (16.7)     | 10 (83.3)   | 0.015 |
|               |                   | Yes      | 64 (59.8)    | 43 (40.2)   |       |
| 5             | Lung disorder     | No       | 2 (9.1)      | 20 (90.9)   | 0.000 |
|               |                   | Yes      | 66 (51.6)    | 62 (48.4)   |       |
| 6             | Cancer            | No       | 0            | 1 (100.0)   | 0.488 |
|               |                   | Yes      | 62 (57.9)    | 45 (42.1)   |       |
| 7             | Impaired kidney   | No       | 4 (18.2)     | 18 (81.8)   | 0.001 |
|               |                   | Yes      | 66 (52.8)    | 59 (47.2)   |       |
| 8             | Liver disorder    | No       | 0            | 4 (100.0)   | 0.054 |
|               |                   | Yes      | 57 (57.6)    | 42 (42.4)   |       |
| 9             | Leukocytosis      | No       | 9 (30.0)     | 21 (70.0)   | 0.012 |
|               |                   | Yes      | 49 (62.0)    | 30 (38.0)   |       |
| 10            | D-dimer high      | No       | 17 (34.0)    | 33 (66.0)   | 0.002 |
|               |                   | Yes      | 64 (54.7)    | 53 (45.3)   |       |
| 11            | Thrombocytopenia  | No       | 2 (16.7)     | 10 (83.3)   | 0.015 |
|               |                   | Yes      | 66 (61.1)    | 42 (38.9)   |       |
| 12            | ICU               | No       | 0            | 21 (100.0)  | 0.000 |
|               |                   | Yes      | 57 (57.6)    | 42 (42.4)   |       |
| 13            | Hypertension      | No       | 9 (30.0)     | 21 (70.0)   | 0.008 |
|               |                   | Yes      | 63 (52.5)    | 57 (47.5)   |       |
| 14            | Neurology problem | No       | 3 (33.3)     | 6 (66.7)    | 0.317 |
|               |                   | Yes      | 64 (51.2)    | 61 (48.8)   |       |
| 15            | Anemia            | No       | 2 (50.0)     | 2 (50.0)    | 1.000 |
|               |                   | Yes      | 68 (54.0)    | 58 (46.0)   |       |
| 16            | Sepsis            | No       | 0            | 5 (100.0)   | 0.026 |
|               |                   | Yes      |              |             |       |

ICU: Intensive care unit.

The COVID-19 typical phase is divided into four stages, namely, Stage 1 is without symptoms starting when the virus enters the body and replicates, Stage 2 begins when the virus begins to spread, Stage 3 begins an inflammatory process in various body systems, and Stage 4 is critical because it damaged endothelial, impaired organ function, and thrombosis [17]. This study found several risk factors that could be predictors

**Table 3: Risk factor for COVID-19 death**

| Variable               | Constanta B | SE    | Wald   | Df | Significance | Exp (B) |
|------------------------|-------------|-------|--------|----|--------------|---------|
| Age                    | 0.070       | 0.020 | 12.061 | 1  | 0.001*       | 1.073   |
| Gender                 | 0.848       | 0.552 | 2.359  | 1  | 0.125        | 2.335   |
| Diabetes mellitus      | 0.873       | 0.634 | 1.896  | 1  | 0.169        | 2.394   |
| Heart disease          | 1.875       | 1.053 | 3.168  | 1  | 0.075        | 6.520   |
| Impaired lung function | 2.143       | 0.854 | 6.298  | 1  | 0.012*       | 8.528   |
| Impaired kidney        | 1.587       | 0.751 | 4.466  | 1  | 0.035*       | 4.891   |
| Leukocytosis           | 0.873       | 0.647 | 1.825  | 1  | 0.177        | 2.395   |
| High D-dimer           | 1.197       | 0.574 | 4.349  | 1  | 0.037*       | 3.309   |
| Thrombocytopenia       | 1.665       | 0.997 | 2.791  | 1  | 0.095        | 5.285   |
| Hypertension           | 0.508       | 0.667 | 0.581  | 1  | 0.446        | 1.662   |
| Stroke                 | 0.894       | 0.977 | 0.838  | 1  | 0.360        | 2.446   |
| Constant               | -7.099      | 1.853 | 14.683 | 1  | 0.000        | 0.001   |

\*Significant  $P < 0.05$ . SE: Standard error.

of patients' mortality caused by SARS-Cov-2 virus infection, namely, increasing age, lung disorders, decreased kidney function, and high levels of D-dimer ( $p < 0.05$ ). These results are similar to those of previous studies, revealing a sign of a cytokine storm [18], and being in stage 4 with a high risk of death [17]. In this study, liver disorders, cancer patients, and admitted to the ICU were not included as a risk factor, although there was a significant association with the incidence of death or survival of patients ( $p < 0.5$ ).

COVID-19 patients with older age are associated with an increase in angiotensin-converting enzyme-2 (ACE-2) receptors, which cause high replication of the virus, in addition to a decrease in the immune system and an increase in comorbidities that increase disease severity [19]. Comorbid diseases such as diabetes mellitus, cardiovascular and chronic lung disease, cancer, and impaired kidney and liver function have a more critical COVID-19 high risk [20], [21]. Lung disorder, a decrease in renal function, and an increase in D-dimer levels are critical signs according to the course of stage 4 disease. Although anticoagulant and anti-inflammatory therapy can be given at this stage; in general, it is very difficult to improve and progress quickly [17]. Patients with decreased kidney function generally experience worsening if infected with COVID-19 [22]. Beside, SARS-CoV-2 can cause acute renal failure caused by a cytokine storm as a systemic inflammatory response to the angiotensin-converting enzyme 2 (ACE2) receptor present in the kidney [23].

Indonesia is a country with a Muslim majority population and inhabited by various ethnicities. Although there have been improvements from the government, the lack of facilities and infrastructure and a referral system for patients with COVID-19 symptoms remain a problem in handling COVID-19 patients. Patients are often referred late for various reasons, such as fear of going to the hospital, lack of coordination between primary and secondary services (hospitals), and lack of availability of medicines [5]. Older patients who come to the hospital generally have symptoms of cough, fever, and short breath [24]. These symptoms are very likely in stages 3–4. Furthermore, in terms of limitation, this study is limited to data obtained from medical records at 1 hospital; thus, caution is needed to make decisions regarding the actions to be given to patients who meet critical criteria.

## Conclusion

Based on the result of this study, it can be concluded that factors that can be used to determine whether a subject died or not included age, lung disease, impaired kidney function, and increased levels of d-dimer.

## Acknowledgment

The researchers would like to thank Universitas Muhammadiyah Yogyakarta for funding this research and the PKU Muhammadiyah Hospital for the permission to collect data.

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