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Original Article

Evaluation of menstrual cycle parameters under the influence of stress

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Abstract

Menstrual cycle is highly sensitive to the influence of external and internal factors. Stress, associated with adverse consequences for the female organism, leads to dysfunction of the menstrual cycle and, consequently, reproductive health disorders. The investigation of the impact of chronic stress on the female reproductive sphere convincingly demonstrates the role of external triggering factors in the development and functioning of the menstrual cycle, which serves as a marker of reproductive health. Simultaneously, it opens up broad possibilities for detailing aspects of this pathological process, taking into account the stress factor. The question of the difficulty of identifying individuals experiencing the effects of chronic stress has always arisen, particularly during the COVID-19 pandemic. Therefore, previous studies have yielded conflicting results regarding the influence on the menstrual cycle under these conditions. In light of these findings, further in-depth research on this issue is crucial and promising.

Keywords: reproductive system, anxiety, COVID-19, stress-induced.

Introduction

A normal menstrual cycle is a fundamental indicator of satisfactory female reproductive health. Its functioning is orchestrated through the coordinated operation of the hypothalamus-pituitary-ovarian system based on the principle of feedback. Dysfunctions in the menstrual cycle are a prevalent issue in today's society and adversely impact the physical and psychoemotional aspects of women's health. Technological disasters, pandemics, and wars have significantly increased the frequency of manifestations of this pathology [1-4].

The COVID-19 pandemic, which has been ongoing for over four years amid the constant mutation of the virus, has manifested in various clinical forms. Over the entire period of the pandemic, as of December 31, 2023, the World Health Organization recorded 773,819,856 cases of the disease, with a death toll of 7,010,568. According to the findings of Nengzhuang Wang, Lina Qin, Long Ma, Hongli Yan, Indu Sharma, Priti Kumari, Anuradha Sharma, and Subhas Chandra Saha, COVID-19, in addition to respiratory disorders, induces disruptions in the reproductive system and is characterized by significant changes in psychoneurological status [5, 6].

Observations of the impact of COVID-19 on the body objectively demonstrate significant disruptions to psychomental health, particularly concerning sleep disorders, anxious reactions, and depressive states, which result from the dysfunction of extrahypothalamic structures [7-11]. Given the substantial role that neurotransmitters play in the regulation of the menstrual

cycle, the negative impact of COVID-19 on the reproductive sphere is entirely predictable.

It is known that the female body is more sensitive to the effects of stressors than the male body. Ongoing research worldwide explores the pathogenesis of the impact of COVID-19 consequences, particularly as a stress trigger on menstrual cycle parameters. The pathogenesis of stress-induced disorders in the reproductive sphere results from the disruption of the hypothalamus-pituitary-adrenal axis: corticotropin-releasing hormone inhibits the secretion of hypothalamic gonadotropin-releasing hormone, especially the pulsatile rhythm generator region of the latter in the hypothalamus. On the other hand, glucocorticoids suppress the synthesis of pituitary luteinizing hormone and the secretion of ovarian steroid hormones. The activation of these stress-responsive system components leads to prolonged adverse effects on female reproductive health [12].

There are often difficulties in determining the correlation of a stressor as the cause of certain diseases due to the lack of objective diagnostic markers for stress-induced pathology.

As of today, there is a limited amount of research on assessing the impact of COVID-19-related stress on the female reproductive system. According to the findings of Omer Demir's study, involving 263 participants, a decrease in the volume of menstrual discharge and the duration of menstruation was observed [13]. However, research by Taha Takmaz, Ibrahim Gundogmus, and others, which included 952 female healthcare workers, showed an increase in the number of irregular menstrual cycles, anxiety, and depressive disorders considered consequences of the COVID-19 pandemic. As a result of this study, it was revealed that 29% of women with irregular menstrual cycles had higher anxiety and stress levels compared to 71% of women with normal menstrual cycles [14].

Two independent studies by R. Muharam, Feranindhya Agiananda, and Shannon M. Malloy have confirmed data regarding an increase in irregular menstrual cycles and menstrual blood volume after recovering from COVID-19 [15, 16]. Data from Brian T. Nguyen and others, who analyzed 18,076 Natural Cycles app users, indicate that 45.4% experienced an increase in anxiety levels associated with the pandemic, with no significant changes in menstrual cycle parameters. As a result, this study did not demonstrate significant associations between changes in stress levels during the pandemic and abnormal cycle parameters [17]. Therefore, existing studies provide evidence of some impact of COVID-19 on the nature of menstrual cycle parameters [18-21].

The wide range of interpretations in research results studying the impact of COVID-19 on various systems and organs of the human body, including the reproductive system, can be explained by the absence of unified approaches in assessing menstrual cycle parameters in conditions of comorbidity and the COVID-19 pandemic.

Therefore, an in-depth study of menstrual cycle characteristics in women of reproductive age will allow researchers to broaden their understanding in this direction and develop an algorithm of actions with a personalized approach for correcting identified disruptions.

Material and methods

An observational study was conducted to assess the menstrual cycle status before and after exposure to a stressor (before and after contracting COVID-19). The survey, titled "Impact of COVID-19-related Stress on the Menstrual Cycle", was developed by us in an online format using Google Forms and in paper format. It was validated for relevance and distributed on various social media platforms, as well as among patients and hospital staff, to achieve a broader sample. The questionnaire comprised several sections, including identification data, obstetric, gynecological, and somatic history, anthropometric indicators, characteristics of the MC, and details about the course of COVID-19 (outpatient/inpatient treatment). The effects of COVID-19-related stress on the menstrual cycle are presented in Table 1.

The questionnaire was divided into two parts: the first included characteristics of menstrual cycle parameters before the episode of COVID-19, and the second covered the characteristics of current menstrual cycle parameters. The assessment of menstrual cycle characteristics was conducted by women independently through responses to questions.

The questionnaire we developed was supplemented with the Perceived Stress Scale (PSS-10), which was used to assess the anxiety level. The self-administered questionnaire for determining the level of subjective stress consisted of 10 questions, evaluated on a 5-point Likert scale (0-never, 1-almost never, 2-sometimes, 3-fairly often, 4-often). The scoring range from 0 to 40 allowed for categorizing stress levels: 0-13 - low, 14-27 - moderate, and 27-40 - high. The Perceived Stress Scale (PSS-10) is presented in Table 2.

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A total of 930 women participated in the survey. The relevance of the study was enhanced by a differential approach in forming the main research groups, consisting of 550 women. Exclusion factors included age below 18 and above 45 years; use of hormonal contraception/antidepressants; presence of concomitant endocrine disorders; body mass index less than 18.5 or greater than 24.9; pregnant and lactating women; chronic gynecological diseases that could affect pathological changes in the menstrual cycle; women with mental and behavioral disorders classified as Class V of ICD 11. Statistical analysis was performed using Microsoft Excel. After forming the research groups, 550 patients remained in the study.

Results and discussion

The average age of the examined patients was 29±11 years. Reproductive history data revealed the following pattern: 16.7% had one pregnancy, 13% had two, and 9% had three or more pregnancies. Among the examined individuals, 21% experienced miscarriages in the form of both early and late abortions, and 11% had preterm labor.

The duration of menstruation before the onset of stress was within the normal range in 86% (475 women), prolonged in 6% (31 women), and shortened in 8% (44 women). The duration of menstruation before stress is presented in Figure 1. After the onset of stress,

Table 1: The effects of COVID-19-related stress on the menstrual cycle.

Age _____

Weight _____

Height _____

Number: pregnancies ☐ births ☐ miscarriages ☐

Treatment of COVID-19: outpatient ☐ /inpatient ☐

	Yes		No	
Hormonal contraception				
Other diseases				
Bad habits				
Menstrual cycle	Before stress		After stress	
	Duration			
<4 days				
4–8 days				
>8 days				
	Frequency			
24 days				
24–38 days				
>38 days				
	Yes	No	Yes	No
Regular				
Painful (estimate in points 3+2+1+0)				
The need to change hygiene products at night				
The presence of blood clots >1 cm				
The maximum number of hygiene products per day				
Intermenstrual bleeding				

Table 2: Perceived Stress Scale (PSS-10).

1. In the last month, how often have you been upset because of something that happened unexpectedly?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

3. In the last month, how often have you felt nervous and stressed?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

4. In the last month, how often have you felt confident about your ability to handle your personal problems?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

5. In the last month, how often have you felt that things were going your way?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

6. In the last month, how often have you found that you could not cope with all the things that you had to do?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

7. In the last month, how often have you been able to control irritations in your life?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

8. In the last month, how often have you felt that you were on top of things?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

9. In the last month, how often have you been angered because of things that happened that were outside of your control?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

this parameter remained normal in 79% (433 women), prolonged menstruation increased to 8% (46 women), and shortened menstruation increased to 13% (71 women). Thus, according to the survey results, disturbances in the duration of menstruation increased by 1.56 times after experiencing COVID-19—the duration of menstruation after stress is presented in Figure 2.

Before the onset of stress, the menstrual cycle duration was within the normal range in 80% (440 women), with a prolonged cycle observed in 14% (77 women) and a shortened cycle in 6% (33 women). The frequency of the menstrual cycle before stress is presented in Figure 3. After experiencing COVID-19, the cycle duration within 24-38 days was maintained in 72% (394 women), cycles >38 days were diagnosed in 17% (93 women), and cycles <24 days increased from 6% to 11%. Thus, under the influence of stress, abnormal menstrual cycle duration increased by 1.41 times compared to the pre-pandemic COVID-19 period. The frequency of the menstrual cycle after stress is presented in Figure 4.

Among all respondents, the menstrual cycle was regular before stress in 86% (472 women), while irregular cycles were observed in 14% (78 women). After experiencing stress, the number of women with regular menstrual cycles decreased by 15%, and the incidence of irregular menstrual cycles increased from 14% to 29%. The regularity of the menstrual cycle before and after stress is presented in Figures 5 and 6.

Having assessed the pain intensity during menstruation before stress, it was found that 15% (82 women) reported complete absence of menstrual pain, 37% (204 women) rated the pain sensations at 1 point, 36% (198 women) at 2 points, and 12% (66 women) indicated maximum menstrual pain at 3 points. The pain

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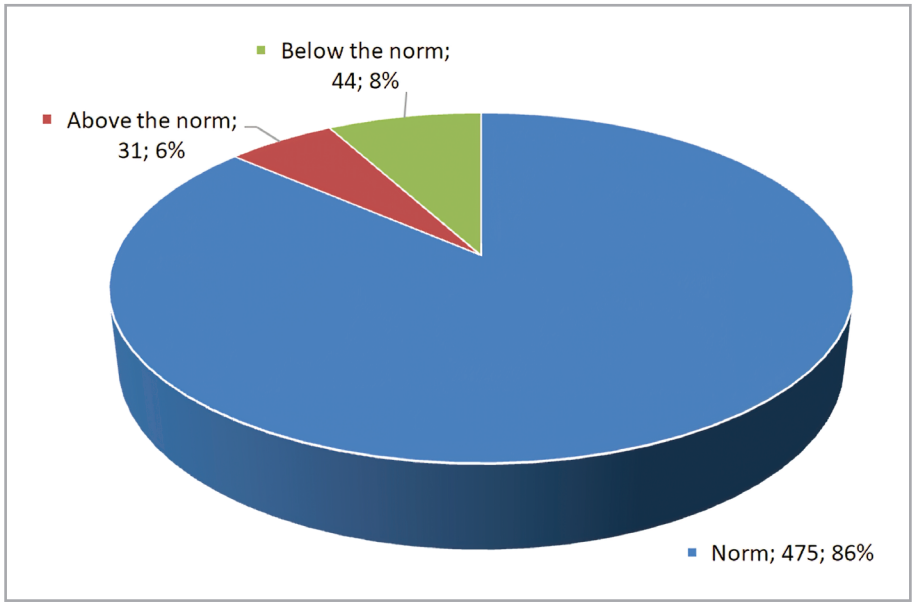

Figure 1: The duration of menstruation before stress.

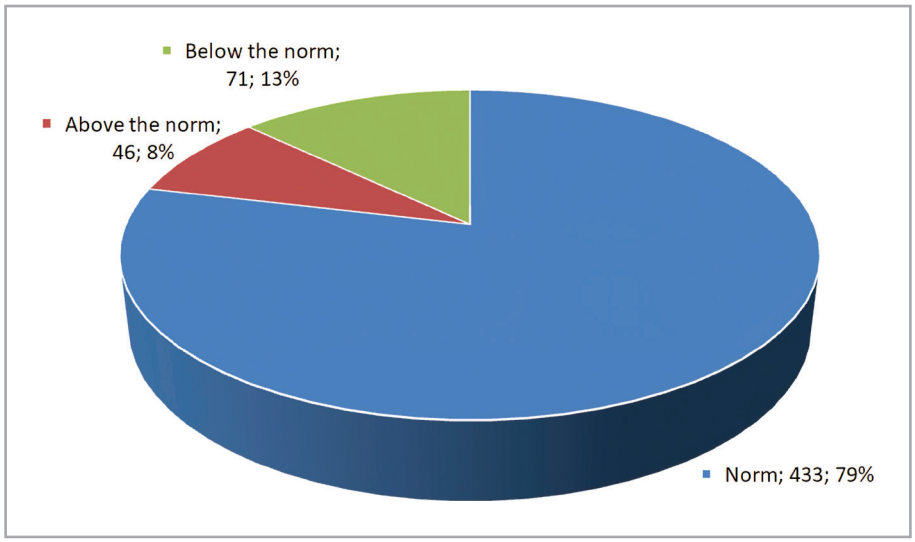

Figure 2: The duration of menstruation after stress.

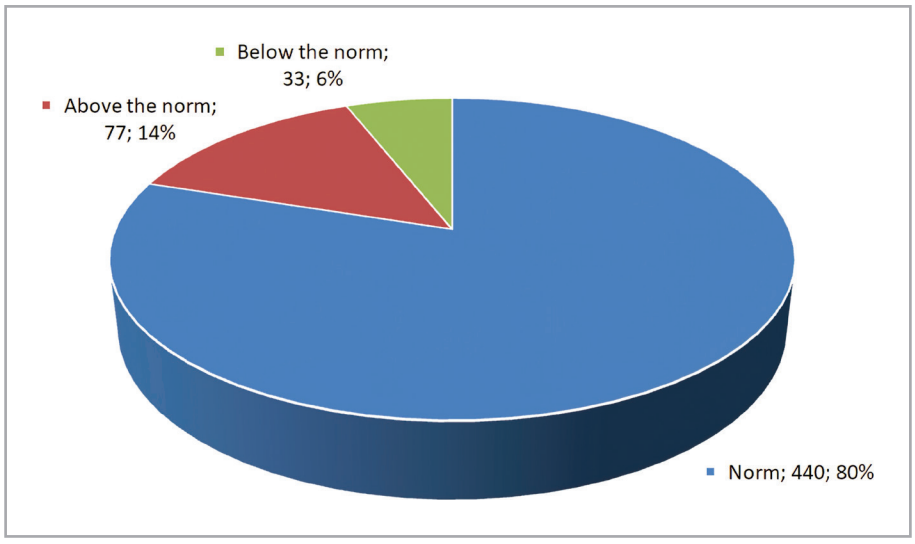

Figure 3: The frequency of the menstrual cycle before stress.

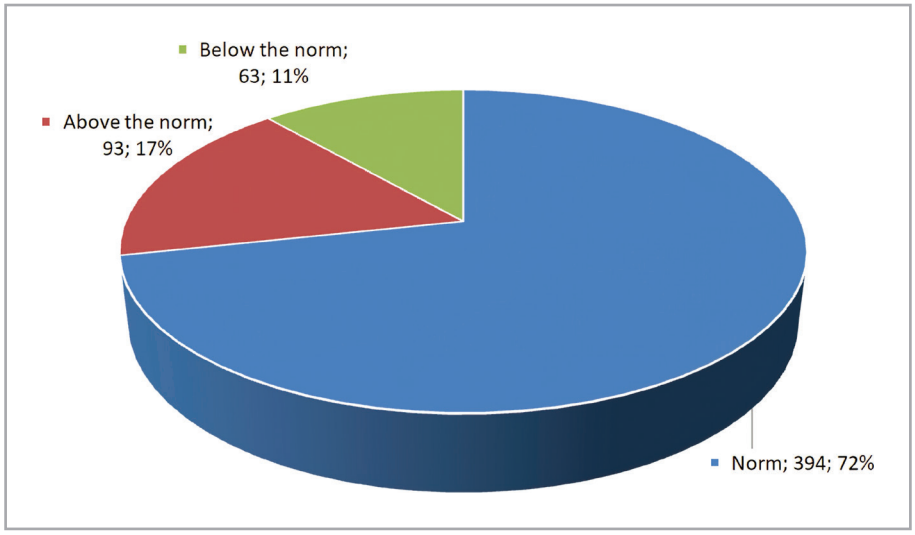

Figure 4: The frequency of the menstrual cycle after stress.

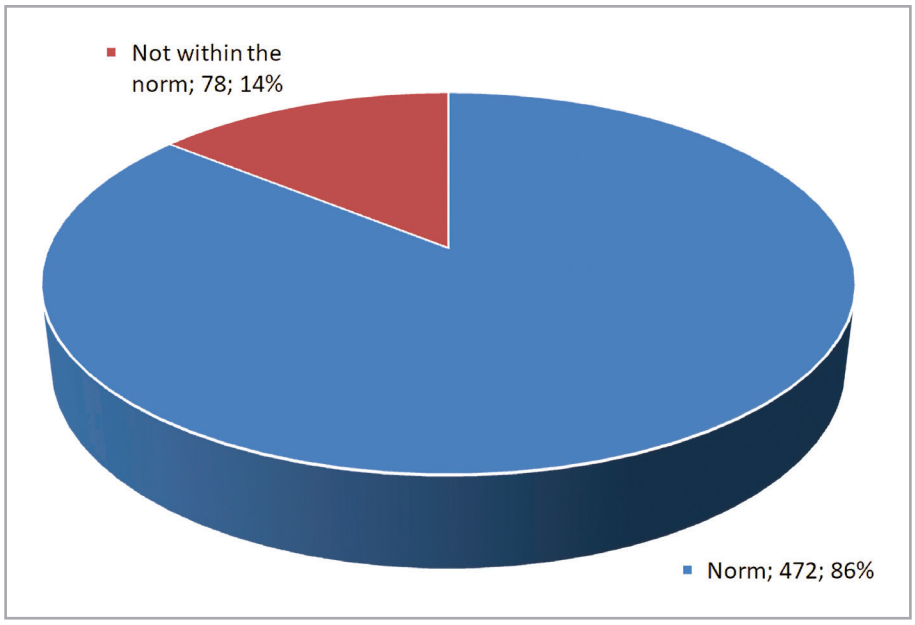

Figure 5: The regularity of the menstrual cycle before stress.

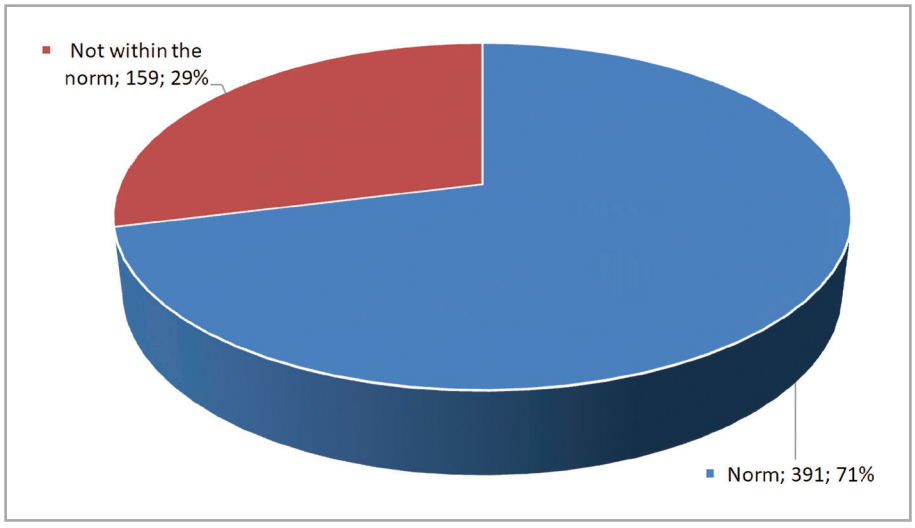

Figure 6: The regularity of the menstrual cycle after stress.

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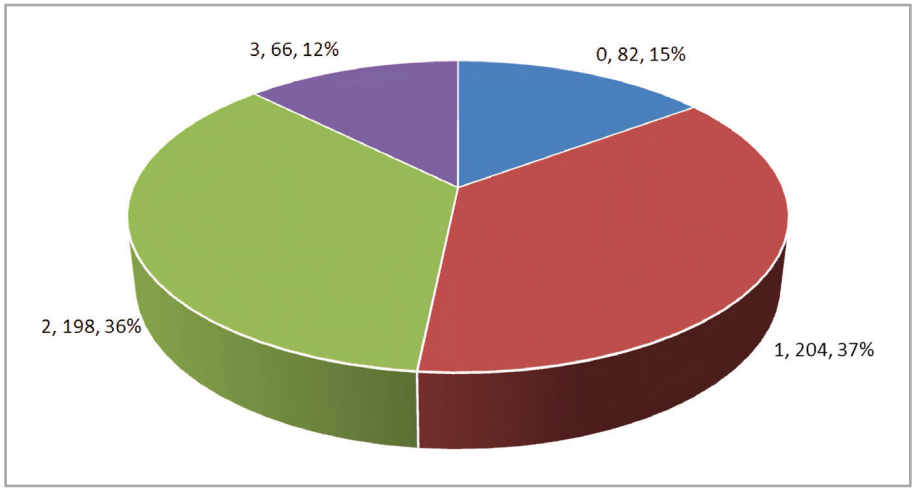

Figure 7: The pain before stress.

before stress is presented in Figure 7. After experiencing stress, the number of women who rated the pain of menstruation at 0 points decreased to 13% (72 women), at 1 point to 33% (181 women), and at 2 points to 31% (171 women). However, the number of women who reported pain at 3 points increased to 23% (126 women). Therefore, after stress, there was a tendency towards progression of pain during menstruation with the most pronounced clinical manifestation. The pain after stress is presented in Figure 8.

The assessment of menstrual blood volume took into account the following data: the maximum number of hygiene products used per day during menstruation, the need to change hygiene products at night, the presence of blood clots larger than 1 cm in menstrual discharge, and intermenstrual bleeding.

During the analysis of respondents' answers regarding the maximum number of hygiene products used per day during menstruation before the stress, the highest material consumption was noted in 20% of women. After experiencing COVID-19, the frequency of maximum use of hygiene products increased to 34%. Assessment of blood loss volume during menstruation is presented in Figure 9.

A comparison of data on the need to change hygiene products at night before and after stress showed an increase in this indicator by 15% (from 14% to 29%). A similar trend was observed for the visualization of blood clots larger than 1 cm in menstrual discharge. This symptom was additionally noted by 56 women (10%) after stress.

We did not find significant changes regarding the occurrence of intermenstrual bleeding before and after stress. Thus, the study revealed an increase in the number of patients with excessive blood loss during menstruation.

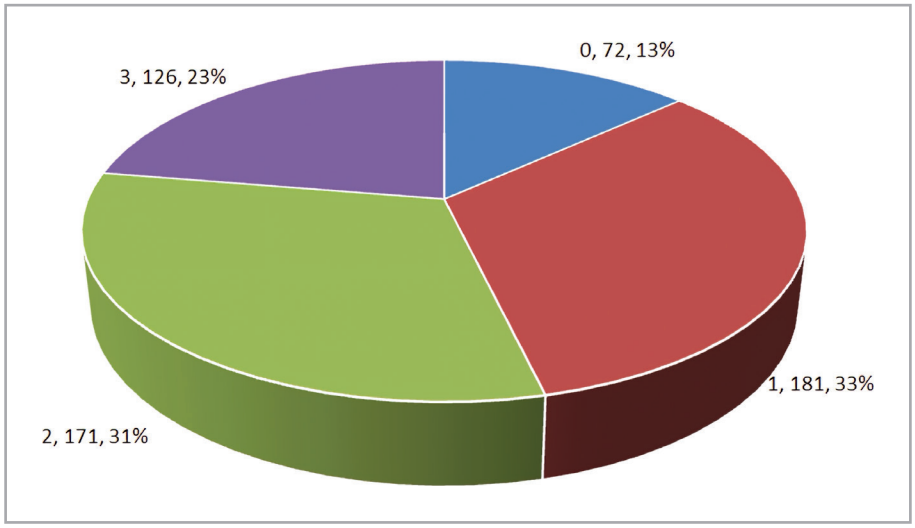

Figure 8: The pain after stress.

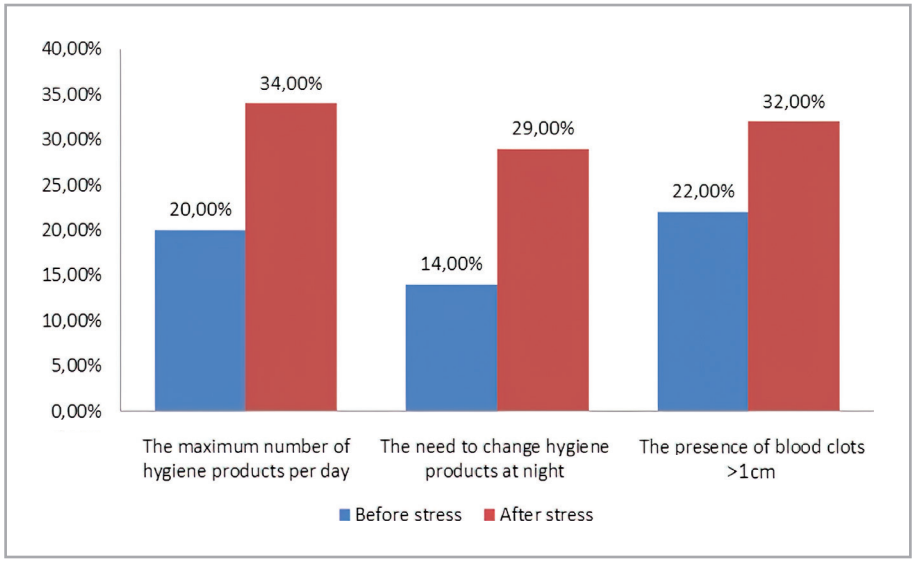

Figure 9: Assessment of blood loss volume during menstruation.

The assessment of the impact of stress levels on various characteristics of the menstrual cycle using the PSS-10-C scale demonstrated the following: in women with a normal menstrual duration, a low level of stress was observed in 79%, moderate in 15%, and high in 6%; among those with altered menstrual duration, a low stress level was found in 49%, moderate in 36%, and high in 15%; in women with a normal cycle length, a low stress level was present in 88%, moderate in 12%; altered cycle length was associated with a low stress level in 39%, moderate in 40%, and high in 21%; in patients with normal cycle regularity, 77% exhibited a low stress level, 19% moderate, and 4% high; among those with irregular cycle regularity, a low stress level was observed in 28%, moderate in 49%, and high in 23%; women with painless menstruation showed a low stress level in 88%, moderate in 9%, and high in 3%; patients with characteristic pain during the critical period had a low

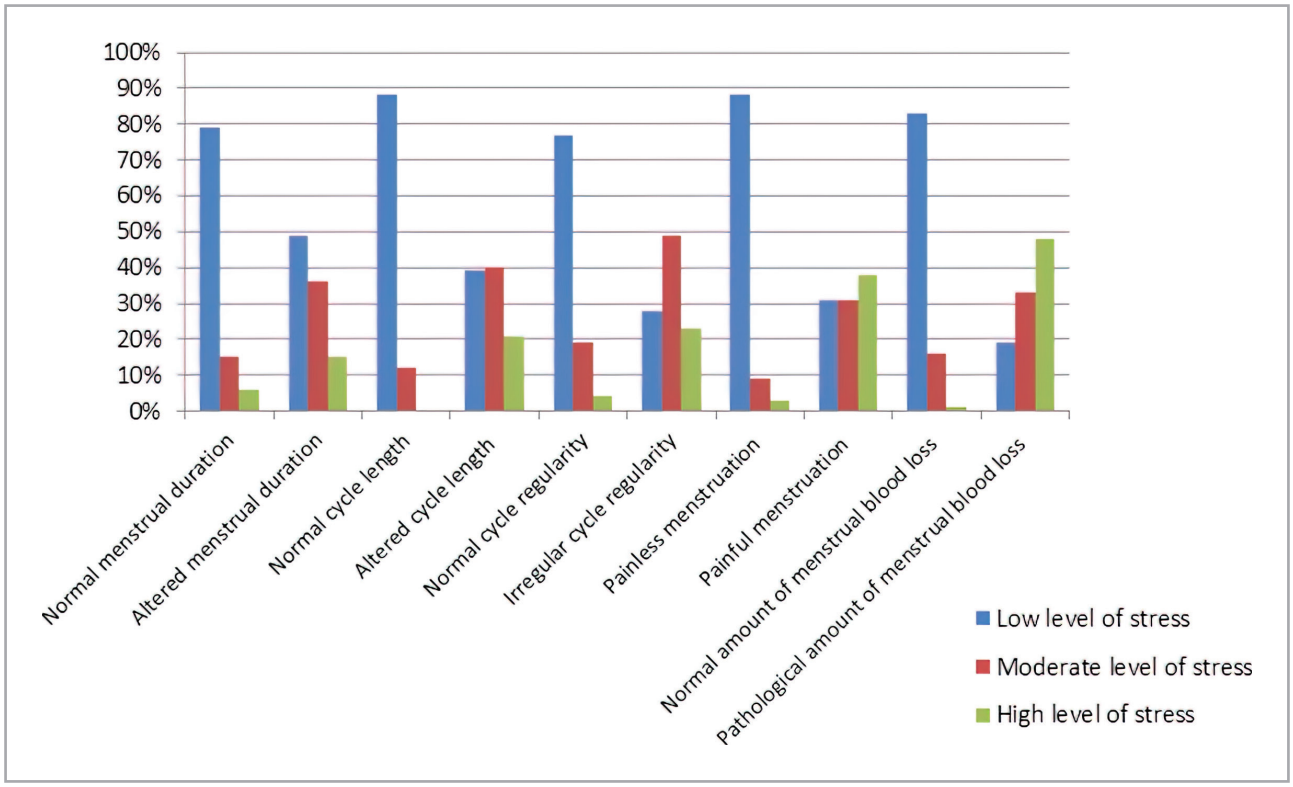

Figure 10: Relationship between stress levels and normal/pathological characteristics of the menstrual cycle.

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stress level in 31%, moderate in 31%, and high in 38%; respondents with a normal amount of menstrual blood loss rated a low stress level at 83%, moderate at 16%, and high at 1%; pathological menstrual blood loss under low stress was observed in 19%, moderate in 33%, and high in 48%. Thus, an increase in anxiety levels was characteristic of patients with deviations in menstrual function parameters compared to women with normal characteristics. These changes were particularly evident in terms of pathological blood loss and menstrual pain. The relationship between stress levels and normal/pathological characteristics of the menstrual cycle is presented in Figure 10.

The combination of all these changes provides grounds to consider COVID-19 infection as a stressor leading to disruptions in the Menstrual Cycle (MC). Failure to respond promptly to the development of pathology can significantly impact a woman's reproductive health.

Conclusion

Therefore, stress-induced disruptions in the Menstrual Cycle (MC) in the context of a past COVID-19 infection in conditions of an unstable and unfavorable epidemiological situation represent a significant socio-medical issue today. This necessitates an in-depth study of the mechanisms underlying the pathological consequences and the development of personalized counseling and treatment programs for affected patients.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the ethics commission at I. Horbachevsky Ternopil National Medical University (minutes no. 41 dated September 1, 2023).

Consent to participate

Written informed consent was obtained from all the participants.

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