Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation

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Daftar Isi

Daftar Isi	2
Submission 20 Mei 2021	3
Author to Editor 31 Juli 2021	4
Submitted Manuscript	5
Peer Review Proses 31 Juli 2021	15
Re ; Peer Review Process 2 Agustus 2021	16
Decision on Manuscript 27 Agustus 2021	17
Revision	20
Transferred Manuscript 15 September 2021	23
Re: Peer Review Process 17 September 2021	24
Editor to Author: Response Letter 17 September 2021	25
Revision Manuscript	26
Decision Letter 29 September 2021	31
Manuscript Accepted 4 Oktober 2021	33
Manuscript Accepted 5 Oktober 2021	34
Editor to Author 26 Oktober 2021	45
Table added 26 Oktober 2021	46
Manuscript Revisions	47
Manuscript Accepted 11 November 2021	57
License was Successfully Submitted 13 November 2021	59
Information: Production	60
Article: Proof 30 November 2021	61
Correction Submitted 30 November 2021	63
Article Published 22 Desember 2021	64
Article Published Online 22Desember 2021	65
Published Article	66

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Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of

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Running Head: Sequelae in COVID-19 Patients

Introduction

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after

recovering from COVID-19. To date, there have been 1,657,035 cases of COVID-19, with 45,116

dead and 1,511,417 recovered in Indonesia. We assessed sequelae in COVID-19 patients and most common sequelae, both those who had self-isolated and those who were hospitalized, who had recovered for more than three months after negative Polymerase Chain Reaction (PCR) swab results. COVID-19 Sequelae is persistent symptomatology and outcomes after hospital discharge or completion of self-isolation with a wide and multifaceted range of clinical manifestations were identified, including respiratory, gastrointestinal, neurological, cardiovascular symptoms, and other organ manifestations. ¹

Methods

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than three months. These sequelae is persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Hospital. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The sequelae of COVID-19 were those reported since the patient was declared negative by a PCR swab and had completed self-isolation or hospitalization for 10 days plus three days at the hospital, as recommended by the World Health Organization and the local Ministry of Health. The data collected were self-reported symptoms that appeared from when the patient was declared recovered from COVID-19 until 90 days later. The data were obtained from various cities in Indonesia.

A total of 214 patients who had been declared recovered from COVID-19 were contacted between January and March 2021 to complete a single electronic questionnaire between one month and three months after being declared recovered. Thirteen participants who did not complete the questionnaire were not included in the analysis. We performed only descriptive analysis due to the small number of participants. Data analysis was conducted using SPSS 23.

Results

A total of 201 participants, took part from Indonesia and were of Asian ethnicity with an average age of 39.35 years old; the participants included 109 (54.2%) males and 92 (45.8%) females with confirmed COVID-19 infection. A total of 19 COVID-19 patients (9.45%) had had no symptoms, 58 (28.85%) patients had undergone self-isolation, and 143 (71%) had required hospitalization (Table 1). Hypertension and diabetes mellitus were the most common comorbidities found in 31 patients (15.42%). A total of 17 (8.46%) participants were active smokers.

Overall, 127 of the 201 (63.18%) patients reported having experienced sequelae (Table 1). Of these 127 patients, sequelae were reported by 61 patients (48.03%) aged 18–39 years, 63 patients (49.60%) aged 40–64 years, and three patients (2.36%) aged ≥ 65 years. A total of 89 participants (62.2%) with sequelae had been hospitalized, and 38 (65.51%) had independently self-isolated. Sequelae were reported by 19 (9.45%) patients who initially had no symptoms, but after PCR was negative and they had completed self-isolation, persistent symptoms appeared and were believed not to derive from another illness condition. Some symptoms appeared to be dominant in the patient's report. A total of 15 out of 31 (48.39%) patients with hypertension or diabetes (comorbidities) had persistent symptoms to date.

Table 1. Demographic and Clinical Characteristics of the Study Participants

	No. %			
	Total	Inpatient	Outpatient	
Characteristics	recovered	(n = 143)	Symptomatic	Asymptomatic
	individuals		(n = 39)	individuals (n
	(n = 201)			= 19)
Age, mean (SD)	39.35	39.1	40.2	39.6
	(11.56)			
Sex				
Women	92 (45.8)	57 (39.9)	27 (69.2)	8 (42.1)
Men	109 (54.2)	86 (60.1)	12 (30.8)	11 (57.9)
BMI, mean (SD)*	26.3	26.3	26.5	26.3
Comorbidities				
Hypertension	19 (9.45)	18 (12.59)	1 (2.6)	0 (0.0)

Diabetes	12 (5.97)	9 (6.29)	3 (7.7)	0 (0.0)
Active smoker	17 (8.46)	13 (9.09)	1 (2.6)	3 (15.8)
Duration of				
persistent				
symptoms (month)				
0	80 (39.8)	56 (39.2)	17 (43.6)	7 (36.8)
1–2	38 (18.9)	28 (19.6)	10 (25.6)	0 (0.0)
<u>></u> 3	9 (4.5)	5 (3.5)	2 (5.12)	2 (10.5)
Missing	74 (36.8)	54 (37.8)	10 (25.6)	10 (52.6)
Worse quality of	47 (23.4)	34 (23.8)	12 (30.8)	1 (5.3)
life				
Symptoms (post-	127 (63.18)	89 (62.2)	27 (69.2)	11 (57.9)
COVID follow-up)				
Excessive	69 (54.3)	44 (49.4)	21 (53.8)	4 (21.0)
fatigue/tiredness				
Dyspnea/shortness	26 (20.47)	18 (20.2)	5 (12.8)	3 (15.8)
of breath				
Sleep disorders	25 (16.68)	17 (19.1)	7 (17.9)	1 (5.3)
Emotional	22 (17.3)	18 (20.2)	4 (10.3)	0 (0.0)
instability				
Difficulty	34 (26.77)	16 (17.97)	14 (35.9)	4 (21.0)
concentrating				
Digestive problems	25 (19.68)	16 (17.97)	8 (20.5)	1 (5.3)
Loss of appetite	9 (7.09)	7 (7.86)	2 (5.1)	0 (0.0)
Loss of smell	10 (7.84)	5 (5.61)	3 (7.7)	2 (10.5)
Muscle pain	24 (11.94)	23 (25.84)	1 (2.6)	0 (0.0)
Sore throat	8 (6.3)	7 (7.86)	1 (2.6)	0 (0.0)
Cough	33 (25.98)	25 (28.1)	7 (17.9)	1 (5.3)
Cold	19 (14.96)	16 (17.97)	3 (7.7)	0 (0.0)
Diarrhea	2 (1.57)	1 (1.1)	0 (0.0)	1 (5.3)

Earache	1 (0.79)	0 (0.0)	1 (2.6)	0 (0.0)
Sweating	15 (11.81)	14 (15.7)	1 (2.6)	0 (0.0)
Burning sensation	8 (6.3)	5 (5.6)	3 (7.7)	0 (0.0)
on the skin				
Chills	2 (1.57)	2 (2.25)	0 (0.0)	0 (0.0)
Felt feverish	13 (10.23)	13 (14.6)	0 (0.0)	0 (0.0)
Nausea	7 (5.51)	7 (7.86)	0 (0.0)	0 (0.0)

^{*}BMI : Body Mass Index; SD : Standard Deviation

Table 2. Number of symptoms

Persistent symptoms	No. (%)
No symptoms	74 (36.8)
1–2 symptoms	83 (41.3)
≥3 symptoms	44 (21.9)

The most frequently reported sequelae were excessive fatigue (69/127 patients [54.33%]), difficulty concentrating (34/127 [26.77%]), and cough (33/127 patients [25.98%]) (Figure 1). A total of 83 (41.35%) participants experienced sequelae for 1–2 months, and 44 (21.9%) people experienced sequelae for three or more months (Table 2 and Figure 2). Overall, 47 out of 201 (23.38%) participants who had undergone self-isolation or who had been hospitalized reported a decrease in quality of life compared to three participants who had no symptoms (7.1%).

Discussion

In this study, patients were studied at three months after being discharged from hospital or declared recovered. A total of 127 (63.18%) patients reported sequelae that were still felt after being declared recovered with negative PCR confirmation. Eighty people (39.8%) reported sequelae lasting less than 1 month. A total of 38 people (18.9%) reported sequelae lasting around 1-2 months, and nine (4.5%) experienced sequelae ≥ 3 months after being discharged from hospital or

being declared recovered. Approximately 143 (71.14%) of the participants in our study had been hospitalized for COVID-19. Sequelae experienced for more than 1 month were reported by 33 (23.1%) of patients who were hospitalized. A study by Sudre et al. stated that as many as 20.1% of participants with COVID-19 still experienced symptoms and who had recovered from COVID-19 for more than 28 days to more than 12 weeks.³

The most reported sequelae in our study were excessive fatigue (69 of 127 patients [54.33%]), difficulty concentrating (34 of 127 patients [26.77%]), and cough (33 of 127 patients [25.98%]). A total of 83 (41.3%) participants experienced 1–2 sequelae symptoms, and 44 (21.9%) people experienced ≥ 3 sequelae. Fourteen out of 27 (51.85%) comorbid patients who had been hospitalized had persistent symptoms for more than 1 month. Garrigues et al revealed that the most reported persistent symptoms were fatigue (55%), shortness of breath (42%), loss of memory (34%), and impaired concentration and sleep (28% and 30.8%, respectively). Comparison of the persistent symptoms that occurred between the usual isolation-treated patients and the patients who received ICU care was statistically significant. Many symptoms persist several months after hospitalization for COVID-19. While there were few differences between health related quality of life (HRQoL) between ward and ICU patients.⁴ A study by Carfi et al. revealed that 87.4% of patients reported persistent symptoms of at least one symptom, especially fatigue and shortness of breath.⁵

A decrease in quality of life was reported in this study, with 47 patients (23.4%) from the total group of participants and 34 (23.8%) of the hospitalized patients experiencing a decrease in quality of life. Logue et al. also reported impaired quality of life in 30.7% of outpatients who had self-isolated.⁶

In the case of health workers who work in the operating room, the risk of contracting COVID-19 can have serious consequences. The importance of proper PPE use, reorganization of the operating schedule, use of safe operating techniques, and user-friendly surgical equipment are all good ways to avoid smoke production. Surgical team members responded to the COVID-19 pandemic with leadership and crisis management principles. Current recommendations are widely adopted in terms of organizational aspects and surgical management. The Surgery Departments implemented changes, including reorganizing surgical schedules, staff preparation, and the departments outbreak response policies and suggestions for surgical techniques and risk management.

Surgeons reported that their apparent lack of safety and comfort, as well as increased fatigue, may

have hampered their ability to perform at their best throughout surgery. 10

This study is limited because of its small sample size. Although the respondents involved in

this study came from several regions in Indonesia, the locations were not included in the

analysis. There is potential for bias in reporting symptoms during the post-recovery period

of up to three months. This study only analyzed symptoms that were observed and followed

up with questionnaire completed by the patients, more than three months after recovery and

which were not observed during hospitalization or self-isolation. This study also did not

differentiate between isolation room in hospital and ICU inpatient care but only between

patients who self-isolated and hospitalized patients. Our study shows that the sequelae of

COVID-19 are still felt by patients even after being discharged from hospital when the PCR

results are negative, thus affecting the participants' quality of life. This study is an initial

report of the sequelae that are still felt by patients after recovery from COVID-19 in

Indonesia.

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The authors declare no conflict of interest for this article.

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All authors had read and approved the final version of the manuscript.

Desdiani Desdiani had full access to all of the data in this study and takes complete responsibility

for the integrity of the data and the accuracy of the data analysis

TRANSPARENCY STATEMENT

Desdiani Desdiani confirms that the manuscript is a honest, accurate, and transparent account of

the study being reported; that no important aspects of the study have been omitted; and that any

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DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the

article and its supplementary materials.

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Deadlines:

Our aim is to publish all Health Science Reports submissions as quickly as possible, and the sooner you are able to resubmit, the quicker our decision and publishing processes will be. If it is not possible for you to submit your revision in September 24th, 2021, please let us know.

Once again, thank you very much for submitting your article to Health Science Reports. Please let us know if you need any help with the revision process, and we look forward to receiving your revised article soon.

Sincerely,
Dr. Qian Chen
Managing Editor, Health Science Reports
qchen@wiley.com, qchen@wiley.com

Reviewer Comments to Author:

Reviewer: 1

No comments.

Reviewer: 2

Comments:

How to define "COVID-19 Sequelae" ? please clarify it in the manuscript.

Reviewer: 3

Comments:

This paper was well written. It's better to provide a figure detailing the enrollment of patients. In addition, the methods section should be restructured as follows: ethics, subjects (period, definition, excluding criteria), methods (such as data collection, questionaire), and statistical methods.

Reviewer: 4

Comments:

An interesting article and timely during this pandemic

An interesting and well wirtten and timely article on the topic of Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation

from a general surgeon perspective in the field of general surgery, I would add a brief mention within the discussion section, discussing the use of PPE during EMergency surgery, the impact of the pandemic on the healtcare system and

about:blank 2/3

especially the changes and delays that impacted surgery and surgical patients. Also important the consequences of the pandemic on the emergency surgery and how this affected the performance of emergency surgery.

Please references to

- 1) International cooperation group of emergency surgery during the COVID-19 pandemic. Eur J Trauma Emerg Surg. 2020 Oct 13:1-9. doi: 10.1007/s00068-020-01521-y. Online ahead of print.
- 2) Adapting to an unprecedented scenario: surgery during the COVID-19 outbreak. Rev Col Bras Cir. 2020;47:e20202701. doi: 10.1590/0100-6991e-20202701. Epub 2020 Aug 12

Worth discussing a bit further the General precautions and strategies for the staff to overcome transmission during clinical practice especially in EMS and Emergncy services and you can add some perspective from the following

3) Impact of Personal Protective Equipment on Surgical Performance During the COVID-19 Pandemic. International Cooperation Group on PPE and Emergency Surgery, World J Surg. 2020 Sep;44(9):2842-2847. doi: 10.1007/s00268-020-05648-2

Perhaps a brief mention on the debate of use minmally invasive techniques and the risk of aeresolization and viral spreading during surgical procedures, and also during EMS

- 4) Laparoscopy at all costs? Not now during COVID-19 outbreak and not for acute care surgery and emergency colorectal surgery: A practical algorithm from a hub tertiary teaching hospital in Northern Lombardy, Italy. J Trauma Acute Care Surg. 2020 Jun;88(6):715-718. doi: 10.1097/TA.000000000002727
- 5) Convert to open: the new paradigm for surgery during COVID-19? Br J Surg. 2020 Jun;107(7):e194. doi: 10.1002/bjs.11662. Epub 2020 May 5

I think enlarging the discussion section would add value to your article as well as increasing the number references (only 6 references at the moment that can be increased to 10). And discussing the above topics in the Dicussion could make your article of more interest for a general reader and raise reders from other subspecialities as general surgery

Revision

Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation

Desdiani Desdiani^{1,2}, Auditya Purwandini Sutarto³, Alfathul Nur Kharisma⁴, Hera Safitri⁵, Amalia Fitri Hakim¹, Salsabila Hanifa Rusyda¹

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Running Head: Sequelae in COVID-19 Patients

Introduction

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after recovering from COVID-19. To date, there have been 1,657,035 cases of COVID-19, with 45,116 dead and 1,511,417 recovered in Indonesia.2 We assessed sequelae in COVID-19 patients and most common sequelae, both those who had selfisolated and those who were hospitalized, who had recovered for more than three months after negative Polymerase Chain Reaction (PCR) swab results.

Methods

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than three months. These sequelae is persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Hospital. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The sequelae of COVID-19 were those reported since the patient was declared negative by a PCR swab and had completed self-isolation or hospitalization for 10 days plus three days at the hospital, as recommended by the World Health Organization and the local Ministry of Health. The data collected were self-reported symptoms that appeared from when the patient was declared recovered from COVID-19 until 90 days later. The data were obtained from various cities in Indonesia.

A total of 214 patients who had been declared recovered from COVID-19 were contacted between January and March 2021 to complete a single electronic questionnaire between one month and three months after being declared recovered. Thirteen participants who did not complete the questionnaire were not included in the analysis. We performed only descriptive analysis due to the small number of participants. Data analysis was conducted using SPSS 23

Results

A total of 201 participants, took part from Indonesia and were of Asian ethnicity with an average age of 39.35 years old; the participants included 109 (54.2%) males and 92 (45.8%) females with confirmed COVID-19 infection. A total of 19 COVID-19 patients (9.45%) had had no symptoms, 58 (28.85%) patients had undergone self-isolation, and 143 (71%) had required hospitalization (Table 1). Hypertension and diabetes mellitus were the most common comorbidities found in 31 patients (15.42%). A total of 17 (8.46%) participants were active smokers.

Overall, 127 of the 201 (63.18%) patients reported having experienced sequelae (Table 1). Of these 127 patients, sequelae were reported by 61 patients (48.03%) aged 18–39 years, 63 patients (49.60%) aged 40–64 years, and three patients (2.36%) aged ≥ 65 years. A total of 89 participants (62.2%) with sequelae had been hospitalized, and 38 (65.51%) had independently self-isolated. Sequelae were reported by 19 (9.45%) patients who initially had no symptoms, but after PCR was negative and they had completed self-isolation, persistent symptoms appeared and were believed not to derive from another illness condition. Some symptoms appeared to be dominant in the patient's report. A total of 15 out of 31 (48.39%) patients with hypertension or diabetes (comorbidities) had persistent symptoms to date.

The most frequently reported sequelae were excessive fatigue (69/127 patients [54.33%]), difficulty concentrating (34/127 [26.77%]), and cough (33/127 patients [25.98%]) (Figure 1). A total of 83 (41.35%) participants span style="font-family: Times New Roman">experienced sequelae for 1-2 months, and 44 (21.9%) people experienced sequelae for three or more months (Figure 2). Overall, 47 out of 201 (23.38%) participants who had undergone self-isolation or who had been hospitalized reported a decrease in quality of life compared to three participants who had no symptoms (7.1%).

Discussion

In this study, patients were studied at three months after being discharged from hospital or declared recovered. A total of 127 (63.18%) patients reported sequelae that were still felt after being declared recovered with negative PCR confirmation. Eighty people (39.8%) reported sequelae lasting less than 1 month. A total of 38 people (18.9%) reported sequelae lasting around 1–2 months, and nine (4.5%) experienced sequelae ≥ 3 months after being discharged from hospital or being declared recovered. Approximately 143 (71.14%) of the participants in our study had been hospitalized for COVID-19. Sequelae experienced for more than 1 month were reported by 33

(23.1%) of patients who were hospitalized. A study by Sudre et al. stated that as many as 20.1% of participants with COVID-19 still experienced symptoms and who had recovered from COVID-19 for more than 28 days to more than 12 weeks.³

The most reported sequelae in our study were excessive fatigue (69 of 127 patients [54.33%]), difficulty concentrating (34 of 127 patients [26.77%]), and cough (33 of 127 patients [25.98%]). A total of 83 (41.3%) participants experienced 1–2 sequelae symptoms, and 44 (21.9%) people experienced ≥ 3 sequelae. Fourteen out of 27 (51.85%) comorbid patients who had been hospitalized had persistent symptoms for more than 1 month. Garrigues et al revealed that the most reported persistent symptoms were fatigue (55%), shortness of breath (42%), loss of memory (34%), and impaired concentration and sleep (28% and 30.8%, respectively). Comparison of the persistent symptoms that occurred between the usual isolation-treated patients and the patients who received ICU care was statistically significant. Many symptoms persist several months after hospitalization for COVID-19. While there were few differences between health related quality of life (HRQoL) between ward and ICU patients. A study by Carfi et al. revealed that 87.4% of patients reported persistent symptoms of at least one symptom, especially fatigue and shortness of breath.

A decrease in quality of life was reported in this study, with 47 patients (23.4%) from the total group of participants and 34 (23.8%) of the hospitalized patients experiencing a decrease in quality of life. Logue et al. also reported impaired quality of life in 30.7% of outpatients who had self-isolated.⁶

This study is limited because of its small sample size. Although the respondents involved in this study came from several regions in Indonesia, the locations were not included in the analysis. There is potential for bias in reporting symptoms during the post-recovery period of up to three months. This study only analyzed symptoms that were observed and followed up with questionnaire completed by the patients, more than three months after recovery and which were not observed during hospitalization or self-isolation. This study also did not differentiate between isolation room in hospital and ICU inpatient care but only between patients who self-isolated and hospitalized patients. Our study shows that the sequelae of COVID-19 are still felt by patients even after being discharged from hospital when the PCR results are negative, thus affecting the participants' quality of life. This study is an initial report of the sequelae that are still felt by patients after recovery from COVID-19 in Indonesia.

ACKNOWLEDGMENT

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FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this article

AUTHOR CONTRIBUTIONS

Conceptualization : Desdiani Desdiani

Formal analysis: Desdiani Desdiani, Auditya Purwandini Sutarto

Investigation: Alfathul Nur Kharisma, Hera Safitri, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

Project Administration: Desdiani Desdiani

Resources: Desdiani Desdiani, Auditya Purwandini Sutarto, Hera Safitri

Supervision: Desdiani Desdiani

Visualization: Hera Safitri, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

Writing - Original Draft Preparation: Desdiani Desdiani, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

Writing - Review & Editing: Desdiani Desdiani, Auditya Purwandini Sutarto, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

All authors had read and approved the final version of the manuscript.

Desdiani Desdiani had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis

TRANSPARENCY STATEMENT

Desdiani Desdiani confirms that the manuscript is a honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Health Science Reports - Manuscript ID HSR-2021-05-0438.R1 [email ref: SE-10-a]

Dari: HealthScienceReports Journal Admin (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

c: desdiani@ymail.com; audityapsutarto@gmail.com; alfathulnurkarisma@gmail.com; herfitsa1983@gmail.com;

amaliafth01@gmail.com; sh.rusyda@gmail.com

Tanggal: Rabu, 15 September 2021 pukul 11.27 WIB

15-Sep-2021

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Your transferred manuscript entitled "Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation" has been successfully submitted online and is presently being given full consideration for publication in the Health Science Reports.

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Health Science Reports Editorial Office

Re: Peer Review Process 17 September 2021

8/11/23, 12:03 PM

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Re: Health Science Reports - Manuscript ID HSR-2021-05-0438 [email ref: SE-6-a]

Dari: desdiani - (desdiani@ymail.com)
Kepada: healthsciencereports@wiley.com

Tanggal: Jumat, 17 September 2021 pukul 09.37 WIB

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I have upload my response letter in step 1, below reviewer comments, but Health Science Report Journal admin was sent email and told me to upload author response letter as a separate file. Please help me to find the right step to submit my response letter.

Thank you for your attention.

Best Regards, Desdiani Desdiani

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Dear Dr. Desdiani,

Your manuscript is in peer review process.

The handling editor is actively inviting reviewers for your manuscript.

Your patience is much appreciated during this time.

Thank you very much. Best regards, Ronald

Ronald Nathanael (Dr.)

Editorial Assistant

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Editor to Author: Response Letter 17 September 2021

8/11/23, 12:04 PM

Yahoo Mail - Health Science Reports - Manuscript ID HSR-2021-05-0438 [email ref: SE-6-a]

Health Science Reports - Manuscript ID HSR-2021-05-0438 [email ref: SE-6-a]

Dari: Health Science Report (healthsciencereports@wiley.com)

Kepada: desdiani@ymail.com

Tanggal: Jumat, 17 September 2021 pukul 13.39 WIB

Dear Dr. Desdiani,

Please send me the response letter so that I could upload it in ScholarOne.

Thank you very much.

Best regards, Magesh (For Ronald)

Dr. Ronald Nathanael

Editorial Assistant

Health Science Reports

healthsciencereports@wiley.com

From: desdiani - <desdiani@ymail.com>

Sent: 17 September 2021 08:07

To: Health Science Report < healthsciencereports@wiley.com>

Subject: Re: Health Science Reports - Manuscript ID HSR-2021-05-0438 [email ref: SE-6-a]



Dear Editorial Health Science Report Journal,

I have upload my response letter in step 1, below reviewer comments, but Health Science Report Journal admin was sent email and told me to upload

Revision Manuscript

Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation

Desdiani Desdiani^{1,2}, Auditya Purwandini Sutarto¹, Alfathul Nur Kharisma⁴, Hera Safitri⁵, Amalia Fitri Hakim¹, Salsabila Hanifa Rusyda¹

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Running Head: Sequelae in COVID-19 Patients

Introduction

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after recovering from COVID-19. To date, there have been 1,657,035 cases of COVID-19, with 45,116 dead and 1,511,417 recovered in Indonesia. We assessed sequelae in COVID-19 patients and most common sequelae, both those who had self-isolated and those who were hospitalized, who had recovered for more than three months after negative Polymerase Chain Reaction (PCR) swab results. COVID-19 Sequelae is persistent symptomatology and outcomes after hospital discharge or completion of self-isolation with a wide and multifaceted range of clinical manifestations were identified, including respiratory, gastrointestinal, neurological, cardiovascular symptoms, and other organ manifestations.

Methods

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than three months. These sequelae is persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Hospital. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The sequelae of COVID-19 were those reported since the patient was declared negative by a PCR swab and had completed self-isolation or hospitalization for 10 days plus three days at the hospital, as recommended by the World Health Organization and the local Ministry of Health. The data collected were self-reported symptoms that appeared from when the patient was declared recovered from COVID-19 until 90 days later. The data were obtained from various cities in Indonesia.

A total of 214 patients who had been declared recovered from COVID-19 were contacted between January and March 2021 to complete a single electronic questionnaire between one month and three months after being declared recovered. Thirteen participants who did not complete the questionnaire were not included in the analysis. We

Results

A total of 201 participants, took part from Indonesia and were of Asian ethnicity with an average age of 39.35 years old; the participants included 109 (54.2%) males and 92 (45.8%) females with confirmed COVID-19 infection. A total of 19 COVID-19 patients (9.45%) had had no symptoms, 58 (28.85%) patients had undergone self-isolation, and 143 (71%) had required hospitalization (Table 1). Hypertension and diabetes mellitus were the most common comorbidities found in 31 patients (15.42%). A total of 17 (8.46%) participants were active smokers.

Overall, 127 of the 201 (63.18%) patients reported having experienced sequelae (Table 1). Of these 127 patients, sequelae were rported by 61 patients (48.03%) aged 18-39 years, 63 patients (49.60%) aged 40-64 years, and three patients (2.36%) aged ≥ 65 years. A total of 89 participants (62.2%) with sequelae had been hospitalized, and 38 (65.51%) had independently self-isolated. Sequelae were reported by 19 (9.45%) patients who initially had no symptoms, but after PCR was negative and they had completed self-isolation, persistent symptoms appeared and were believed not to derive from another illness condition. Some symptoms appeared to be dominant in the patient's report. A total of 15 out of 31 (48.39%) patients with hypertension or diabetes (comorbidities) had persistent symptoms to date.

			No. %	
	Total	Inpatient		patient
Characteristics	recovered individuals (n = 201)	(n = 143)	Symptomatic (n = 39)	Asymptomatic individuals (n = 19)
Age, mean (SD)	39.35 (11.56)	39.1	40.2	39.6
Sex				
Women	92 (45.8)	57 (39.9)	27 (69.2)	8 (42.1)
Men	109 (54.2)	86 (60.1)	12 (30.8)	11 (57.9)
BMI, mean (SD)*	26.3	26.3	26.5	26.3
Comorbidities				
Hypertension	19 (9.45)	18 (12.59)	1 (2.6)	0 (0.0)
Diabetes	12 (5.97)	9 (6.29)	3 (7.7)	0 (0.0)
Active smoker	17 (8.46)	13 (9.09)	1 (2.6)	3 (15.8)
Duration of persistent symptoms (month)				
0	80 (39.8)	56 (39.2)	17 (43.6)	7 (36.8)
1-2	38 (18.9)	28 (19.6)	10 (25.6)	0 (0.0)
> 3	9 (4.5)	5 (3.5)	2 (5.12)	2 (10.5)
Missing	74 (36.8)	54 (37.8)	10 (25.6)	10 (52.6)
Worse quality of	47 (23.4)	34 (23.8)	12 (30.8)	1 (5.3)
life	,			,
Symptoms (post- COVID follow-up)	127 (63.18)	89 (62.2)	27 (69.2)	11 (57.9)
Excessive	69 (54.3)	44 (49.4)	21 (53.8)	4 (21.0)
fatigue/tiredness	26 (20 17)	10 (20 2)	5 (42.0)	2 (4 5 0)
Dyspnea/shortness	26 (20.47)	18 (20.2)	5 (12.8)	3 (15.8)
of breath Sleep disorders	25 (16 60)	17 (10.1)	7 (17 0)	1 (5 2)
Emotional	25 (16.68) 22 (17.3)	17 (19.1) 18 (20.2)	7 (17.9) 4 (10.3)	1 (5.3) 0 (0.0)
instability	22 (17.3)	18 (20.2)	+ (10.3)	0 (0.0)
Difficulty	34 (26.77)	16	14 (35.9)	4 (21.0)
concentrating	34 (20.77)	(17.97)	17 (33.7)	7 (21.0)
Digestive	25 (19.68)	16	8 (20.5)	1 (5.3)
problems	25 (15.00)	(17.97)	5 (20.5)	- (5.5)
Loss of appetite	9 (7.09)	7 (7.86)	2 (5.1)	0 (0.0)
Loss of smell	10 (7.84)	5 (5.61)	3 (7.7)	2 (10.5)
Muscle pain	24 (11.94)	23	1 (2.6)	0 (0.0)
	((25.84)	,	,
Sore throat	8 (6.3)	7 (7.86)	1 (2.6)	0 (0.0)
Cough	33 (25.98)	25 (28.1)	7 (17.9)	1 (5.3)
Cold	19 (14.96)	16 (17.97)	3 (7.7)	0 (0.0)
Diarrhea	2 (1.57)	1 (1.1)	0 (0.0)	1 (5.3)
	= (/	- (/	. ()	- (/

Earache	1 (0.79)	0 (0.0)	1(2.6)	0 (0.0)	
Sweating	15 (11.81)	14 (15.7)	1(2.6)	0 (0.0)	_
Burning sensation on the skin	8 (6.3)	5 (5.6)	3 (7.7)	0 (0.0)	_
Chills	2 (1.57)	2 (2.25)	0 (0.0)	0 (0.0)	_
Felt feverish	13 (10.23)	13 (14.6)	0 (0.0)	0 (0.0)	_
Nausea	7 (5.51)	7 (7.86)	0 (0.0)	0 (0.0)	

^{*}BMI : Body Mass Index; SD : Standard Deviation

Table 2. Number of symptoms

Persistent symptoms	No. (%)
No symptoms	74 (36.8)
1-2 symptoms	83 (41.3)
≥3 symptoms	44 (21.9)

The most frequently reported sequelae were excessive fatigue (69/127 patients [54,33%]), difficulty concentrating (34/127 [26.77%]), and cough (33/127 patients [25.98%]) (Figure 1). A total of 83 (41.35%) participants experienced sequelae for 1–2 months, and 44 (21.9%) people experienced sequelae for three or more months (Table 2 and Figure 2). Overall, 47 out of 201 (23.38%) participants who had undergone self-isolation or who had been hospitalized reported a decrease in quality of life compared to three participants who had no symptoms (7.1%).

Discussion

In this study, patients were studied at three months after being discharged from hospital or declared recovered. A total of 127 (63.18%) patients reported sequelae that were still felt after being declared recovered with negative PCR confirmation. Eighty people (39.8%) reported sequelae lasting less than 1 month. A total of 38 people (18.9%) reported sequelae lasting around 1−2 months, and nine (4.5%) experienced sequelae ≥ 3 months after being discharged from hospital or being declared recovered.

Approximately 143 (71.14%) of the participants in our study had been hospitalized for COVID-19. Sequelae experienced for more than 1 month were reported by 33 (23.1%) of patients who were hospitalized. A study by Sudre et al. stated that as many as 20.1% of participants with COVID-19 still experienced symptoms and who had recovered from COVID-19 for more than 28 days to more than 12 weeks 3

The most reported sequelae in our study were excessive fatigue (69 of 127 patients [54.33%]), difficulty concentrating (34 of 127 patients [26.77%]), and cough (33 of 127 patients [25.98%]). A total of 83 (41.3%) participants experienced 1–2 sequelae symptoms, and 44 (21.9%) people experienced ≥ 3 sequelae. Fourteen out of 27 (51.85%) comorbid patients who had been hospitalized had persistent symptoms for more than 1 month. Garrigues et al revealed that the most reported persistent symptoms were fatigue (55%), shortness of breath (42%), loss of memory (34%), and impaired concentration and sleep (28% and 30.8%, respectively). Comparison of the persistent symptoms that occurred between the usual isolation-treated patients and the patients who received ICU care was statistically significant. Many symptoms persist several months after hospitalization for COVID-19. While there were few differences between health related quality of life (HRQoL) between ward and ICU patients. A study by Carfi et al. revealed that 87.4% of patients reported persistent symptoms of at least one symptom, especially fatigue and shortness of breath. 5

A decrease in quality of life was reported in this study, with 47 patients (23.4%) from the total group of participants and 34 (23.8%) of the hospitalized patients experiencing a decrease in quality of life. Logue et al. also reported impaired quality of life in 30.7% of outpatients who had self-isolated.⁶

In the case of health workers who work in the operating room, the risk of contracting COVID-19 can have serious consequences. The importance of proper PPE use, reorganization of the operating schedule, use of safe operating techniques, and user-friendly surgical equipment are all good ways to avoid smoke production. Surgical team members responded to the COVID-19 pandemic with leadership and crisis management principles. Current recommendations are widely adopted in terms of organizational aspects and surgical management. The Surgery Departments implemented changes, including reorganizing surgical schedules, staff preparation, and the departments outbreak response policies and suggestions for surgical techniques and risk management. Surgeons reported that their apparent lack of safety and comfort, as well as increased fatigue, may have hampered their ability to perform at their best throughout surgery.

This study is limited because of its small sample size. Although the respondents involved in this study came from several regions in Indonesia, the locations were not included in the analysis. There is potential for bias in reporting symptoms during the post-recovery period of up to three months. This study only analyzed symptoms that were observed and followed up with questionnaire completed by the patients, more than three months after recovery and which were not observed during hospitalization or self-isolation. This study also did not differentiate between isolation room in hospital and ICU inpatient care but only between patients who self-isolated and hospitalized patients. Our study shows that the sequelae of COVID-19 are still felt by patients even after being discharged from hospital when the PCR results are negative, thus affecting the participants' quality of life. This study is an initial report of the sequelae that are still felt by patients after recovery from COVID-19 in Indonesia.

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this article

AUTHOR CONTRIBUTIONS

Conceptualization : Desdiani Desdiani

Formal analysis: Desdiani Desdiani, Auditya Purwandini Sutarto

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All authors had read and approved the final version of the manuscript.

Desdiani Desdiani had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis

TRANSPARENCY STATEMENT

Desdiani Desdiani confirms that the manuscript is a honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Decision Letter 29 September 2021

Decision Letter (HSR-2021-05-0438.R1)

From: qchen@wiley.com

To: desdiani@ymail.com, audityapsutarto@gmail.com, alfathulnurkarisma@gmail.com,

herfitsa1983@gmail.com, amaliafth01@gmail.com, sh.rusyda@gmail.com

Subject: Health Science Reports - Decision on Manuscript ID HSR-2021-05-0438.R1 [email ref: DL-SW-1-a]

Body: 29-Sep-2021

Dear Dr. Desdiani,

Thank you for submitting your revised manuscript to Health Science Reports. I very much enjoyed reading the revision.

I've reviewed your revised manuscript and your response to my comments and those of the reviewers, and I think all of the concerns raised have been satisfactorily addressed. I am thereby pleased to inform you that your manuscript has now been accepted for publication in Health Science

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Dr. Qian Chen Managing Editor, Health Science Reports qchen@wiley.com, qchen@wiley.com

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Reviewer Comments to Author:

Reviewer: 3

Recommendation: Accept

Comments: Thank you.

Reviewer: 2

Recommendation: Accept

Comments:

Very nice after revising!

Reviewer: 1

Recommendation: Accept

Comments:

Well written and accurately revised. Now it is too much better with addition of reviewer comments. it is better suited for publication now

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Dari: HealthScienceReports Journal Admin (onbehalfof@manuscriptcentral.com)

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Dari: HealthScienceReports Journal Admin (onbehalfof@manuscriptcentral.com)

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Sincerely,

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Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of

Self-Isolation

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Running Head: Sequelae in COVID-19 Patients

Introduction

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after recovering from COVID-19.¹ To date, there have been 1,657,035 cases of COVID-19, with 45,116 dead and 1,511,417 recovered in Indonesia.² We assessed sequelae in COVID-19 patients and most common sequelae, both those who had self-isolated and those who were hospitalized, who had recovered for more than three months after negative Polymerase Chain Reaction (PCR) swab results.

Methods

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than three months. These sequelae is persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Hospital. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The sequelae of COVID-19 were those reported since the patient was declared negative by a PCR swab and had completed self-isolation or hospitalization for 10 days plus three days at the hospital, as recommended by the World Health Organization and the local Ministry of Health. The data collected were self-reported symptoms that appeared from when the patient was declared

recovered from COVID-19 until 90 days later. The data were obtained from various cities in Indonesia.

A total of 214 patients who had been declared recovered from COVID-19 were contacted between January and March 2021 to complete a single electronic questionnaire between one month and three months after being declared recovered. Thirteen participants who did not complete the questionnaire were not included in the analysis. We performed only descriptive analysis due to the small number of participants. Data analysis was conducted using SPSS 23.

Results

A total of 201 participants, took part from Indonesia and were of Asian ethnicity with an average age of 39.35 years old; the participants included 109 (54.2%) males and 92 (45.8%) females with confirmed COVID-19 infection. A total of 19 COVID-19 patients (9.45%) had had no symptoms, 58 (28.85%) patients had undergone self-isolation, and 143 (71%) had required hospitalization (Table 1). Hypertension and diabetes mellitus were the most common comorbidities found in 31 patients (15.42%). A total of 17 (8.46%) participants were active smokers.

Overall, 127 of the 201 (63.18%) patients reported having experienced sequelae (Table 1). Of these 127 patients, sequelae were reported by 61 patients (48.03%) aged 18–39 years, 63 patients (49.60%) aged 40–64 years, and three patients (2.36%) aged ≥ 65 years. A total of 89 participants (62.2%) with sequelae had been hospitalized, and 38 (65.51%) had independently self-isolated. Sequelae were reported by 19 (9.45%) patients who initially had no symptoms, but after PCR was negative and they had completed self-isolation, persistent symptoms appeared and were believed not to derive from another illness condition. Some symptoms appeared to be dominant in the

patient's report. A total of 15 out of 31 (48.39%) patients with hypertension or diabetes (comorbidities) had persistent symptoms to date.

The most frequently reported sequelae were excessive fatigue (69/127 patients [54.33%]), difficulty concentrating (34/127 [26.77%]), and cough (33/127 patients [25.98%]) (Figure 1). A total of 83 (41.35%) participants experienced sequelae for 1–2 months, and 44 (21.9%) people experienced sequelae for three or more months (Figure 2). Overall, 47 out of 201 (23.38%) participants who had undergone self-isolation or who had been hospitalized reported a decrease in quality of life compared to three participants who had no symptoms (7.1%).

Discussion

In this study, patients were studied at three months after being discharged from hospital or declared recovered. A total of 127 (63.18%) patients reported sequelae that were still felt after being declared recovered with negative PCR confirmation. Eighty people (39.8%) reported sequelae lasting less than 1 month. A total of 38 people (18.9%) reported sequelae lasting around 1–2 months, and nine (4.5%) experienced sequelae ≥ 3 months after being discharged from hospital or being declared recovered. Approximately 143 (71.14%) of the participants in our study had been hospitalized for COVID-19. Sequelae experienced for more than 1 month were reported by 33 (23.1%) of patients who were hospitalized. A study by Sudre et al. stated that as many as 20.1% of participants with COVID-19 still experienced symptoms and who had recovered from COVID-19 for more than 28 days to more than 12 weeks.³

The most reported sequelae in our study were excessive fatigue (69 of 127 patients [54.33%]), difficulty concentrating (34 of 127 patients [26.77%]), and cough (33 of 127 patients [25.98%]). A total of 83 (41.3%) participants experienced 1–2 sequelae symptoms, and 44 (21.9%) people

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All authors had read and approved the final version of the manuscript.

Desdiani Desdiani had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis

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Table 1. Demographic and Clinical Characteristics of the Study Participants

			No. %	
Characteristics	Total	Inpatient		patient
	recovered individuals (n = 201)	(n = 143)	Symptomatic (n = 39)	Asymptomatic individuals (n = 19)
Age, mean (SD)	39.35 (11.56)	39.1	40.2	39.6
Sex				
Women	92 (45.8)	57 (39.9)	27 (69.2)	8 (42.1)
Men	109 (54.2)	86 (60.1)	12 (30.8)	11 (57.9)
BMI, mean (SD)*	26.3	26.3	26.5	26.3
Comorbidities				
Hypertension	19 (9.45)	18 (12.59)	1 (2.6)	0 (0.0)
Diabetes	12 (5.97)	9 (6.29)	3 (7.7)	0 (0.0)
Active smoker	17 (8.46)	13 (9.09)	1 (2.6)	3 (15.8)
Duration of persistent symptoms (month)	,			
0	80 (39.8)	56 (39.2)	17 (43.6)	7 (36.8)
1–2	38 (18.9)	28 (19.6)	10 (25.6)	0 (0.0)
> 3	9 (4.5)	5 (3.5)	2 (5.12)	2 (10.5)
Missing	74 (36.8)	54 (37.8)	10 (25.6)	10 (52.6)
Worse quality of life	47 (23.4)	34 (23.8)	12 (30.8)	1 (5.3)
Symptoms (post- COVID follow-up)	127 (63.18)	89 (62.2)	27 (69.2)	11 (57.9)
Excessive fatigue/tiredness	69 (54.3)	44 (49.4)	21 (53.8)	4 (21.0)
Dyspnea/shortness of breath	26 (20.47)	18 (20.2)	5 (12.8)	3 (15.8)
Sleep disorders	25 (16.68)	17 (19.1)	7 (17.9)	1 (5.3)
Emotional instability	22 (17.3)	18 (20.2)	4 (10.3)	0 (0.0)
Difficulty concentrating	34 (26.77)	16 (17.97)	14 (35.9)	4 (21.0)
Digestive problems	25 (19.68)	16 (17.97)	8 (20.5)	1 (5.3)
Loss of appetite	9 (7.09)	7 (7.86)	2 (5.1)	0 (0.0)
Loss of smell	10 (7.84)	5 (5.61)	3 (7.7)	2 (10.5)
Muscle pain	24 (11.94)	23 (25.84)	1 (2.6)	0 (0.0)

8 (6.3)	7 (7.86)	1 (2.6)	0 (0.0)
33 (25.98)	25 (28.1)	7 (17.9)	1 (5.3)
19 (14.96)	16	3 (7.7)	0 (0.0)
	(17.97)		
2 (1.57)	1 (1.1)	0 (0.0)	1 (5.3)
1 (0.79)	0 (0.0)	1 (2.6)	0 (0.0)
15 (11.81)	14 (15.7)	1 (2.6)	0 (0.0)
8 (6.3)	5 (5.6)	3 (7.7)	0 (0.0)
2 (1.57)	2 (2.25)	0 (0.0)	0 (0.0)
13 (10.23)	13 (14.6)	0 (0.0)	0 (0.0)
7 (5.51)	7 (7.86)	0 (0.0)	0 (0.0)
	33 (25.98) 19 (14.96) 2 (1.57) 1 (0.79) 15 (11.81) 8 (6.3) 2 (1.57) 13 (10.23)	33 (25.98) 25 (28.1) 19 (14.96) 16 (17.97) 2 (1.57) 1 (1.1) 1 (0.79) 0 (0.0) 15 (11.81) 14 (15.7) 8 (6.3) 5 (5.6) 2 (1.57) 2 (2.25) 13 (10.23) 13 (14.6)	33 (25.98) 25 (28.1) 7 (17.9) 19 (14.96) 16 3 (7.7) (17.97) 2 (1.57) 1 (1.1) 0 (0.0) 1 (0.79) 0 (0.0) 1 (2.6) 15 (11.81) 14 (15.7) 1 (2.6) 8 (6.3) 5 (5.6) 3 (7.7) 2 (1.57) 2 (2.25) 0 (0.0) 13 (10.23) 13 (14.6) 0 (0.0)

^{*}BMI : Body Mass Index; SD : Standard Deviation

Table 2. Number of symptoms

Persistent symptoms	No. (%)
No symptoms	74 (36.8)
1–2 symptoms	83 (41.3)
≥3 symptoms	44 (21.9)

Editor to Author 26 Oktober 2021

HSR-2021-05-0438.R1

Dari: Health Science Report (healthsciencereports@wiley.com)

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Tanggal: Selasa, 26 Oktober 2021 pukul 09.10 WIB

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Thank you very much.

Best regards, Magesh (For Ronald)

Dr. Ronald Nathanael

Editorial Assistant Health Science Reports healthsciencereports@wiley.com



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32kB

Table added 26 Oktober 2021

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Best regards, Magesh (For Ronald)

Dr. Ronald Nathanael

Editorial Assistant Health Science Reports healthsciencereports@wiley.com



Sequelae_in_COVID-19_Patients_Final_Rev.docx

41kB

Manuscript Revisions

Sequelae in COVID-19 Patients Three Months after Hospital Discharge or Completion of Self-Isolation

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Running Head: Sequelae in COVID-19 Patients

Introduction

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after recovering from COVID-19. To date, there have been 1,657,035 cases of COVID-19, with 45,116 dead and 1,511,417 recovered in Indonesia. We assessed sequelae in COVID-19 patients and most common sequelae, both those who had self-isolated and those who were hospitalized, who had recovered for more than three months after negative Polymerase Chain Reaction (PCR) swab results. COVID-19 Sequelae is persistent symptomatology and outcomes after hospital discharge or completion of self-isolation with a wide and multifaceted range of clinical manifestations were identified, including respiratory, gastrointestinal, neurological, cardiovascular symptoms, and other organ manifestations. I

Methods

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than three months. These sequelae is persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Hospital. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The sequelae of COVID-19 were those reported since the patient was declared negative by a PCR swab and had completed self-isolation or hospitalization for 10 days plus three days at the hospital, as

recommended by the World Health Organization and the local Ministry of Health. The data collected were self-reported symptoms that appeared from when the patient was declared recovered from COVID-19 until 90 days later. The data were obtained from various cities in Indonesia.

A total of 214 patients who had been declared recovered from COVID-19 were contacted between January and March 2021 to complete a single electronic questionnaire between one month and three months after being declared recovered. Thirteen participants who did not complete the questionnaire were not included in the analysis. We performed only descriptive analysis due to the small number of participants. Data analysis was conducted using SPSS 23.

Results

A total of 201 participants, took part from Indonesia and were of Asian ethnicity with an average age of 39.35 years old; the participants included 109 (54.2%) males and 92 (45.8%) females with confirmed COVID-19 infection. A total of 19 COVID-19 patients (9.45%) had had no symptoms, 58 (28.85%) patients had undergone self-isolation, and 143 (71%) had required hospitalization (Table 1). Hypertension and diabetes mellitus were the most common comorbidities found in 31 patients (15.42%). A total of 17 (8.46%) participants were active smokers.

Overall, 127 of the 201 (63.18%) patients reported having experienced sequelae (Table 1). Of these 127 patients, sequelae were reported by 61 patients (48.03%) aged 18–39 years, 63 patients (49.60%) aged 40–64 years, and three patients (2.36%) aged \geq 65 years. A total of 89 participants (62.2%) with sequelae had been hospitalized, and 38 (65.51%) had independently self-isolated. Sequelae were reported by 19 (9.45%) patients who initially had no symptoms, but after PCR was negative and they had completed self-isolation, persistent symptoms appeared and were believed

not to derive from another illness condition. Some symptoms appeared to be dominant in the patient's report. A total of 15 out of 31 (48.39%) patients with hypertension or diabetes (comorbidities) had persistent symptoms to date.

Table 1. Demographic and Clinical Characteristics of the Study Participants

	No. %			
	Total Inpatient		Outpatient	
Characteristics	recovered individuals (n = 201)	(n = 143)	Symptomatic (n = 39)	Asymptomatic individuals (n = 19)
Age, mean (SD)	39.35 (11.56)	39.1	40.2	39.6
Sex				
Women	92 (45.8)	57 (39.9)	27 (69.2)	8 (42.1)
Men	109 (54.2)	86 (60.1)	12 (30.8)	11 (57.9)
BMI, mean (SD)*	26.3	26.3	26.5	26.3
Comorbidities				
Hypertension	19 (9.45)	18 (12.59)	1 (2.6)	0 (0.0)
Diabetes	12 (5.97)	9 (6.29)	3 (7.7)	0 (0.0)
Active smoker	17 (8.46)	13 (9.09)	1 (2.6)	3 (15.8)
Duration of persistent symptoms (month)				
0	80 (39.8)	56 (39.2)	17 (43.6)	7 (36.8)
1–2	38 (18.9)	28 (19.6)	10 (25.6)	0 (0.0)
<u>> 3</u>	9 (4.5)	5 (3.5)	2 (5.12)	2 (10.5)
Missing	74 (36.8)	54 (37.8)	10 (25.6)	10 (52.6)
Worse quality of life	47 (23.4)	34 (23.8)	12 (30.8)	1 (5.3)
Symptoms (post- COVID follow-up)	127 (63.18)	89 (62.2)	27 (69.2)	11 (57.9)
Excessive fatigue/tiredness	69 (54.3)	44 (49.4)	21 (53.8)	4 (21.0)
Dyspnea/shortness of breath	26 (20.47)	18 (20.2)	5 (12.8)	3 (15.8)
Sleep disorders	25 (16.68)	17 (19.1)	7 (17.9)	1 (5.3)
Emotional instability	22 (17.3)	18 (20.2)	4 (10.3)	0 (0.0)
Difficulty concentrating	34 (26.77)	16 (17.97)	14 (35.9)	4 (21.0)

Digestive	25 (19.68)	16	8 (20.5)	1 (5.3)
problems		(17.97)		
Loss of appetite	9 (7.09)	7 (7.86)	2 (5.1)	0 (0.0)
Loss of smell	10 (7.84)	5 (5.61)	3 (7.7)	2 (10.5)
Muscle pain	24 (11.94)	23	1 (2.6)	0 (0.0)
•		(25.84)		
Sore throat	8 (6.3)	7 (7.86)	1 (2.6)	0 (0.0)
Cough	33 (25.98)	25 (28.1)	7 (17.9)	1 (5.3)
Cold	19 (14.96)	16	3 (7.7)	0 (0.0)
		(17.97)		, ,
Diarrhea	2 (1.57)	1 (1.1)	0 (0.0)	1 (5.3)
Earache	1 (0.79)	0 (0.0)	1 (2.6)	0 (0.0)
Sweating	15 (11.81)	14 (15.7)	1 (2.6)	0 (0.0)
Burning sensation	8 (6.3)	5 (5.6)	3 (7.7)	0 (0.0)
on the skin				
Chills	2 (1.57)	2 (2.25)	0 (0.0)	0 (0.0)
Felt feverish	13 (10.23)	13 (14.6)	0 (0.0)	0 (0.0)
Nausea	7 (5.51)	7 (7.86)	0 (0.0)	0 (0.0)

^{*}BMI: Body Mass Index; SD: Standard Deviation

Table 2. Number of symptoms

Persistent symptoms	No. (%)
No symptoms	74 (36.8)
1–2 symptoms	83 (41.3)
≥ 3 symptoms	44 (21.9)

The most frequently reported sequelae were excessive fatigue (69/127 patients [54.33%]), difficulty concentrating (34/127 [26.77%]), and cough (33/127 patients [25.98%]) (Figure 1). A total of 83 (41.35%) participants experienced sequelae for 1–2 months, and 44 (21.9%) people experienced sequelae for three or more months (Table 2 and Figure 2). Overall, 47 out of 201 (23.38%) participants who had undergone self-isolation or who had been hospitalized reported a decrease in quality of life compared to three participants who had no symptoms (7.1%).

Discussion

In this study, patients were studied at three months after being discharged from hospital or declared recovered. A total of 127 (63.18%) patients reported sequelae that were still felt after being declared recovered with negative PCR confirmation. Eighty people (39.8%) reported sequelae lasting less than 1 month. A total of 38 people (18.9%) reported sequelae lasting around 1–2 months, and nine (4.5%) experienced sequelae ≥ 3 months after being discharged from hospital or being declared recovered. Approximately 143 (71.14%) of the participants in our study had been hospitalized for COVID-19. Sequelae experienced for more than 1 month were reported by 33 (23.1%) of patients who were hospitalized. A study by Sudre et al. stated that as many as 20.1% of participants with COVID-19 still experienced symptoms and who had recovered from COVID-19 for more than 28 days to more than 12 weeks.³

The most reported sequelae in our study were excessive fatigue (69 of 127 patients [54.33%]), difficulty concentrating (34 of 127 patients [26.77%]), and cough (33 of 127 patients [25.98%]). A total of 83 (41.3%) participants experienced 1–2 sequelae symptoms, and 44 (21.9%) people experienced ≥ 3 sequelae. Fourteen out of 27 (51.85%) comorbid patients who had been hospitalized had persistent symptoms for more than 1 month. Garrigues et al revealed that the most reported persistent symptoms were fatigue (55%), shortness of breath (42%), loss of memory (34%), and impaired concentration and sleep (28% and 30.8%, respectively). Comparison of the persistent symptoms that occurred between the usual isolation-treated patients and the patients who received ICU care was statistically significant. Many symptoms persist several months after hospitalization for COVID-19. While there were few differences between health related quality of life (HRQoL) between ward and ICU patients.⁴ A study by Carfi et al. revealed that 87.4% of patients reported persistent symptoms of at least one symptom, especially fatigue and shortness of breath.⁵

A decrease in quality of life was reported in this study, with 47 patients (23.4%) from the total group of participants and 34 (23.8%) of the hospitalized patients experiencing a decrease in quality of life. Logue et al. also reported impaired quality of life in 30.7% of outpatients who had self-isolated.⁶

In the case of health workers who work in the operating room, the risk of contracting COVID-19 can have serious consequences. The importance of proper PPE use, reorganization of the operating schedule, use of safe operating techniques, and user-friendly surgical equipment are all good ways to avoid smoke production. Surgical team members responded to the COVID-19 pandemic with leadership and crisis management principles. Current recommendations are widely adopted in terms of organizational aspects and surgical management. The Surgery Departments implemented changes, including reorganizing surgical schedules, staff preparation, and the departments outbreak response policies and suggestions for surgical techniques and risk management. Surgeons reported that their apparent lack of safety and comfort, as well as increased fatigue, may have hampered their ability to perform at their best throughout surgery.

This study is limited because of its small sample size. Although the respondents involved in this study came from several regions in Indonesia, the locations were not included in the analysis. There is potential for bias in reporting symptoms during the post-recovery period of up to three months. This study only analyzed symptoms that were observed and followed up with questionnaire completed by the patients, more than three months after recovery and which were not observed during hospitalization or self-isolation. This study also did not differentiate between isolation room in hospital and ICU inpatient care but only between patients who self-isolated and hospitalized patients. Our study shows that the sequelae of COVID-19 are still felt by patients even after being discharged from hospital when the PCR results are negative, thus affecting the

participants' quality of life. This study is an initial report of the sequelae that are still felt by patients after recovery from COVID-19 in Indonesia.

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FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

AUTHOR CONTRIBUTIONS

Conceptualization: Desdiani Desdiani

Formal analysis: Desdiani Desdiani, Auditya Purwandini Sutarto

Investigation: Alfathul Nur Kharisma, Hera Safitri, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

Project Administration: Desdiani Desdiani

Resources: Desdiani Desdiani, Auditya Purwandini Sutarto, Hera Safitri

Supervision: Desdiani Desdiani

Visualization: Hera Safitri, Amalia Fitri Hakim, Salsabila Hanifa Rusyda

Writing - Original Draft Preparation: Desdiani Desdiani, Amalia Fitri Hakim, Salsabila Hanifa

Rusyda

Writing – Review & Editing: Desdiani Desdiani, Auditya Purwandini Sutarto, Amalia Fitri Hakim,

Salsabila Hanifa Rusyda

All authors had read and approved the final version of the manuscript.

Desdiani Desdiani had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis

TRANSPARENCY STATEMENT

Desdiani Desdiani confirms that the manuscript is a honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Manuscript Accepted 11 November 2021

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Article ID: HSR2444 Article DOI: 10.1002/hsr2.444 Internal Article ID: 17255988

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Journal: Health Science Reports

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Article ID: HSR2444 Article DOI: 10.1002/hsr2.444 Internal Article ID: 17255988

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Please get in touch with your Production Editor at ejalcoran@wiley.com;Mitchie.Balacanao@straive.com if you have any questions.

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Article DOI: 10.1002/HSR2.444

Article: Proof 30 November 2021

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1 INTRODUCTION

Many patients experience post-COVID-19 sequelae that lead to impaired quality of life after recovering from COVID-19.1 To date, there have been 1 657 035 cases of COVID-19, with 45 116 dead and 1511 417 recovered in Indonesia. 2 We assessed seguelae in COVID-19 patients and most common sequelae, both those who had self-isolated and those who were hospitalized, who had recovered for more than 3 months after negative polymerase chain reaction (PCR) swab results. COVID-19 sequelae are persistent symptomatology, and outcomes after hospital discharge or completion of self-isolation with a wide and multifaceted range of clinical manifestations were identified, including respiratory, gastrointestinal, neurological, cardiovascular symptoms, and other organ manifestations.1

2 METHODS

This study by the Faculty of Medicine, Sultan Ageng Tirtayasa University assessed the sequelae of adult patients who confirmed positive for COVID-19 infection based on PCR examination, who had undergone self-isolation or hospitalization and had been declared recovered for more than 3 months. These sequelae are persistent symptoms that develop during or following a confirmed case of COVID-19 and that continue for >28 days. The patients were retrospectively included in this study. Informed consent was signed by the patients, and this study was approved by the ethics committee of Bhayangkara Brimob Haspital This study follows the Strengthening the Departing of Observational Studies in

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