

Effect of COVID-19 vaccination on menstrual cycle irregularities among females: A cross-sectional study in Pakistan

Alina Arshad¹, Muhammad Usman², Humaira Majeed Khan^{1*}, Zaufishan Rahman¹, Mobina Manzoor¹ and Bazgha Gul¹

¹Institute of Pharmacy, Faculty of Pharmaceutical and Allied Health Sciences, Lahore College for Women University, Lahore, Pakistan

²Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan

Abstract: This study was aimed to assess the type and severity of COVID vaccine-induced menstrual disorders and also to investigate the risk factors for menstrual changes following COVID-19 vaccination in Pakistani females. A cross-sectional survey-based study was conducted in females between 12 -70 years of age from February to July 2022. The survey was conducted via in-person interviews as well as via social media. The data was analyzed using standard descriptive statistical parameters, the sociodemographic and clinical features were evaluated and reported as frequencies (percentages). The study comprised a total of 1023 female subjects. Approximately 36.9% of women reported menstrual abnormalities following immunization, with 30.5% experiencing them following their second dose. However, in majority of these women (21%) the symptoms were resolved after 3 months of irregularity. Vaccine type significantly influenced the incidence of menstrual disorders ($p < 0.001$) which were linked to Pfizer-Biontech, Sinopahrm, Sinovac, Moderna at rates of 14.9%, 9.5%, 4.7% and 2.7%, respectively. Both AstraZeneca and Moderna were implicated in postmenopausal bleeding (1.6% and 0.8%, respectively). The study showed that females receiving COVID-19 vaccines experienced menstrual irregularities such as short duration of periods, decreased volume of bleeding, and frequent menstrual cycles. However, the symptoms were temporary and self-limiting.

Keywords: COVID-19, vaccination, menstrual abnormalities, Pakistan

INTRODUCTION

In 2019, the WHO declared COVID-19, a pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). According to World Health Organization (WHO), there were 753 million confirmed SARS-CoV-2 infections with over 6 million deaths worldwide as of 1st February, 2023. In Pakistan, the number of confirmed cases was 1.57 million with over thirty thousand deaths due to COVID infection, as of 1st February 2023 (World Health Organization 2023). A rapid development of vaccines based on various platforms has been undertaken in order to reduce morbidity and mortality. Several side effects of the vaccine were well-documented, including fever, fatigue and headache (Polack *et al.*, 2020). A less well-known side-effect, namely menstrual irregularities, was then reported by an increasing number of women following vaccination (Merchant 2021).

The menstrual cycle, which is a biologically essential for females and is tightly regulated by endocrine, autocrine, and paracrine factors, varies greatly in length (26-35 days) and hormone levels throughout the cycle. AUB is defined by the FIGO (International Federation of Gynecology and Obstetrics) as abnormal uterine bleeding with abnormal frequency (cycle length of <24 days or more than 38 days), duration (less than 3 days or more

than 8 days) and quantity (light/heavy) (Munro *et al.*, 2018).

Abnormal uterine bleeding (heavy, prolonged) is a significant cause of morbidity and reduced quality of life for women. Furthermore, the association of metabolic disorders with abnormal uterine bleeding like dyslipidemia can also lead to increased mortality (Rostami Dovom *et al.*, 2016, Wang *et al.*, 2020). Therefore, menstrual abnormalities present a substantial problem to the healthcare system, particularly when considering the influence on women's daily responsibilities.

The association between COVID-19 infection and female menstrual irregularities has been brought to light recently by researchers (Li *et al.*, 2021). Numerous cases of menstrual problems after covid-19 vaccinations were reported to the MHRA (UK Medicines and Healthcare Products Regulatory Agency), including heavier or lighter periods, delayed periods, and intermenstrual bleeding. Counseling women about the risks and benefits of vaccination require a clearer understanding of the magnitude and duration of these changes. It is also important to identify vulnerable groups, such as those with preexisting gynecological conditions, so that they can receive appropriate counselling (Male 2021).

According to Pakistan statistics, the female population is 114.14 million as of October 2022. Therefore, the purpose

*Corresponding author: e-mail: humaira.majeed.khan@gmail.com

of this study was to assess the type and severity of COVID vaccine-induced menstrual disorders as well as to investigate the risk factors for menstrual changes following COVID-19 vaccination in females of reproductive age. Moreover, to evaluate the incidence of post-menopausal bleeding after COVID-19 vaccination. This study has would identified the significant cofactors which can be considered for the administration of COVID vaccine in order to minimize the problems related to the menstrual cycles in females.

MATERIALS AND METHODS

Study Design

A cross-sectional survey was conducted between February to July 2022 in order to evaluate the menstrual changes after COVID-19 vaccination among the females in Pakistan. The females were recruited for this study through a convenient sampling technique. A convenience sample of women were recruited for the study and data was collected by conducting web-based survey on google form and also in-person interviews. The sample size was calculated by the following equation 1 (Pourhoseingholi *et al.*, 2013).

$$n = \frac{z^2 p(1-p)}{d^2} \quad \text{Equation 1}$$

Where “n” is sample size, Z is level of confidence, P represent expected prevalence and d is precision.

The poll was disseminated across several digital media platforms to enhance the number of responses, and participants were encouraged to forward it to their friends and acquaintances. Females belonging to the age groups of 12–70 years were included in this study. Age groups were classified as 12-16 years (menarche) (Carroll 2007), 17-40 years (premenopausal) 41-55 years (perimenopausal) (Radhakrishnan 2023) and 56-70 years (post-menopausal) (Carroll 2007). The survey took six minutes to complete and the participation was entirely voluntary. There was a question before the start of actual questionnaire regarding the informed consent “if the participant gives her consent for participation in this survey?”

Study tool development and validation

Based on previous research, an authenticated questionnaire was developed to evaluate the COVID vaccine-associated menstrual disorders (Muhaidat *et al.*, 2022). A team of subject-matter experts conducted the face and content validity checks on the questionnaire's draft. Expert feedback was then compiled and revised. Later, the draft questionnaire was modified as needed.

The questionnaire consists of 30 extensive self-report questions covering six integral topics. The first is demographics, including age, weight, height, education, occupation, socio-economic status, and marital status. The

second section contains questions about the past medical gynecology related history, including bleeding/clotting disorder, autoimmune disease, asthma/allergy problems, PCOS, thyroid disorder, fibroids, endometriosis, hypothalamic amenorrhea, PMDD (Premenstrual dysphoric disorder) and adenomyosis. The third category is about previous COVID-19 infections and the severity of the symptoms of the infection, type of vaccine administered along with the number of doses and dates of vaccination. The fourth category includes questions about menarche age, menstrual abnormalities before and after vaccination, including menstrual cycle length, duration, frequency, amount of bleeding experienced before and after vaccination, time of symptoms' emergence after vaccination, the duration of symptoms' emergence, their relationship to the dose, and response to change in menstrual cycle. The fifth category consists of hormonal treatment including contraceptives, acne, endometriosis, hypo/hyperthyroidism, and the sixth category consists of questions related to pregnancy and breastfeeding.

The questionnaire was then tested on 30 women vaccinated with COVID-19 to assess its structure, clarity, length and overall impression, resulting in several minor changes to the original. Pilot testing results were not included in the final analysis.

Ethical permission was taken from the Office of Research, Innovation and commercialization (ORIC) vide letter No. ORIC/LCWU/381 dated 05-10-2022. Written informed consent was obtained from all the participants after explaining them the objectives of the study. All ethical factors were considered including participants' rights to privacy, confidentiality, and self-determination. The study adhered to ethical standards of voluntary participation, and did not cause them any emotional distress.

STATISTICAL ANALYSIS

All statistical analysis was performed using SPSS version 25.0. Based on the variability analysis (standard deviation), descriptive statistics were employed to describe the data. Using standard descriptive statistical parameters, the sociodemographic and clinical features were evaluated and reported as frequencies (percentages). The Chi-square test was performed to evaluate the relationship between vaccine type and dose and menstrual irregularity. A p-value of 0.05 or less was found to be statistically significant.

RESULTS

A total of 1345 females were enrolled in the study but 322 participants were excluded. Out of 322 excluded participants, 91 did not fill the online survey form completely while 231 participants were excluded for different reasons: Did not give written consent (56),

pregnant women (35), underwent hysterectomy (32), not vaccinated (60), didn't know the type of vaccine (48). Among 1023 included participants 678 were interviewed in person and 345 participants filled out the form via online survey. The flowchart of participants inclusion and exclusion is shown in fig. 1.

More than half of the respondents (62.3%) were between the ages 17–40 years, and 56.4% had a normal BMI. During the study, around half of the participants (55%) were students, and 65.9% were from the middle class. The majority of our study's respondents (61.9%) were single, while 36.3% were married. In terms of COVID-19 infection, 23% of participants had a confirmed infection. The majority of participants received Sinopharm, Pfizer-Biontech, And Sinovac (34.1%, 26.9%, and 19.3%, respectively) and a large percentage of people (82.8%) had two doses of the COVID-19 vaccine. Among the participants, the great majority of subjects (85%) were disease-free. However, PCOS was present in 9.2% of the participants. The Participants' socio-demographics and clinical characteristics are shown in table 1.

The effect of COVID-19 vaccine on menstrual disturbance is shown in table 2. The increased intervals between menstrual cycle (>35 days cycle) was observed mostly after the administration of 2nd dose which is 7.5% while increased frequency after administration of 1st and booster dose was observed in 2.2% and 5.9% females respectively. Similarly, increase in the frequency of menstrual cycles (< 24 days cycle) was also observed after the administration of 2nd dose. The disturbance in duration of bleeding was also observed after the administration of 2nd dose where the duration of bleeding was decreased in majority of females (10.6%) while increase in duration of bleeding was reported by 3.9% participants. The volume of bleeding was also decreased in 11.2% females while it was increased in 3.3% females after the administration of 2nd dose. The moderate nature of menstrual cramps was observed in 3.2% females after the administration of 3rd (booster) dose while severe menstrual cramps were reported in 6.2% females after getting 1st dose, 14.3% females after getting 2nd dose while 4.4% females reported sever cramps after the administration of 3rd dose of vaccine. However, intermenstrual bleeding was mostly reported after the administration of 1st dose (0.3%) while post-menopausal bleeding was reported by 1.6% females who received 2nd dose of vaccine. The association of number of doses of vaccine with menstrual disturbance was significant for all types of problems except for amenorrhea as shown in table 2.

The disturbance in menstrual cycles was also associated with the type of vaccines as shown in table 3 as well as in fig. 2. The change in duration of bleeding, frequency of bleeding, volume of bleeding and menstrual cramps were compared for different types of vaccines. The decrease in

duration of bleeding (< 3 days) was mostly observed with Pfizer-Biotech 131 (12.8%) followed by Sinopharm 71 (6.9%). However, increase in duration of bleeding (> 7 days) was mostly observed with Sinopharm 29 (2.8%) followed by Sinovac vaccine 24 (2.3%) (fig. 2a). The increase in frequency of periods (< 24 days cycle) was mostly observed with Pfizer-Biotech 84 (8.2%) and decrease in frequency of periods (> 35 days cycle) was also associated with the administration of Pfizer-Biotech 69 (6.7%). The disturbance in frequency of periods was also observed in few patients who received Sinovac (fig. 2 b). The volume of bleeding was also significantly influenced by the type of vaccine and decrease in volume of bleeding was observed in most of the females 131 (12.8%) who received Pfizer-Biotech vaccine followed by Sinopharm 71 (6.9%) (fig. 2c). The occurrence of menstrual cramps of moderate nature were mostly observed in females administered with Sinopharm vaccine 138 (13.5%) while that of severe nature were mostly caused by Pfizer-Biotech vaccine 111 (10.9%) (fig. 2d).

The occurrence of menstrual irregularities after one month, two months and three months of vaccination was observed in 112 (10.9%), 130 (12.7%) and 74 (7.23%) females respectively. Whereas, 24 (2.5%) postmenopausal females reported one time spotting after vaccination. The occurrence of menstrual irregularities has been shown in table 4.

The study revealed that age, BMI, socio-economic status, marital status, education, COVID-19 infection, hormonal treatment, stopping or starting any type of contraceptive method, had no significant association with menstrual cycle length, duration, and frequency as ($p > 0.05$), whereas vaccine type and doses had statistical significance with the menstrual cycle length, duration, and frequency ($p < 0.001$).

Following vaccination, only 4% of women who experienced irregular menstruation consulted a gynecologist while 25.3% of women with menstrual irregularities after vaccination did not take any action to address the issue. The participant's reaction to post-vaccination menstrual irregularities is shown in table 5.

DISCUSSION

Vaccination is the best public health measure for preventing the spread of infectious diseases like COVID-19. New research on COVID-19 is constantly being published, the lack of high-quality research on COVID-19 and the menstrual cycle reflects the broader focus of medical research, which does not prioritize women's health, particularly outside of the context of pregnancy. Although there are studies with focus on impact of COVID-19 vaccination in females with global perspective (Sarfraz *et al.*, 2022), this is probably the first study reporting the menstrual disturbances associated with the COVID-vaccine among Pakistani females.

Table 1: Demographic and clinical characteristics of study participants

Variables	N (%)
Age (years)	
12-16 (menarche)	160 (15.6)
17-40 (pre-menopausal)	636 (62.3)
41-55 (peri-menopausal)	140 (13.7)
56-70 (post-menopausal)	87 (8.5)
BMI (kg/m ²)	
Underweight (< 18)	108 (10.6)
Normal weight (18.5-24.9)	577 (56.4)
Overweight (25-29.9)	238 (23.3)
Obesity (30 or above)	100 (9.8)
Marital status	
Single	633 (61.9)
Married	371 (36.3)
COVID Infection	
Yes, diagnosed	235 (23.0)
No	541 (52.9)
I think so, but not diagnosed	247 (24.1)
Severity of COVID symptoms	
I didn't have symptoms	541 (52.9)
Mild symptoms (fever, cough, sore throat)	440 (43.0)
Moderate symptoms (difficulty in breathing)	41 (4.0)
Vaccine doses	
1 dose	98 (9.6)
2 doses	847 (82.8)
Booster dose	78 (7.6)
Types of COVID-19 vaccines	
Sino Pharm	349 (34.1)
Pfizer-Biontech	275 (26.9)
Astrazeneca	27 (2.6)
Moderna	45 (4.4)
Cansino	53 (5.2)
Sputnik V	5 (0.5)
Sinovac	197 (19.3)
Sino Pharm + Pfizer	68 (6.6)

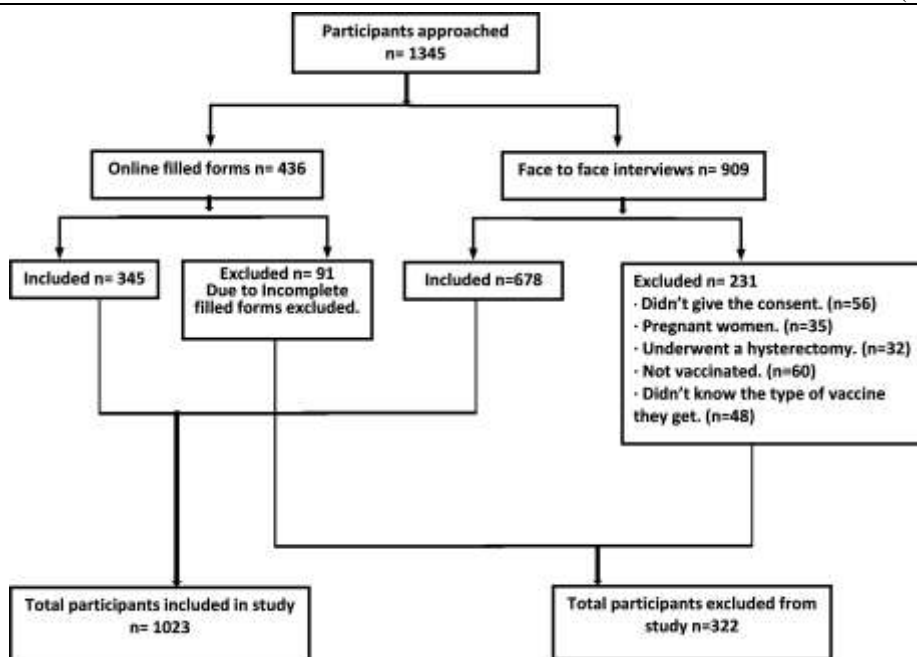


Fig. 1: Flowchart of participants' inclusion.

Table 2: Menstrual disorders and doses of vaccines

Menstrual disorder	Doses of vaccine n (%)				p-value
	1st dose	2nd dose	3rd dose	both doses	
Increase period frequency	23 (2.2)	77 (7.5)	60 (5.9)	1 (0.1)	0.01*
Decrease period frequency	49 (4.8)	88 (8.7)	28 (2.7)	18 (1.7)	0.01*
Increase duration of bleeding	15 (1.4)	40 (3.9)	12 (1.2)	0 (0)	0.027*
Decrease duration of bleeding	55 (5.3)	109 (10.6)	76 (7.4)	18 (1.8)	0.027*
Increase volume of bleeding	15 (1.4)	34 (3.3)	12 (1.2)	0 (0)	0.027*
Decrease volume of bleeding	57 (5.5)	115 (11.2)	76(7.4)	18(1.7)	0.027*
Menstrual cramps					
Moderate	2 (0.2)	9 (0.9)	33(3.2)	2 (0.2)	0.015*
Severe	63(6.2)	144 (14.3)	46 (4.4)	6 (0.6)	0.015*
Amenorrhea	5 (0.5)	5 (0.5)	3 (0.3)	3(0.3)	0.06
Intermenstrual bleeding	3(0.3)	0 (0)	1 (0.1)	0 (0)	0.001*
Post-menopausal bleeding	8 (0.8)	16 (1.6)	0 (0)	0 (0)	0.001*

*p < 0.05 is considered statistically significant.

Table 3: Association of types of vaccines and menstrual disorders

Menstrual disorders	Type of vaccine n (%)							p-value	
	Sinopharm	Pfizer-Biontech	Sinovac	Moderna	Cansino	Sputnik-V	Astrazeneca		Sinopharm + Pfizer
Increase period frequency	39 (3.8)	84 (8.2)	28 (2.7)	6 (0.6)	4 (0.4)	2 (0.2)	0 (0)	1 (0.1)	0.019
Decrease period frequency	58 (5.7)	69 (6.7)	22 (2.2)	21 (2.1)	12 (1.2)	1 (0.1)	0 (0)		
Increase duration of bleeding	29 (2.8)	10 (1.0)	24 (2.3)	2 (0.2)	0 (0)	1 (0.1)	0 (0)	1 (0.1)	0.01
Decrease duration of bleeding	71 (6.9)	131(12.8)	22 (2.2)	12 (1.2)	13 (1.3)	2 (0.2)	0 (0)	7 (0.7)	
Increase volume of bleeding	29 (2.8)	10 (1.0)	18 (1.8)	2 (0.2)	0 (0)	1 (0.1)	0 (0)	1 (0.1)	0.035
Decrease volume of bleeding	71 (6.9)	131(12.8)	30 (2.9)	12 (1.2)	13 (1.3)	2 (0.2)	0 (0)	7 (0.7)	
Moderate cramps	138 (13.5)	117(11.4)	88 (8.6)	14 (1.4)	27 (2.6)	2 (0.2)	0 (0)	14 (1.4)	0.018
Severe cramps	65 (6.4)	111(10.9)	43 (4.2)	14 (1.4)	17 (1.7)	3(0.3)	0 (0)	6 (0.6)	
Amenorrhea	1 (0.1)	1 (0.1)	6 (0.6)	0 (0)	5 (0.5)	0 (0)	0 (0)	2 (0.2)	0.073
Intermenstrual bleeding	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0.011
Post-menopausal bleeding	0 (0)	0 (0)	2 (0.2)	0 (0)	0 (0)	0 (0)	14(1.4)	0 (0)	0.028

*p value less than 0.05 was considered statistically significant.

Table 4: Time frame of menstrual irregularities

	Duration of irregularity						One-time spotting	No change	Total
	1 week	2 weeks	1 week	2 weeks	**More than 3 months				
Onset of symptoms after vaccination	2 weeks	1	2	7	0	0	0	0	10
	1 month	0	0	34	19	51	8	0	112
	*2 months	2	0	1	10	109	8	0	130
	3 months	1	0	0	7	57	8	1	74
	No change	0	0	0	0	0	0	697	697

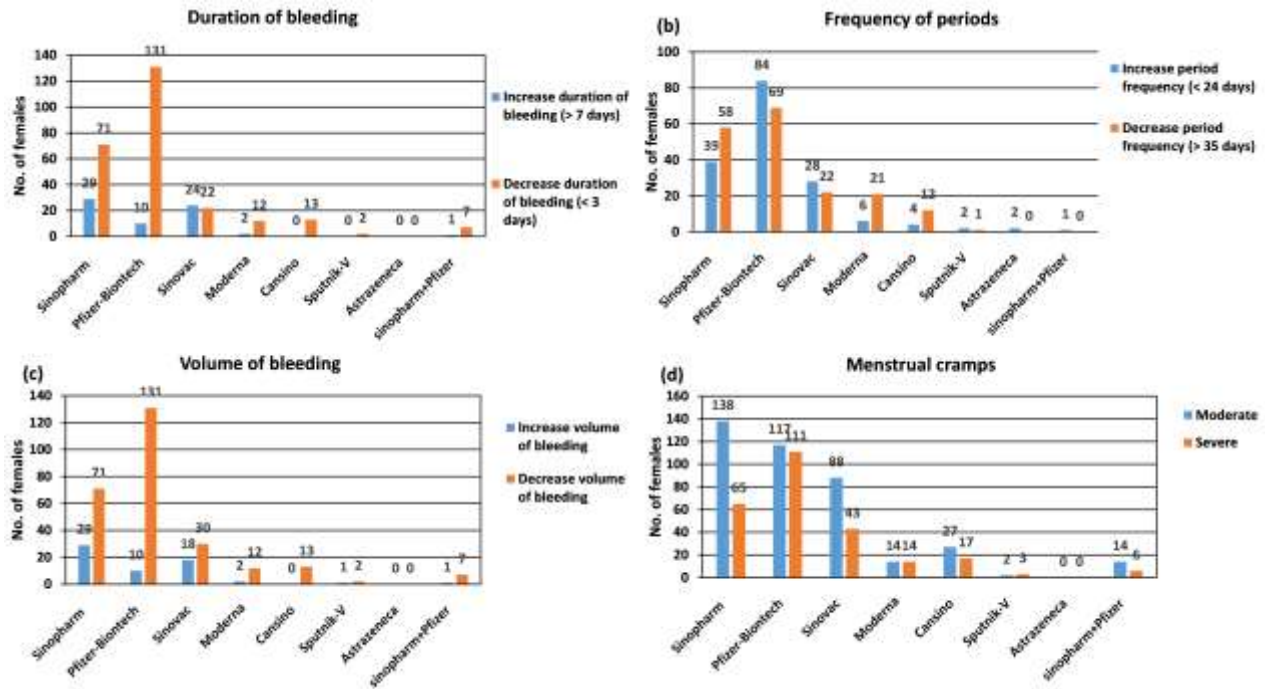


Fig. 2: Association of type of COVID-19 vaccination with duration of bleeding (a), frequency of bleeding (b), volume of bleeding (c), and menstrual cramps (d).

Table 5: Participants Reaction to Post-Vaccination Menstrual Irregularities.

Participants reaction	n (%)
No action took on menstrual irregularities	259 (25.3)
Consult gynecologist	42 (4.1)
Self-treatment	21 (2.1)
Searched online	4 (0.4)
No symptoms	697 (68.1)

According to the findings of study, 36.9% of the women in Pakistan who were vaccinated against COVID-19 reported experiencing menstrual irregularities after receiving the vaccination, especially after the second dose (30.5%). The results demonstrated that at least one of the four parameters described by FIGO to characterize the menstrual cycle was outside the normal range after vaccination, indicating a change in the menstrual cycle. When compared to their pre-vaccination status, women who received the vaccine had significantly decreased frequency of periods as well as shorter duration of bleeding after the administration of covid-vaccine. However, after more than three months of irregularity, these symptoms were relieved for 21% of respondents. A similar finding was observed in females of Iraq and Jordan where the change in number of days between two periods was also observed (Al-Najjar *et al.*, 2022). However, a prolonged cycle of menstruation is also reported in few studies (Lebar *et al.*, 2022). The ethnic variation can be the justification of this difference in response to COVID-vaccine.

The number of females who experienced decreased volume of bleeding was significantly higher than those increased volume of bleeding after the administration of vaccine. This might be due to the fact that the female menstrual cycle is influenced by a variety of factors, some of which are chronic and call for treatment, such as fibroids, endometriosis, and polycystic ovary syndrome (Phelan *et al.*, 2021). Some of these factors are transient and include infections, weight gain, stress, hormonal changes, and times of psychological stress (Kurdoğlu). A change in volume of bleeding has also been reported in Iraq and Jordan in a similar study (Al-Najjar *et al.*, 2022). The study shows that 4.8% had a decrease in period frequency, 5.3% had a decrease in the duration of bleeding, and 5.5% had a decrease in the volume of bleeding after the first dose of vaccination. Whereas after the second dose of vaccination, 8.7% had a decrease in period frequency, 10.6% had a decrease in duration of bleeding, and 11.2% had a decrease in volume of bleeding post-vaccination, and 1.6% had post-menopausal bleeding after the second dose of vaccination. However, in another study conducted in females of Middle East and North Africa (MENA), majority of females (46.7%) experienced menstrual abnormalities after the administration of first dose (Muhaidat *et al.*, 2022). As a reaction to vaccination, increased energy expenditure promotes processes such as leukocyte activation of T lymphocytes, which results in the production of antibodies against COVID-19 (Alvergne *et al.*, 2021). One hypothesis for the effect seen is that the immune response to the vaccine affects the hypothalamic-

pituitary-ovarian axis resulting in menstrual irregularities (Paces *et al.*, 2020). Even though the hypothalamic-pituitary-gonadal axis is responsible for maintaining a regular reproductive cycle, it can be temporarily disrupted by exposure to stress or an exacerbated immune response, such as that caused by immunization (Taylor *et al.*, 2020).

In comparison of the vaccine type, the decrease in period frequency by sinopharm was 5.7%, Pfizer-biontech 6.7%, sinovac 2.2%, and moderna 2.1% and a decrease in the duration of bleeding by sinopharm 6.9%, Pfizer-biontech 12.8%, and sinovac 2.2%. and a decrease in the volume of bleeding by sinopahrm 6.9%, Pfizer-biontech 12.8%, and sinovac 2.2% and 1.3% by cansino. In our study, amenorrhea was caused by sinovac 0.6% and by cansino 0.5% and inermenstrual bleeding by sinopharm 0.3%. Our study suggests that 1.4% of post-menopausal bleeding was caused by Astrazeneca and 0.8% by Moderna. There is a significant association between the menstrual disturbances caused by the types of vaccine. ($p < 0.001$). To the best of our knowledge no other study has reported the comparison of vaccine type in term of their effect of menstrual cycle. However, the results of a study of menstrual irregularity post-vaccination in the MECOVAC survey suggest that after the second dose, 62.5% of women who received Vaxzevria (AstraZeneca), 46.9% of women who received Comirnaty (Pfizer-BioNTech), and 64.3% of women who received Spikevax (Moderna) reported a change in the quantity of their subsequent menstrual flow, which is in accordancewith our results (Lebar *et al.*, 2022).

In this study, 25.3% of women did nothing regarding menstrual irregularity and only 4.1% of women went to a gynecologist. There are numerous explanations for this observed lack of assistance-seeking behavior (Alvergne *et al.*, 2021). First, some people, according to their evaluation, may have suffered moderate symptoms that did not necessitate care. Furthermore, the COVID-19-induced state of emergency may have produced a psychological or physical barrier that hindered people from seeking help for non-COVID-19-related problems. There is a paucity of understanding about the potential mechanism via which the vaccination could produce menstruation symptoms. It is possible, however, that it is due to immune-mediated vaccine-induced thrombocytopenia (Hunter 2021). Vaccine-induced thrombocytopenia, which results in irregular menstruation, has previously been related to a number of other vaccines, including the measles, mumps, and rubella (MMR), hepatitis A and B, diphtheria, tetanus, and acellular pertussis (DTaP), varicella and even influenza (Perricone *et al.*, 2014). This theory is backed up by this research, which identified trends and characteristics that may indicate the symptoms are the result of an immunological response. More research is needed to establish the mechanism by which the COVID-19 immunization induces menstrual abnormalities.

CONCLUSION

This study shows COVID vaccine-induced menstrual abnormalities such as short duration of periods, decreased volume of bleeding, and frequent menstrual cycles. These abnormalities may have an impact on women daily activities, ultimately lowering their overall quality of life. The findings also provide preliminary evidence that these symptoms are self-limiting and transient therefore, no clinical intervention is recommended. However, this study has identified the factors which can be considered for the administration of COVID vaccine in order to minimize the problems related to the menstrual cycles in females. The findings therefore call for routine menstrual data collection in COVID-19 and vaccination studies, as well as research into the mechanisms of menstrual disturbance after vaccination. There is a need for additional research that includes information on other menstrual health-related parameters and the evaluation of larger cohorts in order to determine the proportion of women with long-term changes. There are only a few limitations to this research. First, because this is a cross-sectional study with recall bias, more prospective longitudinal studies to confirm these findings should be conducted. Second, the study did not assess females' psychological status during the COVID-19 pandemic.

REFERENCES

- Al-Najjar MAA, Al-Alwany RR, Al-Rshoud FM, Abu-Farha RK and Zawiah M (2022). Menstrual changes following COVID-19 infection: A cross-sectional study from Jordan and Iraq. *PLoS One*, **17**(6): e0270537.
- Alvergne A, Kountourides G, Argentieri MA, Agyen L, Rogers N, Knight D, Sharp GC, Maybin A and Olszewska Z (2021). COVID-19 vaccination and menstrual cycle changes: A United Kingdom (UK) retrospective case-control study. *medRxiv*. 2021.2011.2023.21266709.
- Carroll RG (2007). Female reproductive system. Elsevier's Integrated Physiology. Mosby, Philadelphia, pp.177-187.
- Hunter PR (2021). Thrombosis after covid-19 vaccination. *BMJ*, **373**: n958.
- Kurdoğlu Z (2021). Do the COVID-19 vaccines cause menstrual irregularities? *Int. J. Women's Health Reprod.*, **9**(3): 158-159.
- Lebar V, Laganà AS, Chiantera V, Kunič T and Lukanović D (2022). The effect of COVID-19 on the menstrual cycle: A systematic review. *J. Clin. Med.*, **11**(13): 3800
- Li K, Chen G, Hou H, Liao Q, Chen J, Bai H, Lee S, Wang C, Li H, Cheng L and Ai J (2021). Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age. *Reprod. Biomed. Online*, **42**(1): 260-267.
- Male V (2021). Menstrual changes after covid-19 vaccination. *BMJ*, **374**: n2211.

- Merchant H (2021). CoViD-19 post-vaccine menorrhagia, metrorrhagia or postmenopausal bleeding and potential risk of vaccine-induced thrombocytopenia in women. *BMJ*, **373**: 958.
- Muhaidat N, Alshrouf MA, Azzam MI, Karam AM, Al-Nazer MW and Al-Ani A (2022). Menstrual symptoms after COVID-19 vaccine: A cross-sectional investigation in the MENA region. *Int. J. Womens Health*, **14**: 395-404.
- Munro MG, Critchley HOD and Fraser IS (2018). The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int. J. Gynaecol. Obstet.*, **143**(3): 393-408.
- Paces J, Strizova Z, Smrz D and Cerny J (2020). COVID-19 and the immune system. *Physiol. Res.*, **69**(3): 379-388.
- Perricone C, Ceccarelli F, Neshor G, Borella E, Odeh Q, Conti F, Shoenfeld Y and Valesini G (2014). Immune thrombocytopenic purpura (ITP) associated with vaccinations: A review of reported cases. *Immunol. Res.*, **60**(2-3): 226-235.
- Phelan N, Behan LA and Owens L (2021). The impact of the COVID-19 pandemic on women's reproductive health. *Front Endocrinol (Lausanne)*, **12**: 642755.
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW, Hammitt Jr. LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU and Gruber WC (2020). Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N. Engl. J. Med.*, **383**(27): 2603-2615.
- Pourhoseingholi MA, Vahedi M and Rahimzadeh M (2013). Sample size calculation in medical studies. *Gastroenterol. Hepatol. Bed Bench*, **6**(1): 14-17.
- Radhakrishnan R (2023). What is the average age a woman stops menstruating? *MedicineNet*, https://www.medicinenet.com/what_is_the_average_age_a_woman_stops_menstruating/article.htm
- Rostami Dovom M, Tehrani FR, Djalalinia S, Cheraghi L, Gandavani SB and Azizi F (2016). Menstrual cycle irregularity and metabolic disorders: A population-based prospective study. *PLoS One*, **11**(12): e0168402.
- Sarfraz A, Sarfraz Z, Sarfraz M, Nadeem N, Felix M and Cherrez-Ojeda I (2022). Menstrual irregularities following COVID-19 vaccination: A global cross-sectional survey. *Ann Med Surg (Lond)*, **81**: 104220.
- Taylor S, Landry CA, Paluszczek MM, Fergus TA, McKay D and Asmundson GJG (2020). COVID stress syndrome: Concept, structure and correlates. *Depress Anxiety*, **37**(8): 706-714.
- UK Medicines and Healthcare Products Regulatory Agency (2023). from <https://www.emergobyul.com/resources/mhra-uk-medicines-and-healthcare-products-regulatory-agency>.
- Wang YX, Arvizu M, Rich-Edwards JW, Stuart JJ, Manson JE, Missmer SA, Pan A and Chavarro JE (2020). Menstrual cycle regularity and length across the reproductive lifespan and risk of premature mortality: prospective cohort study. *BMJ*, **371**: m3464.
- World Health Organization (2023). WHO Coronavirus (COVID-19) Dashboard. <https://covid19.who.int/>.