Menstrual Symptom Disorders After COVID-19 in Relation To Anxiety and Long COVID Symptoms

Buket Akinci[1], Damla Korkmaz Dayican[1], Eyüp Günay[1], Nilgün Coşar[1], Hakan Ötün[1], Rumeysa Kılınç[1], İnci Kurban[1], Kübra Punar[1], Elif Karagülle[1], Ecem Nasırlı[1], Ezgi Altıparmak[1], Semiha Açıkalın[1], and Serhat Başçi[1]

[1]Biruni University, Faculty of Health Sciences

April 05, 2024

Abstract

Aim and objectives: Coronavirus disease (COVID-19) can affect the menstrual cycle and menstrual volume. We aimed to examine the changes in menstrual symptoms of women who had recovered from COVID-19 and determine the factors affecting these changes. Methods: A questionnaire, prepared using Google Forms, was completed online in May 18-31, 2021 by 180 women (26.08±6.62 years) who had recovered from COVID-19. Menstrual symptoms, menstrual pain severity, fatigue severity and anxiety levels of the participants were assessed with Menstrual Symptom Questionnaire (MSQ), Visual Analogue Scale (VAS) and Fatigue Severity Scale (FSS), Coronavirus Anxiety Scale (CAS), respectively. Results: Post-COVID-19 individuals' MSQ total scores and subgroup scores, FSS scores and menstrual pain showed a statistically significant increase compared to pre-COVID-19 ($p < 0.001$ for all). Multiple linear regression analysis identified age at menarche and change in FSS and VAS scores as significant contributors to 38.4% of the variance explained in the significant regression for change in MSQ score ($F(3.176) = 38.23$, $p < 0.001$). Individuals with prolonged fatigue, muscle–joint pain and dyspnea symptoms showed increased MSQ total scores ($p = 0.006$, $p = 0.009$, $p = 0.046$ respectively) and negative effects/somatic complaints subgroup scores ($p = 0.004$, $p = 0.002$, $p = 0.017$ respectively). Also, individuals with prolonged gastrointestinal symptoms showed increased pain symptoms ($p = 0.029$) and coping methods subgroup scores ($p = 0.002$), while those with prolonged muscle and joint pain showed increased coping methods ($p = 0.022$) subgroup scores. Conclusion: In this study, we observed worsened menstrual symptoms, fatigue, and menstrual pain severity in women recovered from COVID-19. In addition, age at menarche and fatigue and menstrual pain scores differences after COVID-19 were determiners of the changes in menstrual symptoms. Menstrual symptoms were more severe in women who have prolonged fatigue, dyspnea, muscle–joint pain, and gastrointestinal symptoms.

INTRODUCTION

Coronavirus disease (COVID-19) is a viral infectious disease that affects many organs of the body, most commonly the lungs, and has short- and long-term consequences.[1] Regardless of disease severity, the most frequently reported persisting symptoms after COVID-19 are fatigue and dyspnea.[2]

The World Health Organization has revealed that women's health is more adversely affected by COVID-19 than that of men.[3]Angiotensin-converting enzyme 2 (ACE2), which plays a key role in the entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells, is expressed in high amounts in the female genital organs, such as the ovaries, uterus, vagina, and placenta,[4]which may pose a risk for female reproductive functions, leading to infertility, fetal distress, or menstrual cycle disorders.[5] ACE2 is responsible for balancing the levels of angiotensin II enzyme, which initiates menstruation.[5] ACE2 expression in the uterine tissue varies according to age and menstrual cycle phase,[6]and these changes may result in impaired uterine bleeding.[5]

Limited number of studies have examined the effects of COVID-19 on the menstrual cycle. Li et al. examined menstrual cycle in women who had recovered from COVID-19 and determined that one-fifth of infected women, more commonly those with severe disease, have decreased menstrual volume or prolonged menstrual cycle.[7] Different phases of menstruation are associated with distinctive hormonal, physical, and mental changes.[8] Stress, exercise, and life changes can cause menstrual problems.[9] Dysmenorrhea is the most common menstrual problem.[10] In a study examining the effect of pandemic stress on the menstrual cycle, 36.9% of women had irregular menstrual cycles and 38.8% experienced dysmenorrhea.[11] In addition, 52.6% of women have reported a change in their menstrual cycle during the quarantine period. Therefore, stress during the pandemic is significantly associated with changes in the menstrual cycle.[12]

The effects of COVID-19 on body systems and functions are being investigated from the different perspectives. The studies examining the effects of COVID-19 on the menstrual cycle are limited and to the best of our knowledge, no study evaluated the changes in menstrual symptoms of women who have had COVID-19.[7,11,12] We hypothesized that menstrual symptoms may worsen in women who had recovered from COVID-19. Therefore, we aimed to examine the changes in menstrual symptoms of women who had recovered from COVID-19 and determine the factors affecting these changes.

METHODS

This cross-sectional study was based on retrospective and prospective inquiries. An online questionnaire prepared using Google Forms application was sent to 196 women between May 18 and 31, 2021. We included all volunteers who answered the questionnaire, were aged 18–45 years, had been diagnosed with COVID-19 (based on a confirmed positive polymerase chain reaction test result that was emailed to us), were fluent in Turkish, and were in the menstrual phase at the time of inclusion. Individuals who were in the premenopausal–postmenopausal period, unable to email their PCR results, or unable to answer the questionnaire adequately were excluded. The study protocol was approved by the Non-Interventional Ethics Committee of Biruni University (No: 2021/47-45) and registered at the ClinicalTrials.gov (NCT04806815). The study was conducted according to the principles of the Declaration of Helsinki, and all participants provided informed consent at the beginning of the study.

Data on sociodemographic characteristics, the history of COVID-19, and prolonged symptoms were recorded. Menstrual symptoms, menstrual pain severity, fatigue severity, and anxiety levels were assessed using the Menstrual Symptom Questionnaire (MSQ), Visual Analogue Scale (VAS), Fatigue Severity Scale (FSS), and Coronavirus Anxiety Scale (CAS), respectively.

Participants were asked to answer all questions included in the MSQ, taking into account their menstrual periods before and after their COVID-19 diagnosis. The MSQ consists of 22 items divided into three subgroups (Factor 1-negative effects/somatic complaints [1-13], Factor 2-pain symptoms [14-19], and Factor 3-coping methods [20-22]), with each item scored from 1 and 5, designed to assess menstrual pain and symptoms. The total MSQ score is calculated by adding the mean scores of the items included in the subgroups and ranges from 22 to 110. Higher scores indicate increased menstrual symptom severity.[13,14]

VAS was used to score patients' menstrual pain severity, with scores ranging from 0 (no pain) to 10 (most severe pain).[15]

The FSS questionnaire consists of nine Likert-type questions, with each question scored from 1 to 7, and scores [?]4 indicating severe fatigue. The participants were asked to answer all questions, while considering what they experienced before and after their COVID-19 diagnosis. The total score ranges from 9 to 63, with higher scores indicating greater severity.[16,17]

The CAS is used to assess dysfunctional anxiety. Participants were asked to rate their frequency of anxiety episodes when exposed to thoughts or information about COVID-19 on a five-point scale, ranging from 0 (not at all) to 4 (almost every day). A total score of [?]9 indicated coronavirus-related anxiety.[18,19]

Statistical Analysis

The Statistical Package for Social Science program (v23; SPSS, Chicago, IL) was used for statistical analysis. Data were expressed as mean ± standard deviation or percentages. The Kolmogorov–Smirnov test was used to analyze the normality of the variables, all parameters were non-normally distributed. The Wilcoxon signed rank test used for the comparison of menstrual symptoms, menstrual pain severity, and fatigue severity of individuals before and after COVID-19. Inter correlations between the changes ((post COVID-19) - (pre-COVID)) in MSQ, MSQ subgroup scores, fatigue and menstrual pain and coronavirus anxiety were computed using Spearman correlation. Independent variables based on univariate analysis were analyzed by multiple linear regression analysis to determine the multivariate influence of the predictors of the Δ MSQ scores. The adjusted R^2 was used to explain the total variance. Subjects' the Δ MSQ scores and subgroup scores compared based on demographic features and prolonged COVID-19 symptoms using Mann Whitney-U test or Kruskal-Wallis test. Statistical significance was set at $p < 0.05$ for all analysis.

RESULTS

A total of 196 individuals initially met the inclusion criteria; however, 16 individuals were excluded from the study because they did not complete the questionnaire. Therefore, 180 participants were included. The mean age was 26.08 ± 6.62 years, while the mean age at menarche was 13.28 ± 1.35 years.

The patients' sociodemographic and COVID-19 disease related data are shown in Table 1. None of the participants were diagnosed with female reproductive diseases. Three (1.7%) participants had been admitted due to pneumonia and hypoxemia, 17 (9.4%) participants had COVID-19-related pulmonary radiological findings, and 95 (52.8%) participants had been treated with favipiravir. The most common prolonged COVID-19 symptoms were fatigue (52.8%), muscle–joint pain (38.3%), and headache (32.2%).

Pre- and post-COVID-19 MSQ scores, FSS scores, and VAS scores are shown in Table 2. After the diagnosis of COVID-19, the individuals had significantly higher MSQ total scores (Z = -4.196), negative effects/somatic complaints (Z = -3.970), pain symptoms (Z = -3.342), coping methods subgroup scores of MSQ (Z = -2.469), FSS scores (Z = -8.929), and menstrual pain scores (Z = -5.265) than those before the diagnosis of COVID-19.

The correlation between Δ MSQ scores and age, body mass index, age at menarche, Δ FSS scores, Δ menstrual pain, and CAS scores was examined. Δ MSQ scores had a significant negative mild-to-moderate correlation with the age at menarche (r = -0.158) and a significant positive mild-to-moderate correlation with the Δ FSS score (r = 0.516) and the Δ menstrual pain score (r = 0.334). A negative significant correlation was found between age at menarche and Δ MSQ-negative effects/somatic complaints subgroup scores (r = -0.160) and Δ MSQ-coping methods subgroup scores (r = -0.185). Δ FSS and Δ menstrual pain scores were positively correlated with negative effects/somatic complaints subgroup scores (r = 0.528 and r = 0.299, respectively), pain symptoms subgroup scores (r = 0.45 and r = 0.337, respectively) and coping methods subgroup scores (r = 0.368 and r = 371, respectively) (Table 3).

Multiple linear regression analysis identified age at menarche and FSS and VAS scores as significant contributors to 38.4% of the variance explained in the significant regression for MSQ scores (F (3.176) = 38.23, p < 0.001; Table 4).

The Δ MSQ scores of the individuals did not differ according to education level, smoking status or time passed after the diagnosis of COVID-19. The Δ MSQ scores of the individuals were compared according to the prolonged COVID-19 symptoms. Individuals with prolonged fatigue, muscle–joint pain, and dyspnea symptoms showed increased Δ MSQ total scores (Z = -2.775, Z = -2.594, Z = -1.994, respectively) and Δ negative effects/somatic complaints subgroup scores (Z = -2.907, Z = -3.052, Z = -2.393, respectively). Individuals with prolonged gastrointestinal symptoms showed increased Δ pain symptoms subgroup scores (Z = -2.182) and coping methods subgroup scores (Z = -3.082), while those with prolonged muscle and joint pain symptoms showed increased Δ coping methods subgroup scores (Z = -2.288) (Table 5).

The sample size of the study was calculated using the G*Power 3.1.9.4 Sample Size Calculator program (Universitat Düsseldorf), considering the 180-person sample and the Δ MSQ total score after COVID-19 diagnosis (2.29 ± 8.16). Accordingly, the power of the study was calculated to be 96.2% ($\alpha = 0.05$).

DISCUSSION

Our cross-sectional study aimed to examine the changes in menstrual symptoms of women had recovered from COVID-19 and determine the factors associated with these changes. Our results showed that menstrual symptoms, fatigue, and menstrual pain severity worsened in women after being diagnosed with COVID-19. In addition, age at menarche and fatigue and menstrual pain scores differences after COVID-19 were determiners of the changes in menstrual symptoms. Menstrual symptoms were more severe in women with prolonged fatigue, dyspnea, muscle–joint pain, and gastrointestinal symptoms.

Menstruation, which is controlled by the uterus, ovary, and brain, can be affected by various infections, medications, or other organ dysfunctions.[20] SARS-CoV-2 has been reported to cause menstrual cycle disorders by affecting female reproductive functions.[5] Among the women who had been diagnosed with COVID-19, 20% and 19% reported a reduced menstrual volume and prolonged menstrual cycle, respectively. The changes in sex hormones as a result of ovarian suppression have been suggested as a possible cause.[7] In a previous study, 38.8%, 37%, and 29.8% young adolescents reported menstrual pain, menstrual volume changes, and menstrual cycle duration changes, respectively.[11]Previous studies have primarily focused on the effects of COVID-19 on menstrual volume and menstrual cycle duration. To our knowledge, our study is the first to identify increased menstrual symptoms and related factors in women who recovered from COVID-19. We believe that the negative effects of COVID-19 on the female genital organs responsible for menstrual cycle control as well as persisting post-infection symptoms may have led to this finding.

The rapid decrease in estrogen levels during menstruation causes menstrual pain, muscle–joint pain, and gastrointestinal symptoms.[21] The prevalence of dysmenorrhea varies between 67.2% and 90.0%.[22] During menstruation, as the basal contraction level of the uterus rises from 10 mmHg to 150–180 mmHg, uterine ischemia develops and the released anaerobic metabolites stimulate Type-C pain fibers, causing dysmenorrhea. In addition, the incidence of symptoms, such as nausea, vomiting, and diarrhea, increases with the stimulation of the gastrointestinal system by prostaglandins.[23] In our study, individuals with prolonged gastrointestinal symptoms after COVID-19 had higher pain symptoms and coping methods subgroup scores. In addition subjects with prolonged muscle–joint pain had higher changes in MSQ total score, negative/somatic effects and coping methods subgroup scores. Similarities between persistent post-infection symptoms and the physiological symptoms that occur during the menstrual period may lead to the disturbed menstrual symptoms.

Regardless of disease severity, the most frequently reported persist symptoms were fatigue and dyspnea.[2] In our study, 21.7% individuals had prolonged dyspnea and had increased negative effects/somatic complaints subgroup scores. In studies investigating airway sensitivity during menstrual periods, a significant increase in bronchial hyperactivity was found during the luteal phase.[24,25] In a study by Gibbs et al.,[26] 40% patients with asthma experienced worsening symptoms and reduced peak expiratory flow during the premenstrual period. In our study, individuals with prolonged dyspnea symptoms after COVID-19 had higher difference in MSQ total score and negative/somatic effects subgroup scores. This result shows that there is a link between the subjective respiratory symptoms and menstrual symptom disorders especially associated with somatic complaints after recovery from COVID-19.

Fatigue is a premenstrual symptom and has been associated with excessive bleeding during menstruation.[27,28] Juhi et al.[29] reported that muscle fatigue occurs with decreased estrogen levels in the early follicular and luteal phases. Among women who were evaluated 60 days after being diagnosed with COVID-19, 53.1% reported persistent fatigue.[2] El Sayed et al.[30] emphasized that the symptoms of fatigue and anhedonia persist in individuals who had recovered from COVID-19. Therefore we specifically focused on fatigue as a frequent ongoing symptom in those subjects. Consistent with this finding, fatigue was the most common persistent COVID-19 symptom in our study, and individuals with prolonged fatigue had higher changes in MSQ total score and negative/somatic effects subgroup scores subgroup scores.

Individuals with increased menstrual pain severity showed higher anxiety levels.[10] The risk of developing depression, anxiety, and post-traumatic stress disorder is high in people who had recovered from COVID-

19, and this tendency is more common in women.[31] In our study, although the negative effects/somatic complaints subgroup scores increased in women after COVID-19, no correlation was identified between the coronavirus anxiety and changes in menstrual symptom scores. A possible reason is that the CAS is not a sensitive scale for evaluating anxiety disorders caused by post-traumatic stress or other reasons. In future studies, using a more comprehensive measurement tool to evaluate the relationship between menstrual symptoms and anxiety is recommended.

Zurawuecka et al.[32] have reported that an early age at menarche is associated with menstrual pain, and Anikwe et al.[33] have reported that the mean age at menarche is 13 ± 1.0 years and that menstrual pain is more common in this age group. However, Çakir et al.[34] did not identify ant relationship between menstrual pain and age at menarche.[34] We found no relationship with between age at menarche and the pain symptoms but observed a negative relationship with the coping methods subgroup scores. Moreover, the regression analysis showed that, each 1-year decrease in the age at menarche increased the change in MSQ by 0.82.

This finding may indicate an increased incidence of menstrual symptoms in women recovering from COVID-19 who were younger at menarche, and that women's ability to cope with menstrual symptoms may not have developed at an early age.

Li et al.[7] reported no difference in menstrual volume, sex hormones, and Anti-Müllerian hormone between women who had recovered from mild and severe COVID-19. Furthermore, the menstrual cycle duration was longer in women who had severe COVID-19 than in those who had recovered from mild COVID-19. In our study, only three individuals had moderate COVID-19, while the other individuals were asymptomatic or had only a mild disease. Therefore, menstrual symptoms were not compared according to the disease severity in our study. However, when the individuals were examined according to the time after COVID-19 diagnosis, the changes in the MSQ total scores and subgroup scores were not affected by the time after the illness. This result may be related to the presence of prolonged COVID-19 symptoms. Furthermore, it suggests that menstrual symptoms may also consider as an ongoing symptom of COVID-19.

Our study has some limitations. Since the menstrual cycle duration, menstrual volumes and sexual activity of the individuals were not evaluated. Therefore the relationship between increased menstrual symptoms after COVID-19 and these variables could not be explained. Since our participants were aged 18–45 years, our results may not be applicable to women beyond that age range who had been diagnosed with COVID-19 and are actively menstruating. The retrospective assessment of pre-COVID-19 menstrual symptoms is another limitation of our study.

In conclusion, we observed worsened menstrual symptoms, fatigue, and menstrual pain severity in women after diagnosis of COVID-19. In addition, we found that age at menarche, fatigue, and menstrual pain severity changes determined the changes in menstrual symptoms after COVID-19 diagnosis. Menstrual symptoms were more severe in women with prolonged fatigue, dyspnea, muscle–joint pain, and gastrointestinal symptoms. We examined the effects of COVID-19 on menstrual symptoms and determined the factors associated with menstrual symptom changes. We believe that the relationship between menstrual symptoms and menstrual cycle characteristics and long COVID-19 symptoms should be further examined in future studies with long-term follow-up periods.

REFERENCES

1. Huang H-H, Wang P-H, Yang Y-P, et al. A review of severe acute respiratory syndrome coronavirus 2 infection in the reproductive system. Journal of the Chinese Medical Association. 2020;83(10):895.

2. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. Jama. 2020;324(6):603-605.

3. Organization WH. Coronavirus disease 2019 (COVID-19): situation report, 82. 2020;

4. Seymen CM. Effects Of Covid-19 Pandemic On Female Fertility. Gazi Journal of Health Sciences. 5(3):1-7.

5. Jing Y, Run-Qian L, Hao-Ran W, et al. Potential influence of COVID-19/ACE2 on the female reproductive system. Molecular human reproduction. 2020;26(6):367-373.

6. Abhari S, Kawwass JF. Endometrial susceptibility to SARS CoV-2: explained by gene expression across the menstrual cycle? Fertility and Sterility. 2020;114(2):255-256.

7. Li K, Chen G, Hou H, et al. Analysis of sex hormones and menstruation in COVID-19 women of childbearing age. Reproductive biomedicine online. 2021;42(1):260-267.

8. Turpoğlu Çelik A. The Impacts Of Early Childhood Period On Family And Community Health, Democracy And Development. The Journal of Academic Social Sciences. 2015;13:240-263.

9. Güney E, Ünver H, Derya YA, Tuba U. Effects of Physical Exercise Levels on Menstrual Cycle. Journal of Duzce University Health Sciences Institue. 017;7(3):137-142.

10. Sönmezer E, Yosmaoğlu HB. Changes of menstrual attitude and stress perception in women with dysmenorrhea. Turkish Journal of Physiotherapy and Rehabilitation. 2014;25(2):56-62.

11. Malik VS, Kumar K, Kumar A, Behmani RK. Effect of Stress on Menstrual Cycle in Young Adolescent Female During COVID-19 Lockdown in India. 2020;

12. Bruinvels G, Goldsmith E, Blagrove R, Martin D, Shaw L, Piasecki J. How lifestyle changes within the COVID-19 global pandemic have affected the pattern and symptoms of the menstrual cycle. medRxiv. 2021;

13. Chesney MA, Tasto DL. The development of the menstrual symptom questionnaire. Behaviour Research and Therapy. 1975;13(4):237-244.

14. Güvenç G, Seven M, Akyüz A. Adaptation of the Menstrual Symptom Questionnaire into Turkish. TAF Prev Med Bull. 2014;13:367-374.

15. Langley G, Sheppeard H. The visual analogue scale: its use in pain measurement. Rheumatology international. 1985;5(4):145-148.

16. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of neurology. 1989;46(10):1121-1123.

17. Armutlu K, Korkmaz NC, Keser I, et al. The validity and reliability of the Fatigue Severity Scale in Turkish multiple sclerosis patients. International Journal of Rehabilitation Research. 2007;30(1):81-85.

18. Lee SA. Coronavirus Anxiety Scale: A brief mental health screener for COVID-19 related anxiety. Death studies. 2020;44(7):393-401.

19. Şayık D, Yiğit D, Açıkgöz A, Çolak E, Mumcu Ö. Turkish Validity and Reliability of the Coronavirus Anxiety Scale. Eskisehir Medical Journal. 2(1):16-22.

20. Kala M, Nivsarkar M. Role of cortisol and superoxide dismutase in psychological stress induced anovulation. General and comparative endocrinology. 2016;225:117-124.

21. Graziottin A, Zanello P. Menstruation, inflammation and comorbidities: implications for woman health. Minerva ginecologica. 2015;67(1):21-34.

22. Al-Jefout M, Seham A-F, Jameel H, Randa A-Q, Luscombe G. Dysmenorrhea: prevalence and impact on quality of life among young adult Jordanian females. Journal of pediatric and adolescent gynecology. 2015;28(3):173-185.

23. Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. Obstetrics & Gynecology. 2006;108(2):428-441.

24. Weinmann G, Zacur H, Fish J. Absence of changes in airway responsiveness during the menstrual cycle. Journal of allergy and clinical immunology. 1987;79(4):634-638.

25. Tan K, McFarlane L, Coutie W, Lipworth B. Effects of exogenous female sex-steroid hormones on lymphocyte β2-adrenoceptors in normal females. British journal of clinical pharmacology. 1996;41(5):414-416.

26. Gibbs C, Coutts I, Lock R, Finnegan O, White R. Premenstrual exacerbation of asthma. Thorax. 1984;39(11):833-836.

27. Başoğul C, Aydın Özkan S, Karaca T. The effects of psychoeducation based on the cognitive-behavioral approach on premenstrual syndrome symptoms: A randomized controlled trial. Perspectives in psychiatric care. 2020;56(3):515-522.

28. Kocaoz S, Cirpan R, Degirmencioglu AZ. The prevalence and impacts heavy menstrual bleeding on anemia, fatigue and quality of life in women of reproductive age. Pakistan journal of medical sciences. 2019;35(2):365.

29. Juhi A, Deepali A. Assessment of onset of the duration of fatigue in muscle using surface electromyography on women during the different phases of menstrual cycle. National Journal of Physiology, Pharmacy and Pharmacology. 2019;9(8):751-755.

30. El Sayed S, Shokry D, Gomaa SM. Post-COVID-19 fatigue and anhedonia: A cross-sectional study and their correlation to post-recovery period. Neuropsychopharmacology Reports. 2021;41(1):50-55.

31. Dai L-L, Wang X, Jiang T-C, et al. Anxiety and depressive symptoms among COVID-19 patients in Jianghan Fangcang Shelter Hospital in Wuhan, China. Plos one. 2020;15(8):e0238416.

32. Zurawiecka M, Wronka I. The Influence of Age at Menarche on the Menstrual Pattern of Polish University Students. Journal of Adolescent Health. 2021;68(1):210-212.

33. Anikwe CC, Mamah JE, Okorochukwu BC, Nnadozie UU, Obarezi CH, Ekwedigwe KC. Age at menarche, menstrual characteristics, and its associated morbidities among secondary school students in Abakaliki, southeast Nigeria. Heliyon. 2020;6(5):e04018.

34. Cakir M, Mungan I, Karakas T, Girisken I, Okten A. Menstrual pattern and common menstrual disorders among university students in Turkey. Pediatrics International. 2007;49(6):938-942.

Acknowledgments: The authors have no conflicts of acknowledgement.

Conflicts of Interest Disclosure: The authors have no conflicts of interest to disclose.

Clinical Trial Number: NCT04806815

TABLES

Table 1. Sociodemographic and clinical characteristics of the women who had COVID-19

	N (%) or Mean ±SD
Age (years)	26.08±6.62
BMI (kg/m²)	23.05±4.24
Menarche age (years)	13.28±1.35
Marital status	
Single	129 (71.7 %)
Married	51 (28.3 %)
Education	
Secondary School	9 (5 %)
Higher School	33 (18.3 %)
Bachelor	125 (69.4 %)
Master/Doctoral	13 (7.2 %)
Smoking history	

	N (%) or Mean ±SD
Smoking	36 (20 %)
Never smoked	124 (68.9 %)
Ex-smoker	20 (11.1 %)
Comorbidities	
None	154 (85 %)
Asthma	10 (5.6 %)
Vascular pathologies	5 (2.8 %)
Thyroid gland pathologies	3 (1.7 %)
Type 2 diabetes	4 (2.2 %)
Dislipidemia	5 (2.8 %)
Time after positive PCR test (days)	104.66±60.22
4-12 weeks	85 (47.2 %)
12 weeks-6 months	80 (44.4 %)
> 6 months	15 (8.3 %)
Prolonged COVID-19 symptoms	
Fatigue	95 (52.8 %)
Headache	58 (32.2 %)
Cough	33 (18.3 %)
Dyspnea	39 (21.7 %)
Muscle and joint pain	69 (38.3 %)
Secretion	28 (15.6 %)
Loss of smell and taste	45 (25 %)
Gastrointestinal problems	21 (11.7 %)
Coronavirus Anxiety Scale (0-20)	3.22±3.99

SD: standard deviation, BMI: body mass index, kg: kilogram, m: meter.

Table 2. Menstrual Symptom Questionnaire, Fatigue Severity Scale and menstrual pain scores before and after COVID-19

	Pre COVID-19 Mean±SD	Post COVID-19 Mean±SD	Δ Mean±SD	P
MSQ (22-110)	64.96±16.61	67.26±17.37	2.29±8.16	<0.001*
Factor 1- Negative effects / somatic complaints	36.14±9.72	37.46±10.11	1.32±4.70	<0.001*
Factor 2- Pain symptoms	18.04±5.24	18.76±5.44	0.72±2.96	0.001*
Factor 3- Coping methods	7.39±3.56	7.57±3.61	0.17±0.89	0.009*
FSS (9-63)	38.17±12.66	44.51±13.29	6.33±9.25	<0.001*
Menstrual Pain (0-10)	3.47±2.79	4.19 ±2.99	0.72±1.97	<0.001*

Δ: (post COVID-19) - (pre-COVID), MSQ: menstrual symptom questionnaire, FSS: fatigue severity scale, CI: confidence interval, *p<0.05.

Ταβλε 3. Τηε ςορρελατιονς βετωεεν Δ ΜΣΧ ανδ αγε, BMI, μεναρςη αγε ΄ΑΣ, Δ ΦΣΣ,

ανδ Δ μενστρυαλ παιν

	Δ MSQ	Δ Factor 1- Negative effects / somatic complaints	Δ Factor 2- Pain symptoms
Age	p=0.334	p=0.282	p=0.658
BMI	p=0.796	p=0.613	p=0.870
Menarch age	p=0.035*	p=0.032*	p=0.051
Coronavirüs anxiety scale	p=0.320	p=0.347	p=0.469
Δ FSS	p<0.001	p<0.001	p<0.001
Δ Menstrual Pain	p<0.001*	p<0.001*	p<0.001*

Δ: (post COVID-19) - (pre-COVID), BMI: body mass index, FSS: fatigue severity scale, MSQ: menstrual symptom questionnaire, CAS: coronavirus anxiety scale, *p<0.05.

Ταβλε 4. Μυλτιπλε ρεγρεσσιον αναλψσις φορ Δ ΜΣΧ

Dependent variables	Independent variables	B	Standart Error B	β	T	P	95% CI
ΔMSQ	ΔFSS	0.447	0.052	0.507	8.626	<0.001*	0.34/0.54
	Menarch age	-0.822	0.355	-0.136	-2.315	0.022*	-1.52/-0.12
	Δ Menstrual pain	1.379	0.242	0.334	5.697	<0.001*	0.90/1.85

Δ: (post COVID-19) - (pre-COVID), MSQ: menstrual symptom questionnaire, FSS: fatigue severity scale, CI: confidence interval, *p<0.05.

Ταβλε 5. Τηε ςομπαρισον οφ ΔΜΣΧ ιν τερμς οφ σοςιοδεμογραπηις φεατυρες, τιμε αφτερ ΠCΡ τεστ, ονγοινγ ̃Ο″ΙΔ-19 σψμπτομς ανδ μεδιςαλ τρεατμεντ δυρινγ ̃Ο″ΙΔ-19

	ΔΜΣΧ Mean±SD	P	Δ Φαςτορ 1 Mean±SD	Δ Φαςτορ 1 Mean±SD	p	Δ Φαςτορ 2 Mean±SD	p	Δ Φαςτορ 3 Mean±SD	P
Education level	**Education level**	**Education level**	**Education level**	**Education level**	**Education level**	**Education level**	**Education level**	**Education level**	**Ed lev**
Secondary School (n=9)	- 0.66±3.77	0.507	- 0.22±2.10	- 0.22±2.10	0.434	- 0.33±1.11	0.315	- 0.11±0.78	0.6
High School (n=33)	1.09±9.44		0.60±4.68	0.60±4.68		0.18±3.84		0±0.79	
Bachelor (125)	2.64±7.93		1.52±4.85	1.52±4.85		0.88±2.71		0.22±0.90	
Master/Doctoral (n=13)	4.00±8.97		2.23±4.43	2.23±4.43		1.30±3.49		0.38±1.12	
Prolonged COVID-19 symptoms	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Prolonged COVID-19 symptoms**	**Pr CO 19 sy to**
Headache yes=58 no= 122	3.01±8.53 1.95±7.99	0.264	1.50±5.0 1.23±4.56	0.290	0.290	1.01±2.99 0.58±2.95	0.454	0.27±0.89 0.13±0.89	0.2

	ΔMΣX Mean±SD	**P**	**Δ Φαστορ 1 Mean±SD**	**Δ Φαστορ 1 Mean±SD**	**p**	**Δ Φαστορ 2 Mean±SD**	**p**	**Δ Φαστορ 3 Mean±SD**	**P**
Fatigue yes=95 no=85	3.62±9.09 0.81±6.72	0.006*	2.12±4.94 0.42±4.26	0.004*	0.004*	1.03±3.43 0.37±2.29	0.340	0.27±1.01 0.07±0.73	0.0
Cough yes=33 no=147	4.24±12.15 1.85±6.94	0.800	2.03±6.80 1.16±2.03	0.956	0.956	1.54±4.19 0.53±2.59	0.163	0.48±1.41 0.10±0.72	0.1
Dyspnea yes=39 no= 141	4.61±9.14 1.65±7.78	0.046*	2.89±5.58 0.88±4.34	0.017*	0.017*	1.23±3.03 0.58±2.94	0.148	0.33±0.95 0.13±0.88	0.0
Muscle and joint pain yes=69 no=111	4.23±10.89 1.09±5.58	0.009*	2.33±6.05 0.69±3.50	0.002*	0.002*	1.31±4.01 0.35±1.99	0.271	0.37±1.16 0.05±0.65	0.0
Secretion yes=28 no=152	3.67±11.98 2.03±7.27	0.285	1.96±6.17 1.20±4.39	0.544	0.544	1.25±4.72 0.62±2.52	0.287	0.28±1.21 0.15±0.83	0.1
Loss of smell and taste yes=45 no=135	2.62±10.49 2.18±7.26	0.519	1.42±6.06 1.28±4.17	0.390	0.390	0.91±3.83 0.65±2.62	0.718	1.14±0.17 0.80±0.06	0.5
Gastrointestinal problems yes=21 no=159	5.04±9.76 1.93±7.89	0.183	2.71±6.82 1.13±4.34	0.196	0.196	1.61±2.87 0.69±2.96	0.022*	0.57±0.87 0.12±0.89	0.0
Smoking history	**Smoking history**	**Smoking history**	**Smoking history**	**Smoking history**	**Smoking history**	**Smoking history**	**Smoking history**	**Smoking history**	**Sm his to**
Never smoked (n=124)	2.03±7.90	0.634	1.14±4.41	1.14±4.41	0.292	0.69±2.98	0.999	0.14±0.82	0.6
Smoking (n=36)	2.41±7.72		1.33±4.86	1.33±4.86		0.83±2.64		0.13±0.68	
Ex-smoker (20)	3.7±10.53		2.4±6.05	2.4±6.05		0.70±3.46		0.45±1.50	
Time after positive PCR test	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Time after positive PCR test**	**Ti aft po tiv PC tes**
4-12 weeks (n=85)	2.61±8.15	0.891	1.36±4.46	1.36±4.46	0.876	0.85±3.06	0.570	0.27±1.06	0.4

	ΔΜΣΧ Mean±SD P	**Δ Φαστορ 1 Mean±SD**	**Δ Φαστορ 1 Mean±SD p**	**Δ Φαστορ 2 Mean±SD p**	**Δ Φαστορ 3 Mean±SD P**
12 weeks-6 months (n=80)	1.80±6.64	1.21±4.24	1.21±4.24	0.47±2.21	0.08±0.65
> 6 months (n=15)	3.13±14.18	1.66±7.80	1.66±7.80	1.26±5.24	0.13±0.99

SD: standard deviation, Δ: (post COVID-19) - (pre-COVID), Factor 1: negative effects/somatic complaints, Factor 2: pain symptoms, Factor 3: coping methods, PCR: polymerase chain reaction, *p<0.05.