DOI 10.11603/24116-4944.2025.2.15792
УДК 618.17-008:618.3-059-02:616.98:578.834.1

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ANALYSIS OF STRESS-INDUCED EFFECTS ON MENSTRUAL DYSFUNCTION IN WOMEN OF REPRODUCTIVE AGE

The aim of the study – to determine the nature and strength of the correlation between the level of COVID-19-related psychological stress and menstrual cycle parameters in women of reproductive age.

Materials and Methods. The observational study was conducted in the form of a questionnaire developed by us: "Impact of COVID-19-related stress on the menstrual cycle." The mental health status of women was assessed using the Perceived Stress Scale (PSS-10). The next step involved determination of the presence of correlation relationships between the stress-inducing factor and deviations from normal menstrual cycle parameters, which was performed using Statistica 10 software.

Results and Discussion. The study involved 550 reproductive-age patients. The processing of correlation analysis results revealed different degrees of strong positive correlation between all menstrual cycle parameters and stress. Stress predominantly influences menstrual blood volume: the need to replace sanitary products at night during menstruation (GC = 1.00) and the presence of blood clots >1 cm in menstrual discharge (GC = 0.99), as well as the regularity of the menstrual cycle (GC = 0.98). The stress-inducing factor has the least impact on the parameter of menstrual cycle frequency (SROC = 0.77).

Conclusions. Elevated levels of psychological stress correlate with a higher degree of menstrual changes. Future research on stress-induced menstrual disturbances and the long-term consequences of these changes is necessary.

Key words: COVID-19; stress-induced; menstrual cycle; correlation; parameters.

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АНАЛІЗ СТРЕС-ІНДУКОВАНИХ ЕФЕКТІВ ПОРУШЕННЯ МЕНСТРУАЛЬНОЇ ФУНКЦІЇ У ЖІНОК РЕПРОДУКТИВНОГО ВІКУ

Мета дослідження – встановити характер та силу кореляційних зв'язків між рівнем психологічного стресу, пов'язаного з COVID-19, та параметрами менструального циклу в жінок репродуктивного віку.

Матеріали та методи. Спостережне дослідження було проведено у формі розробленої нами анкети: «Вплив стресу, пов'язаного з COVID-19, на менструальний цикл». Психічний стан жінок оцінювали за допомогою Шкали сприйняття стресу (PSS-10). Наступним етапом було статистичне визначення наявності кореляційних зв'язків між стресорним фактором та відхиленнями від нормальних параметрів менструального циклу, що здійснювали з використанням програмного забезпечення Statistica 10.

Результати дослідження та їх обговорення. У дослідженні взяли участь 550 пацієнток репродуктивного віку. Обробка результатів кореляційного аналізу виявила різні ступені прямого, сильного взаємозв'язку між усіма параметрами менструального циклу та рівнем стресу. Стрес переважно впливає на об'єм менструальної крововтрати: потребу зміни гігієнічних засобів вночі під час менструації (GC = 1.00) та наявність згустків крові >1 см у менструальних виділеннях (GC = 0.99), а також на регулярність менструального циклу (GC = 0.98). Найменший вплив стресорного чинника відзначено на тривалість менструального циклу (SROC = 0.77).

Висновки. Підвищений рівень психологічного стресу корелює з більшим вираженням змін менструального циклу. Необхідні подальші дослідження стрес-індукованих порушень менструального циклу та довгострокових наслідків цих змін.

Ключові слова: COVID-19; стрес-індукований; менструальний цикл; кореляція; параметри.

INTRODUCTION. The menstrual function (MF) is a crucial biological feature of the female body, providing conditions for reproduction. Complex regulation of cyclic changes in the female body is controlled by hormonal support from the hypothalamic-pituitary-ovarian system and is realized at the level of the target organs [1, 2]. Additionally, it is important to consider the effects of hormonal activity from other peripheral hormone-producing organs (such as the adrenal glands, and thyroid gland), which can significantly alter system functioning [3]. In recent years, numerous large-scale studies have investigated the causes and consequences of the impact of COVID-19 on the female reproductive function [4, 5]. The pathogenesis involves both direct action, due to SARS-CoV-2 penetration into the ovaries, and indirect action, due to high levels of psychological stress caused by the pandemic [6–11]. The consequences of COVID-19 include disruption of the adequate functioning of the hypothalamic-pituitary-ovarian system, which may lead to infertility [12, 13]. Therefore, an in-depth study of MC parameters in reproductive-aged women who have experienced COVID-19 is a current task, as the lack of timely and adequate response to MF-related changes over time may become a prerequisite for reproductive dysfunction [14–17].

THE AIM OF THE STUDY – to determine the nature and strength of the correlation between the level of COVID-19-related psychological stress and menstrual cycle parameters in women of reproductive age.

MATERIALS AND METHODS. Using a systematic approach, we conducted an observational study on the impact of stress on the menstrual cycle (MC). We developed a questionnaire using Google Forms, which was distributed through several online platforms as well as in offline format. The questionnaire, titled «Impact of COVID-19-related Stress on the Menstrual Cycle», consisted of several sections, including personal information, anthropometric data, obstetric, gynecological, and somatic history, as well as characterization of MC parameters.

The questionnaire comprised two sections. The first section assessed MC parameters before the onset of COVID-19 illness, while the second section evaluated the current state of MC. The survey included questions regarding the duration of menstruation before and after stress (DMBS, DMAS; categorized as <4 days, 4–8 days, >8 days), frequency of the menstrual cycle before and after stress (FMCBS, FMCAS; categorized as <24 days, 24–38 days, >38 days), regularity of the menstrual cycle to and after stress (RTS, RAS; yes, no), menstrual pain to and after stress (PTS, PAS; rated on a 4-point verbal scale according to Ohnhaus EE and Adler R., where 0 represents no pain, 1 represents mild pain, 2 represents moderate pain, and 3 represents severe pain), maximum number of hygiene products used per day during menstruation before and after stress (MNHPPDBS, MNHPPDAS), need for overnight change of hygiene products before and after stress (CHPNBS, CHPNAS; yes, no), and presence of blood clots >1 cm before and after stress (PBCBS, PBCAS; yes, no) [18]. To assess the stress level of all participants, we additionally administered The Perceived Stress Scale-10 [19].

The applied research was conducted using Statistica 10 software. For this purpose, all evaluated MC parameters were divided into two groups: numerical and ordinal data. Numerical values included: duration of menstruation, frequency of the menstrual cycle, and maximum quantity of hygiene products used per day during menstruation. The ordinal data included: regularity of the menstrual cycle, menstrual pain intensity, need for overnight replacement of hygiene products, and presence of blood clots >1 cm. Therefore, four out of the seven examined parameters were ordinal, and the analysis of the numerical characteristics revealed that they did not adhere to a normal distribution (Fig. 1).

The preliminary graphical analysis provides grounds to suggest a dependency of all investigated attributes on stress. The next step is to establish the degree of dependency of all the aforementioned parameters on stress.

According to the above data, non-parametric methods of analysis were employed to identify the influence of stress on MC characteristics. This ensures accurate measurement of the strength of these relationships.

To measure the level of correlation between each pair of analyzed numerical factors before and after stress, we utilized one of the rank-order density estimations – Spearman Rank Order Correlations (SROC) ρ. In its calculation, the rank differences d of the factorial and resultant features for each unit of the population are used:

$$SROC = 1 - \frac{6\sum_{i=1}^{n} d_i^2}{n(n^2-1)}$$

In the formula provided above: n represents the number of patients who participated in the study, d_i denotes the difference in the value of the corresponding attribute before and after stress.

Spearman Rank Order Correlations (SROC) range from 0 to 1, characterizing the density of the relationship and indicating its direction - whether it's positive or negative.

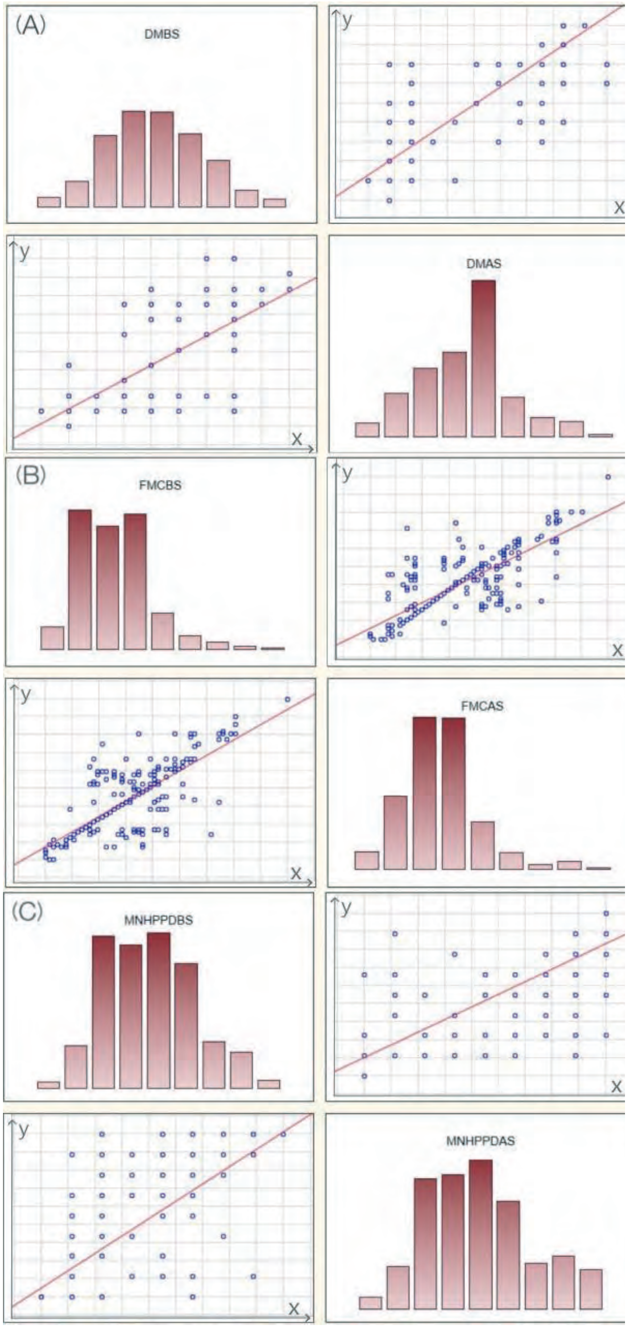

Fig. 1. (A) Scatterplot matrix for the DMBS (duration of menstruation before stress) and DMAS (duration of menstruation after stress).

(B) Scatterplot matrix for the FMCBS (frequency of the menstrual cycle before stress) and FMCAS (frequency of the menstrual cycle after stress).

(C) Scatterplot matrix for the MNHPPDBS (maximum number of hygiene products per day before stress) and MNHPPDAS (maximum number of hygiene products per day after stress).

The relationship between attributes is considered statistically significant if the value of the Spearman rank correlation coefficient SROC > 0.5 [20].

To assess the strength of the relationship between pairs of ordinal parameters before and after stress, Gamma Correlations (GC) were employed. This is a measure of ordinal association between two vectors of numbers. The GC estimation is performed using the formula:

$$GC = \frac{N_S - N_d}{N_S - N_d},$$

Where Ns is the number of pairs of cases ranked in the same order for both variables, and Nd is the number of pairs of cases ranked in the opposite order for both variables [21].

RESULTS AND DISCUSSION. Overall, 930 women participated in the survey. The eligibility criteria for participating in the survey required having had a COVID-19 infection no more than two months prior to the study. Each participant provided informed consent for the processing of personal data. Respondents had the option to complete the survey anonymously if they wished. Exclusion criteria included: pregnant women, women in the postpartum period and lactation period, body mass index outside the range of 18.5–24.9, presence of endocrine or gynaecological pathology affecting the MC, as well as women with diagnosed mental and behavioural disorders classified as class V of the ICD-11. As a result, the empirical database of the study consisted of data from the examination of 550 patients aged 18 to 45 years. The results of applying Spearman rank-order correlation allow us to conclude that various degrees of strong direct correlation have been established for statistical significance at p<0.05 regarding all analyzed pairs of numerical variables: duration of menstruation before and after stress (SROC = 0.86), frequency of the menstrual cycle before and after stress (SROC = 0.77), maximum number of hygiene products used per day during menstruation (SROC = 0.83) (Fig. 2–4).

The results of applying Gamma Correlations (GC) have provided evidence of a very strong direct correlation between the parameters: regularity of menstrual cycles before and after stress (GC = 0.98), severity of menstrual pain before and after stress (GC = 0.81), presence of blood clots >1 cm before and after stress (GC = 0.99), and a linear correlation between the need to replace hygiene products at night before and after stress (GC = 1.00) (Fig. 5–8).

Spearman Rank Order Correlations
MD pairwise deleted
Marked correlations are significant at p <,05000

Variable	DMBS	DMAS
DMBS	1,000000	0,862654
DMAS	0,862654	1,000000

Fig. 2. Spearman Rank Order Correlations for the DMBS (duration of menstruation before stress) and DMAS (duration of menstruation after stress).

Spearman Rank Order Correlations
MD pairwise deleted
Marked correlations are significant at p <,05000

Variable	FMCBS	FMCAS
FMCBS	1,000000	0,771525
FMCAS	0,771525	1,000000

Fig. 3. Spearman Rank Order Correlations for the FMCBS (frequency of the menstrual cycle before stress) and FMCAS (frequency of the menstrual cycle after stress).

Spearman Rank Order Correlations
MD pairwise deleted
Marked correlations are significant at p <,05000

Variable	MNHPPDBS	MNHPPDAS
MNHPPDBS	1,000000	0,832314
MNHPPDAS	0,832314	1,000000

Fig. 4. Spearman Rank Order Correlations for the MNHPPDBS (maximum number of hygiene products per day before stress) and MNHPPDAS (maximum number of hygiene products per day after stress).

Gamma Correlations
MD pairwise deleted
Marked correlations are significant at p <,05000

Variable	PTS	PAS
PTS	1,000000	0,812588
PAS	0,812588	1,000000

Fig. 5. Gamma Correlations for the RTS (regularity of menstrual cycle to stress) and RAS (regularity of menstrual cycle after stress).

Gamma Correlations
MD pairwise deleted
Marked correlations are significant at p <,05000

Variable	PTS	PAS
PTS	1,000000	0,812588
PAS	0,812588	1,000000

Fig. 6. Gamma Correlations for the PTS (menstrual pain to stress) and PAS (menstrual pain after stress).

Gamma Correlations
MD pairwise deleted
Marked correlations are significant at p <,0500

Variable	CHPNBS	CHPNAS
CHPNBS	1,000000	1,000000
CHPNAS	1,000000	1,000000

Fig. 7. Gamma Correlations for the PBCBS (presence of blood clots >1 cm before stress) and PBCAS (presence of blood clots >1 cm after stress).

Variable	Gamma Correlations MD pairwise deleted Marked correlations are significant at p <,05000 CHPNBS	CHPNAS
CHPNBS	1,000000	1,000000
CHPNAS	1,000000	1,000000

Fig. 8. Gamma Correlations for the CHPNBS (need to change hygiene products at night before stress) and CHPNAS (need to change hygiene products at night after stress).

Based on the statistical summary of the aforementioned results of applied analysis regarding the influence of stress on menstrual cycle parameters, the following conclusions were drawn: stress exerts the greatest effect on the indicator of the need to replace hygiene products at night. Processing the results revealed that this parameter characterizes an increased volume of bloody discharge during menstruation. A significant influence of the stress factor is observed on the parameters of the presence of blood clots >1 cm and menstrual cycle regularity. The least impact of the stress factor is realized on the parameter of menstrual cycle frequency.

CONCLUSIONS. In today's conditions, stress-induced disruptions of the menstrual cycle are highly prevalent. According to the results of our study, under these conditions, there is a significant increase in the risk of abnormal uterine bleeding associated with ovulatory dysfunction. The latter is associated with reduced reproductive potential and requires further investigation of the mechanisms of therapeutic and preventive measures.

PROSPECTS FOR FURTHER RESEARCH. A promising direction for future research is the detailed investigation of stress-induced menstrual cycle disturbances as a potential marker of deeper changes in women’s reproductive health. It is important to determine whether the observed fluctuations in menstrual parameters are associated with long-term fertility risks. Expanding research in this field may contribute to the development of approaches for early detection and prevention of stress-associated reproductive disorders.

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Received 02.09.2025
Accepted for publication 03.10.2025
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