



Characteristics, Clinical Manifestations, Length of Hospitalization, and Nutritional Status of COVID-19 Patients

Erika Martining Wardani^{1*}, Riezky Faisal Nugroho², Difran Nobel Bistara¹, Lono Wijayanti¹, Siti Nurhasina¹, Fety Susanti Cahyaningsih³

¹Department of Nursing, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, 60237 Surabaya, East Java, Indonesia; ²Department of Nutrition, Politeknik Kesehatan Kemenkes Surabaya, 60282 Surabaya, East Java Indonesia; ³Department of Nursing, Dr. Soetomo Hospital, 60237 Surabaya, East Java, Indonesia

Abstract

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***Correspondence:** Erika Martining Wardani, Department of Nursing, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, 60237 Surabaya, East Java, Indonesia. E-mail: erika@unusa.ac.id
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BACKGROUND: The disease that is endemic and has become a global pandemic is COVID-19 due to reports of thousands of cases. The pandemic is weighing on intensive care units with an influx of COVID-19 patients. The clinical manifestations of COVID-19 vary, diagnostic examinations and treatment are also experiencing dynamic developments. This study aims to provide an overview of the characteristics, clinical manifestations, length of treatment, and nutritional status of COVID-19 patients.

METHODS: This study used a descriptive analytic cross-sectional method with inclusion criteria that were positive for COVID-19. The research data were obtained from 130 hospital medical records for the period June to August 2021. The collected data were then analyzed using SPSS.

RESULTS: The study found that men were more exposed to COVID-19 (71.5%) and 70% of patients worked as medical personnel. The age range of the majority of patients was more than 40 years (78.5%). Most of the comorbidities were hypertensive patients. Clinical manifestations of COVID-19 patients were cough (44.6%), fever (40%), flu-like symptoms (32.3%), painful swallowing (26.2%), anosmia (16.2%), shortness of breath (15.4%), nausea (14.6%), vomiting (13.8%), and diarrhea (0.9%). The average length of stay is 7–14 days (9.2%) with adequate nutritional status (14.6%). Patients with length of treatment ($p = 0.01$) and poor nutritional status ($p = 0.000$) were significantly different.

CONCLUSION: The majority of COVID-19 sufferers are male, over 40 years old, with cough symptoms, and the most comorbid hypertension, as well as deaths from hypertension and the elderly. Better treatment is needed for people with COVID-19.

Introduction

Coronaviruses are a large family of viruses that cause disease. There are at least two types of coronaviruses that cause disease causing severe symptoms such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). The corona virus spreads faster even though the risk of death is not as big as SARS (transmitted from civet cats) let alone MERS (transmitted from camels). SARS-CoV-2 is the virus that causes corona virus disease (COVID-19) [1].

The number of confirmed cases of coronavirus disease 2019 (COVID-19) continues to rise in several countries. According to the latest data on August 9, 2020 from the World Health Organization, there are 216 countries with confirmed cases of COVID-19 with the number of confirmed cases of COVID-19 19,462,112 people [2]. Until now, the country that occupies the highest position in the world for confirmed cases of the COVID-19 is the United States with a total of

4,897,958 people [2]. The COVID-19 Handling Task Force (2021) reported that as of January 3, 2021, data on the distribution of COVID-19 in Indonesia were 765,350 confirmed cases, 22,734 cases died, and 110,679 cases were active or under treatment, 11.3% (86,361 cases) were confirmed in Indonesia. East Java Province and most of them came from Surabaya City (18,288 cases) [3]. The number of cases treated at Dr. Soetomo Surabaya hospital starting from March to July 2020 as many as 1432 cases (Medical Record Data at Dr. Soetomo Hospital Surabaya, 2020). COVID-19 appears in varying degrees of severity [4].

Symptoms of COVID-19 are often non-specific. Common symptoms that often appear include fever, cough, and fatigue, which then recover quickly or progress to respiratory problems such as: shortness of breath, dyspnea, and pneumonia, causing ARDS, kidney failure, coagulation dysfunction, multiple organ failure, and even death. Another rare symptoms are heart infections, mysterious blood clots, unexpected strokes, and rashes. Symptoms include pain, nasal congestion, sore throat, headaches, and even loss of the sense of smell or taste [5].

Patients with COVID-19 require hospitalization because this disease is an infectious disease in the respiratory tract that is contagious and can cause respiratory, physical, and psychological dysfunction, as well as various other dysfunctions, the impact of which can reduce the patient's functional capacity. Patients with COVID-19 who require hospitalization are divided into two rooms, namely, the ordinary treatment room and the intensive care room [6].

Various nutritional interventions, such as oral nutritional supplements, dietary management, and counseling, have shown positive results in different patient populations. For example, in hospitalized malnourished patients, nutritional interventions have been shown to reduce length of stay and rates of unplanned 30-day re-admissions, while improving quality of life and saving costs. A recent study showed that a comprehensive nutrition-focused quality improvement program in malnourished hospital inpatients reduced health care costs by reducing 30-day re-admissions and reducing length of stay [7].

Efforts to stop COVID-19 in 2020 must have two aspects: the first is the treatment of infected patients and avoiding the spread of the virus. This study aims to analyze the relationship between the characteristics, clinical manifestations, length of stay, and nutritional status of COVID-19 patients with the severity of COVID-19 disease. It is hoped that by knowing the significant relationship between characteristics, clinical manifestations, length of stay, and nutritional status with the severity of COVID-19, patients will receive optimal therapy, thereby reducing mortality [9].

Methods

This study uses a cross-sectional observational-analytic study conducted at Dr Soetomo Hospital Surabaya from June to August 2021 with existing medical records. The inclusion criteria of this study were all confirmed COVID-19 patients or real-time polymerase chain reaction or by the GeneXpert SARS-CoV-2 method with samples taken from nasal or pharyngeal swabs. All patients were treated in the Isolation Room of Dr Soetomo Hospital, Surabaya. This research has passed ethical standards from the ethics committee of Airlangga University faculty of dental medicine, number: 732/HRECC.FODM/VII/2021.

Statistical analysis using SPSS version 25. Categorical data are presented in terms of frequency and percentage with Chi-Square test and Fischer exact test as alternative tests. Meanwhile, numerical data are presented in the form of mean \pm standard deviation with independent t-test and Mann-Whitney test as alternative tests.

Results

Patient characteristics

Characteristics of COVID-19 patients at Soetomo Hospital Surabaya, Indonesia are shown in Table 1. The results showed that men were more at risk of experiencing COVID-19 with severe symptoms compared to women ($p = 0.040$; OR = 2.201; 95% CI = 0.992–4.876). Age did not correlate with the severity of COVID-19 ($p = 0.149$; OR = 1.152; 95% CI = 0.432–2.182). Occupation also had no effect on the severity of COVID-19 ($p = 0.302$; OR = 0.714; 95% CI = 0.325–1.571). Patients who were exposed to cigarette smoke (active smokers, former smokers, and passive smokers) had a higher chance of getting COVID-19 with severe symptoms compared to those who were not exposed to cigarette smoke ($p = 0.001$; OR = 13.440; 95% CI = 4.250–42.502).

Table 1: Characteristics of COVID-19 patients at Soetomo Hospital Surabaya, Indonesia

Variable	Severity		p-value
	Heavy (%)	Not heavy (%)	
Gender			0.040
Man	47 (36.2)	31 (23.8)	
Woman	27 (20.8)	25 (19.2)	
Age (years)			0.149
<12	2 (1.5)	4 (3.1)	
12–29	18 (13.8)	17 (13.2)	
30–40	12 (9.2)	6 (4.6)	
>40	36 (27.7)	35 (26.9)	
Profession			0.302
Health workers	40 (30.8)	38 (29.2)	
Other	37 (28.5)	15 (11.5)	
Smoke			0.001
Exposed	39 (30)	14 (10.8)	
Tidak	35 (26.9)	42 (32.3)	

Clinical manifestations

Based on Table 2, the results of the clinical manifestations of COVID-19 patients assessed include a history of cough, not correlated with the degree of severity ($p = 0.435$; OR = 1.325; 95% CI = 0.5763.175). Symptoms of fever did not correlate with the degree of severity ($p = 0.620$; OR = 1.289; 95% CI = 0.4433.750). Patients with severe symptoms tended to experience headaches that correlated with severity ($p = 0.011$; OR = 9.574; 95% CI = 1.17777.865). Flu symptoms did not correlate with severity ($p = 0.347$; OR = 1.823; 95% CI = 1.528–2.172). Patients with severe symptoms tended to experience painful swallowing ($p = 0.249$; OR = 1.815; 95% CI = 1.535–2.209). Complaints of anosmia did not correlate with the degree of severity ($p = 0.293$; OR = 2.588; 95% CI = 0.497–13.481). Patients with severe symptoms tend to experience symptoms of shortness of breath with a degree of severity ($p = 0.001$; OR = 9.286; 95% CI = 3.476–24.805). Complaints of nausea did not correlate with the degree of severity ($p = 1.000$; OR = 0.800; 95% CI = 0.108–5.909). Symptoms of vomiting did not correlate with severity ($p = 0.157$; OR = 0.1856; 95% CI = 0.781–4.409). Symptoms of diarrhea did not correlate with the degree of severity ($p = 0.504$; OR = 0.617; 95%

Table 2: Clinical manifestations of COVID-19 patients at Soetomo Hospital Surabaya, Indonesia

Variable	Severity		p-value
	Heavy (%)	Not heavy (%)	
Clinical manifestation			
Cough	49 (37.7)	38 (29.2)	0.435
Fever	43 (33.1)	36 (27.7)	0.620
Headache	38 (29.2)	2 (1.5)	0.011
Flu-like symptoms	31 (23.8)	28 (21.5)	0.347
Swallowing pain	8 (6.2)	2 (1.5)	0.249
Anosmia	5 (3.8)	3 (2.3)	0.293
Shortness of breath	64 (49.2)	22 (16.9)	0.001
Nausea	21 (16.2)	11 (8.5)	1.000
Vomiting	19 (14.6)	9 (6.9)	0.157
Diarrhea	8 (6.2)	10 (7.7)	0.504
Comorbid			
Comorbid	49 (37.7)	28 (21.5)	0.002
Non-comorbid	28 (21.5)	38 (29.2)	

CI = 0.154–2.441).

Patients with comorbidities tended to experience severe symptoms compared to patients without comorbidities ($p = 0.002$; OR = 3.518; 95% CI = 1.494–7.705). Most of the comorbidities were hypertensive patients.

Length of treatment and nutritional status

Based on Table 3, it can be assessed that the length of treatment correlates with the degree of severity ($p = 0.01$; OR = 13.220; 95% CI = 4.250–42.502). Patients with poor nutritional status tend to experience severe symptoms compared to patients with adequate nutritional status ($p = 0.000$; OR = 3.216; 95% CI = 1.2929–6.604).

Table 3: Length of treatment and nutritional status of COVID-19 patients at Soetomo Hospital Surabaya, Indonesia

Variable	Severity		p-value
	Heavy (%)	Not heavy (%)	
Length of treatment (days)			
<7	8 (6.2)	6 (4.6)	0.001
7–14	12 (9.2)	14 (1.1)	
14–21	64 (49.2)	26 (20)	
Nutritional status			0.000
Moderate	19 (14.6)	21 (16.2)	
Sever	20 (15.4)	17 (13.1)	
Critical	37 (28.5)	16 (12.3)	

Discussion

The results of this study found that men were more exposed to COVID-19 (71.5%) where men were more at risk of experiencing COVID-19 with severe symptoms compared to women ($p = 0.040$; OR = 2.201; 95% CI = 0.992–4.876). This is in line with Liu *et al.* who found that gender was mostly found in 56 males (55.4%) and 45 females (44.6%) [10]. Ahmed and Dumanski said in 2020 that the angiotensin enzyme 2 (ACE2), an integral part of the human renin-angiotensin-aldosterone system “RAAS,” enables SARS-CoV-2 to attack humans. This may be because it is a functional receptor for Alveolar epithelial cells. Overall, males show higher her RAAS activity than females [11].

In this study, the mean age of severity was above 40 years (78.5%). This is in accordance with Liang who stated that the average age was 56 years [12]. Liu *et al.* stated that the mean age of patients with severe and critical grades was higher than that of moderate grades. This is in line with this study where the average age of severe and critical patients was 60 and 56 [10]. According to Wu and McGoogan, this may be due to a decrease in the immune system in old age so that they have a greater risk of ARDS and death [13].

From our research data, it was found that 70% of patients worked as medical personnel and 20.75% did not work. According to the centers for disease control and prevention, the working age group is more susceptible to exposure, because to work, some people have to travel and meet many people. This is related to close contact and history of travel to infected areas which are risk factors for COVID-19 exposure [14], [15]. However, in our study, it was found that there was no significant association between the working group of patients and the risk of exposure to COVID-19.

On smoking status, this study classified patients based on who was exposed (28.13%) and not exposed to cigarettes and found that 18 of 20 patients were in the severe category. This study is in line with the study of Feng Y, *et al.* which stated that smoking status was related to the severity of the disease in patients treated in intensive care [16]. Another study by Wu, *et al.* stated that smoking status was related to the severity and mortality of COVID-19 patients [13]. Another meta-analysis study by Harapan, *et al.* stated that smoking increases the risk of COVID-19 severity by twofold [17].

Based on clinical symptoms, the most common symptoms were cough (44.6%), fever (40%), and flu-like symptoms (32.3%). In patients with severe symptoms, shortness of breath, fever, and cough are predominant. This is similar to the symptoms of COVID-19 pneumonia in China which show prominent symptoms in patients with severe pneumonia [18].

In this study, 23 patients with comorbid hypertension (30.7%) were found to have a moderate degree, 8 people (47.1%) to a severe degree, and 12 people (66.7%) to a critical degree. Other investigators Hu and Wang also concluded that the most common comorbidities among COVID-19 patients with ARDS were hypertension (27%), diabetes (19%), and cardiovascular disease (6%) [19]. Lim and Sim, in their study, also found hypertension in mild COVID-19 13% and severe degrees 48.6% [20]. Huang *et al.* found that 36.5% of COVID-19 patients with hypertension and hypertensive patients with COVID-19 tended to show a higher mortality rate [21]. This is also supported by Liang hypertension is significantly associated with independent risk for predicting the severity and mortality of COVID-19 patients [12]. This according to Zhang *et al.* can be caused by direct injury mediated through the ACE2. A study in China showed that SARS-CoV-2 infection was caused by the binding of viral proteins

to the ACE2 receptor after protein activation. ACE2 is a monocarboxy peptidase that is best known for cleaving several peptides in the renin-angiotensin system. Since its discovery in 2000, ACE2 has been considered a protective factor against elevated blood pressure. Binding of SARS-CoV-2 to ACE2 can reduce the physiological function of ACE2 and then lead to adverse outcomes of hypertension such as multi-organ dysfunction [12]. In addition, according to Kuba *et al.*, ACE2 plays an important role in acute lung disease, especially acute respiratory distress syndrome [22]. Meanwhile, according to Rodilla *et al.*, hypertension is associated with a higher risk for all-cause mortality [23].

In this study, the average length of stay was 7–14 days. The incubation period for people infected with the SARS-CoV-2 virus that causes COVID-19 is 14 days. In patients with severe and critical COVID-19, intravenous insulin should be the first line of treatment. Patients who are on continuous renal replacement therapy, the proportion of glucose and insulin in the replacement solution should be increased or decreased according to the results of monitoring glucose levels to avoid hypoglycemia and severe glucose fluctuations. During this period, the patient feels sick about 4 days after being infected with the coronavirus. Pain symptoms in patients infected with the coronavirus vary from mild, moderate to severe, depending on the person. All of these symptoms also affect the immune system and risk factors for comorbidities or comorbidities that the patient had before being infected with the SARS-CoV-2 coronavirus [27], [29]. COVID-19 patients with severe comorbidities are immediately admitted to the negative pressure intensive care unit, and patients with moderate-to-mild medical conditions are treated in the usual ward. Patients with uncontrolled comorbidity will have special monitoring on days 5 and 6 of treatment. This is because unpredictable conditions, or more severe conditions, can occur. After two swab tests, the patient was declared cured and the result was negative. The duration of treatment from admission to the declaration of cure was 2 weeks for patients without comorbid and 3 weeks for patients with comorbid. Treatment duration and patient recovery depend on each patient's condition [24].

In this study, the average nutritional status of the patients was adequate. This is especially noticeable in bedridden patients with inadequate food intake. Therefore, nutritional support for patients with severe COVID-19 is extremely important and can improve the immune response to infection and thus the prognosis of the disease. COVID-19 is a highly contagious disease, and severely ill patients usually exhibit other organ dysfunction and are prone to malnutrition. Appropriate nutritional intervention can prevent an increase in the incidence of multiple organ failure in time. The results of this retrospective study show that nutritional risk screening is an important basis for clinical management and prognostic assessment of COVID-19. The

results of the study are in line with the research of Yu *et al.* in 2021, comparing COVID-19 patients without malnutrition with COVID-19 patients with malnutrition, the results of the study show that COVID-19 patients with malnutrition have a longer stay in hospital than COVID-19 patients without malnutrition [25]. Proper diet and good nutritional status are considered as essential elements for an optimal immune response to prevent infection. Nutritional status and diet modulate inflammation and immune function and influence the outcome of COVID-19. The nutritional status of the host is considered a key factor in the outcome of various infectious diseases [26], [28].

Conclusion

The results showed that clinical characteristics such as gender, smoking history, clinical manifestations (fever, shortness of breath, and cough), length of stay, and nutritional status had a significant effect on the severity of COVID-19 infection. Knowing the severity of the disease, it is hoped that patients will receive optimal therapy and reduce mortality.

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References

1. Kementerian Kesehatan RI. Pedoman Kesiapan Menghadapi COVID-19. In: Kementerian Kesehatan RI. Indonesia: Direktorat Jenderal Pencegahan dan Pengendalian Penyakit (P2P); 2020a.
2. World Health Organization. COVID-19 Weekly Epidemiological Update, 27 December 2020. Geneva: World Health Organization; 2020a.
3. Pemerintah Kota Surabaya. Surabaya Tanggap COVID-19. Available from: <https://lawancovid-19.surabaya.go.id/visualisasi/graph> [Last accessed on 2021 Jan 03].
4. Rees EM, Nightingale ES, Jafari Y, Waterlow NR, Clifford S, Carl CA, *et al.* COVID-19 length of hospital stay: A systematic review and data synthesis. *BMC Med.* 2020;18(1):270. <https://doi.org/10.1186/s12916-020-01726-3> PMID:32878619
5. Tresnasari C, Dharmmika S. COVID-19 dan Tatalaksana Kedokteran Fisik Serta Rehabilitasi Pasien. Pusat Penerbitan

- Unisba (P2U). Indonesia: LPPM UNISBA; 2020.
6. Wardani EM, Nugroho RF, Ainiyah N, Nurhasina S. Mask wearing behavior, type of mask, frequency replacement of mask, and duration of mask wearing with skindemic. *AIP Conf Proc*. 2023;1(2595):090012-1-5. <https://doi.org/10.1063/5.0123955>
 7. Sauer AC, Li J, Partridge J, Sulo S. Assessing the impact of nutrition interventions on health and nutrition outcomes of community-dwelling adults: A systematic review. *Nutr Diet Suppl*. 2018;10:45-57. <https://doi.org/10.2147/NDS.S177248>
 8. Zhang XY, Huang HJ, Zhuang DL, Nasser MI, Yang MH, Zhu P, *et al*. Biological, clinical and epidemiological features of COVID-19, SARS and MERS and AutoDock simulation of ACE2. *Infect Dis Poverty*. 2020;9(1):99. <https://doi.org/10.1186/s40249-020-00691-6>
PMid:32690096
 9. Feng X, Li P, Ma L, Liang H, Lei J, Li W, *et al*. Clinical characteristics and short-term outcomes of severe patients with COVID-19 in Wuhan, China. *Front Med (Lausanne)*. 2020;7:491. <https://doi.org/10.3389/fmed.2020.00491>
PMid:32850926
 10. Liu XQ, Xue S, Xu JB, Ge H, Mao Q, Xu XH, *et al*. Clinical characteristics and related risk factors of disease severity in 101 COVID-19 patients hospitalized in Wuhan, China. *Acta Pharmacol Sin*. 2021;43(1):64-75. <https://doi.org/10.1038/s41401-021-00627-2>
PMid:33742107
 11. Ahmed SB, Dumanski SM. Sex, gender and COVID-19: A call to action. *Can J Public Health*. 2020;111(6):980-3. <https://doi.org/10.17269/s41997-020-00417-z>
PMid:32990927
 12. Maji R, Bhattacharjee A, Elango A, Ghosh S, Gantait K. Laboratory biomarkers of COVID-19 outcome: findings from a high dependency unit of South Bengal. *Int J Res Med Sci [Internet]*. 2021;9:3074-8. Available from: <https://www.msjonline.org/index.php/ijrms/article/view/10049> [Last accessed on 2023 Jul 06].
 13. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus disease 2019 (COVID-19) Outbreak in China: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323(13):1239-42. <https://doi.org/10.1001/jama.2020.2648>
PMid:32091533
 14. Susilo A, Rumende CM, Pitoyo CW, Santoso WD, Yulianti M, Sinto R, *et al*. Coronavirus Disease 2019: Tinjauan literatur terkini Coronavirus disease 2019: Review of current literatures. *J Penyakit Dalam Indones*. 2020;7(1):45-67.
 15. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel Coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet*. 2020;395(10223):507-13. [https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)
PMid:32007143
 16. Feng Y, Xu B, Feng J, Xianyu J. Association of procalcitonin and the severity of COVID-19: A meta-analysis. *Case Stud Opin*. 2021;1(7):166-74.
 17. Harapan H, Itoh N, Yufika A, Winardi W, Keam S, Te H, *et al*. Coronavirus disease 2019 (COVID-19): A literature review. *J Infect Public Health*. 2020;13(5):667-73. <https://doi.org/10.1016/j.jiph.2020.03.019>
PMid:32340833
 18. Gong XM, Song L, Li H, Li L, Jin W, Yu KH, *et al*. CT characteristics and diagnostic value of Covid-19 in pregnancy. *PLoS One*. 2020;15(7):e0235134. <https://doi.org/10.1371/journal.pone.0235134>
PMid:32614854
 19. Hu J, Wang Y. The clinical characteristics and risk factors of severe COVID-19. *Gerontology*. 2021;67(3):255-66. <https://doi.org/10.1159/000513400>
PMid:33406518
 20. Keddie S, Ziff O, Chou MK, Taylor RL, Heslegrave A, Garr E, Lakdawala N, *et al*. Laboratory biomarkers associated with COVID-19 severity and management. *Clinical immunology*. 2020;221:108614.
 21. Huang S, Wang J, Liu F, Liu J, Cao G, Yang C, *et al*. COVID-19 patients with hypertension have more severe disease: A multicenter retrospective observational study. *Hypertens Res*. 2020;43(8):824-31. <https://doi.org/10.1038/s41440-020-0485-2>
PMid:32483311
 22. Kuba K, Imai Y, Ohto-Nakanishi T, Penninger JM. Trilogy of ACE2: A peptidase in the renin-angiotensin system, a SARS receptor, and a partner for amino acid transporters. *Pharmacol Ther*. 2010;128(1):119-28. <https://doi.org/10.1016/j.pharmthera.2010.06.003>
PMid:20599443
 23. Rodilla E, Saura A, Jiménez I, Mendizábal A, Pineda-Cantero A, Lorenzo-Hernández E, *et al*. Association of hypertension with all-cause mortality among hospitalized patients with COVID-19. *J Clin Med*. 2020;9(10):3136. <https://doi.org/10.3390/jcm9103136>
PMid:32998337
 24. Wardani EM, Bistara DN, Septianingrum Y. Karakteristik klinis dan lama rawat inap pasien covid-19 dengan komorbid dan tanpa komorbid. *Holistik Jurnal Kesehatan*. 2021;15(4):666-73.
 25. Yu Y, Ye J, Chen M, Jiang C, Lin W, Lu Y, *et al*. Malnutrition prolongs the hospitalization of patients with COVID-19 infection: A clinical epidemiological analysis. *J Nutr Health Aging*. 2021;25(3):369-73. <https://doi.org/10.1007/s12603-020-1541-y>
PMid:33575730
 26. Im JH, Je YS, Baek J, Chung MH, Kwon HY, Lee JS. Nutritional status of patients with COVID-19. *Int J Infect Dis*. 2020;100:390-3. <https://doi.org/10.1016/j.ijid.2020.08.018>
PMid:32795605
 27. Wardani EM, Nugroho RF, Bistara DN, Afriyah RK, Hasina SN, Septianingrum Y. Clinical manifestations of COVID-19 patients with comorbid and non-comorbid at Dr. Soetomo hospital, Surabaya. *Open Access Maced J Med Sci*. 2022;10(G):330-4. <https://doi.org/10.3889/oamjms.2022.7582>
 28. Wardani EM, Nugroho RF, Bistara DN, Fitriyani A, Wijayanti L, Ainiyah N, *et al*. Level of student education and knowledge about sinovac vaccine with immunization participation. *Bali Med J*. 2022;11(2):738-41. <https://doi.org/10.15562/bmj.v11i2.3153>
 29. Wardani EM, Nugroho RF. *Buku Saku Vaksin Langkah Preventif Cegah Covid-19*. Surabaya: Unusa Press; 2021.