

# Features of Hemostasis in Women with Menstrual-Ovarian Cycle Disorders Against the Background of COVID-19

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**Abstract** The study included 120 women with menstrual-ovarian cycle disorders against the background of COVID-19. According to the clinical course of COVID-19, all patients were divided into three groups. The first group consisted of 45 women (37.5%) with a mild form of COVID-19, the second group included 43 women (35.8%) with moderate COVID-19, and the third group comprised 32 women (26.7%) with severe COVID-19. The study results demonstrate a significant impact of COVID-19 on the hemostasis state in 92% of women with menstrual-ovarian function disorders against the background of COVID-19. The levels of fibrinogen are 1.8 times and D-dimer on average 2.0 times higher than in healthy women. A correlation has been established between the levels of D-dimer, fibrinogen, and the severity of the clinical course of COVID-19, specifically, the presence of a direct correlation of these indicators with the severe form of COVID-19.

**Keywords** Hemostasis, Women, Menstrual-Ovarian Cycle Disorders, COVID-19

## 1. Introduction

In recent years, the world has faced an unprecedented challenge in the form of the COVID-19 pandemic caused by the SARS-CoV-2 virus [1-3]. This pandemic has had a significant impact on all aspects of healthcare, including women's reproductive health. The SARS-CoV-2 virus demonstrates a wide range of clinical manifestations, including effects on the blood system and hemostasis [4-5]. Hemostasis is a complex process that maintains the circulation of stationary blood within the vascular bed, preventing blood loss when vessels are damaged, and also prevents the formation of thrombi within vessels under normal conditions [6-7]. Disorders in the hemostasis system can lead to various pathological conditions, from thrombosis to bleeding. At the same time, a woman's menstrual cycle is closely linked to various physiological processes in the body, including the hemostasis system [8-9]. Menstrual cycle disorders can indicate various diseases and conditions, including hormonal imbalances, reproductive system problems, and even the overall state of health. It is reported that COVID-19 infection can affect the menstrual cycle, causing its disorders, making the study of this topic relevant and necessary for understanding the possible interactions

between COVID-19, the menstrual-ovarian cycle, and the hemostasis system [1-11].

The relevance of this study is driven by the growing need to understand the features of COVID-19's impact on women's reproductive health, particularly on the menstrual-ovarian cycle and hemostasis [12-14]. Despite extensive research on the impact of COVID-19 on the human body, data on the interaction of the infection with the women's reproductive system and the hemostasis system remain insufficient [15-17]. This creates a necessity for conducting targeted research to identify potential mechanisms of interaction and to develop appropriate methods of prevention and treatment.

**The aim of this study** is to investigate the features of hemostasis in women with menstrual-ovarian cycle disorders against the background of past or current COVID-19 infection.

## 2. Materials and Methods

The studies were conducted from 2021 to 2023, involving women aged 18 to 36. The study included 120 women with menstrual-ovarian cycle disorders against the background of COVID-19. According to the clinical course of COVID-19, all patients were divided into three groups. The first group consisted of 45 women (37.5%) with a mild form of COVID-19, the second group included 43 women (35.8%) with moderate COVID-19, and the third group comprised 32 women (26.7%) with severe COVID-19. All participants underwent hemostasis tests, such as thromboelastography, coagulogram, studies of the anticoagulant system, as well as

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the level of D-dimer. A complex of statistical methods was used for data analysis. Descriptive statistical methods (mean, median, standard deviation) as well as inferential statistics (t-test, analysis of variance (ANOVA), nonlinear methods when necessary) were applied to assess the significance of differences between the groups. The significance level was set at  $p < 0.05$ .

### 3. Research Results

The study showed that significant changes in the hemostasis system were observed in 87% of women with menstrual-ovarian function disorders against the background of COVID-19, 42% and 45% respectively in the groups. In 73.2% of women in these groups, increased levels of D-dimer and fibrinogen were identified, 34.8% and 38.4% respectively in the groups. An increase in the levels of blood coagulation factors V and VIII was noticed in 24.2%, which may indicate a tendency towards thrombus formation and thromboembolism. Moreover, the study results showed that the state of the hemostasis system in 120 women with menstrual-ovarian function disorders against the background of COVID-19 varies depending on the severity of COVID-19.

The APTT analysis in the first group of women with menstrual-ovarian function disorders against the background of COVID-19 showed an increase in this indicator's time, respectively  $42.4 \pm 1.2$ ,  $43.2 \pm 1.4$ , and  $44.4 \pm 1.02$  sec in the subgroups against  $28.2 \pm 0.1$  sec in the control group.

The D-dimer level in the first group of women with menstrual-ovarian function disorders against the background of COVID-19 was higher compared to the control group, being respectively  $276.3 \pm 0.2$ ,  $278.2 \pm 0.1$ , and  $280.1 \pm 0.4$   $\mu\text{g/mL}$  against  $240.4 \pm 0.4$   $\text{ng/mL}$  in the control group. The fibrinogen level analysis in the first group showed that in the subgroups, this indicator was  $5.0 \pm 1.6$ ,  $5.4 \pm 1.3$ , and  $5.8 \pm 1.3$   $\text{g/L}$  against  $3.5 \pm 1.1$   $\text{g/L}$  in the control group. It was found that the fibrinogen level increased by 2.0 times in women with menstrual-ovarian function disorders against the background of COVID-19.

The PTI analysis in the first group of women with menstrual-ovarian function disorders against the background

of COVID-19 showed growth of this indicator in the subgroups, respectively  $112.1 \pm 0.1$ ,  $114.2 \pm 0.2$ , and  $118.2 \pm 0.4$ .

The study of thrombin time showed that in the first group, this indicator was  $34.0 \pm 0.7$ ,  $35.2 \pm 0.2$ , and  $36.7 \pm 0.4$  respectively in the subgroups. The average level of platelets in the subgroups of the first group was  $480.0 \pm 0.2$ ,  $482.0 \pm 0.4$ , and  $484.0 \pm 0.1 \times 10^9/\text{L}$  against  $364.4 \pm 0.1 \times 10^9/\text{L}$  in the control group (see table).

The APTT analysis in the second group of women with menstrual-ovarian function disorders against the background of COVID-19 also showed an increase in this indicator's time depending on the severity of COVID-19 in the subgroups, respectively,  $43.0 \pm 0.2$ ,  $44.0 \pm 0.3$ , and  $45.2 \pm 0.1$  sec against  $28.2 \pm 0.1$  sec in the control group. The D-dimer level in the second group of women with menstrual-ovarian function disorders against the background of COVID-19 was higher compared to the control group, being respectively  $275.2 \pm 0.4$ ,  $278.2 \pm 0.2$ , and  $280.2 \pm 0.4$   $\mu\text{g/mL}$  against  $240.4 \pm 0.4$   $\text{ng/mL}$  in the control group.

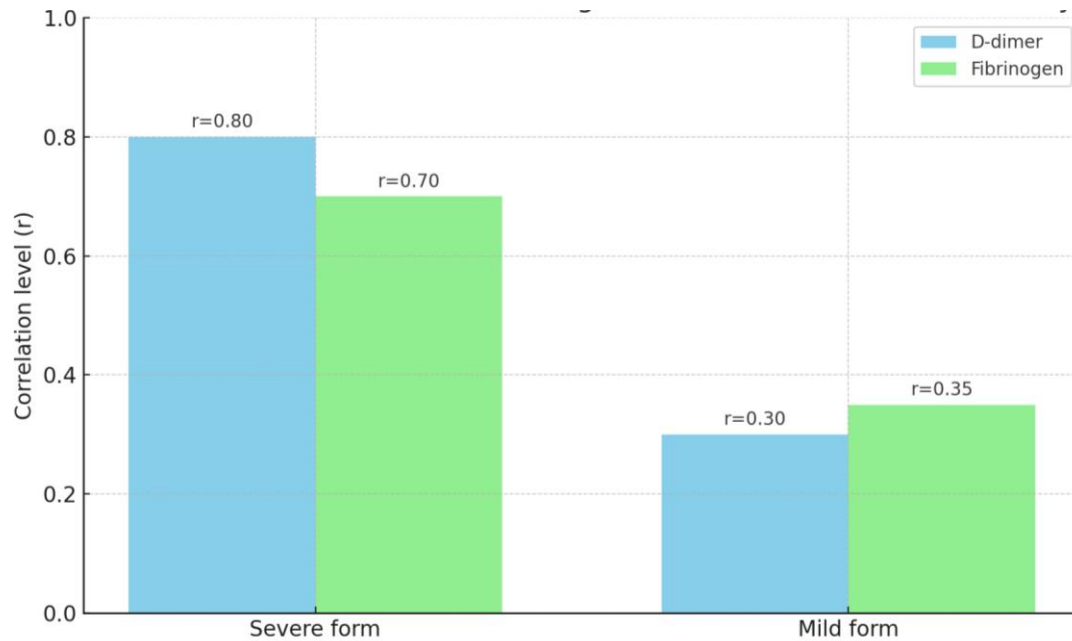
The fibrinogen level analysis in the second group showed that in the subgroups, this indicator was  $5.2 \pm 0.2$ ,  $5.5 \pm 0.2$ , and  $5.7 \pm 0.2$   $\text{g/L}$  against  $3.5 \pm 1.1$   $\text{g/L}$  in the control group. It was found that the fibrinogen level increased by 1.7 times in women with menstrual-ovarian function disorders against the background of COVID-19. The PTI analysis in the second group of women with menstrual-ovarian function disorders against the background of COVID-19 showed growth of this indicator in the subgroups, respectively,  $113.2 \pm 0.2$ ,  $116.2 \pm 0.2$ , and  $118.4 \pm 0.1$ . The study of thrombin time showed that in the second group, this indicator was  $33.0 \pm 0.6$ ,  $34.1 \pm 0.2$ , and  $35.0 \pm 0.2$  sec. The average level of platelets in the subgroups of the second group was  $478.2 \pm 0.1$ ,  $480.0 \pm 0.4$ , and  $482.2 \pm 0.2 \times 10^9/\text{L}$  against  $364.4 \pm 0.1 \times 10^9/\text{L}$  in the control group.

The study results indicate a significant increase in all hemostasis system indicators by 2.1-2.2 times in women with menstrual-ovarian function disorders and COVID-19. Specifically, there was an increase in fibrinogen levels by 1.8 times, D-dimer by 2.0 times, activated partial thromboplastin time (APTT) by 1.6 times, and prothrombin time (PT) by 1.7 times.

**Table 1.** Hemostasis system indicators in women with menstrual-ovarian function disorders in women with COVID-19,  $M \pm m$

Indicators	Group I, n=60			Group II, n=60			Control group, n=30
	Mild form of COVID-19, n=22	Moderate severity COVID-19, n=20	Severe form of COVID-19, n=18	Mild form of COVID-19, n=23	Moderate severity COVID-19, n=22	Severe form of COVID-19, n=15	
APTT, (sek)	$42,4 \pm 1,2^*$	$43,2 \pm 1,4^*$	$44,4 \pm 1,02^*$	$43,0 \pm 0,2^*$	$44,0 \pm 0,3^*$	$45,2 \pm 0,1^*$	$28,2 \pm 0,1$
PTI, %	$112,1 \pm 0,1^*$	$114,2 \pm 0,2$	$118,2 \pm 0,4$	$113,2 \pm 0,2$	$116,2 \pm 0,2$	$118,4 \pm 0,1$	$105,6 \pm 0,1$
Fibrinogen, (g/l)	$5,0 \pm 1,6^*$	$5,4 \pm 1,3^*$	$5,8 \pm 1,3^*$	$5,2 \pm 0,2^*$	$5,5 \pm 0,2^*$	$5,7 \pm 0,2^*$	$3,5 \pm 1,1$
Thrombin time, (sec)	$34,0 \pm 0,7^*$	$35,2 \pm 0,2^*$	$36,7 \pm 0,4^*$	$33,0 \pm 0,6^*$	$34,1 \pm 0,2^*$	$35,0 \pm 0,2^*$	$21,0 \pm 0,1$
D-dimer, ng/ml	$276,3 \pm 0,2^*$	$278,2 \pm 0,1^*$	$280,1 \pm 0,4^*$	$275,2 \pm 0,4^*$	$278,2 \pm 0,2^*$	$280,2 \pm 0,4^*$	$240,4 \pm 0,4$
Platelets, $10^9/\text{l}$	$480,0 \pm 0,2^*$	$482,0 \pm 0,4$	$484,0 \pm 0,1$	$478,2 \pm 0,1$	$480,0 \pm 0,4$	$482,2 \pm 0,2$	$364,4 \pm 0,1$

Note: \*significantly different from the indicators of the first group,  $p < 0.001$ ; \*\* significantly different from the indicators of the control group,  $p < 0.001$ .



**Figure 1.** Correlation between D-dimer and fibrinogen levels and the severity of the clinical course of COVID-19

We also established a correlation between the levels of D-dimer, fibrinogen, and the severity of the clinical course of COVID-19, in particular, the presence of a direct correlation of these indicators with the severe form of COVID-19. The correlation coefficient was respectively ( $r=0.80$ ) and ( $r=0.70$ ), and a weak correlation with the mild form of COVID-19, with the correlation coefficient being respectively ( $r=0.30$ ) and ( $r=0.35$ ) (see Fig. 1).

Thus, the study results demonstrate a significant impact of COVID-19 on the hemostasis state in 92% of women with menstrual-ovarian function disorders and COVID-19. The levels of fibrinogen and D-dimer in women with menstrual-ovarian function disorders and COVID-19 are significantly higher than those in the control group.

In this context, it is important to consider the risk of thrombotic complications in managing women with menstrual-ovarian function disorders and COVID-19. Early detection and prevention of thrombotic complications can significantly reduce the risk of adverse outcomes for the mother. In conclusion, our study highlights the need for more in-depth monitoring of hemostasis in women with menstrual-ovarian function disorders against the background of COVID-19. This will allow for timely detection and prevention of thrombotic complications and improve the quality of life for women.

## 4. Conclusions

The study results demonstrate a significant impact of COVID-19 on the hemostasis state in 92% of women with menstrual-ovarian function disorders against the background of COVID-19. The levels of fibrinogen are 1.8 times and D-dimer on average 2.0 times higher than in healthy women. A correlation has been established between the levels of

D-dimer, fibrinogen, and the severity of the clinical course of COVID-19, specifically, the presence of a direct correlation of these indicators with the severe form of COVID-19. The correlation coefficient was respectively ( $r=0.80$ ) and ( $r=0.70$ ), and a weak correlation with the mild form of COVID-19, with the correlation coefficient being respectively ( $r=0.35$ ) and ( $r=0.30$ ). Therefore, it is important to conduct research on the hemostasis state in such patients for early detection and prevention of thrombotic complications.

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