

## Research Article

# Assessing Stress, Anxiety, and Depression in Women with Menstrual Disorders Caused by COVID-19 Vaccines

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## Abstract

**Introduction:** One of the most effective solutions to control the COVID-19 pandemic is vaccination. However, possible side effects of the vaccine can negatively affect the vaccination process. The present study was conducted to determine the levels of stress, anxiety, and depression in women with menstrual disorders caused by COVID-19 vaccines.

**Methods:** In this retrospective cohort study, DASS-21 online questionnaire was used to assess anxiety, stress, and depression following menstrual cycle disorders after receiving the COVID-19 vaccine in 916 eligible women aged between 18 and 45.

**Results:** The participants' mean age was  $34.34 \pm 8.37$ , 77.79% of the participants were married, and 61.47% of them were government employees. Menorrhagia was the most prevalent menstrual disorder (n=189). Hypermenorrhea was 5.3 times more likely in women using no contraception method compared to those using natural family planning methods (OR=5.13 and P=0.00). This risk was also 2.77 times higher in women without high school education compared to those with diploma (OR=0.36 and P=0.01). Stress, anxiety, and depression levels increased in the group with menstrual disorders within three months and also showed a significant increase compared to the control group (P<0.05).

**Conclusion:** Stress, anxiety, and depression occurred as a result of menstrual disorders caused by COVID-19 vaccines. Lack of awareness of possible side effects and how to deal with them aggravates mental disorders. Proper education and counseling before vaccination, follow-up of possible side effects, and guidance can prevent negative attitudes toward vaccines.

**Keywords:** Abnormal uterine bleeding; Mental health; COVID-19

## Introduction

The coronavirus disease (COVID-19) pandemic has disrupted not only the health care systems and the economy, but also the lives of millions around the world. Vaccination is probably the most effective solution to control and end the pandemic. The efficiency of vaccination programs depends on individuals' inclination to receive the vaccines. Doubts and concerns about vaccination can negatively affect this tendency. The biggest concerns leading to individuals' reluctance to receive COVID-19 vaccines are allergic reactions, limitations in daily life, autoimmune reactions, neurological side effects, and unknown long-term consequences [1].

Recent studies have reported changes in the menstrual cycle after receiving both mRNA and adenovirus-based COVID-19 vaccines [2].

The menstrual cycle involves the activity and interaction of hormones affecting the uterus released from the hypothalamus, pituitary gland, and ovaries [3].

Factors affecting menstrual disorders include ethnicity, age, menstrual age, Body Mass Index (BMI), history of surgical or medical problems, kidney problems, socioeconomic status, and mental disorders [4]. Types of menstrual disorders include menstrual irregularities, hypermenorrhea, hypomenorrhea, polymenorrhagia, oligomenorrhea, dysmenorrhea, amenorrhea, menorrhagia, and Premenstrual Syndrome (PMS) [5,6]. Pathological conditions caused by menstrual disorders, including infertility and reduced fertility, malignancies, Abnormal Uterine Bleeding (AUB), breast and endometrial diseases, and complications secondary to them, cause health problems and reduced quality of life [7,8].

Various studies have shown that physical illnesses can affect an individual's mood and emotions and cause stress, anxiety, and depression [9,10]. Additionally, gynecological diseases can lead to mental disorders such as stress, anxiety, and depression by causing hormonal imbalances [11,12].

In addition, mental disorders such as stress, anxiety, and depression could affect the body and cause physical problems and symptoms. As researchers have shown, stress can cause a variety of menstrual disorders. Furthermore, stress and sleep deprivation among adolescent girls have been strongly associated with abnormal menstrual patterns. Anxiety is also known to be a potential contributing factor for menstrual disorders. Some studies have shown that people with high levels of anxiety are more prone to menstrual

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disorders compared to those with lower levels of anxiety [13].

Since women often consider menstruation as an indication of their reproductive health, its disorder causes concern, reduced quality of life, and mental disorders; these disorders and the resulting mental disorders enter a vicious cycle, further exacerbating the problem. Therefore, the present study was conducted to determine the effect of menstrual disorders caused by COVID-19 vaccines on stress, anxiety, and depression in women to determine effective clinical interventions. These interventions may be used to increase the women's tendency to get vaccinated through reducing the possible negative attitudes towards vaccines.

## Materials and Methods

We conducted a retrospective cohort study on stress, anxiety, and depression resulting from menstrual period changes after COVID-19 vaccination. The study population consisted of women of reproductive age (18 to 45 years old) living in southeast Iran in 2001. The samples were women who had received the COVID-19 vaccine. Sampling was done online among the eligible women.

Women 18 to 45 years old with regular periods of 21 to 35 days with normal bleeding before vaccination without women's diseases affecting female sex hormones, such as premature ovarian failure, polycystic ovary syndrome, and endocrine disorders, such as hypothyroidism and pituitary adenoma, who had not experienced stressful incidents from three days before vaccination until completing the questionnaire were included in the study.

Women receiving treatments for menstrual disorders due to vaccination during the three-month period of the study and those who did not complete the three questionnaires were excluded.

### Research tools

A demographic and obstetrics history questionnaire. The first part investigated age, occupation, education, marital status, BMI, women's diseases, and other diseases, such as cardiovascular diseases, anemia, etc., using pharmaceutical, hormonal, and non-hormonal treatment, the number of pregnancies and abortions, contraception methods before and after vaccination, pregnancy or (peri) menopause status, and the COVID-19 vaccine type.

The second part assessed the menstrual status before and after receiving the vaccine in terms of menstrual cycle lengths, bleeding days, bleeding volume, dysmenorrhea, amenorrhea, PMS, and the duration of the effect in case of irregular periods and/or abnormal uterine bleeding.

**The DASS-21 anxiety and depression scale:** The DASS-21 is the short form of the DASS-42; it has been validated for the Iranian population by Sahebi, Asghari, and Salari (2005), and its Cronbach's alpha has been reported to be 0.94, 0.92, and 0.82 in the depression, anxiety, and stress subscales, respectively. This scale is employed to simultaneously measure the severity of the main symptoms of depression, anxiety, and stress [14,15]. Each subscale consists of 7 questions, and the final score of each variable result from the sum of the scores of the questions related to it. The questions have 4 options and are answered through self-assessment. The answers range from "never" to "always" and participants can choose among "never", "sometimes", "often", and "always." Scores range from 0 to 3; the options "never", "sometimes", "often", and "always" are assigned a score of 0, 1, 2, and 3, respectively. Since the DASS-21 is the short form of the DASS-42 scale, the final score of each subscale must be doubled.

Therefore, the total score for each scale ranges from 0 to 42 [16].

The survey was done only in Persian and was distributed using social media. The research purpose and manner of completing the questionnaire in the three-time spans (one month, two months, and three months after vaccination) were explained, and the participants could only complete the questionnaire after completing a consent form.

Overall, 1520 participants completed the questionnaire, but 531 of them were excluded since they did not meet the inclusion criteria (irregular periods before vaccination, experiencing stressful incidents, taking hormonal medications, having diseases such as PCOS and thyroid disorders, and taking contraceptive pills). Twenty-six of the 989 eligible participants were excluded because they did not complete the questionnaire, and 47 of them were excluded due to referring to a doctor to receive treatments. Among the remaining 916 participants, 196 had experienced at least one menstrual disorder after vaccination; these participants were placed in the menstrual disorders group, and the other 720 participants who did not experience any change in their menstrual cycle, dysmenorrhea, or PMS were considered as the control group.

### Data analysis

Statistical analysis was performed on 916 participants using the SPSS 17 with the measures of central tendency and dispersion, tests for equality of proportions, chi-square, and one-way ANOVA.

## Results

The participants' mean age was  $34.34 \pm 8.37$ . The majority of the participants were married (86.16%), housekeeper (73.07%), and had university degrees (62.09%). The most common method of contraception used by the participants was the natural method. In terms of vaccine types, 246 (26.85%), 275 (30.02%), 317 (34.6%), and 78 of the participants had received Sputnik, AstraZeneca, Sinopharm, and other vaccines (Barekat, Bharat, or Pasteurcovac), respectively (Table 1).

In the group of individuals with menstrual disorders after vaccination, 149 (16.26%), 147 (16.04%), 47 (5.13%), 157 (17.13%), 88 (9.6%), 189 (20.63%), 112 (12.22%), 93 (10.15%), 18 (1.96%), and 162 (17.68%) of the participants developed polymenorrhagia, oligomenorrhagia, hypomenorrhagia, hypermenorrhagia, bleeding for less than 3 days, Menorrhagia, Metrorrhagia, increased dysmenorrhagia, amenorrhagia, and increased PMS symptoms, respectively (Table 2).

The risk of polymenorrhagia after vaccination in women who did not use any contraception methods was 1.7 times higher than in those who used natural methods (OR=1.7, P=0.045). This risk in women over 50 was 7.1, 5.2, and 6.66 times higher than in women between 20 and 30 (OR=0.19, P=0.00), 30 and 40 (OR=0.19, P=0.01), and 40 and 50 (OR=0.15, P=0.00), respectively.

Women with a university degree were 7.79 times more likely to develop hypomenorrhagia after vaccination compared to those without a high school diploma (OR=7.79, P=0.01). The risk of hypomenorrhagia after vaccination was 5.13 times higher in women using no contraception methods compared to those using natural methods (OR=5.13, P=0.00).

The risk of hypermenorrhagia after vaccination in women without high school diplomas was 2.77 and 3.44 times higher compared to women with high school diplomas (OR=0.36, P=0.01) and women

**Table 1:** Demographic characteristics of the samples.

Variable		With AUB	Without AUB
		N (%)	
Marital status	Single	21 (10.71)	85 (11.8)
	Married	169 (86.22)	620 (86.11)
	Widow	6 (3.06)	15 (2.08)
Job	Housekeeper	143 (72.95)	527 (73.19)
	self-employment	11 (5.61)	49 (6.8)
	Employee	42 (21.42)	144 (20)
Education	High school	24 (12.24)	129 (17.91)
	Diploma	47 (23.97)	156 (21.66)
	College education	125 (63.77)	435 (60.41)
Type of vaccine received	Sputnik	42 (21.42)	204 (28.33)
	AstraZeneca	61 (31.12)	214 (29.72)
	Sino pharm	67 (34.18)	250 (34.72)
	Others	26 (13.26)	52 (7.22)
Contraceptive Use	DEPO	1 (0.51)	13 (1.8)
	IUD	2 (1.02)	14 (1.94)
	Withdrawal	128 (65.3)	528 (73.33)
	LD or HD	2 (1.02)	13 (1.8)
	Minipill	0	4 (0.55)
	Condom	20 (10.2)	63 (8.75)
	Non	43 (21.93)	85 (11.8)
Breastfeeding status	No	189 (96.42)	695 (96.52)
	Yes	7 (3.57)	25 (3.47)
Age	<20	6 (3.06)	38 (5.27)
	20 -30	61 (31.12)	239 (33.19)
	30-40	71 (36.22)	224 (31.11)
	40-50	56 (28.57)	207 (28.75)
	>50	2 (1.02)	12 (1.66)
BMI	18.5<	6 (3.06)	28 (3.88)
	18.5 to 24.9	122 (62.24)	463 (64.3)
	25 to 29.9	52 (26.53)	167 (23.19)
	>30	16 (8.16)	62 (8.61)

**Table 2:** Status of vaccination complications on menstrual cycle (n=916).

Variable		Frequency	Percent
Polymenorrhagia	Yes	149	16.26
	No	767	83.73
Oligomenorrhea	Yes	147	16.04
	No	769	83.95
Hypomenorrhea	Yes	47	5.13
	No	869	94.86
Hypermenorrhea	Yes	157	17.13
	No	759	82.87
Bleeding less than 30 cc	Yes	88	9.6
	No	828	90.39
Menorrhagia	Yes	189	20.63
	No	727	79.36
Metrorrhagia	Yes	112	12.22
	No	804	87.77
Amenorrhea	Yes	18	1.96
	No	898	98.03
Dysmenorrhea	Without change	823	89.84
	Increased	93	10.15
PMS	Without change	754	82.31
	Increased	162	17.68

with university degrees (OR=0.29, P=0.00), respectively. This risk was also 16.6 times higher in women who used natural contraception methods than in those using an intrauterine device (IUD) (OR=0.06, P=0.01). However, women using no contraception method were 1.75 times more likely to develop hypermenorrhea compared to those using natural methods (OR=1.76, p=0.01).

The risk of intermenstrual bleeding in single women was 1.9 times higher than in married women (OR=0.52, p=0.02). The risk of dysmenorrhea in women without high school diplomas was 2.85

times higher than in those with high school diplomas (OR=0.35, P=0,01) and 3.12 times higher than those with university degrees (OR=0.32, P=0.01).

Women taking LD or HD pills were 12.94 times more at risk of developing amenorrhea after vaccination compared to those using natural methods (OR=12.94, P=0.00). Moreover, this risk was 5.26 times higher in women with no experience of breastfeeding compared to those with this experience (OR=0.19, P=0.00).

Comparing stress levels in the two groups indicated that in the group with menstrual disorders the stress level was at its highest in the third month followed by the second and first months. Furthermore, stress levels were significantly increased compared to the control group. The anxiety levels in the group with menstrual disorders also increased within the three months and showed a significant increase compared to the control group. In addition, depression levels in the group with menstrual disorders increased within the three months and showed a significant increase compared to the control group (P<0.05) (Table 3).

## Discussion

The aim of the present study was to determine the effect of menstrual disorders caused by COVID-19 vaccines on stress, anxiety, and depression in women and results showed 21.39% of the participants developed menstrual disorders after vaccination.

Recent studies have reported changes in the menstrual cycle after receiving both mRNA- and adenovirus-based COVID-19 vaccines, suggesting that if there is a link, it might be due to the immune response to vaccination [2]. Alison also concluded that COVID-19 vaccines cause insignificant, temporary, and self-limiting changes in the length of the menstrual cycle [17]. According to Lagana's report, most women experienced menstruation 1 to 5 days earlier than expected, and the most prevalent change was heavy menstrual bleeding. In fact, the menstrual cycle can be affected by the activation of the immune system in response to various stimuli, including viral infections. A study conducted on women reported that about a quarter of women infected with SARS-CoV-2 developed menstrual disorders [18].

The findings showed that people with menstrual disorders experienced stress, anxiety, and depression, which worsened along the three months. Physical illnesses can cause mental illnesses in patients. For example, Lui showed that people with chronic illnesses develop stress, anxiety, and depression [9]. Pourmansouri also found that patients with thalassemia major have a low quality of life and a high percentage of these patients suffer from moderate to severe depression, anxiety, and stress [10].

The inflammatory responses associated with acute or chronic physical conditions can affect access to neurotransmitter precursor amino acids, and these changes are associated with mental health [19].

In women, changes and instability in female sex hormones that cause menstrual irregularities can cause stress, anxiety, and depression. In women, changes and imbalances in female sex hormones leading to menstrual disorders can cause stress, anxiety, and depression. In this regard, Sule argued that the quality of life of women affected by this form of stress and anxiety was significantly lower in the menorrhagia group compared to the control group (without menorrhagia) [12]. Furthermore, a study in Oman showed that the risk of depression, anxiety, and stress in women with Polycystic Ovary Syndrome

**Table 3:** Comparison of stress, anxiety and depression between two groups (with AUB and without AUB).

Mental Disorder	First Cycle following the Vaccine		P-value	Second Cycle following the Vaccine		P-value	Third Cycle following the Vaccine		P-value
	With AUB	Without AUB		With AUB	Without AUB		With AUB	Without AUB	
	Mean ± SD			Mean ± SD			Mean ± SD		
Stress	23.86 ± 8.74	8.86 ± 5.45	<0.001	24.16 ± 8.65	8.72 ± 5.53	<0.001	24.96 ± 8.77	8.73 ± 5.47	<0.001
Anxiety	13.6 ± 6.54	3.33 ± 2.98		13.89 ± 6.53	3.31 ± 2.85		14.11 ± 6.58	3.12 ± 2.91	
Depression	17.87 ± 9.9	4.6 ± 5.09		18.80 ± 9.6	4.71 ± 5.1		18.91 ± 9.8	4.59 ± 5.08	

(PCOS) increased compared to the control group [11]. The role of sex hormones in regulating women's emotions has been confirmed by many studies [20,21]. Steroid hormones, progesterone, and estradiol play vital roles in regulating brain morphology and function. Sex hormone fluctuation can cause changes in the neurotransmitter system, potentially and permanently affecting mood and behavior. Steroid hormones, also known as active neurosteroids, play a role in cognitive emotion regulation by organizing and activating the central nervous system [22,23].

Stress is mental/psychological distress that arises from different aspects of life, including physical, psychological, social, and emotional pressures, affecting both the body and mind. Dysfunctional thought patterns can cause stress or exacerbate it [24]. Anxiety is also expressed as an emotional state including feelings of tension and fear and increased activity of the autonomic nervous system [25]. Fear of the unknown and lack of awareness can cause anxiety. As the findings suggested, the participants' levels of stress, anxiety, and depression increased over time. Lack of awareness of possible side effects, their mechanisms, and their treatments leads to a negative attitude. According to the findings of the study conducted by Christopher, the greatest fear leading to individuals' reluctance to receive the vaccines was the fear of their short-term and long-term side effects [1].

Since mental disorders can exacerbate menstrual disorders, educating people about possible short-term side effects and how to deal with them can help them recover more quickly and often without need for treatment. Previous studies have shown that most women who had had menstrual disorders recovered spontaneously within the next month. Most importantly, there is no evidence that COVID-19 vaccination adversely affects fertility.

In clinical trials, the rate of unwanted pregnancies was similar in vaccinated and unvaccinated individuals. In assisted reproduction clinics, the pregnancy rate was also similar in the two groups [26].

## Conclusions

One-fifth of women developed menstrual disorders after receiving COVID-19 vaccines. These disorders were followed by mental disorders such as stress, anxiety, and depression. Informing people about the temporary nature of these complications can reduce the psychological effects and prevent people from entering the vicious cycle of menstrual disorders exacerbation. It also prevents the development of negative attitudes toward the vaccines and the unwillingness to receive further doses and negative publicity among women.

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## Ethics Approval and Consent to Participate

This manuscript was derived from a project code No. 400000874 and was approved by the Ethics Committee of Kerman University of Medical Sciences, Iran (the code of ethics No. Kmu.ac.ir.1400.594).

Special codes were used for each of the participants to ensure the information confidentiality.

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