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ORIGINAL ARTICLE

CHANGES IN WOMEN'S MENSTRUATION PATTERNS FOLLOWING COVID-19 INFECTION

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ABSTRACT

The Coronavirus Disease 2019 (COVID-19) has been demonstrated to disrupt the body's immune response, adversely affecting the reproductive system. Consequently, this study has focused on the changes in the menstruation patterns of survivors of the disease in women of reproductive age with asymptomatic, mild, and severe cases. This study employed an observational cross-sectional approach. The sample comprised 207 women who had recovered from COVID-19 within the past six months and met the inclusion and exclusion criteria. The sampling technique utilized consecutive sampling, and menstrual characteristics were assessed using a questionnaire. Several respondents in the severe group experienced changes in their menstrual patterns. Their duration of menstruation was shortened by 11.11%, and 13.58% had a more extended menstrual period. Some respondents' cycles were elongated by 20.98%, some decreased their initial menstrual volume by 32.09%, and some increased by 27.16%. Meanwhile, their menstrual volume decreased by 17.28% at the end of menstruation, and their duration lengthened by 24.69%. 12.1% of respondents also reported changes in menstrual regularity. Additionally, 19.75% of respondents stated that their menstrual pain decreased, and 13.58% had increased menstrual pain. The multivariate analysis revealed that the severity of the COVID-19 infection was the primary factor influencing menstrual patterns.

Keywords: *Menstrual patterns; menstrual cycle; severity of infection; survivor of COVID-19.*

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INTRODUCTION

In 2019, a new Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-2) was discovered and was first identified in Wuhan, China. Named Coronavirus Disease 2019 (COVID-19), this virus spread very quickly through respiratory droplets of infected people. COVID-19 can cause symptoms ranging from mild to severe, such as coughing, fever, and shortness of breath. Its initial symptoms are similar to common cold systems caused by the influenza virus (UNICEF, 2020).

On January 30, 2020, the World Health Organization (WHO) declared a public health emergency of international concern (PHEIC), and on March 11, 2020, COVID-19 was determined as a pandemic situation (WHO, 2023). The pandemic continued for three years, and COVID-19 cases rapidly

increased in waves of variants worldwide. A survey result on September 2023 reported over 771 million confirmed cases of COVID-19 worldwide, with almost 7 million deaths. Within the first two years, the highest increase in infections occurred in the Americas, which was reported to have increased by 7%. Meanwhile, the number of cases decreased by around 12% in the South and East Asia regions. Conversely, some regions experienced an increased mortality rate, especially in Africa, at 72% (WHO, 2021).

COVID-19 has significantly contributed to global morbidity and mortality rates and dramatically affected the health service system. Special planning and handling were needed to maintain the continuity of health services worldwide (Khan et al., 2020). Meanwhile, the clinical manifestations of COVID-19 infection range widely. A total of 81% of patients had mild clinical symptoms, 14% had severe symptoms, and the remaining 5% required critical treatment for organ failure, sepsis, shock, and multiple organ dysfunction. However, initial epidemiological findings identified that most confirmed cases were asymptomatic based on a study of more than 44,000 infected patients in China (The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020).

According to Wiersinga et al. (2020), COVID-19 infection causes inflammation in the tissues and endothelial cells of the lungs. This pathogenesis then results in micro-thrombi formation and contributes to the occurrence of thrombotic complications, such as limb ischemia, ischemia stroke, and myocardial infarction and can eventually lead to multiple organ failures. Jing et al. (2020) also explained that COVID-19 infection can interfere with the body's immune system and affect the reproductive system.

Previous research on the effect of COVID-19 infection on the reproductive system was also conducted by Li et al. (2021). Their study observed menstrual changes in severe-level COVID-19 patients. They found that the menstrual cycle was lengthened, and the volume decreased in severe patients' menstrual cycles. Hoffmann et al. (2020) explained that in COVID-19 infection, the COVID-19 pathogen enters cells via the angiotensin-converting enzyme-2 (ACE2) receptor. Zhang et al. (2020) further described how COVID-19 attacks organs that produce ACE2. One of these sources is the cell ovarian granulosa that makes ACE2 (Honorato-Sampaio et al., 2012). These findings suggest that the COVID-19 virus can target the ovaries.

However, little to no clinical data have been published regarding the impact of the COVID-19 virus on ovarian function (Li et al., 2021). Meanwhile, some changes in ovarian function can be seen by observing changes in menstruation.

This study compared changes in women's menstruation patterns following COVID-19 infection. Based on the Living Guidance for Clinical Management of COVID-19 (2021) issued by the WHO, COVID-19 severity can be divided into three groups: asymptomatic (no symptoms), mild (mild-moderate symptoms), and severe (severe symptoms) (WHO, 2021). Monin et al. (2020) explained the immune system's response to a viral infection would trigger an adaptive protective response. Additionally, this cascade response will induce hormonal changes in the uterus, which is thought to cause menstrual changes.

These changes in the uterus are also produced because when an infection occurs, a person will experience disturbances in their sleep duration, time, and quality (Baker & Lee, 2022) and changes in their thermoregulation system (Baker et al., 2020). These changes make their menstrual cycle abnormal (shorter or longer). Sundström-Poromaa (2018) reported that significant changes in sleep patterns in women, for example, sleeping less than 6 hours, typical sleep disturbances, and changes in emotional adaptation and mental health, can cause changes in a woman's premenstrual syndrome.

Research on women's menstruation pattern changes after COVID-19 infection needs to be conducted. Wang et al. (2021) stated that most researchers have focused on damages to the respiratory system rather than the reproductive system as a post-infection effect of SARS-CoV-2. Meanwhile, the research at Tongji Hospital on 177 patients showed that most respondents experienced decreased and increased menstrual volume, lengthening and shortening of the menstrual cycle, and changes in menstrual pain (Li et al., 2021). Additionally, Davis et al. (2022) researched 1,752 women from 56 countries and found that 36% had menstrual problems and 26% had irregular menstrual periods after COVID-19 infection.

However, few studies have focused on changes in women's menstrual cycles after COVID-19 infection in Indonesia. According to COVID-19 Survivor Indonesia (CSI) data, around 70% of female survivors of COVID-19 experience long-term COVID-19 symptoms, one of which is a change in their menstrual cycle (CNN Indonesia, 2021). Therefore, this study is important, given the scarcity of research on this topic in Indonesia.

Furthermore, changes in the menstrual cycle following SARS-CoV-2 infection can induce anxiety and concern about reproductive health, which impacts sexual well-being with partners. Therefore, this study has the following three objectives: to examine women's menstrual changes post-COVID-19 infection in women of reproductive age with asymptomatic, mild, and severe symptoms; to determine the relationship between the respondents' characteristics and the severity of infection with changes in menstrual patterns; and to identify the most dominant factor associated with changes in menstrual patterns.

METHOD

Study design

This observational study used a cross-sectional approach and primary data to investigate the changes in the menstrual cycle of asymptomatic, mild, and severe COVID-19 survivors.

Sample

Data on asymptomatic patients or those who experienced mild COVID-19 symptoms were collected from one of the shelters treating COVID-19 patients in Daerah Istimewa Yogyakarta (DIY). Meanwhile, data for COVID-19 survivors with severe symptoms were collected from patients treated at RSUP Dr. Sardjito General Hospital.

The study's population was patients who had recovered from asymptomatic, mild, and severe COVID-19 in DIY and met the inclusion criteria. The following inclusion criteria were used in this study: women of reproductive age (16-45 years) who experience menstruation; have experienced asymptomatic, mild, or severe COVID-19 in the last six months, confirmed through medical records, and have fully recovered; and willing to become research subjects by signing an informed consent form.

Meanwhile, the following exclusion criteria were used in this study: patients who have had reproductive organ surgery that affects their menstrual cycle; patients who experienced menstrual disorders before being infected with COVID-19 (based on patient information); and patients who cannot use the Google Form application.

The consecutive sampling technique was employed. Therefore, all research subjects who were found and met the inclusion criteria were included in the study until the minimum number of samples was met. The Slovin formula was used to determine the minimum number of samples, which was 58 people in each group. The researchers compiled the questionnaire with several alternative answers describing the respondents' menstrual characteristics before and after being infected with COVID-19, up to a maximum of 6 months after COVID-19 infection.

Instrument

The researcher compiled the women's menstruation pattern instrument based on previous research references about menstruation pattern. The changes in menstrual patterns studied included menstrual duration, frequency, volume at the beginning of menstruation, volume at the end of menstruation, and menstrual pain. These were defined as follows: 1) The duration of menstruation starts from the first day of bleeding until the bleeding finishes; the answer choices are 1-3 days, 4-8 days, and > 8 days; 2) The menstrual cycle is the duration from the start of menstruation in this period until the start of the next period; the answer choices are < 28 days, 28-35 days, and > 35 days; 3) Menstrual regularity is the regularity of menstruation. The answer choices are if the period is the same every month, it is called regular, whereas if the time range is different every month, it is called irregular; 4) Volume at the beginning of menstruation is the average amount of blood secreted during the initial menstrual period per day. The answer choices are 0.5 ml, > 05-2 ml, > 2-3.5 ml, > 3.5-6 .5 ml and >6.5-12.5 ml; 5) Volume at the end of menstruation is the average amount of blood secreted during the final menstrual period per day, the answer choices are 0.5 ml, > 05-2 ml, > 2-3.5 ml, > 3.5-6 .5 ml and >6.5-12.5 ml.; and 6) Menstrual pain is an unpleasant sensation that arises when a woman is menstruating, with the answer choices of no menstrual pain and menstrual pain.

The instrument used in this study went under subject matter expert review, involving 3 experts whose expertise are related to the instrument being assessed. This study's relevance aspect has an I-CVI of 0.98, and its accuracy aspect has an I-CVI value of 0.97. Additionally, its essence aspect has an I-CVI of 0.98, clarity aspect has an I-CVI of 1.00, and ease of understanding aspect has an I-CVI value of 0.96. Therefore, it the I-CVI of each aspect of the Menstrual Change Instrument questionnaire is valid. The researchers did not conduct a reliability test. In addition, the instrument was piloted with a comprehension test on 10 respondents who indicated that they understood the questions and answered according to the questions.

Data collection

The data collection process was conducted online using WhatsApp and Google Forms. The researchers worked with the UGM Covid-19 Task Force to collect active WhatsApp numbers of patients who had been treated. The researchers contacted the WhatsApp of each potential respondent who met the inclusion criteria and then explained the research. In addition, the researcher asked about their willingness to become a research respondent by sharing a link to a Google form containing an informed consent form and the research questionnaire. The respondents then completed the research questionnaire within the time limit agreed with the researcher.

Data analysis

To observe changes in menstrual patterns, the respondents were asked to answer the questionnaire based on their experience before and after they were infected with COVID-19. The menstrual pattern component is declared to have changed if the measurement results before COVID-19 are different after being infected with COVID-19. They then illustrated their responses with a diagram of menstrual characteristics before and after being infected with COVID-19. Next, a comparative test was conducted using Chi-square analysis with significance set as $p<0.05$ to determine whether there were differences in the menstrual pattern changes in each type of case. A multivariate analysis was also conducted using logistic regression.

Ethical consideration

The research was conducted after obtaining approval from the Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada in Yogyakarta, Indonesia with the approval number: KE/FK/0187/EC/2022.

RESULT

A total of 207 respondents were involved in this study, consisting of 58 asymptomatic COVID-19 survivors, 68 mild COVID-19 survivors, and 81 severe COVID survivors. Table 1 shows the respondents' characteristics. Most of the respondents were late adolescents aged 17-25 years (64.3%), and the most common body mass index (BMI) status was a normal BMI status of 18.5-25 (61.8%). Most respondents experienced menarche at the age of 12-16 years (80.2%), most do not smoke (96.6%), and all respondents do not use contraception (100%). A homogeneity test was conducted between the asymptomatic, mild, and severe respondent groups. The tests revealed that the respondent's age and menarche's age were not homogeneous between the three groups. In comparison, BMI and smoking status showed homogeneity between the three groups.

Table 1. Respondents' Characteristics n = 207

Characteristics of respondents	Asymptomatic		Mild		Severe		Total		p
	n	%	n	%	n	%	n	%	
Age									
Late teens 17-25 years old	41	19.8	54	26.1	38	18.4	133	64.3	0.000*
Early adulthood 26-35 years old	16	7.7	9	4.3	18	8.7	43	20.8	
Late adulthood 36-45 years	1	0.5	5	2.4	25	12.1	31	15.0	
Body Mass Index									
Underweight < 18.5	12	5.8	9	4.3	12	5.8	33	15.9	0.820
Normally 18.5-25	33	15.9	44	21.3	51	24.6	128	61.8	
Fat >25	13	6.3	15	7.2	18	8.7	46	22.2	
Menarche									
Children aged 5-11 years	9	4.3	15	7.2	8	3.9	32	15.5	0.010*
Early adolescence aged 12-16 years	49	23.7	52	25.1	65	31.4	166	80.2	
Late adolescence 17-25 years	0	0	1	0.5	8	3.9	9	4.3	
Smoking behavior									
Do not smoke	55	26.6	64	30.9	81	39.1	200	96.6	0.074
Smoke	3	1.4	4	1.9	0	0	7	3.4	
History of contraceptive use									
Not using contraception	58	28	68	32.9	81	39.1	207	100	-
Using contraception	0	0	0	0	0	0	0	0	

Table 2 presents the findings of an analysis that examined the number of respondents who experienced alterations in their menstrual patterns. Comparative tests of the respondents' menstrual durations were conducted on those with asymptomatic, mild, and severe cases, and they revealed significant differences in the changes in menstrual duration across the three groups, with a p-value of 0.004.

Conversely, no statistically significant differences were observed in the menstrual cycles of the three groups (p = 0.363). A p-value of 0.000 was obtained for the three groups, indicating a statistically significant correlation between changes in menstrual regularity. Significant differences were observed in the initial volume of menstrual bleeding between the three groups (p = 0.000). Similarly, significant differences were observed in the changes in menstrual volume at the end of menstruation between the three groups, with a p-value of 0.000. Additionally, significant differences were observed in the changes in menstrual pain across the three groups, with a p-value of 0.000.

Table 2. Changes in women's menstrual patterns before and after asymptomatic, mild, and severe COVID-19 infection (n = 207)

Pattern of Menstruation	Asymptomatic		Mild		Severe		Total		*P*
	n	%	n	%	n	%	n	%	
Duration of Menstruation									
There is no change in duration	53	25.6	63	30.4	62	29.5	177	85.5	0.004*
There has been a change in duration	5	2.4	5	2.4	20	9.7	30	14.5	
Total	58	28	68	32.9	81	39.1	207	100	
Menstrual Cycle									
There is no cycle change	43	20.8	54	26.1	56	27.1	153	73.9	0.363
There is a cyclical change	15	7.2	14	6.8	25	12.1	54	26.1	
Total	58	28	68	32.9	81	39.1	207	100	
Menstrual Regularity									
There is no change in regularity	47	22.7	67	32.4	56	27.1	170	82.1	0.000*
There is a change in regularity	11	5.3	1	0.5	25	12.1	37	17.9	
Total	58	28	68	32.9	81	39.1	207	100	
Volume at the beginning of menstruation									0.000*
There is no change in volume	40	19.3	55	26.6	33	15.9	128	61.8	
There is a volume change	18	8.7	13	6.3	48	23.2	79	38.2	
Total	58	28	68	32.9	81	39.1	207	100	
Volume at the end of menstruation									0.000*
There is no change in volume	48	23.2	66	31,9	47	22.7	161	77.8	
There is a volume change	10	4.8	2	1	34	16.4	46	22.2	
Total	58	28	68	32,9	81	39.1	207	100	
Menstrual Pain									0.000*
There was no change in menstrual pain	40	19.3	64	30,9	79	38.2	183	88.4	
There are changes in menstrual pain changes	18	8.7	4	1,9	2	1	24	11.6	
Total	58	28	68	32,9	81	39.1	207	100	

*Note * p < 0,005*

Figure 1 exhibits that most respondents' menstruation duration did not change. However, in the severe group, the number of respondents whose menstrual duration was shortened was nine people (11.11%), and 11 people (13.58%) had prolonged menstrual duration.

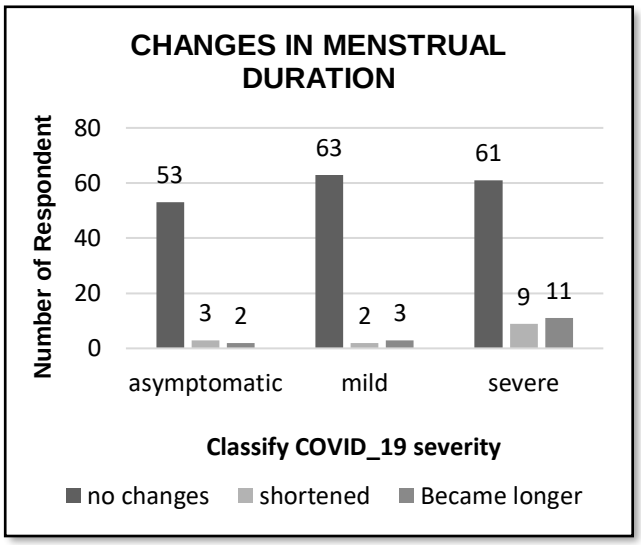

Figure 1. Changes in menstrual duration

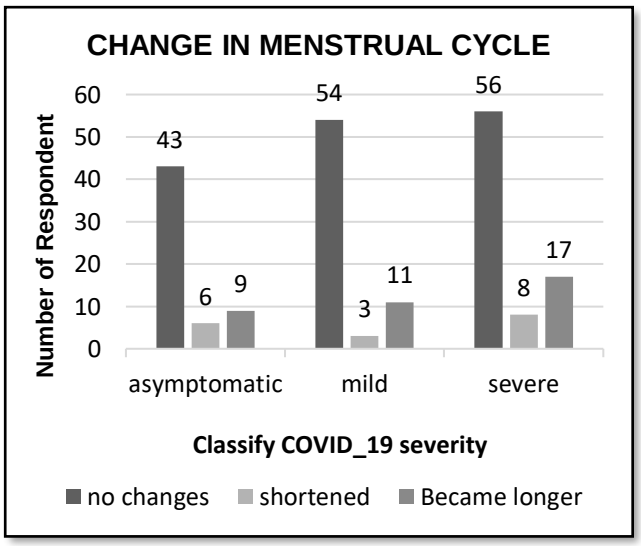

Figure 2. Changes in menstrual cycle

Figure 2 exhibits that most respondents' menstrual cycles remained unchanged. However, there has been a slight change in the respondents' menstrual cycles for each type of COVID-19 severity. The respondents' cycle length changes are almost the same for all COVID-19 severities. The respondents who experienced the most changes through an elongated cycle were the those who had severe COVID-19, with 17 people or 20.98% of the total number of respondents in the severe group.

Figure 3 shows that most respondents did not experience changes in menstrual regularity. Nevertheless, there were slight changes in the respondents' menstrual regularity in each type of COVID-19 severity. The respondents who experienced severe COVID-19 symptoms had the most significant change in menstrual regularity, with 25 people or 30.86% of the total number of respondents in the severe group.

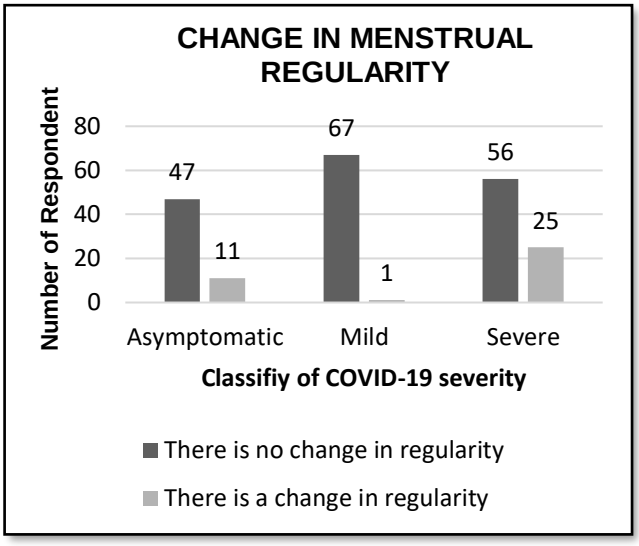

Figure 3. Changes in menstrual regularity

Based on Figures 4 and 5, the respondents' volume of menstruation at the beginning and end of their menstruation period was the same as the volume before and after being infected with COVID-19. However, respondents who experienced severe COVID-19 symptoms experienced more changes in menstrual volume than those of other severity types. Menstrual volume at the beginning of menstruation, for the respondents in the severe group, 26 (32.09%) respondents' volume of menstruation decreased, and 22 (27.16%) increased. Meanwhile, 14 (17.28%) respondents' menstruation volume at the end of menstruation in the severe group decreased, while 20 (24.69%) people had prolonged volume changes.

Figure 6 shows that most respondents' menstrual pain did not change between before and after being infected with COVID-19 for each type of COVID-19 severity. However, of the respondents with severe COVID-19 symptoms, 16 (19.75%) stated that their menstrual pain decreased, and 11 (13.58%) had increased menstrual pain.

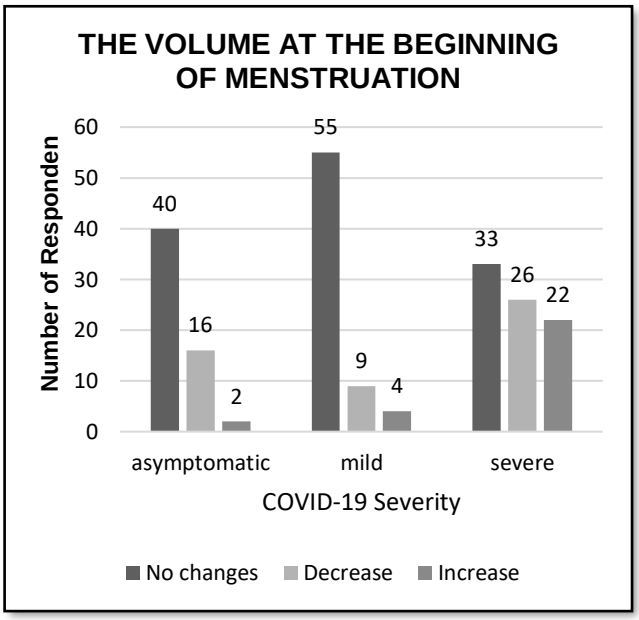

Figure 4. The volume at the beginning of menstruation

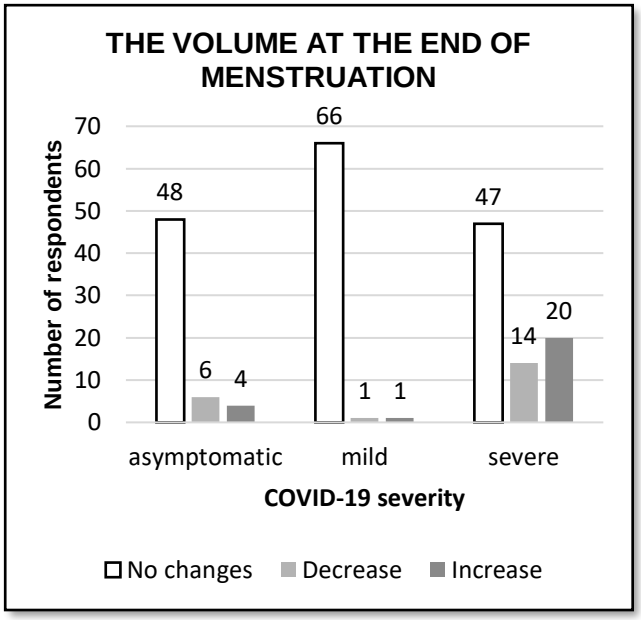

Figure 5. The volume at the end of menstruation

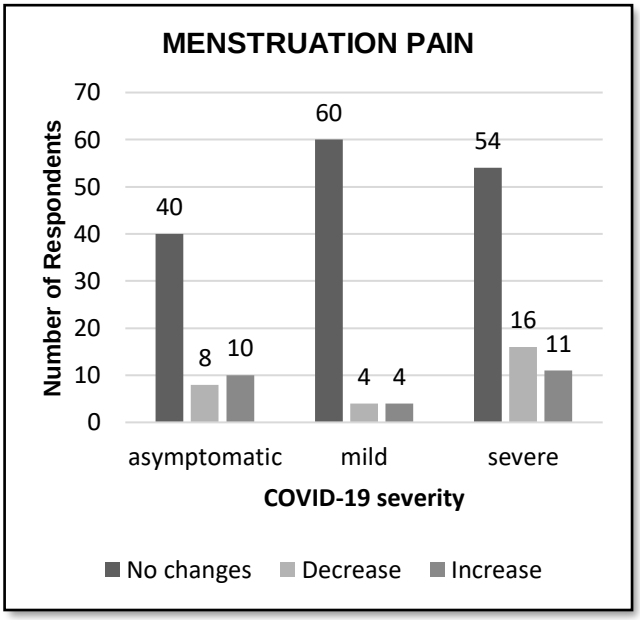

Figure 6. Menstruation pain

Table 4. Multivariate analysis of the respondents' characteristics and the severity of infection with menstrual pattern changes

Variabel	Koefisien	S.E	Wald	df	Nilai p	OR	CI (95%)		R-square
							Min	Max	
	Duration of menstruation								
Severity of infection	-1,679	0,571	8,656	1	0,003	0,187	0,061	0,571	0,102
Age	1,570	0,840	3,495	1	0,062	4,807	0,927	24,626	
Body mass index	1,263	0,777	2,845	1	0,104	3,536	0,772	16,198	
Menarche	-0,415	1,320	0,099	1	0,753	0,661	0,050	8,783	
	Menstrual cycle								
Severity of infection	-0,561	0,423	1,760	1	0,125	0,570	0,249	1,307	0,045
Age	1,187	0,595	3,948	1	0,047	3,264	1,016	10,484	
Body mass index	-0,698	0,527	1,753	1	0,186	0,498	0,177	1,398	
Menarche	-0.271	0,906	0,090	1	0,764	0,762	0,129	4,497	
	Menstrual regularity								
Severity of infection	-0,771	0,449	2,967	1	0,085	0,461	0,191	0,113	0,154
Age	0,072	0,574	0,016	1	0,901	1,074	0,349	3,309	
Body mass index	-0,206	0,643	0,102	1	0,749	0,814	0,231	2,872	
Menarche	1,941	1,253	2,399	1	0,121	6,967	0,597	81,253	
	The volume of the beginning of menstruation								
Severity of infection	-1,661	0,416	15,909	1	0,000	0,190	0,084	0,430	0,188
Age	0,845	0,525	2,585	1	0,108	2,327	0,831	6,516	
Body mass index	-0,852	0,544	2,406	1	0,121	0,427	0,145	1,252	
Menarche	0,847	0,894	0,897	1	0,343	2,333	0,404	13,465	
	The volume of the end of menstruation								
Severity of infection	-1,108	0,455	5,916	1	0,015	0,330	0,135	0,806	0,196
Age	-0,355	0,717	0,422	1	0,516	0,701	0,240	2,047	
Body mass index	-0,269	0,652	0,170	1	0,680	0,764	0,213	2,745	
Menarche	-0,586	0,960	0,373	1	0,542	0,557	0,085	3,651	
	Menstrual Pain								
Severity of infection	3,470	1,046	11,014	1	0,001	32,132	4,140	249,401	0,299
Age	-0,798	1,057	0,570	1	0,450	0,450	0,057	3,576	
Body mass index	-0,086	0,724	0,014	1	0,906	0,918	0,222	3,794	
Menarche	-0,575	1,441	0,159	1	0,690	0,563	0,033	9,491	

The relationship between the respondents' characteristics and the severity of infection with changes in menstrual patterns was analyzed. The factors that play a role vary greatly and can be explained as follows: 1) The dominant factor associated with the duration of menstruation is the severity of infection. The four variables tested have an influence of 10.2% on the duration of menstruation, while the rest are influenced by other factors not examined in this study. 2) The dominant factor associated with the menstrual cycle is the respondent's age. The four variables tested have an influence of 4.5% on the menstrual cycle, while the rest are influenced by factors not examined in this study. 3) For menstrual regularity, none of the four variables examined in this study are dominantly associated with the incidence of menstrual regularity. These variables have an influence of 15.4% on the menstrual cycle, while the rest are influenced

by factors not examined in this study. 4) The dominant factor associated with menstrual volume at the beginning of menstruation is the severity of infection. The four variables tested have an influence of 18.8% on the volume of the beginning of menstruation, while the rest are influenced by factors examined in this study. 5) The dominant factor associated with menstrual volume at the end of menstruation is the severity of the infection. The four variables tested have an influence of 19.6% on the volume of the end of menstruation, while the rest are influenced by factors not examined in this study. 6) The dominant factor associated with menstrual pain is the severity of infection. The four variables tested have an influence of 29.9% on menstrual pain, while the rest is influenced by factors not examined in this study.

The multivariate analysis revealed that of the four variables suspected of being related to changes in menstrual pattern, the severity of COVID-19 infection is the dominant factor affecting the duration of menstruation, the menstrual volume at the beginning and the end of menstruation, and menstrual pain.

DISCUSSION

Based on epidemiological studies about COVID-19 infection, the frequency of men infected with COVID-19 is higher than women in several countries, including China, South Korea, Italy, and worldwide (Mo et al., 2020; Chen et al., 2020; Remuzzi and Remuzzi, 2020). The rate and fatality of COVID-19 infection in women is lower than in men because women can produce higher levels of circulating antibodies, especially IgG and IgM immunoglobulins, than men (Butterworth et al., 1967). In addition, compared with men, women can also develop higher levels of immune cells, such as CD4+ T helper cells (Amadori et al., 1995). Nevertheless, for epidemiological research purposes, the influence of COVID-19 infection on female patients is worthy of further study.

Based on this study's results, the changes in the respondents' menstrual patterns varied based on the severity of COVID-19 infection. As illustrated in the preceding figures, most respondents reported alterations in their menstrual patterns, such as duration, regularity, volume at the beginning and end of menstruation, and intensity of menstrual discomfort. These observed variations were statistically significant across the three groups.

In contrast, menstrual cycle characteristics exhibited minimal variation across the three groups. The group with a history of severe COVID-19 infection demonstrated the most pronounced alterations in menstrual patterns. The three groups had only one similar pattern, namely the menstrual cycle (Mardliyah et al., 2023; Rahmawati et al., 2023; Ramadhani et al., 2023).

The symptomatic changes experienced by women infected by COVID-19 result in physiological changes in their bodies, especially in their reproductive organs. This statement aligns with Huang et al.'s (2020) findings in their mini-review. Infection with the COVID-19 virus can affect host cells through the cellular receptor, angiotensin-converting enzyme 2 (ACE2). Theoretically, human cells with ACE2 expression are believed to affect the targets of SARS-CoV-2 infection, including the lungs, digestive tract, kidneys, and heart, as well as the ovaries and testes, which have a dominant role in fertility. ACE2 is also related to oocyte maturation, ovulation, and spermatogenesis. ACE2 can also be found in endometrial epithelial cells. Huang et al. (2020) also found some uncertainty about whether COVID-19 infection can damage the reproductive system.

Moreover, previous viral infections are widely known to affect the female reproductive system and cause menstrual disorders, such as hepatitis B and C virus infections and human immunodeficiency virus (HIV). Anovulation has also been reported in acute illness and may be transient. The disease causes suppression of ovarian function, thereby affecting its regular function (Li et al., 2021).

Furthermore, endometrial tissue expresses receptors and proteins involved in SARS-CoV-2 infectivity, but it is unknown whether this can alter endometrial receptivity and embryo implantation (Delamuta et al., 2021). Therefore, the effects of SARS-CoV-2 on the male/female reproductive system must be studied in the long term. Most researchers currently focus on studying respiratory system damage rather than the reproductive system after COVID-19 infection. However, some results imply that SARS-CoV-2 infection can be detrimental. Meanwhile, the male reproductive system also functions through ACE2 receptor mediation. Several studies have shown that SARS-CoV-2 may impact male/female reproduction, so the best efforts are to control and prevent SARSCoV-2 infection with vaccinations and strategies to avoid transmission (Wang et al., 2021).

This study's multivariate analysis revealed that the severity of infection is the dominant factor affecting menstrual duration, the menstrual volume at the beginning and end of menstruation, and menstrual pain. To date, there is limited existing literature on the impact of the SARS-CoV-2 infection on menstrual patterns. However, the available research provides insight into the infection's effect on each of these patterns. The prevailing view is that the SARS-CoV-2 infection affects the female reproductive system (Li et al.,2021). SARS-CoV-2 can invade target cells by binding to ACE2, thus affecting female fertility. ACE2, widely expressed in the ovaries, uterus, vagina, and placenta, regulates the levels of angiotensin II (Ang II) and Ang-(1-7) to perform its physiological functions. ACE2, Ang II, and Ang-(1–7) can regulate follicle development and ovulation, regulate angiogenesis and corpus luteum degeneration, and influence endometrial tissue growth. ACE2 expression in the ovaries may affect ovarian reserve; reduced ovarian reserve can affect fecundity by reducing egg quality (Steiner et al., 2017). The ovarian hormone levels in question are basal concentrations of stimulating hormone (FSH), basal luteinizing hormone (LH), estradiol (E(2)), AMH anti-Müllerian hormone (AMH) (Tal et al., 2017; Jhonson et al., 2006). Therefore, ACE2 expression in the ovaries may affect the changes in women's menstrual cycle and menstrual volume. Kolanska et al. (2021) stated that the ovarian reserve of patients with a history of asymptomatic and mild COVID-19 did not change, as proven by comparing the results of an examination of AMH levels in COVID-19 rapid diagnostic test-positive patients and COVID-19 quick diagnostic test negative patients. This finding may also be related to the reports of fewer menstrual pattern changes in patients with asymptomatic infection and more menstrual cycle changes in the group with severe infection. However, further studies with a larger sample size are needed.

This study's results also demonstrate that menstrual pain was experienced by patients with a history of asymptomatic, mild, and severe types of COVID-19. Although all respondents experienced changes to their menstrual pain, the most changes occurred in the severe group, as 16 (19.75%) respondents stated that their menstrual pain had decreased

and 11 (13.58%) had increased menstrual pain. This study also included menstrual pain as one of the menstrual pattern variables because it is commonly experienced by women who are menstruating.

According to a study by Negriff et al. (2009), one of the most common physical and emotional symptoms of menstruation is menstrual pain, also known as dysmenorrhea (Negriff et al, 2009). The menstrual pain studied in this study was specifically classified as primary dysmenorrhea, defined as pain during menstruation without any pathological problems found in the reproductive organs (Davis et al., 2005).

These changes in menstrual patterns add further evidence that COVID-19 infection influences women's reproductive organs and may also affect fertility. This research was conducted by asking 207 patients with a history of COVID-19 infection with a six-month time limit. Most changes in menstrual patterns occurred in patients with severe symptoms, while very few changes occurred in mild and asymptomatic types. Several respondents stated that the changes in menstrual patterns were felt early after infected with COVID-19; as their body's condition improved, their menstrual patterns tended to return to how they were before being COVID-19 infection.

According to Li et al. (2021), COVID-19 infection causes suppression of ovarian function, causing changes in sexual hormone levels and raising the possibility of a woman experiencing menstrual disorders, which tend to be reversible. Hormonal imbalances can also affect changes in the menstrual cycle, and some causes include exposure to environmental stressors such as excessive physical activity, low energy intake, cigarette smoke, and psychosocial stress (Attarchi et al., 2013). Patients with COVID-19 experience very high levels of psychological distress because they feel that COVID-19 is a new disease with no known cure and a high risk of death. This psychological stress can also affect changes in the menstrual cycle. The findings of this study may serve as an educational resource for healthcare professionals seeking to reduce patient anxiety following a diagnosis of COVID-19. It is important to note that COVID-19 infection, particularly in severe cases, can lead to alterations in the menstrual cycle, including changes in duration, volume, and pain levels of menstruation.

Nevertheless, this study's sample is still limited, and menstrual data taken before and after being infected with COVID-19 were taken up to a maximum of 6 months after being infected with COVID-19, making it possible for respondents to forget their menstrual history. This study also did not examine psychological stress factors that are often experienced by COVID-19 patients, which can also affect changes in women's menstrual patterns. Finally, the questionnaire used also does not meet the reliability test criteria.

CONCLUSION AND RECOMMENDATION

There were significant differences in the changes in women's menstrual patterns based on the severity group (asymptomatic, mild, and severe) of COVID-19. The menstrual pattern changes examined were duration, regularity, beginning and end menstrual volume, and menstrual pain. The respondents in the severe COVID-19 group experienced the most frequent changes in menstrual patterns. Age of menarche and infection severity also correlate with changes in menstrual patterns.

The multivariate analysis revealed that the severity of COVID-19 infection is the dominant factor affecting menstrual duration, the menstrual volume at the beginning and end of menstruation, and menstrual pain. Knowledge about the potential for changes in menstrual patterns after COVID-19 infection is essential for patient education to reduce their anxiety about the impacts that arise after COVID-19 infection. Future research should employ a larger sample size and a longitudinal observational design when examining changes in the menstrual cycle in other infectious diseases. Doing so will enable a more comprehensive understanding of the impact of such diseases on reproductive organs. In addition, researchers need to examine other factors that can affect changes in menstrual patterns that have not been examined in this study, such as psychological stress factors.

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