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## The relationship between history of physical activity and COVID-19 severity with post COVID-19 syndrome

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### ABSTRACT

**Background and purpose:** The COVID-19 pandemic has resulted in severe symptoms for many patients, continuing into the formation of post-COVID syndrome which affects the quality of life of patients. This study aims to assess relationship between history of physical activity and COVID-19 severity with post-COVID-19 syndrome.

**Methods:** This was a cross-sectional study involving 87 randomly selected adult COVID-19 patients treated at Udayana University Hospital from January 2022 to December 2023. Data collected were characteristics of the participants, the history of physical activity measured with IPAQ questionnaire, the severity of COVID-19 based on several indicators on the medical records, and post-COVID syndrome assessed with questionnaire. Data analysis method used for the Bivariate test is Chi-Square, and Multivariate uses the Logistic Regression Test to find the relationship between all variables.

**Results:** Of the 87 patients, 56.3% were men with age range from 19 to 56 years. The majority, 83.9% of patients had severe COVID symptoms and 43.7% experienced post-COVID syndrome, with the highest distribution being fatigue, at 81.6%. Low physical activity was associated with post-COVID syndrome ( $p=0.004$ ), 60.5% patients with low physical activity experience post-COVID syndrome compared to 27.3% with moderate physical activity. A significant relationship was also found between the severity of COVID-19 symptoms and the incidence of post-COVID syndrome ( $p=0.002$ ). As many as 35.6% of patients who experienced mild COVID-19 experienced post-COVID syndrome, while 85.7% of COVID-19 patients who experienced moderate-severe COVID-19 experienced post-COVID syndrome. The multivariate test also provided significant results between history of physical activity and post-COVID syndrome ( $p=0.014$ ) and the relationship between COVID-19 severity and post-COVID syndrome ( $p=0.011$ ).

**Conclusion:** A relationship was found between the history of pre-COVID physical activity and the severity of COVID symptoms with the incidence of post-COVID syndrome. On the other hand, there is no relationship between gender, age and comorbidity with post-COVID syndrome.

**Keywords:** physical activity, COVID-19 severity, post-COVID syndrome

## INTRODUCTION

At the end of 2019, a new communicable disease was discovered named coronavirus disease 19, abbreviated as COVID-19. The disease is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), an RNA virus.<sup>1</sup> The virus was first discovered in Wuhan, China. A study showed that 66% of people infected with SARS-CoV-2 have visited or been associated with a seafood market in Wuhan.<sup>2</sup> Then, the following case appeared in Bangkok, Thailand, on January 13, 2020, and eventually spread to many other countries.<sup>1</sup> The spread of this virus is very fast due to the high mobility between countries. Thus, on March 11, 2020, the World Health Organization (WHO) declared COVID-19 as a global pandemic.<sup>3</sup>

Like other coronaviruses, SARS-CoV-2 attacks the respiratory tract and is transmitted by waterborne transmission through droplets that enter the mouth, nose, or eyes.<sup>4</sup> After entering the human body, the SARS-CoV-2 S protein will bind to the ACE-2 receptor and replicate in the nasal cavity. The virus will continue migrating from the upper respiratory tract, and the immune response will become more aggressive. Most people infected with SARS-CoV-2 have mild symptoms that do not require special treatment, but the other 20% may have a lung infiltrate that will lead to moderate to severe symptoms.<sup>5</sup> People with comorbidities, such as cardiovascular disease, chronic respiratory disease, diabetes, and cancer, and older people exposed to SARS-CoV-2 have a higher risk of moderate to severe symptoms compared to people who do not have comorbid disease.<sup>3</sup>

The mild clinical manifestations of COVID-19 are fever, cough, fatigue, nasal obstruction, nasal discharge, anosmia, sore throat, and diarrhea. Severe accompanying symptoms include dyspnea, hypoxemia, acute respiratory distress syndrome (ARDS), sepsis shock, metabolic acidosis, bleeding, and coagulation dysfunction.<sup>6</sup> Within 2 weeks to 3 months of viral clearance, patients who have been infected with SARS-CoV-2 may experience varying prolonged symptoms, such as fatigue, headaches, attention deficit, alopecia, dyspnea, cough, myalgia, arthralgia, etc. The event is a post-COVID syndrome that is suspected to occur because the activation of mast cells causes long-term symptoms that vary due to the involvement of many organs.<sup>7</sup>

In connection with the occurrence of this idiopathic syndrome, post-COVID syndrome is still a particular concern, and all symptoms that appear after the acute period of COVID-19 will be categorized as post-COVID syndrome.<sup>4</sup> A study that involve 2412 COVID-19 patients showed more than half, 59.7% experienced post-COVID syndrome. A meta-analysis shows symptoms that persist after two years of being infected with COVID-19, such as fatigue and cognitive impairments. There are also psychological symptoms such as anxiety and depression, as well as sleep disorders in post-COVID syndrome. Post-COVID syndrome therapy that can only be given as a symptomatic therapy, whilst preventive measures is the best effort to reduce post-COVID syndrome. Physical activity was suggested reduced the likelihood of experiencing post-COVID syndrome.<sup>8</sup>

Physical activity defines as all body movements produced by skeletal muscles that require energy. People who regularly do moderate or high physical activity tend to have good health and improved quality of life.<sup>8</sup> Physical activity is also assessed as a modulator of clinical manifestations and prognosis of various chronic diseases. Routine and adequate physical activity help to stimulate the regular immune system, reduce physical syndrome, improve lung function, improve the cardiovascular system, stimulate brain plasticity, and maintain

mental health.<sup>9</sup>

A literature review has shown that adequate physical activity can be an effective preventive measure for the onset of multisystemic symptoms according to the diversity of cases and symptoms experienced by the patient. In the same study, it was shown that exercise has an effect on immunological health and help to manage and mitigate physical syndromes, especially pulmonary complications.<sup>9</sup> Research related to the relationship between the history of physical activity and COVID-19 severity with post-COVID syndrome in Indonesia, particularly in Bali, has not been conducted. Therefore, this study aims to assess the association between physical activity history and COVID-19 severity with post-COVID syndrome.

## METHOD

This is an analytical observational study with a cross-sectional design. Researchers have compiled a list of COVID-19 patients at Udayana Hospital through databases and medical records to obtain a sample frame. A simple random sampling was used, with a total of 87 subjects agreed to participate in this study. The criteria for inclusion in this study were COVID-19 patients at the Udayana Hospital and registered in the database. The exclusion criteria are COVID-19 patients who have heart abnormalities or do not complete the questionnaire. The samples are patients who have completed COVID-19 treatment.

The primary data collection was carried out through online questionnaires with Google Forms. The International Physical Activity Questionnaire was used to assess the history of physical activity, the aspects included are how many days study subjects did vigorous or moderate physical activity and how much time did the study subject usually spend for vigorous or moderate physical activity, how many days study subjects walk at least 10 minutes at a time and how much time did the study subject usually spend for walking, how much time did the study subject usually spend sitting on a week day. After study subjects fulfilled the questionnaire, we accumulate the duration and type of physical activity and then we can divide it to low, moderate, and high based on International Physical Activity Questionnaire guideline.

Medical records of study subjects were used to determine COVID-19 severity, which has already been written in the medical records and determined by the internist at Udayana University Hospital. A questionnaire designed by researchers was used to assess post-COVID syndrome 2 weeks to 3 months after infected COVID-19, we contact every study subject through messages and send them online questionnaire link. The variables studied came from three research instruments, including pre-COVID physical activity history, severity of COVID-19 symptoms, and post-COVID syndrome.

Primary data from the questionnaire is compiled in Ms. Excel along with secondary data from medical records. Next, the data was processed using the Statistical Package for the Social Science (SPSS) to go through Bivariate and Multivariate tests. The method used for the Bivariate test is Chi-Square, and Multivariate uses the Logistic Regression Test to find the relationship between all variables. Ethics approval was released on May 23<sup>rd</sup> 2023 with grant number 1364/UN14.2.2.VII.14/LT/2023.

## RESULT

## COVID-19 Patients' Characteristics

Based on data in Table 1, it can be seen that of the 87 patients, 49 (56.3%) were male with age range from 19 to 56 years old, more than three quarter (77.0%) were less than 40 years old. One fifth (21.8%) of the patients have comorbid, almost half (49.4%), reported low physical activity, and moderate physical activity (48.3%), while only 2.3% with high physical activity, hence we combined the high physical activity to the moderate physical activity for further analysis.

The majority (83.9%) of the COVID-19 patients was categorized as mild cases, while the others (16.1%) were moderate to severe. The patients who experienced post-COVID syndrome were 38 people (43.7%), with the most frequent post-COVID symptoms was fatigue (81.6%), followed by myalgia (42.1%), headaches (42.1%), anxiety disorders (36.8%), sleep disturbances (36.8%), cough (31.6%), shortness of breath (23.7%), tinnitus (21%), fever (18.4%), and anosmia (13.2%). The rarest symptoms were alopecia, vertigo, and excess sputum at 2.7%, respectively.

**Table 1. COVID-19 patients' characteristics**

Characteristics	f (%)
Male	49 (56.3)
Female	38 (43.7)
<40 years old	67 (77.0)
≥40 years old	20 (23.0)
With comorbidity	19 (21.8)
Without comorbidity	68 (78.2)
Low physical activity	43 (49.4)
Moderate physical activity	42(48.3)
High physical activity	2 (2.3)
Mild COVID-19	73 (83.9)
Moderate-Severe COVID-19	14 (16.1)
With post COVID syndrome	38 (43.7)
Without post COVID syndrome	49 (56.3)

## Post COVID-19 syndrome based on patients' characteristics

In this study, bivariate analysis by chi-square test was conducted to identify the relationship between the history of physical activity and COVID-19 severity with post-COVID syndrome at Udayana Hospital.

From Table 2, it can be seen that post COVID-19 syndrome was higher among women (52.6%) compare to men (36.7%) with odd ratio almost two, however, it was not statistically significant ( $p=0.206$ ). The older patients (40 years old and above) were more likely to experience COVID-19 syndrome compare to younger groups at 55.0% and 40.3%, respectively. This was also not statistically significant ( $p=0.365$ ). Based on the comorbidity status, patients with comorbidities were suffered from post-COVID-19 syndrome slightly higher (47.4%) compare to those with no comorbidities (42.6%).

Meanwhile two variables showed significant association with the post-COVID-19 syndrome status, level of physical activity and COVID-19 severity. COVID-19 patients with moderate to high physical activity level showed lower odds ( $OR=0.25$ ; 95%CI 0.10-0.60) of experiencing post-COVID-19 syndrome compare to those with low physical activity. This signifies the physical activity as protective factor of post-COVID syndrome. On the other hand, patients with more severe COVID-19 were more likely to experience post COVID-19 syndrome by around ten times. ( $OR=10.85$ , 95%CI: 2.25-52.22).

**Table 2. Distribution of post COVID-19 syndrome based on patients' characteristics**

Characteristics	Post COVID Syndrome		OR	95%CI	p
	Yes f (%)	No f (%)			
<b>Gender</b>					
Female	20 (52.6)	18 (47.4)	1.91	0.81 – 4.53	0.206
Male	18 (36.7)	31 (63.3)			
<b>Age</b>					
≥40 years old	11 (55.0)	9 (45.0)	1.81	0.66 – 4.96	0.365
<40 years old	27 (40.3)	40 (59.7)			
<b>Comorbidity</b>					
With comorbidity	9 (47.4)	10 (52.6)	1.21	0.44 – 3.36	0.916
Without comorbidity	29 (42.6)	39 (57.4)			
<b>Physical Activity</b>					
Moderate-high	12 (27.3)	32 (72.7)	0.25	0.10 – 0.60	0.004
Low	26 (60.5)	17 (39.5)			
<b>COVID-19 Severity</b>					
Moderate-Severe	12 (85.7)	2 (14.3)	10,85	2.25 - 52.22	0.002
Mild	26 (35.6)	47 (64.4)			

### Factors associated with post COVID-19 syndrome

We carried out a multivariate analysis by logistic regression test to measure the relationship between each variable with post-COVID syndrome at Udayana Hospital. Table 3 shows that there is a significant relationship between history of physical activity and post covid syndrome, patient with moderate to high physical activity has 70% lower odds to have post-covid syndrome compared to those with low level physical activity

(AOR=0.29, p=0.014). There is also significant relationship with severity of COVID-19 with more than eight times likelihood to experience post-COVID-19 syndrome (AOR=8.49, p=0.011).

**Table 3. Factors associated with post COVID-19 syndrome**

Variable	AOR*	95%CI	p
Gender	1.45	0.53 – 3.96	0.468
Age	1.66	0.49 – 5.60	0.412
Comorbidity	1.22	0.37 – 4.12	0.741
Physical Activity	0.29	0.11 – 0.78	0.014
Severity of COVID-19	8.49	1.64 – 44.04	0.011

\*AOR=adjusted odd ratio

## DISCUSSION

The multivariate analysis indicates that higher physical activity is significantly associated with a lower likelihood of developing post COVID-19 syndrome, while higher severity of COVID-19 is significantly associated with a higher likelihood of developing post COVID-19 syndrome. Other variables such as gender, age, and comorbidity do not show statistically significant associations with post COVID syndrome in this analysis. Physical activity has been shown to enhance immune system function. Individuals who engage in regular exercise tend to have a more effective immune response, which can help the body better combat viral infections like COVID-19, thereby reducing the likelihood of developing post-COVID complications. Regular physical activity can reduce chronic inflammation levels in the body. Chronic inflammation is known to exacerbate COVID-19 symptoms and contribute to the severity of post-COVID syndrome. By reducing inflammation, physical activity may mitigate the severity and duration of post-COVID symptoms.<sup>9</sup> This study shows that moderate to high physical activity can be a promising preventive treatment for post-COVID syndrome and severe COVID-19. This result indicates that health promotion about physical activity should be further enhanced to raise public awareness about the benefits of physical activity, particularly in preventing post-COVID syndrome and moderate-severe COVID-19. For patients that has low pre-COVID physical activity and experience post-COVID syndrome and moderate-severe COVID-19, requires additional healthcare attention.

On the other hand, higher severity of COVID-19 is significantly associated with a higher likelihood of developing post-COVID syndrome. This can be attributed to the extensive damage and stress that a severe COVID-19 infection can inflict on the body's systems. Severe cases of COVID-19 often lead to prolonged inflammation, organ damage, and significant physiological stress, which can result in a higher incidence of long-term symptoms and complications known as post-COVID syndrome. Other variables such as gender, age, and comorbidity did not show statistically significant associations with post-COVID syndrome in this analysis. This may be due to the complex interplay of various biological, environmental, and lifestyle factors that

influence the development of post-COVID syndrome, which might not be fully captured in this study.<sup>9</sup>

In this study, it was found that COVID-19 patients at Udayana Hospital were female and had post-COVID syndrome of 52.6%, this percentage was higher compared to the male COVID-19 patients and those who had post-COVID syndrome of 36.7%. This distribution is the same as the previous study by Bai et al. (2022), i.e., female study subjects experienced post-COVID syndrome more than males.<sup>10</sup> Based on the chi-square test, the results of this study were that there was no relationship between gender and the occurrence of post-COVID syndrome. The results are the same as the previous research conducted by Uniyal et al. (2022), while the research conducted by Bai et al. (2022) proves a relationship between gender and post-COVID syndrome. The variable measuring instruments, bias, and confounding factors present in this study can influence these differences in results, one of which is the distribution of gender, which is different from this study, there is no literature that explains the tendency of women to be infected with COVID-19.

In this study, it was found that the COVID-19 patients at Udayana Hospital who are  $\geq 40$  years old and have post COVID syndrome of 55%, where this percentage is higher compared to COVID-19 patients who are  $< 40$  years of age and have post-COVID syndrome of 27%. This result is the same as the previous study by Bai et al. (2022) which also shows the number of older study subjects who have post-COVID syndrome compared with the young study subjects.<sup>10</sup> Based on the chi-square test, this study's results show no relationship between age and post-COVID syndrome occurrences. The results are the same as the previous study by Uniyal et al. (2022), whereas the study conducted by Bai et al. (2022) proved a relationship between age and the occurrence of post-COVID syndrome. The previous study conducted by Bai et al. (2023) had similarities with this study, which used questionnaires to measure the occurrence of post-COVID syndrome. However, it had different methods and results from this study.

In this study, it was found that the COVID-19 patients at Udayana Hospital who have a comorbid disease and have post-COVID syndrome of 47.4%, where this percentage is higher compared to COVID-19 patients who have no comorbid disease and experience post-COVID syndrome is 42.6%. This result is the same as the study carried out by Uniyal et al. (2022), i.e., the number of research subjects with comorbid disease more experienced post-COVID syndrome compared with the research subjects who did not have comorbid syndrome. Patients with comorbidities are more susceptible to contracting COVID-19 for several reasons. First, these underlying health conditions, such as diabetes, heart disease, or chronic lung disease, can weaken the immune system's ability to fight viral infections like COVID-19. Second, individuals with comorbidities often experience poorer overall health, characterized by chronic inflammation or metabolic disorders, which further lowers the body's resistance to infection. Additionally, certain comorbidities affect respiratory function, such as chronic lung disease or asthma, making individuals more susceptible to severe respiratory illnesses such as COVID-19. These factors collectively contribute to the increased susceptibility of comorbid patients to COVID-19 infection.<sup>11</sup>

Based on the data of this study, COVID-19 patients at Udayana Hospital who performed low physical activity in the pre-COVID period and experienced post-COVID syndrome 60.5% and who did not experience post-COVID syndromes of 39.5%. This result shows that physical activity has a negative relationship with post-COVID syndrome. Furthermore, COVID-19 patients at Udayana Hospital who did moderate physical activities in the pre-COVID period suffered post-COVID syndrome incidents of 27.3%, and those who did not experience

post-COVID syndrome of 72.7%. In this study, many subjects performed moderate physical activity while those performing high physical activity performed only two people, so more moderate physical activity was demonstrated in this study. This is possible because physical activity is known to bring benefits to health and improve quality of life.<sup>12</sup> Physical activity is also assessed as a modulator of clinical manifestations and prognosis of various diseases.<sup>9</sup> In addition, one previous study has also proven that adequate physical activity can reduce post-COVID syndrome.<sup>13</sup> The study has similarities with this study because it investigated the relationship between physical activity during pre-COVID periods and post-COVID syndrome. The study differs from this because it selected the research subjects who reported positive COVID-19 test results. In contrast, this study chose the subject of research from the database of patients who confirmed positive for COVID-19 at Udayana Hospital. Previous research by Feter et al. (2023) and this study have similar results, namely, that physical activity is related to post-COVID syndrome. In this study, people who performed moderate physical activity increased their risk of developing post-COVID syndrome by 2.2 times, while people who did moderate-intensive physical activity reduced their risk of having post-COVID syndrome. Due to the limited availability of previous research, until the writing of the results of this research, there are no other results different from this research, so they cannot be compared.

In this study, it was found that COVID-19 patients at Udayana Hospital were male and performed moderate physical activity at 61.2%, which is a higher percentage compared to the COVID-19 patients who were female and did moderate physical activities at 36.8%. This result was the same as the previous study, which said that the number of subjects who performed male-intensive physical activity was more than those of the research who performed female.<sup>14</sup> The researchers also did a chi-square test to prove the relationship between gender and physical activity. The asymptotic significance value (2-sided) in the Continuity Correction<sup>b</sup> test is 0.041, which is less than 0.05, so it can be concluded that  $H_0$  is rejected, which means there is a significant relationship between gender and history of physical activity in the Udayana Hospital. According to the data, it can be concluded that physical activity can be influenced by gender, affecting post-COVID syndrome. In other words, male subjects are more likely to engage in moderate physical activity, reducing the post-COVID syndrome risk. So, gender and physical activity go hand in hand to increase or decrease the risk of post-COVID syndrome.

A person who has confirmed a negative may still experience a variety of symptoms, and these events are known as post-COVID syndrome.<sup>3</sup> Based on the data of this study, COVID-19 patients at Udayana Hospital had a severe COVID-19, 85.7% experienced post-COVID syndrome and 14.3% did not experience post-COVID syndrome. This is possible because a person with moderate-severe COVID-19 has certain conditions, such as a comorbid disease or an unhealthy lifestyle that causes further organ damage and eventually develops post-COVID syndrome.<sup>15</sup> The previous study conducted by Uniyal et al. (2022) had similarities with this study, which used the questionnaire as a measurement tool for the occurrence of post-COVID syndrome but had a different study location. This study had similar results to the study by Uniyal et al. (2022), where there was a relationship between COVID-19 severity and post-COVID syndromes.<sup>11</sup> The study obtained data COVID-19 severity from one of the hospitals in Milan. It used a post-COVID syndrome measurement device with blood tests, periodic medical examinations, and two questionnaires.

However, the main weakness of this study is the small sample size of 87 participants, which limits the generalizability of the findings. Additionally, the cross-sectional design restricts the ability to establish causality

between physical activity, COVID-19 severity, and post-COVID syndrome. The reliance on self-reported data, particularly for assessing physical activity levels and post-COVID symptoms, introduces the potential for recall bias and inaccuracies in reporting. Furthermore, the study did not account for potential confounding factors that could influence the results, such as socioeconomic status, access to healthcare, and other lifestyle factors.

## CONCLUSION

The conclusion that can be drawn from this research is there is a relationship between the history of physical activity and post-COVID syndrome among patients at Udayana Hospital, with moderate physical activity has a more negligible risk of experiencing post-COVID syndrome. There is a relationship between COVID-19 severity and post-COVID syndrome, with the risk of post-COVID syndrome occurring is 10.846 times higher in people with moderate-severe COVID-19. There is no relationship between gender, age and comorbidity with post-COVID syndrome.

To address the study limitations, future research should consider employing a larger sample size to improve the reliability and generalizability of the findings. A longitudinal study design would be beneficial in establishing causal relationships and temporal sequences between physical activity, COVID-19 severity, and post-COVID syndrome. Incorporating objective measures of physical activity and post-COVID symptoms, such as wearable activity trackers and clinical assessments, can enhance data accuracy. Additionally, adjusting for potential confounding factors and exploring the role of socioeconomic status, healthcare access, and other lifestyle variables would provide a more comprehensive understanding of the associations under study.

## COMPETING INTEREST

We have no conflict of interest in this study.

## FUNDING

This study was self-funded by researcher.

## AUTHOR'S CONTRIBUTION

OT developed the study design, collected and analyzed the data, and drafted the manuscript. PA, MM, and SP provide suggestions from developing the study design until the manuscript is prepared. PA also as the correspondence author.

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