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Hotma Martogi Lorensi Hutapea
Universitas Indonesia, Depok, hotm002@brin.go.id

Mondastri Korib Sudaryo
Universitas Indonesia, Depok, maqo19@gmail.com

Arli Aditya Parikesit
Indonesia International Institute for Life Sciences, Jakarta, arli.parikesit@i3l.ac.id

Tri Yunis Miko Wahyono
Universitas Indonesia, Depok, triyunis@yahoo.com

Nelda Aprilia Salim
Mohammad Hoesin Hospital, Palembang, neldasalim@fk.unsri.ac.id

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Risk Factors Associated with Long COVID Among Hospitalized Adults in Several Hospitals in Palembang City, Indonesia

Hotma Martogi Lorensi Hutapea[1,2], Mondastri Korib Sudaryo[3*], Arli Aditya Parikesit[4], Tri Yunis Miko Wahyono[3], Nelda Aprilia Salim[5]

[1]Doctoral Program, Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia
[2]Center for Biomedical Research, National Research and Innovation Agency, Bogor, Indonesia
[3]Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia
[4]Department of Bioinformatics, School of Life Sciences, Indonesia International Institute for Life Sciences, Jakarta, Indonesia
[5]Department of Internal Medicine, Mohammad Hoesin Hospital, Palembang, Indonesia

Abstract

Long COVID is characterized by one or more symptoms experienced by individuals prior to a COVID-19 infection that last for ≥2 months, and its risk factors remain unclear. This study aimed to identify risk factors associated with long COVID among patients admitted between June 1, 2020, and October 31, 2023, at three referral COVID-19 hospitals in Palembang City, Indonesia. This cohort study included adults who were admitted for ≥5 days. The participant's medical records were reviewed for admission and discharge dates, sociodemographic and clinical characteristics, and vaccination and therapy status. A standardized and validated instrument was used to assess fatigue during admission, and a structured questionnaire was used to evaluate long COVID. Cox regression was employed to determine factors associated with long COVID. Among 256 patients, long COVID was identified in 39.1%. Fatigue during admission, chronic kidney disease, thrombocytosis, and positive RT-PCR test at hospital discharge increased the risk of long COVID, whereas being fully vaccinated decreased its risk. This study identifies five risk factors for long COVID and determines that fatigue during admission is the strongest.

Keywords: coronavirus disease 2019, hospitalized patients, long COVID, risk factors

Introduction

Since the first coronavirus disease 2019 (COVID-19) case in Indonesia was reported on March 2, 2020, several policies have been implemented by the government to limit the transmission of the disease. Although daily reports of COVID-19 showed a decrease in new cases since the first quarter of 2023 compared to prior data (October to December 2022), studies showed that patients still experienced one or more symptoms after the acute phase and prolonged to 12 weeks or more, known as long COVID.[1] Studies revealed that patients with long COVID suffer from various systemic symptoms such as persistent fatigue, cough, dyspnea, eyesight problems, hair loss, and depression.[2,3] Although regulations or guidelines are available for managing COVID-19 patients, a comprehensive guideline for treating long COVID patients in Indonesia is lacking.[4]

Several studies have been conducted to understand long COVID and its distribution. In 2024, the global prevalence of long COVID-19 was 23%, with sleep disorder as the most common symptom.[2] A large survey from China reported that 35% of COVID-19 patients experienced long COVID with memory decline as the most frequently observed symptom.[3] A study in Indonesia reported that the prevalence of long COVID in 2022 was 43%, with fatigue as the most frequent symptom (29.4%).[5] Studies performed in several countries to understand the risk factors of long COVID revealed that older adults, females, depression or anxiety history, comorbidities, autoimmune history and the increment anti-nuclear antibody, and high ferritin or vitamin D levels increased the risk of long COVID.[2,3]

Palembang City has one vertical hospital (managed by the Indonesian Ministry of Health), which is the biggest COVID-19 referral hospital in the southern area of Sumatra. This hospital serves five provinces on Sumatra Island.[6] Data from the vertical hospital in Palembang City has not yet been fully explored compared to data from referral hospitals in Java Island.[7]

***Correspondence**:* *Mondastri Korib Sudaryo, Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, Email: maqo19@gmail.com.*

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This study aimed to understand the comprehensive important risk factors of long COVID by including the factors of sociodemographic characteristics, symptoms during hospitalization, clinical manifestations, vaccination, and therapy status among hospitalized adults in Palembang City. Currently, 1,465 COVID-19 active cases remain reported,[8] thus, the long COVID risk factors determined in this study may provide valuable insights to improve the management and prevention of long COVID in Indonesia.

Method

This cohort study was conducted in one vertical hospital (Hospital A), one Type B hospital (Hospital B), and one Type C hospital (Hospital C) in Palembang City and examined individuals with an inpatient history of COVID-19 by doing interviews from March 1 to December 21, 2024. Hospital A was the main study site, and two other neighboring hospitals (Hospital B and C) were included to obtain more samples as minimally required. Research permission from the three hospitals was acquired through an agreement to follow regulations from the hospitals. After obtaining ethical clearance and permission, all data were collected and anonymously kept in a personal computer with a secured identifier number accessible to only the authors.

In this study, fatigue was a symptom experienced by participants at onset and during hospitalization. The Fatigue Assessment Scale (FAS), developed and standardized by Michielsen and used by other studies to assess fatigue in COVID-19, was utilized as a data collection tool to assess fatigue during hospitalization and as a long COVID symptom.[9] The FAS was translated into the Indonesian language and validated (Cronbach's Alpha = 0.812).[10] To assess fatigue during admission, 256 participants were interviewed by phone. The FAS questionnaire consisting of 10 statements was read to the participants, and responses using Likert scales of 1 ("never") to 5 ("always") were obtained. The COVID-19 pandemic has an unforgettable history; therefore, participants may have had good memories related to the admission period. Time probing was performed to minimize recall bias and help recall the memory of fatigue during admission.

The long COVID status of 256 participants was assessed through phone interviews according to World Health Organization guidelines.[1] The participants were asked about the indication of their hospitalization, experienced symptoms during hospitalization, and prolonged symptoms after hospital discharge and its duration. Long COVID was determined based on when the symptom started (onset) and the duration of the symptom experienced. Participants were considered to be experiencing long COVID if their symptoms were due to COVID-19 and lasted for ≥2 months or the symptoms newly developed within 3 months after initial COVID-19 onset and lasted for ≥2 months.

The symptoms of long COVID were obtained as self-reported by the participants. The study variables included sociodemographic characteristics: age (18–49, 50–59, and ≥60 years), sex (female or male), education (below junior high school or above junior high school), occupation (employed or unemployed), and ethnicity (Melayu Palembang, non-Melayu Palembang, mixed (Melayu Palembang and non-Melayu Palembang); body mass index (BMI) (underweight: BMI <18.5; normal: BMI of 18, 5–25; and overweight: BMI >25); symptoms at hospitalization, such as fatigue (yes if FAS score was ≥22), dyspnea, nausea, fever (temperature >36.5°C), and cough; hematology abnormality, including thrombocytopenia (thrombocyte $<189\times10^3/\mu L$), thrombocytosis (thrombocyte $>436\times10^3/\mu L$), and erythrocytopenia (erythrocyte $<4.0\times10^6/\mu L$); RT-PCR result at discharge; type of comorbidities, such as hypertension, diabetes mellitus (DM), cancer, chronic kidney disease (CKD), lupus, asthma, anemia, cardiovascular disease (CVD), and chronic co-infection; number of comorbidities and severity; and vaccination and therapy (i.e., antivirus, oxygen therapy, and anti-inflammatory drugs).

The participants were considered partially vaccinated if they had received one dose of the COVID-19 vaccine at least 14 days before admission and fully vaccinated if they had received at least two doses of the COVID-19 vaccine at least 14 days before admission. Moreover, the participants were considered antiviral RdRp-inhibitor-treated if they received at least one loading dose at 1,600 mg/12 hours for the first day and followed with 2×600 mg of favipiravir for the next 4 days or one loading dose at 200 mg for the first day and followed with 100 mg remdesivir for the next 4 days and NA-inhibitor-treated if they received 800 mg/12 hours of molnupiravir for 5 days. Unless stated otherwise, all the variables were categorized as written in the medical record.

Participant recruitment was based on patients' admission between June 1, 2020, and October 31, 2023. Convenience sampling was employed based on the recentness of admission. The sample size was estimated using the Kelsey formula for the different proportion hypothesis test, with a minimum of 246 samples required to obtain 0.8 statistical power. During data collection, 256 patients were examined (Figure 1).

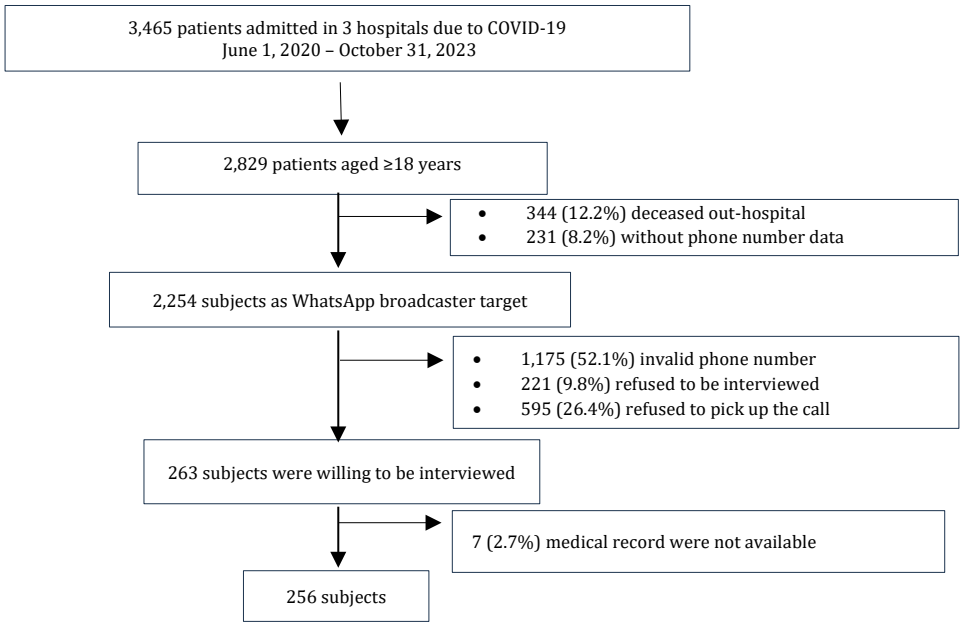

Figure 1. Sample Recruitment Flow Chart

Univariate analysis was conducted to calculate the proportion (%) of long COVID and all independent variables. Moreover, bivariate analysis was performed to measure the association between independent variables and long COVID using the Chi-square test. Further analysis using multivariate Cox regression was performed in two steps: selecting candidate risk factor variables based on p-value <0.25 and determining the final significant risk factors of long COVID based on p-value <0.05.

Strength of association was measured using risk ratio (RR), together with the 95% confidence interval (CI) and corresponding p-value. RR was interpreted as a multiplication of long COVID risk incidents among exposed people compared to the risk among nonexposed individuals. All statistical analyses were performed using a computer with a statistical analysis package licensed to the Faculty of Public Health, Universitas Indonesia (no. 501809408022).

Results

Approximately 39.1% of the participants experienced long COVID, with fatigue as the most common symptom (48 out 100). Over half of the participants were female (57.4%), aged 18–49 years (62.1%), and did not finish junior high school (57%), and 26.1% worked in the private sector. Additionally, most participants had mixed ethnicity (37.9%) (Table 1). Over half of the participants had normal BMI (55.1%). Furthermore, 70.1% experienced fatigue, 55.1% had cough, and 50% suffered from dyspnea. Concerning hematology, erythrocytopenia was common among the participants (55%). Viral genetic material was still detected in 87 participants (33.9%) upon discharge (Table 2).

Table 1. Sociodemographic Characteristics of Participants

Variable	Frequency (N = 256)	Percentage (%)
Long COVID	100	39.1
Fatigue	48	18.7
Dyspnea	30	11.7
Weakness	11	4.3
Allergic	5	2.0
Easily get ill	2	0.8
Others (cough, anorexia, chest pain)	4	1.6
Age, year	43.5 ±15.3	
Age		
18–49	159	62.1
50–59	58	22.7
≥60	39	15.2
Sex		
Female	147	57.4
Male	109	42.6
Education		
<Junior high school	146	57.0
≥Junior high school	110	43.0
Occupation		
Private sector	67	26.1
Housewives	60	23.3
Civil servant	37	14.4
Self-employed	20	7.8
Freelance	7	2.7
Others (farmers, fishermen)	12	12.7
Unemployed	53	20.6
Ethnicity		
Melayu Palembang	93	36.3
Non-Melayu Palembang	66	25.8
Mixed (Melayu Palembang and Non-Melayu Palembang)	97	37.9

Table 2. Body Mass Index, Symptoms, and Hematology of Participants During Admission with COVID-19

Variable	Frequency (N=256)	Percentage (%)
Body Mass Index		
Underweight	16	6.2
Overweight	55	21.5
Normal	141	55.1
Fatigue during admission		
Yes	181	70.1
No	75	29.3
Dyspnea **)		
Yes	128	50.0
No	128	50.0
Nausea **)		
Yes	37	14.5
No	219	85.5
Fever >36.5°C		
Yes	103	40.2
No	153	59.8
Cough **)		
Yes	141	55.1
No	115	44.9
Weakness **)		
Yes	63	24.6
No	193	75.4
Thrombocytopenia*)		
Yes	60	24.0
No	190	76.0
Thrombocytosis*)		
Yes	25	10.0
No	225	90.0
Erythrocytopenia*)		
Yes	104	55.0
No	85	46.0
RT-PCR result at discharge **)		
Positive	87	34.0
Negative	169	66.0

*) Missing data were found in several variables, i.e., BMI (44 cases), thrombocytopenia (6 cases), thrombocytosis (6 cases), and erythrocytopenia (67 cases).
**) Symptom history was taken from patients' reports as written in the medical record
Note: RT-PCR, real-time polymerase chain reaction

Hypertension was the most frequent comorbidity (24.2%), followed by DM (16.4%) and CKD (16%). Almost all participants (93%) suffered from moderate to severe COVID-19 (Table 3). Moreover, 44.5% of the participants were unvaccinated, and 36.4% received full COVID-19 vaccination. Most participants received an antiviral RdRp inhibitor (62.9%), and only 11.7% received an antiviral NA inhibitor. Additionally, 48.6% of the participants received oxygen therapy, and only 16% received anti-inflammatory drugs (Table 4).

Table 3. Type and Number of Comorbidities and Disease Severity of Participants During Admission

Variables	Frequency (n = 256)	Percentage (%)
Hypertension		
Yes	62	24.2
No	194	75.8
Diabetes Mellitus		
Yes	42	16.4
No	214	83.6
Cancer		
Yes	19	7.4
No	237	92.6
Chronic Kidney Disease		
Yes	41	16.0
No	215	84.0
Lupus		
Yes	8	3.1
No	248	96.9
Asthma		
Yes	6	2.3
No	250	97.7
Anemia		
Yes	19	7.4
No	237	92.6
Cardiovascular Disease		
Yes	21	8.2
No	235	91.8
Chronic Co-infection		
Yes	12	4.7
No	244	95.3
Others		
Yes	4	1.6
No	252	98.4
Number of comorbidities		
0	109	42.6
1	91	35.5
>1	56	21.9
Severity		
Moderate-severe	239	93.3
Asymptomatic-mild	17	6.7

Table 4. Vaccination Status and Therapy of Participants in Palembang City, Indonesia

Variable	Frequency (N = 256)	Percentage (%)
Vaccination status		
Unvaccinated	114	44.5
Partially vaccinated	49	19.1
Fully vaccinated	93	36.4
Antivirus therapy		
Untreated	65	25.4
RdRp inhibitor	161	62.9
NA inhibitor	30	11.7
Oxygen therapy *)		
Received therapy	125	50.6
Did not receive therapy	122	49.4
Anti-inflammatory drug		
Received therapy	41	16.0
Did not receive therapy	215	84.0

*) Missing data were found in oxygen therapy variables (9 cases)

Table 5. Bivariate Analysis to Obtain the Association Between Each Factor and Long COVID

Variable	Long COVID (+)	Long COVID (-)	RR (95% CI)	p-value
Age				
50–59	28 (48.3)	30 (51.7)	1.51 (0.97–2.33)	0.067
≥60	17 (43.6)	22 (56.4)	1.35 (0.77-2.37)	0.295
18–49	55 (34.6)	104 (65.4)	1.0	
Sex				
Male	44 (40.4)	65 (59.6)	1.06 (0.78–1.44)	0.713
Female	56 (38.1)	91 (61.9)	1.0	
Education				
<Junior high school	34 (30.6)	77 (69.4)	0.67 (0.48–0.94)	0.016
≥Junior high school	66 (45.5)	79 (54.5)	1.0	
Occupation				
Employed	24 (45.3)	29 (54.7)	1.21 (0.86–1.71)	0.297
Unemployed	76 (37.4)	127 (62.6)	1.0	
Ethnicity				
Non-Palembang	20 (30.3)	46 (69.7)	0.74 (0.48–1.15)	0.173
Mixed (Palembang and Non-Palembang)	42 (43.3)	55 (56.7)	1.06 (0.76–1.48)	0.734
Palembang	38 (40.9)	55 (59.1)	1.0	
Dyspnea				
Yes	45 (35.2)	83 (64.8)	0.82 (0.60–1.11)	0.200
No	55 (43.0)	73 (57.0)	1.0	
Nausea				
Yes	15 (40.5)	22 (59.5)	1.05 (0.68–1.60)	0.842
No	85 (38.8)	134 (61.2)	1.0	
Fever >36.5°C				
Yes	23 (22.3)	80 (77.7)	0.44 (0.30–0.66)	<0.001
No	77 (50.3)	76 (49.7)	1.0	
Cough				
Yes	43 (30.5)	98 (69.5)	0.62 (0.45–0.84)	0.002
No	57 (49.6)	58 (50.4)	1.0	
Weakness				
Yes	32 (50.8)	31 (49.2)	1.44 (1.06–1.96)	0.028
No	68 (35.2)	125 (64.8)	1.0	
Fatigue during admission				
Yes	85 (47.0)	96 (53.0)	2.35 (1.46–3.79)	<0.001
No	15 (20.0)	60 (80.0)	1.0	
Hypertension				
Yes	25 (40.3)	37 (59.7)	1.04 (0.73–1.48)	0.815
No	75 (38.7)	119 (61.3)	1.0	
Diabetes Mellitus				
Yes	17 (40.5)	25 (29.5)	1.04 (0.70–1.56)	0.864
No	83 (38.8)	131 (61.2)	1.0	
Cancer				
Yes	11 (57.9)	8 (42.1)	1.54 (1.02–2.34)	0.080
No	89 (37.6)	148 (62.4)	1.0	
Chronic Kidney Disease				
Yes	27 (65.9)	14 (34.1)	1.94 (1.45–2.59)	<0.001
No	73 (34.0)	142 (66.0)	1.0	
Lupus				
Yes	5 (62.5)	3 (37.5)	1.63 (0.93–2.86)	0.167
No	95 (38.3)	153 (61.7)	1.0	
Asthma				
Yes	5 (83.3)	1 (16.7)	2.19 (1.48–3.24)	0.025
No	95 (38.0)	155 (62.0)	1.0	
Anemia				
Yes	9 (47.4)	10 (52.6)	1.23 (0.75–2.04)	0.441
No	91 (38.4)	146 (61.6)	1.0	
Cardiovascular Disease				
Yes	11 (52.4)	10 (47.6)	1.38 (0.89–2.15)	0.192
No	89 (37.9)	146 (62.1)	1.0	
Chronic Co-infection				
Yes	8 (66.7)	4 (33.3)	1.77 (1.15–2.72)	0.045
No	92 (37.7)	152 (62.3)	1.0	
Number of comorbidities				
1	42 (46.2)	49 (53.8)	1.68 (1.15–2.44)	0.006
>1	28 (50.0)	28 (50.0)	1.82 (1.22–2.72)	0.004
0	30 (27.5)	79 (72.5)	1.0	
RT-PCR result at discharge				
Positive	45 (51.7)	42 (48.3)	1.59 (1.18–2.14)	0.003
Negative	55 (32.5)	114 (67.5)	1.0	

Variable	Long COVID (+)	Long COVID (-)	RR (95% CI)	p-value
Vaccination status				
Partially vaccinated	28 (57.1)	21 (42.9)	1.30 (0.95–1.79)	0.119
Fully vaccinated	22 (23.7)	71 (76.3)	0.54 (0.35–0.83)	0.002
Unvaccinated	50 (43.9)	64 (56.1)	1.0	
Antivirus therapy				
NA inhibitor	6 (20.0)	24 (80.0)	0.46 (0.22–1.00)	0.029
RdRp inhibitor	66 (41.0)	95 (59.0)	0.95 (0.68–1.33)	0.773
Untreated	28 (43.1)	37 (56.9)	1.0	
Oxygen therapy				
Received therapy	45 (36.0)	80 (64.0)	0.83 (0.61–1.13)	0.232
Did not receive therapy	53 (43.4)	69 (56.6)	1.0	
Anti-inflammatory drug				
Received therapy	18 (43.9)	23 (56.1)	1.15 (0.78–1.69)	0.488
Did not receive therapy	82 (38.1)	133 (61.9)	1.0	
Severity				
Moderate-Severe	93 (38.9)	146 (61.1)	0.88 (0.51–1.50)	0.643
Asymptomatic-Mild	8 (44.4)	10 (55.6)	1.0	
Body Mass Index	22.16±3.52	23.80±3.46		0.682
Underweight	11 (68.8)	5 (31.3)	1.64 (1.12–2.41)	0.040
Overweight	17 (30.9)	38 (69.1)	0.74 (0.48–1.15)	0.158
Normal	59 (41.8)	82 (58.2)	1.0	
Thrombocytosis				
Yes	15 (60.0)	10 (40.0)	1.59 (1.11–2.28)	0.031
No	85 (37.8)	140 (62.2)	1.0	
Thrombocytopenia				
Yes	32 (53.3)	28 (46.7)	1.49 (1.10–2.02)	0.016
No	68 (35.8)	122 (64.2)	1.0	
Erythrocytopenia				
Yes	59 (56.7)	45 (43.3)	1.38 (1.02–1.87)	0.033
No	35 (41.2)	50 (58.8)	1.0	

Notes: RR, risk ratio; CI, confidence interval; RT-PCR, real-time polymerase chain reaction; RdRp, rna-dependent rna polymerase; NA, neuroamidase.

Bivariate analysis evaluated the association between each factor and long COVID among hospitalized participants during the COVID-19 pandemic (Table 5). Based on all associations in the bivariate analysis, 19 risk factor variables with p-value <0.250 were selected to proceed to the final multivariate Cox regression analysis (table not shown). The final Cox model showed that the risk factors for long COVID in three hospitals of Palembang City were fatigue during admission (RR = 2.17; 95% CI: 1.24–3.78; p-value = 0.007), CKD (RR = 1.66; 95% CI: 1.05–2.61; p-value = 0.030), thrombocytosis (RR = 1.99; 95% CI: 1.13–3.49; p-value = 0.017), positive RT-PCR result upon discharge from the hospital (RR = 1.60; 95% CI: 1.07–2.40; p-value = 0.022), and being fully vaccinated (RR = 0.54; 95% CI: 0.54–0.89; p-value = 0.015) (Table 6).

Table 6. Final Cox Model Risk Factors of Long COVID

Characteristics	RR (95%CI)	p-value
Fatigue during admission	2.17 (1.24–3.78)	0.007
Chronic Kidney Disease	1.66 (1.05–2.61)	0.030
Thrombocytosis	1.99 (1.13–3.49)	0.017
RT-PCR result when discharged	1.60 (1.07–2.40)	0.022
Vaccination status		
Partially	1.05 (0.65–1.69)	0.836
Fully	0.54 (0.32–0.89)	0.015

Notes: RT-PCR, real-time polymerase chain reaction

Discussion

In this study, the proportion of long COVID among the hospitalized adults as the participants was 39.1%. Several studies reported long COVID proportions of 12.5%–35.5% for patients who experienced symptoms for ≥2 months.[11–13] A study in 2024 reported that the long COVID proportion in low- and middle-income countries was 42.4%, which was significantly lower than that in high-income countries, which was 69.7%.[14] The current health and economic burden of long COVID may have already exceeded that of other chronic diseases. The long-term guidelines concerning long COVID remain unavailable, and this could be a significant drain on businesses, third-party payers, the healthcare system, and society.[14] Therefore, these findings may provide valuable insights to help health providers address the importance of long COVID treatment and of other post-viral infections caused by other coronavirus or other viruses with similar characteristics.

Fatigue was the most common symptom among patients with long COVID (48.0%) in this study and several other studies.[9,15,16] Furthermore, 57.2% of the participants experienced fatigue during hospitalization, contributing to an increasing risk of long COVID 2.17 times compared to those without fatigue history during hospitalization. Moreover, other studies reported fatigue in the acute phase as a crucial predictor of long COVID.[17,18] This study's finding was strengthened by a meta-analysis concluding that fatigue in the acute phase may be used as a predictor for long COVID. Therefore, early fatigue management is critical to prevent long-term consequences of fatigue.[19] Fatigue occurs during the acute phase of COVID-19 because of systemic impairment[20] and could be the consequence of neuroinflammatory processes.[21] This phenomenon was also observed in other viral infections such as Epstein–Barr virus, SARS, AIDS, and enterovirus-infected diseases, wherein the pathogenic pathway in acute fatigue was similar.[22] Acute-phase fatigue in COVID-19 should not be taken only as an acute symptom but also as a clinical indicator or risk factor for chronic conditions.

Chronic Kidney Disease is characterized by decreased glomerulus filtration speed, uremic toxin accumulation, chronic systemic inflammation, and immunity dysregulation.[23] In long COVID patients with CKD, the existing immune response dysregulation may prolong the inflammation phase following acute infection, which leads to continuous chronic inflammation and increased risk of long COVID.[23] In this study, 16% of the participants had preexisting CKD upon hospitalization, which was consistent with previous studies that reported that CKD was found in 12%–20% of admitted patients with COVID-19.[23,24] The authors estimated that the risk of long COVID increased 1.66 times in patients with CKD compared to those without CKD. Another study also reported that COVID-19 patients with CKD had a significantly higher risk of experiencing persistent fatigue, cognitive disturbance, and cardiovascular disease, which were all the manifestations of long COVID than those without CKD.[25] In addition, CKD is associated with endothelial dysfunction and severe oxidative stress. The tropism of SARS-CoV-2 includes endothelial cells facilitated by the ACE2 receptor, which is expressed in numerous kidney tissue and vascular.[26] Predisposition endothelial damage and viral effects combination worsen vasculopathy, tissue hypoxia, and multi-organ dysfunction.[26] Moreover, coagulopathy is a concern owing to the higher risk of hypercoagulability among patients with CKD.[27]

Thrombocytosis may occur in patients with COVID-19; however, it is rare and related to serious health conditions. In this study, the percentage of participants with thrombocytosis was 9.7%, higher than that in a study in the United States, which reported that 7% of hospitalized patients with COVID-19 experienced thrombocytosis.[28] Moreover, the proportion of thrombocytosis cases among participants with long COVID in this study was 14.9%. It increased the risk of long COVID 1.99 times compared to those without thrombocytosis. Thrombocytosis may cause blood clots, which lead to myocardial infarction, stroke, and mesenteric ischemia.[29] Fibrinolysis-resistance microclots, thrombocyte activation, and persistent coagulation abnormality were found among patients with long COVID even months after the acute phase.[2,3,12,14] These findings indicated that thrombocytosis was not only a reactive phenomenon during acute infection but also a potential biological marker for long-term risk. Therefore, thrombocytosis may be an independent risk factor for long COVID.

In this study, the percentage of participants with positive RT-PCR tests upon discharge from the hospital was 33.9%. This was relatively higher than that in a previous study, which reported that 18% of patients had positive results with recovered clinical conditions upon discharge from the hospital.[30] This disparity may be due to the difference in viral variants, the RT-PCR method used, and the difference between the duration and criteria of patient discharge regulation in the hospital. Among participants with long COVID, the proportion of those with positive RT-PCR tests at hospital discharge increased to 44.6%. This result was consistent with a previous study in 2020, which reported that viral RNA was still detected in 47% of patients with persistent symptoms after weeks of admission.[31] This finding indicated that prolonged viral ribonucleic acid (RNA) was associated with a longer duration of the disease and its complications. This study also found that a positive RT-PCR test increased the risk of long COVID 1.6 times after treatment. Another study also reported the same findings, stating that persistent symptom was associated with prolonged viral shedding.[32] Viral or RNA persistence enhances prolonged immune activation, which leads to persistent symptoms such as dyspnea, fatigue, and muscle pain.[33,21] This study strengthened the hypothesis that a positive RT-PCR test at hospital discharge was not only a marker of viral replication but also evidence of the presence of RNA fragments, which reflected immunological dysfunction that led to long COVID risk.

The proportion of partially vaccinated participants was 19.1%, and 36.2% of fully vaccinated participants. Further analysis showed that being fully vaccinated was associated with a lower long COVID risk at almost 1.9 times as compared to being unvaccinated. This finding was consistent with meta-analysis studies showing full vaccination as more effective

in significantly reducing long COVID.[34] A similar result was also found in a cohort study showing that two doses of vaccine were associated with a decreased risk of long COVID, around 49%.[35] These results revealed that vaccination is crucial to protect individuals from experiencing post-viral persistent symptoms such as long COVID. The COVID-19 vaccine prepares the immune system by inducing an adaptive immune response, including activating B-cell memory and T-cell specific to SARS-CoV-2. This mechanism enhances viral elimination and reduces systemic inflammation burden during acute infection. Viral load decrement and shortening viremia duration were found to directly reduce the risk of long-term immune dysfunction and persistent tissue damage.

This study contributed to a better understanding of the association between clinical effects (hospitalized patients' symptoms, comorbidities, hematology abnormality, RT-PCR status at hospital discharge, and vaccination and therapy status) and long COVID. To assess fatigue during hospitalization, a translated, valid, and reliable FAS questionnaire was utilized to recall the participants' memories using a probing technique. To assess long COVID, the information from the participants and clinical data in medical records were combined. The temporality of the association between determinants and long COVID could be ascertained by using a cohort design.

This study had several limitations. First, almost all the participants were admitted with moderate severity; therefore, the number of followed long COVID patients in the mild and severe stages was sufficient. Second, phone interviews were conducted; therefore, only those who had a phone and were willing to participate in the study could be observed, and thus, results may not be generalized to the whole population. Third, recall bias may have occurred when asking about fatigue history; however, the bias may be minimal as the fatigue history was asked when the participants were hospitalized during the COVID-19 pandemic. The validity of the response was strengthened by using the standardized FAS questionnaire.

Conclusion

Five significant risk factors are identified in this study. Four of them (fatigue during hospitalization, CKD, thrombocytosis during admission, and viral RNA still being detected at discharge from hospital) increase the risk of long COVID. Meanwhile, one risk factor, full COVID-19 vaccination, decreases the risk of developing long COVID. Fatigue is the strongest risk factor for long COVID. Early identification of these five risk factors and their adequate corresponding clinical intervention or management in Indonesian health facilities can prevent or reduce the possibility of the occurrence of long COVID, which is estimated to contribute significant long-term health problems globally. Therefore, future studies are warranted to develop dynamic modeling to estimate and project health impacts of long COVID.

Abbreviations

COVID-19: coronavirus disease 2019; FAS: Fatigue Assessment Scale; BMI: body mass index; DM: diabetes mellitus; CKD: chronic kidney disease; CVD: cardiovascular disease; RR: risk ratio; CI, confidence interval; RT-PCR: real-time polymerase chain reaction; RdRp: rna dependent rna polymerase; NA: neuroamidase; RNA: ribonucleic acid.

Ethics Approval and Consent to Participate

The patients' data was obtained from the medical records of Mohammad Hoesin General Hospital after being approved by the Health Research Ethics Committee, Faculty of Public Health, Universitas Indonesia No. Ket-5/UN2.F10.D11/PPM.00.02/2024 and Mohammad Hoesin General Hospital No.DP.04/03/D.XVIII.6.8/ETIKRSMH/04/2024. Subjects gave their consent to participate in text messages.

Competing Interest

The authors have no conflicts of interest to declare.

Availability of Data and Materials

The datasets are not publicly available but are available from the corresponding author upon reasonable request.

Authors' Contribution

Conceptualization: HMLH, MKS, AAP, TYMW, NAS; Data curation: HMLH, MKS; Formal analysis: HMLH, MKS; Funding acquisition: HMLH, MKS; Investigation: HMLH, MKS, AAP, NAS; Methodology: HMLH, MKS, AAP; Project administration: HMLH, MKS, TYMW; Resources: HMLH, MKS ; Software: HMLH, MKS; Supervision: MKS, AAP; Validation: MKS, AAP, TYMW; Visualization: HMLH, MKS, AAP; Writing–original draft: HMLH, MKS; Writing–review & editing: all authors.

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