P-ISSN : 2527-4627
Warmadewa Medical Journal
Available online http://ejournal.warmadewa.ac.id/index.php/warmadewa_medical_journal

WMJ (Warmadewa Medical Journal), Vol. 7 No. 1 Mei 2022, Hal. 33-40

Factors Associated with Long-Term COVID-19: An Observational Cross-Sectional Study in Indonesia

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Abstract

Long-term COVID-19 could occur in COVID-19 patients, affecting the patient's quality of life, and becoming a problem for public health. However, information is rarely on factors associated with the occurrence of long COVID-19 cases. This study analyzed factors associated with long-term COVID-19. The study was an observational cross-sectional, conducted in August 2021. The data were collected through a Google form questionnaire distributed to COVID-19 survivors in Indonesian. They must be aged more than 17 years to meet the inclusion criteria, while those with incomplete data were excluded. The data were processed by using SPSS 21 with an ordinal regression test in which an alpha level was 5%. As many as 101 from 16 men (15.8%) and 85 women (84.2%) were obtained. Comorbid status (p-value = 0.001) and duration of treatment (p -value = 0.034 and 0.015) had a significant association with the occurrence of long-term COVID-19. Meanwhile, age, gender, occupation, type of care, and vaccination status were not likely associated with long-term COVID-19. COVID-19 patients with comorbidity and a long duration of treatment are more likely to experience long-term COVID-19.

Keywords: COVID-19, long-term COVID-19, factor, public health

INTRODUCTION

COVID-19 infection can manifest a wide severity spectrum from asymptomatic to life-threatening conditions; likewise, the symptoms may persist in various periods among the COVID-19 patients.[1,2] Typically, people recover from COVID-19 after two to six weeks.[3] However, about 30% of COVID-19 patients experienced long-term symptoms, e.g., fatigue, brain fog, sleep difficulties, arthralgia, pharyngitis, myalgia, headaches, fever, gastrointestinal upset, and skin rashes.[4,5] At least 5-20% of COVID-19 patients will have symptoms lasting over four weeks.[6]

As the World Health Organization (WHO), the long-term symptoms of COVID-19 occur in individuals with a history of probable or confirmed SARS-CoV-2 infection, lasting for at least 2 months. It cannot be explained by an alternative diagnosis and is thus often referred to long COVID-19.[7] Cellular damage, a robust innate immune response with inflammatory cytokine production, and a pro-coagulant state induced by COVID-19 infection may contribute to these long-term symptoms. A decline in quality of life, as measured by the EuroQol visual analog scale, was noted in 44.1% of patients with long-term COVID-19.[8] People experiencing long-term COVID-19 were consistently older, and they were more likely female and required hospital assessment than the group with short-term symptoms.[2] Information

on factors associated with the occurrence of long-term COVID-19 cases is still limited in Indonesia. Therefore, this current study analyzed factors associated with the occurrence of long-term COVID-19. A better understanding of the factors will be beneficial to sending messages about public health.

METHOD

Study design

The study design was an observational cross-sectional, conducted in August 2021. Data were collected through Google Forms, and a saturated sample technique was used for the sampling method. The respondents were required to complete the informed consent before completing the questionnaire. This study had passed an ethical approval by the Ethics Committee of the Faculty of Public Health, Universitas Airlangga with the registered number of ethical approval: 50/EA/KEPK/2021.

Eligibility criteria

The respondents were COVID-19 survivors in Indonesia aged more than 17 years, while the exclusion criteria were respondents with incomplete data. 196 respondents completed the questionnaire, and 95 respondents were excluded due to incomplete data. Overall, 101 respondents were eligible for this study.

RESULT AND DISCUSSION

Characteristics of the Respondents

Out of 101 respondents, there were 16 men (15.8%) and 85 women (84.2%). Most of the respondents were younger than 39 years old, and about 83% were health workers. About 95% of the respondents were in self-quarantine during COVID-19 infection, while others were hospitalized (5%). About 31% of the respondents were treated for less than 10 days, about 64% were treated for more than 10 days but less than 28 days, and about 5% were treated for more than 28 days. About 67% of the respondents had been fully vaccinated. Most of our respondents (90%) did not have comorbidities. The majority (76%) were categorized as acute long-term COVID-19. Most of the respondents lived on Jawa island. Table 1 shows further characteristics of the respondents.

Table 1. Respondents Baseline Characteristic

Variable	Number of Respondents (n=101)
Gender	
Women	85 (84.16%)
Men	16 (15.84%)
Years	
< 25	11 (10.89%)
25-29	33 (32.67%)
30-39	39 (38.61%)
40-49	12 (11.88%)
50-59	4 (3.96%)
≥ 60	2 (1.98%)
Occupation type	
Health worker	84 (83.17%)
Office worker	9 (8.91%)
Work at home	2 (1.98%)
Others	6 (5.94)
Type of care	
Self Isolation	95 (94.1%)
Hospital	6 (5.9%)
Duration of Treatment	
Short (0-10 days)	32 (31.7%)
Intermediete (11-27 days)	65 (64.4%)
Long (≥ 28 days)	4 (4.0%)

DOI: https://doi.org/10.22225/wmj.7.1.4784.33-39

Vaccination Status	
Fully vaccinated*	68 (67.3%)
Not fully vaccinated	33 (32.7%)
Disease History	
Asthma	6 (5.94%)
Hypertension	3 (2.97%)
Cardiac Disease	1 (0.99%)
No Comorbidity	91 (90.10%)
Long COVID Category	
Acute COVID-19	77 (76.24%)
Ongoing Symptomatic COVID-19	22 (21.78%)
Post-COVID-19 Syndrome	2 (1.98%)
Domicile Location	
Jawa	82 (81.19%)
Sumatera	5 (4.95%)
Bali	2 (1.98%)
Kalimantan	10 (9.9%)
Papua	1 (0.99%)
NTT-NTB	1 (0.99%)

*28 days after the second vaccine

Statistical analysis

The data were processed on SPSS 21 with an ordinal regression test in which an alpha level was 5%. The ordinal regression test was employed as there were three categorical data. The long-term COVID-19 categories based on the National Institute for Health and Care Excellence guidelines were shown in Table 2.[9]

The variables analyzed were gender, age, comorbidity, occupation, vaccination status, type of care, and duration of treatment. People experiencing long-term COVID-19 were usually older females, in need of hospital assessment than the group with short-term symptoms.[2] There were six categories of age: < 25 years, 25-29 years, 30-39 years, 40-49 years, 50-59 years, and 60 and above. Meanwhile, the respondents were also categorized as having comorbidity and no comorbidity. The comorbidities included are diabetes, hypertension, cancer, asthma, chronic obstructive pulmonary disease (CPOD), cardiac disease, and stroke.[10] By occupation, the respondents were identified as healthcare workers and non-healthcare workers. They were also categorized based on having full vaccination or not. As antibody responses were formed 28 days after vaccination[11], respondents who had passed 28 days after the second vaccine were categorized as fully vaccinated. Those experiencing long-term COVID-19 were more likely to require hospital assessment.[2] This was used to identify whether they need to be hospitalized and self-quarantined during COVID -19 infection. Meanwhile, the duration of treatment was categorized into short (0-10 days), intermediate (11-27 days), and long (≥ 28 days).

Table 2. Long-Term COVID-19 Category[9]

Category	Definitions
Acute COVID-19	signs and symptoms of COVID-19 for up to 4 weeks.
Ongoing symptomatic COVID-19	signs and symptoms of COVID-19 from 4 weeks up to 12 weeks.
Post-COVID-19 syndrome	signs and symptoms that emerge during or after an infection, continue for more than 12 weeks and are not explained by an alternative diagnosis. It usually presents clusters of symptoms, often overlapping, which can fluctuate and change over time, as well as affect the body's system.

Besides gender, age, comorbidity, occupation, vaccination status, type of care, and duration of treatment analyzed, the other variable, domicile location, was included. Firstly, the multivariate analysis was performed using ordinal regression toward all variables above. A bivariate analysis was then conducted to identify the significance of the association. Table 3 presents the results of multivariate analysis and bivariate analysis.

Table 3. Factors Associated with Long COVID-19

Variables	n(%) 101 (100%)	OR	95% CI	P-value	aOR	95% CI	P-value
Gender							
Women	85 (84.16%)	Ref	Ref	Ref			
Men	16 (15.84%)	0.659	-2.386 - 1.552	0.678			
Age							
< 25 years	11 (10.89%)	Ref	Ref	Ref			
25-29 years	33 (32.67%)	1.918	-2.238 - 3.542	0.659			
30-39 years	39 (38.61%)	4.320	-1.065 - 3.992	0.257			
40-49 years	12 (11.88%)	4.444	-1.380 - 4.363	0.309			
50-59 years	4 (3.96%)	2.420	-3.508 - 5.276	0.693			
60 and above	2 (1.98%)	0.000	(-14.576) - (-14.576)	1.000			
Comorbidity							
Non-comorbid	91 (90.1%)	Ref	Ref	Ref	Ref	Ref	Ref
Comorbid	10 (9.9%)	29.308	1.369 - 5.386	0.001*	14.531	1.216 - 4.136	**0.0003***
Occupation							
Non-Health care	17 (16.8%)	Ref	Ref	Ref			
Health care	84 (83.2%)	0.589	-2.211 - 1.152	0.537			
Type of care							
Self Isolation	95 (94.1%)	Ref	Ref	Ref	Ref	Ref	Ref
Hospital	6 (5.9%)	29.660	0.355 - 6.424	0.029*	3.153	-0.496 - 2.793	0.171
Duration of							
Short	32 (31.7%)	Ref	Ref	Ref	Ref	Ref	Ref
Intermediate	65 (64.4%)	10.512	0.180 - 4.525	0.034*	6.183	0.292 - 3.352	0.020*
Long	4 (4.0%)	66.629	0.828 - 7.570	0.015*	69.134	1.671 - 6.801	**0.001***
Vaccination							
Fully vaccinated	68 (67.3%)	Ref	Ref	Ref			
Not fully vaccinated	33 (32.7%)	0.380	-2.306 - 0.373	0.157			
Domicile							
Jawa	82 (81.19%)	Ref	Ref	Ref			
Sumatera	5 (4.95%)	4.452	-0.950 - 3.937	0.231			
Bali	2 (1.98%)	0.000	-17908.415 - 17867.352	0.998			
Kalimantan	10 (9.9%)	0.642	-2.622 - 1.737	0.691			
Papua	1 (0.99%)	1.033	-5.842 - 0.991	0.991			
NTT-NTB	1 (0.99%)	21.049	-2.048 - 8.142	0.241			

*p-value cut off < 0.05

DOI: https://doi.org/10.22225/wmj.7.1.4784.33-39

Factors Associated with Long-Term COVID-19

The multivariate analysis showed comorbidity (OR 14.531; 95% CI=1.216 - 4.136; p= 0.0003), type of care, and duration of treatment were significantly associated with long-term COVID-19. Duration of treatment i.e., intermediate duration of treatment (aOR 6.183; 95% CI=0.292-3.352; p = 0.020) and long duration of treatment (aOR 69.134; 95% CI=1.671-6.801; p = 0.001) was significantly associated with long-term COVID-19. Whereas, gender, age, occupation type, type of care, vaccination status, and domicile location had no significant association with long-term COVID-19 among the respondents.

DISCUSSION

COVID-19 can cause persistent sickness. Around a quarter of people infected experienced symptoms that lasted for at least a month or even after 12 weeks. Symptoms of long-term COVID-19 include generalized chest and muscle pain, fatigue, shortness of breath, and cognitive dysfunction; the symptoms involved affect multiple body systems and include persisting inflammation, thrombosis, and autoimmunity.[12,13] By sexes and occupation, women and healthcare workers seem to be at greater risk of suffering long-term COVID-19.[6] It even results in harmful consequences including scarring in multiple organs (especially the lungs, heart, kidneys, liver, adrenal glands, and gastrointestinal tract), autoimmunity, and blood clots, causing strokes or other tissue damage.[14,15] As many as 51% of patients with long-term COVID-19 persistently had reduced quality of life, and 50% had shortness of breath at 12 weeks after having symptoms.[16] While 19.9% of patients with long COVID-19 were readmitted, 9.1% died and 27% were readmitted or died within 60 days after being discharged.[17]

Female and older groups are more likely infected.[2] Persistent fatigue at 10-week post-discharge following COVID-19 infection more frequently occurred in females and persons with a history of anxiety or depression diagnosis or antidepressant usage.[18] On the contrary, about 84% of the respondents were women who were younger than 39 years old and had no need of being hospitalized during COVID-19 infection (95%).

Other surveys also suggested that increasing age, previous health status, comorbidities, and the number of symptoms during the acute phase are all associated with the frequency of long-term COVID-19 symptoms an individual may subsequently have.[6,19] Comorbidity like asthma and diseases attacking the heart and lungs are also reported to be associated with a risk of long-term COVID-19 infection.[2,6] Comorbidity and duration of treatment are likely associated with long-term COVID-19. Those with comorbidities were more likely 14.5 times at risk of having long COVID-19 than those without comorbidities. Those with intermediate treatment were more likely six times at risk of having long-term COVID-19 than those with short treatment. Those with long treatment were more likely 69 times at risk of having long-term COVID-19 than those with short treatment. It could be assumed that those with comorbidities treated with intermediate treatment (11-27 days) and long treatment (≥ 28 days) should be more at risk of prolonged symptoms.

Limitation

The total Indonesian population is about 270.2 million[20] and thus the number of respondents in this study is not enough to generalize the results. Most of the respondents lived in Jawa, making disproportional distribution of respondents across other regions. Although 83.2% of respondents were healthcare workers, the data in this study were self-reported by respondents, instead of direct interviews or the results of assessments from healthcare workers, thus it could cause bias. However, because the research respondents came from all over Indonesia and produced valuable data, the results of the research are

expected to be an initial study that can be continued by further research with a wider population, and involving health care workers as assessors.

CONCLUSION

COVID-19 patients with comorbidity and a long duration of treatment are more likely to experience long-term COVID-19.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

ACKNOWLEDGMENTS

The authors would like to thank Universitas Airlangga for providing support in this research and the authors would like to thank all respondents for their kind support by completing the questionnaire for this study.

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