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Original Article

Impact of COVID-19 on the symptoms of premenstrual syndrome

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Abstract

Background and aims: Individuals affected by COVID-19 exhibit a range of symptoms, including, but not limited to, cough and dyspnea. However, there is a limited understanding of the effects of this infection on the physiological well-being of women.

Methods: This quasi-experimental investigation aimed to examine the impact of COVID-19 on premenstrual syndrome (PMS). Participants included Iranian women of reproductive age (18-50 years) who completed a self-reported questionnaire regarding the occurrence of PMS symptoms in the first menstrual cycle following a COVID-19 infection, compared to the occurrence of these symptoms in the menstrual cycles prior to contracting the disease. The data were analyzed using SPSS software version 23, employing descriptive statistics, analysis of variance, and repeated measures analysis.

Results: Approximately 63.7% of participants experienced changes in the length of their menstrual cycles following a COVID-19 infection. Furthermore, COVID-19 exacerbated PMS symptoms in 80.65% of the participants. The most pronounced impact was observed on mood-emotional symptoms, followed by behavioral, physical, and personality symptoms, respectively. Statistical analysis revealed a significant difference in the mean scores among the four symptom categories ($P<0.001$).

Conclusion: The study indicates that COVID-19 may exacerbate both the physical and psychological symptoms of PMS in some women, significantly affecting mood, behavior, and personality. These findings underscore the potential negative effects of the virus on women's reproductive health and highlight the need for further research to explore the relationship between COVID-19 and women's health.

Keywords: COVID-19, Coronavirus, Genitalia, Menstruation, Premenstrual syndrome

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Introduction

In December 2019, a severe respiratory disease was first identified in Wuhan, China, rapidly spreading to numerous countries and affecting a significant number of individuals worldwide. The World Health Organization (WHO) designated this pandemic as COVID-19, which has since emerged as a critical international public health concern. Currently, it is understood that COVID-19 is caused by a novel virus belonging to the Coronaviridae family (1). COVID-19 presents clinically with symptoms such as fever, cough, fatigue, shortness of breath, and in some cases, more severe manifestations (2). A possible mechanism for acquiring COVID-19 involves the virus entering cells through its receptor, the angiotensin-converting enzyme 2 (ACE2) receptor. By penetrating the host cell membrane and fusing with it, the virus releases its genome into the host cell. This process enables the virus to utilize the host cell's organelles to replicate its RNA and form new virions, which are subsequently released to infect other cells (3) (Figure 1). In addition to respiratory symptoms, COVID-19 patients have been reported to experience multi-organ injuries, including cardiovascular and gastrointestinal disorders, as well as hepatic and kidney injuries (4,5). Although further studies

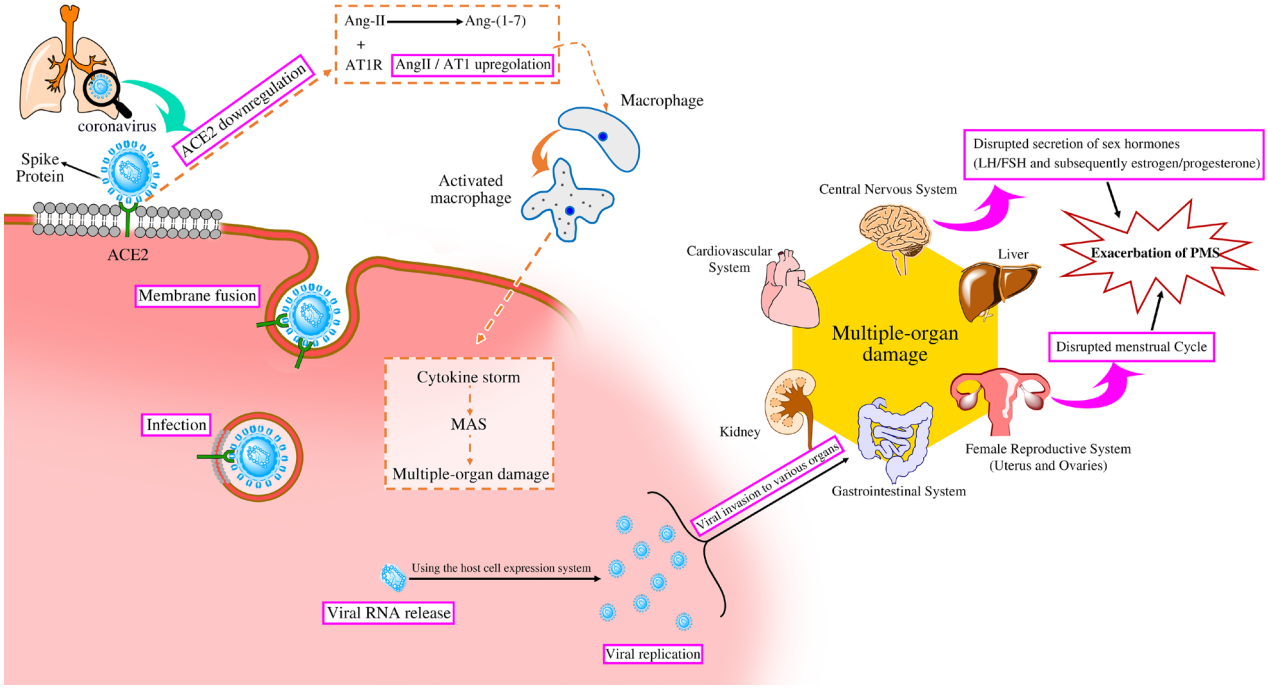

Figure 1. Mechanism of ACE2 downregulation and macrophage activation in COVID-19 pathology

are needed to confirm this claim, there is a possibility that the coronavirus may also attack and damage reproductive organs.

The prevalence of COVID-19 has negatively impacted various aspects of society's lives (6). As a consequence of the pandemic, individuals may experience changes in their sexual behavior (7). However, according to the WHO, sexual and reproductive health services are essential and should continue even during the coronavirus outbreak (8).

There have been several reports regarding the effects of COVID-19 and other epidemics on female reproductive system health (9-11). However, a study by Yuksel et al. found that there was an increase in menstrual disorders rather than vaginal infections during the COVID-19 pandemic (12).

Despite the efforts of various research groups worldwide to understand how COVID-19 affects the female reproductive system, the exact mechanisms underlying this phenomenon remain unclear (13). Consequently, there is a continued need for further studies in this area.

Given the widespread expression of ACE2 in the ovary, vagina, uterus, and placenta, along with the roles of ACE2, Ang-(1-7), and Ang-II in various processes related to the female reproductive system—including the regulation of follicle growth and ovulation (14,15)—it is plausible to hypothesize that the interaction between ACE2 and COVID-19 may potentially lead to damage in female reproductive tissues and processes.

Additionally, the brain's role in regulating the female menstrual cycle is evident. The hypothalamic-pituitary-ovarian (HPO) hormonal axis plays a crucial role in the female reproductive system (16). Given the expression of ACE2 in endocrine organs, including the pituitary gland and hypothalamus, it has been hypothesized that the hormonal functions of these endocrine glands may be affected by the coronavirus (17) (Figure 1).

Some previous studies indicate that the renin-angiotensin system (RAS) plays vital roles in various female reproductive organs, including the ovary (18,19). For instance, Angiotensin II (AngII) and its associated receptors, AT1R and AT2R, are known to regulate oocyte maturation and ovulation (20). Additionally, the RAS significantly influences the regulation of sex hormones (18).

Menstruation is a cycle characterized by the activity and balance of hormones secreted by the hypothalamus, pituitary gland, and ovaries, which periodically (monthly) affect the endometrium of the uterus (Figure 2) (21). Menstrual regulation can be disrupted by external factors such as infections, drug therapies, and dysfunctions in other organs (22).

Menstrual disorders can manifest as increased or decreased menstrual duration, changes in bleeding volume, painful menstruation, and premenstrual syndrome (PMS) (23). PMS is a collection of physical, psychological, emotional, and behavioral symptoms that typically arise about a week before menstrual bleeding (during the last week of the luteal phase) and can persist for several days after the onset of menstruation (Figure 2) (24). Common symptoms of PMS include anxiety, depression, irritability, nervous tension, unexplained crying, hot flashes, bloating, and breast pain. Approximately 80-90% of women of reproductive age experience PMS (25). While PMS is not life-threatening, it can significantly reduce the quality of life, fertility, and mental health of women (26).

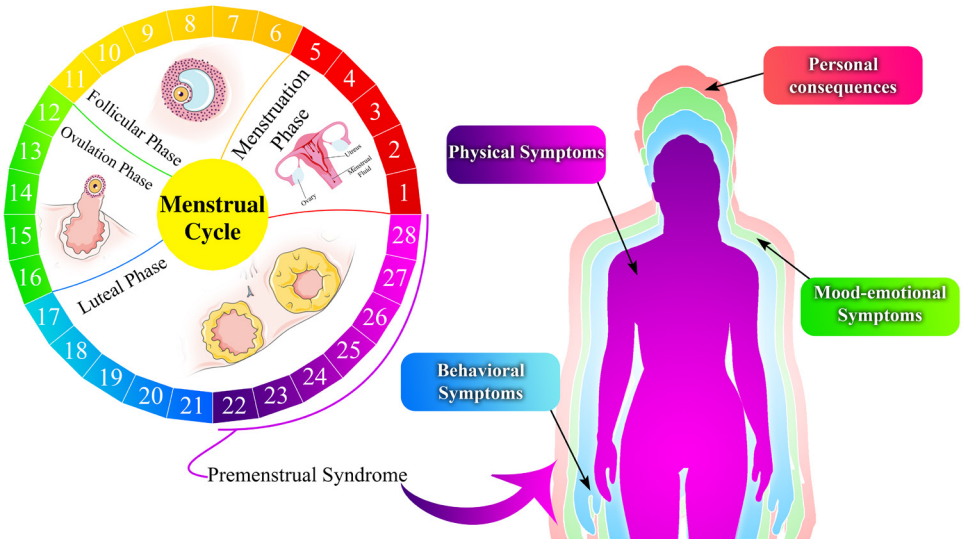

Figure 2. Phases of the menstrual cycle: from menstruation to PMS

In the present study, we investigate the effects of COVID-19 on the severity of PMS symptoms among Iranian women of childbearing age. Evaluating the impact of COVID-19 on PMS is crucial for increasing awareness regarding changes in PMS symptoms and for improving the physical and mental health of the target population. Furthermore, early detection of factors adversely affecting women's reproductive health is essential for preserving fertility within society and mitigating the multi-organ damage associated with the coronavirus.

Despite emerging evidence suggesting that COVID-19 may influence menstrual health, there is a significant lack of comprehensive studies specifically focusing on PMS among Iranian women. Prior research has indicated that psychological stressors related to the pandemic, such as heightened anxiety and changes in lifestyle, can exacerbate PMS symptoms; however, these findings are not universally applicable across different cultural contexts.

This research aims to fill this information gap by providing localized data that reflects the unique experiences of Iranian women during this unprecedented time. By examining how COVID-19 infection and associated stressors correlate with PMS severity, we hope to highlight critical areas for intervention and support within healthcare systems. Additionally, understanding these dynamics can inform public health strategies aimed at improving women's reproductive health outcomes in the face of ongoing global health challenges.

Materials and Methods

Study design and study population

This study, conducted in 2021, employed a retrospective, descriptive-analytical, and cross-sectional design to examine the effects of COVID-19 on the prevalence and severity of changes in PMS symptoms. The sample size was determined to be 146 individuals, based on calculations from Singh et al. and accounting for a 15% attrition rate (27). Participants included women of childbearing age (18–50 years) from various cities in Iran who had contracted COVID-19 within the four months preceding the study. Recruitment was conducted through voluntary sampling.

Inclusion criteria for the study included: consent to participate, normal physical and mental health, familiarity with PMS symptoms, no surgeries or medications affecting the menstrual cycle within three months prior to the study, COVID-19 infection within the past four months, and completion of all questions on the questionnaire.

Exclusion criteria comprised a history of menstrual irregularities regarding the duration of the menstrual period, volume of bleeding, and abnormal pain; use of medications affecting the menstrual cycle; a history of neuropsychiatric disorders and related medication use; as well as pregnancy or breastfeeding.

Data collection tools, participant consent and data analysis methods

To gather data, an online questionnaire was developed that assured participants of confidentiality regarding their responses. This questionnaire was structured based on the trajectory of PMS symptoms and demonstrated a high level of reliability, with a Cronbach's alpha exceeding 0.93 as reported by Endicott et al (28). Notably, in the present study, Cronbach's alpha was calculated to be 0.92, indicating strong internal consistency. The content validity of the questionnaire was affirmed by three experts in the field.

The initial section of the questionnaire collected demographic information, including age, height, weight, age of menstrual onset, and any changes in menstrual cycle length following COVID-19 infection. The subsequent 28 questions focused on common PMS symptoms, prompting participants to compare their experiences during their first menstrual period after COVID-19 with those from previous cycles. All participants provided

informed consent for their responses to be utilized in this study.

Responses were evaluated using a five-point Likert scale ranging from "none" (0) to "very severe" (4), allowing for a comprehensive assessment of symptom severity. The total possible score ranged from 0 to 112, where a score of 0 indicated no change in PMS symptom severity and a score of 112 reflected significant variation. Symptoms were categorized into four groups:

1. Physical symptoms: These included migraine, breast tenderness, joint or muscle pain, body rigidity, obesity, bloating, blurry vision, poor motor coordination, fatigue, dark circles under the eyes, and watery eyes.
2. Mood-emotional symptoms: This category encompassed depression, sudden anger, restlessness, frustration, crying, hypersensitivity to negative responses, feelings of being out of control, lack of interest in normal activities, difficulty concentrating, sensitivity to unforeseen events, panic levels, mood swings, and anxiety.
3. Behavioral symptoms: Symptoms in this group included insomnia or hypersomnia, overeating or cravings for certain foods, excessive alcohol consumption, and lack of energy.
4. Personality consequences: This category specifically addressed the parameter of suspicion.

Upon completion of data collection, questionnaires were coded for analysis using descriptive statistics and analysis of variance (ANOVA) in SPSS software version 23. A repeated measures test was applied to compare mean scores across different symptom categories, with statistical significance set at a P value of < 0.05.

Results

Menstrual cycle changes due to COVID-19

The questionnaires completed by 146 Iranian women of childbearing age (18-50 years old) who had experienced COVID-19 within the last four months were statistically analyzed. Among the participants, 63.7% reported changes in their menstrual cycle length, indicating either an increase or decrease in the number of days. Additionally, 80.65% of respondents experienced an exacerbation of PMS symptoms following COVID-19 infection.

Table 1 illustrates the changes in menstrual cycle length in relation to body mass index (BMI) and age range.

Table 1. The analysis of alterations in menstrual cycle length following COVID-19 by age and body mass index (BMI)

	% People with a change in menstrual cycle length
BMI	
<18.5 (Underweight)	66.67
18.5-24.9 (Normal Weight)	65.56
25.0-29.9 (Overweight)	63.41
≥30.0 (Obese)	44.44
Age	
18-25	67.44
26-35	68.18
36-50	57.63

Changes in PMS symptoms due to COVID-19 (changes in distribution of symptoms and scores)

According to the score averages of the respondents, the highest effect of COVID-19 was observed in the mood-emotional aspects of PMS, followed by behavioral, physical, and personality consequences, respectively (Figure 3a). It is important to note that due to the unequal number of questions for each symptom category, the average score of each group of symptoms was considered for further analysis. The hypothesis that there was a significant change in the severity of each symptom after being infected with coronavirus was confirmed, with a P value of 0.

Additionally, Figure 3b illustrates that the most substantial changes in the distribution of symptoms were related to physical, mood-emotional, and behavioral symptoms, followed by personality consequences.

To determine whether there was a significant difference between the means of the four symptom categories, dependent response tests, or repeated measures ANOVA, were utilized. The assumption of homogeneity of variance was assessed using Mauchly's Sphericity test. The value of the test statistic was 38.410, and with a P value of 0, the assumption of homogeneity of variances was rejected. Consequently, the Greenhouse-Geisser test statistic was employed to examine the differences between the overall mean scores of the symptoms. The results indicated a significant difference, with $F = 61.567$ and a p-value of 0, demonstrating that the mean scores of individuals across the four symptom categories were significantly different.

Figure 3a presents a representation of the mean scores for each symptom category. The severity (Mean ± SD) and distribution (Percentage) of changes in PMS symptoms due to COVID-19 are detailed in Table 2. According to the obtained data, the most severe changes were noted in symptoms of fatigue, insomnia or hypersomnia, and lack of energy, while the least changes were observed in symptoms of excessive alcohol consumption, watery eyes, and suspicion (Figure 3c).

Moreover, the highest distribution of change in symptoms was related to fatigue, lack of energy, and mood swings, whereas the lowest distribution of change was observed in excessive alcohol consumption, watery eyes, and suspicion (Figure 3d).

BMI and age-related analysis

A descriptive representation of the four general symptoms in relation to BMI categories is shown in Table 3. According to the results, women classified as obese experienced more severe changes (Mean ± SD) in PMS symptoms compared to those who were overweight, of healthy weight, and underweight, respectively. However,

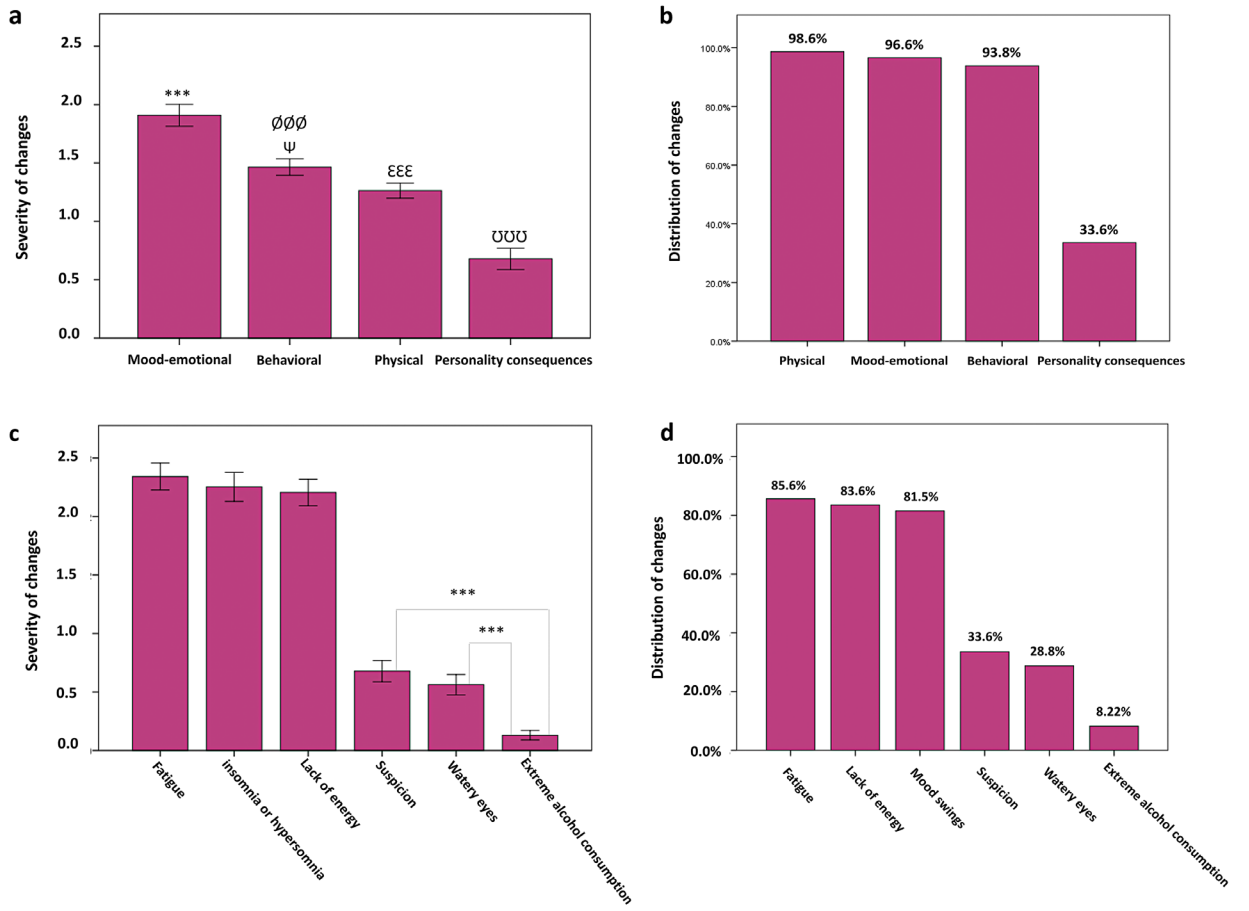

Figure 3 (a, b, c, d). Impact of COVID-19 infection on PMS symptom distribution and severity: statistical analysis of mood-emotional, physical, behavioral, and personality consequences. * Statistically significant differences between mood-emotional and physical symptoms or personality consequences. Ψ: statistically significant differences between mood-emotional and behavioral symptoms group. Ø: statistically significant differences between behavioral symptoms group and personality consequences. Ɛ: statistically significant differences between physical symptoms and personality consequences. Ʊ: statistically significant differences between personality consequences and mood-emotional, behavioral or physical symptoms. (c and d) All symptoms were analyzed separately (mean ± SD, *** $P<0.001$).

as indicated in Table 1, the group of underweight women had a higher number of individuals affected by COVID-19 compared to the group of obese women, which had fewer affected individuals relative to the other groups. Notably, all underweight participants reported experiencing all symptoms except for personality consequences (Table 3).

The analysis revealed that the changes in mood-emotional symptoms ($P=0.849$) and behavioral symptoms ($P=0.749$) were not significantly different among women across various BMI categories. While the severity of changes in physical symptoms tended to increase with higher BMI, the analysis of variance did not show a significant difference ($P=0.073$). Furthermore, in the analysis regarding the difference in scores for personality outcomes across the four BMI categories, no significant difference was observed at a significance level of 0.05 ($P=0.347$).

Table 4 provides a descriptive representation of the incidence of the four symptoms across different age groups. The data reveal that COVID-19 had the highest impact, both in terms of distribution (percentage) and severity (Mean ± SD), in the age range of 26-35 years for all assessed symptoms.

In examining the various age groups, a consistent trend emerged, indicating that the greatest influence of COVID-19 was observed on mood-emotional symptoms, followed by behavioral, physical, and personality symptoms, respectively. This pattern suggests that individuals aged 26-35 may experience more pronounced effects from COVID-19 regarding their PMS symptoms, highlighting a potential area for targeted support and intervention for this demographic.

Discussion

The COVID-19 pandemic has profoundly influenced numerous aspects of life, including cultural, social, economic, and psychological challenges. A wealth of studies has explored its effects on health during and after infection, highlighting the multifaceted nature of this global crisis (29,30). Among the various health-related issues impacted by COVID-19, the menstrual cycle and PMS have emerged as significant areas of concern (22,31,32).

The present study, based on self-reported questionnaires from 143 Iranian women of childbearing age (18-50 years), indicates that menstrual cycle parameters—

Table 2. Distribution of severity and percentage changes in PMS parameters

	% people with changes in symptoms	Mean ± SD
Parameter (Physical)		
Migraine symptoms	43.15	1.06 ± 0.12
Breast tenderness	41.78	0.95 ± 0.11
Joint or muscle pain	67.12	1.71 ± 0.12
Rigid body	72.60	1.66 ± 0.11
Obesity	60.96	1.40 ± 0.12
Swelling	45.21	1.09 ± 0.12
Blurry vision	35.62	0.71 ± 0.10
Poor motor coordination	43.15	0.88 ± 0.10
Fatigue	85.62	2.34 ± 0.11
Dark circles under the eyes	61.64	1.54 ± 0.12
Watery eyes	28.77	0.56 ± 0.09
Parameter (Mood-emotional)		
Depression	69.17	1.53 ± 0.11
Sudden anger	76.03	1.99 ± 0.12
Restlessness	79.45	1.99 ± 0.12
Frustration	71.92	1.76 ± 0.12
Crying, hypersensitivity to a negative response	71.23	1.69 ± 0.12
Feeling out of control	71.92	1.74 ± 0.12
Lack of interest in normal activities	69.86	0.76 ± 0.12
Difficulty concentrating	72.60	1.77 ± 0.12
Sensitivity to unpredictable events	72.60	1.82 ± 0.12
Level of getting panic	56.84	1.18 ± 0.11
Mood swings	81.51	2.09 ± 0.12
Level of anxiety	74.65	1.83 ± 0.12
Parameter (Behavioral)		
Insomnia or hypersomnia	80.14	2.25 ± 0.12
Overeating or cravings for certain foods	54.79	1.27 ± 0.12
Excessive alcohol consumption	8.22	0.13 ± 0.04
Lack of energy	83.56	2.21 ± 0.11
Parameter (Personal consequences)		
Suspicion	33.56	0.68 ± 0.09

including period length and various PMS symptoms (such as physical, mood-emotional, behavioral symptoms, and personality consequences)—may be affected by COVID-19 infection.

Supporting this, a recent 2023 study examining the relationship between COVID-19 and the menstrual cycle in over 15 000 individuals found that 75% reported changes in their menstrual cycle, including alterations in cycle length and duration of bleeding. Additionally, 50% indicated a worsening of psychological symptoms associated with PMS (33). Furthermore, a 2021 study by Li et al found that 25% of participants reported changes in menstrual volume, while 28% experienced alterations in cycle duration due to COVID-19 (22).

In the present study, it was observed that while the highest percentage of individuals reporting changes in menstrual cycle length and PMS alterations were underweight women, the most severe PMS changes were noted among obese women. This suggests a complex relationship between BMI and the severity of PMS symptoms in the context of COVID-19.

Abnormal concentrations of sex hormones in some women with COVID-19 can directly affect menstrual cycle length (22). Notably, patients with severe forms of COVID-19 tend to experience more pronounced menstrual disorders and are more likely to be obese or

Table 3. Descriptive analysis of the prevalence of four symptoms across various BMI groups

BMI	Symptom	% People with symptoms change	Mean ± SD
<18.5 (Underweight)	Mood-emotional	100	1.653 ± 0.478
	Behavioral	100	1.500 ± 0.323
	Physical	100	1.030 ± 0.210
	Personality consequences	33.33	0.5 ± 0.34
18.5-24.9 (Normal Weight)	Mood-emotional	97.78	1.814 ± 0.110
	Behavioral	94.44	1.406 ± 0.083
	Physical	98.89	1.148 ± 0.077
	Personality consequences	36.67	0.71 ± 0.16
25.0-29.9 (Overweight)	Mood-emotional	92.68	1.650 ± 0.157
	Behavioral	92.68	1.579 ± 0.147
	Physical	97.56	1.488 ± 0.142
	Personality consequences	26.82	0.51 ± 0.15
≥30.0 (Obese)	Mood-emotional	100	1.824 ± 0.370
	Behavioral	88.89	1.500 ± 0.331
	Physical	100	1.546 ± 0.262
	Personality consequences	33.33	1.22 ± 0.62

Table 4. Descriptive analysis of the prevalence of four general symptoms according to age classification

Age	Symptom	% people with symptoms change	Mean ± SD
18-25	Mood-emotional	97.67	1.672 ± 0.165
	Behavioral	93.02	1.361 ± 0.122
	Physical	97.67	1.203 ± 0.101
	Personality consequences	34.88	0.7 ± 0.18
26-35	Mood-emotional	95.45	1.858 ± 0.151
	Behavioral	97.73	1.511 ± 0.123
	Physical	100	1.238 ± 0.126
	Personality consequences	38.64	0.73 ± 0.16
36-50	Mood-emotional	96.61	1.755 ± 0.134
	Behavioral	91.53	1.504 ± 0.116
	Physical	98.31	1.325 ± 0.111
	Personality consequences	28.81	0.63 ± 0.15
18-50	Mood-emotional	96.57	1.762 ± 0.086
	Behavioral	93.83	1.465 ± 0.07
	Physical	98.63	1.263 ± 0.066
	Personality consequences	35.56	0.68 ± 0.09

have metabolic syndrome (34).

Moreover, several studies indicate that COVID-19 vaccination, similar to contracting the virus, is associated with menstrual cycle disorders in a significant percentage of women (35). Notably, these disorders appear to worsen following the administration of the second dose of the vaccine (36). While the impact of the COVID-19 vaccine on PMS has been minimally studied, some research has demonstrated changes in PMS symptoms following the first, second, and third doses of certain COVID-19 vaccines (37,38).

While Eshaghi et al. reported that the frequency of PMS symptoms was not influenced by age (39), the present study found a significantly greater change in symptom severity among women aged 26-35 compared to other age groups. Notably, this age range also exhibited the highest percentage of individuals experiencing changes in menstrual cycle length.

The adverse psychological effects of COVID-19 have been extensively documented across various studies. For instance, research conducted among a Chinese population by Wang et al found that 16.5% of participants reported symptoms of depression, while 28.8% reported symptoms of anxiety during the pandemic (40). Similarly, Sahin et al. examined PMS symptoms in individuals with and without COVID-19, revealing that those affected by the virus experienced more pronounced depression and sleep disorders (31).

In a study conducted in Turkey that investigated the relationship between PMS symptoms and COVID-19 distress, the highest prevalence of changes in PMS symptoms was associated with physical symptoms, such as abdominal pain (78.6%), and psychological symptoms, including mood changes (76.3%) (32). The present study also observed the highest percentage of changes in physical symptoms, followed by mood-emotional changes, indicating consistency with existing literature.

Notably, the study by Yüksekol et al reported that the rate of complaints regarding the exacerbation of PMS symptoms during the COVID-19 pandemic was 22% (32). In contrast, the present study found that COVID-19 exacerbated PMS symptoms in 80.65% of participants. This discrepancy may be attributed to social and cultural differences, variations in age ranges, and the characteristics of the populations studied. Additionally, individual personality traits could influence the prevalence of PMS symptom complaints (41).

Disorders such as depression, stress, mood swings, irritability, anger, attention deficit, emotional numbness, and sleep disturbances resulting from COVID-19 restrictions bear a striking resemblance to PMS symptoms (42,43). Research indicates that effective stress management can significantly reduce mood and behavioral symptoms, although it tends to have a lesser impact on the physical symptoms of PMS (39). This aligns with the present study's findings, which demonstrate the greatest severity in mood-emotional and behavioral symptoms. However, in terms of distribution, physical symptoms had the highest percentage, followed by mood-emotional, behavioral, and personality symptoms.

The present study does have some limitations. First, the sample size was relatively small. Although this limitation can be addressed through various statistical analysis methods, it is acknowledged that a larger sample population would likely yield more reliable results. Second, we lacked access to biological samples (such as blood samples) from participants, who were drawn from different provinces of the country.

Conclusion

The results of this study indicate that COVID-19 may exacerbate the physical and psychological symptoms of PMS in some women. The most pronounced effects of COVID-19 were observed in mood-emotional, behavioral, and physical symptoms, as well as personality consequences. These findings offer valuable insights into the potential negative impact of the coronavirus on women's reproductive health. Furthermore, they underscore the necessity for additional research to deepen our understanding of the relationship between COVID-19 and women's health.

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Authors' Contribution

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Writing–review & editing: Maryam Khaleghi, Manizheh Goudarzi, Seyyed Shamsadin Athari, Zahra Gorgin Karaji.

Competing Interests

This study does not present any conflicts of interest.

Ethical Approval

It is important to highlight that, in accordance with the ethics code 1400-791, Ayatollah Boroujerdi University has certified the ethical standards adhered to in this research. It is noteworthy that no clinical tests or drug consumption have been conducted by the target population in this study.

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