

Self-Reported Adverse Events of COVID-19 Vaccines on Menstrual Cycles

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Abstract

Aim of Study: To investigate the adverse events of COVID-19 vaccinations on menstrual abnormalities in women in their reproductive period.

Methods: Following a cross-sectional research design, this study included 102 women who had received the COVID-19 vaccinations. A study questionnaire adapted from the Menstruation after COVID vaccine (MECOVAC) survey was used for data collection.

Results: Almost half of participants (48%) reported the incidence of menstrual abnormalities after receiving COVID-19 vaccinations, manifested as changes in frequency, length or quantity of menstruation. Participants received one, two or three doses of either Pfizer-BioNTech or Oxford-AstraZeneca vaccines. Adverse events of COVID-19 vaccines occurred mainly after the third doses of Pfizer and AstraZeneca (12.5% for both). The most frequent changes in quantity of menstrual blood among participants were variation in its quantity and having heavier menstruation (17.2% and 15.6%, respectively), which occurred after receiving the third dose of Pfizer vaccine, while menstrual blood became less among 25% of participants after receiving the third dose of AstraZeneca. Disturbance of personal life occurred in 44.9%, while 38.8% needed to visit a doctor, 26.5% underwent investigations and 32.7% took medications. Menstrual cycles of 51% returned to normal within 1-2 cycles, while those of 49% returned after more than two cycles.

Conclusions: Women who receive COVID-19 vaccinations may have menstrual abnormalities. This change mainly occurs after the third dose, regardless of the brand of received vaccine. It is recommended that women be clearly informed after vaccination of the possibility of short-term menstrual abnormality and to seek proper medical advice in such conditions. Further studies are required to investigate the possible mechanisms behind these COVID-19 vaccines' adverse events.

Keywords: COVID-19 vaccination, adverse events, menstrual abnormality, Saudi Arabia

Introduction

The global COVID-19 pandemic has shown an accelerated geographic spread over the last two years, (1) and caused devastating effects on public health and the global economy worldwide. Preventive strategies constituted the central role in limiting its spread, along with successful disease isolation and community containment. Moreover, a mass vaccination strategy was globally adopted to build up sufficient herd immunity, being the only effective tool to manage the situation (2).

Currently, there are several types of vaccines for COVID-19. The BNT162b2 (Pfizer-BioNTech), ChAdOx1 (Oxford-AstraZeneca), Sinopharm and Sputnik vaccines have been approved for use in many parts of the world (3). Despite the fact that COVID-19 vaccinations have been effective in reducing hospitalizations and mortalities, many studies have reported various side effects, ranging from mild symptoms, e.g., fatigue, headache, cramps in the arms, to severe symptoms, e.g., hemorrhage, thrombosis, anaphylaxis, venous blood clots and neurological events, including stroke and myocardial infarction (4-8).

Vaccination against SARS-CoV-2 was recommended for all women, including those who are pregnant or planning to become pregnant. However, since the beginning of the COVID-19 pandemic, there have been endless discussions on social media, during clinic visits or telemedicine, reporting that some women may experience menstrual changes related to vaccination, which has fueled vaccine hesitancy or its refusal (9-12).

Studying menstrual cycle features is challenging, since normal variations exist within women over their lifespan and in relation to characteristics, such as age, parity, history of infertility, body mass index and exercise. However, a worldwide increase in visits to the Obstetrics and Gynecology clinics was reported after receiving COVID-19 vaccination (13,14).

The cohort study of Edelman et al. reported that COVID-19 vaccination was associated with a less than one day change in cycle length for both vaccine-dose cycles, compared with pre-vaccine cycles (9). Moreover, a cross-sectional survey conducted in Italy reported slight changes in menstruation cycles after the second dose of vaccination (15). A cross-sectional study in the Middle East and North Africa (MENA) region reported that women experienced a longer duration of menstruation and cycle length after vaccination, which had a negative impact on their quality of life (16).

The information on incidence and types of menstrual irregularities associated with COVID-19 vaccination and its impact in KSA is lacking. Therefore, this study aimed to assess the incidence of menstrual irregularities among women in the region and to investigate the impact of the menstrual abnormalities on their lives. The study will also explore if there is any correlation between the type of administered vaccine and the associated menstrual abnormalities.

Findings of this study are expected to determine if the rates and severity are similar to those reported in the literature and will help in making subsequent decisions for optimal management.

Materials and Methods

The present study followed a descriptive cross-sectional design. A study questionnaire was adapted from the Menstruation after COVID vaccine (MECOVAC) survey (15). The questionnaire included two sections; the first section recorded the demographic and clinical characteristics, hormonal treatments, number of previous pregnancies and abortions, reproductive or peri-menopausal status, and type of COVID-19 vaccine received for the first, second, and third doses; and the second section assessed frequency, length, and quantity of the menstrual cycles after the administration of the first, second and third doses of the COVID-19 vaccine, how long the menstrual abnormalities lasted, whether participants required consultation, and if the experienced abnormality affected their normal daily life.

The ethical approval for conducting this study was obtained from Alkharj Military Hospital Institutional Research Board. An electronic survey form was sent to women fulfilling the inclusion criteria during the period from June to July 2022. All participants were clearly informed that their responses were anonymous and that they could withdraw at any point if they decided to.

The inclusion criteria involved all women of reproductive age, below 50 years old, attending Alkharj Military Hospital, who had received at least one dose of any of the COVID-19 vaccines, and had not been infected with COVID-19. On the other hand, women with gynecological diseases, undergoing hormonal and non-hormonal treatments that can affect menstrual cycle, in the menopause stage, or with a history of irregular menstrual cycles within the last 12 months before receiving the COVID-19 vaccine, or with past history of COVID-19 were not included.

Collected data were analyzed by the Statistical Package for Social Sciences (IBM, SPSS, version 28). Descriptive analyses were applied to describe the frequency and percentages for qualitative variables. The Chi-square (χ^2) test was used to assess significance of differences in changes in menstrual cycles after receiving different doses of COVID-19 vaccines. All the tests of significance were two-tailed, and a p-value < 0.05 was considered statistically significant.

Results

Within the present study, electronic survey forms were sent to 200 women fulfilling the inclusion criteria. However, 102 responses were received, with a response rate of 51%.

Table 1: Personal characteristics of participant women (n=102)

Personal characteristics	No.	%
Age groups		
• <30 years	39	38.2
• 30-40 years	39	38.2
• >40 years	24	23.5
Marital status		
• Single	46	45.1
• Married	56	54.9
Number of received vaccine doses		
• One	3	2.9
• Two	21	20.6
• Three	78	76.5
Type of first dose		
• Pfizer-BioNTech	60	58.8
• Oxford-AstraZeneca	42	41.2
Type of second dose		
• Pfizer-BioNTech	64	62.7
• Oxford-AstraZeneca	35	34.3
Type of third dose		
• Pfizer-BioNTech	64	62.7
• Oxford-AstraZeneca	8	7.8

Table (1) shows that 38.2% of participants were less than 30 years old, 38.2% were 30-40 years old, while 23.5% were older than 40 years. More than half of the participants (54.9%) were married, and 48% had previous infection with COVID-19. Most participants (77.5%) received 3 doses of the vaccine, while 20.6% received two doses and 2% received one dose. Pfizer-BioNTech was the main received vaccine for the first, second and third doses (58.8%, 62.7%, and 62.7%, respectively), followed by Oxford-AstraZeneca (41.2%, 34.3%, and 7.8%, respectively).

Figure 1: Incidence of menstrual changes after receiving COVID-19 vaccines among participating women (n=102)

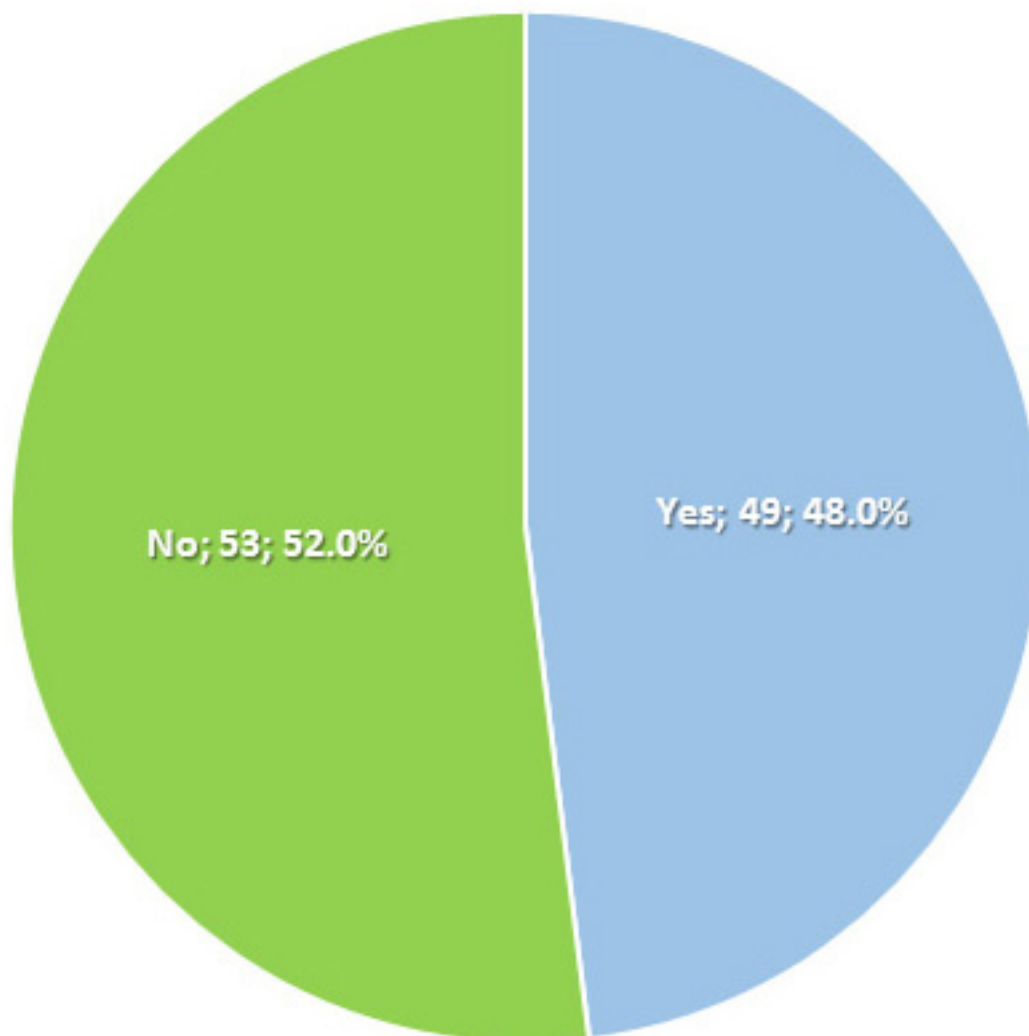


Figure (1) shows that menstrual changes occurred in 48% of participating women after receiving COVID-19 vaccines.

Table 2: Frequency distribution of variations in menstruation after first, second and third doses of COVID-19 vaccines

Changes in Menstrual Cycle	Pfizer			AstraZeneca			P Value
	1 st	2 nd	3 rd	1 st	2 nd	3 rd	
	(n=60)	(n=64)	(n=64)	(n=42)	(n=35)	(n=8)	
Changes in frequency							
Amenorrhea	2 3.3%	1 1.6%	1 1.6%	1 2.4%	0 0.0%	0 0.0%	
Period arrived 1–5 days earlier	2 3.3%	12 18.8%	7 10.9%	1 2.4%	2 5.7%	1 12.5%	
Period arrived 5–10 days earlier	1 1.7%	6 9.4%	6 9.4%	2 4.8%	3 8.6%	0 0.0%	
Period arrived >10 days earlier	1 1.7%	1 1.6%	3 4.7%	1 2.4%	1 2.9%	0 0.0%	<0.001
Period arrived 1–5 days later	2 3.3%	5 7.8%	8 12.5%	0 0.0%	2 5.7%	0 0.0%	
Period arrived 5–10 days later	1 1.7%	1 1.6%	8 12.5%	0 0.0%	3 8.6%	0 0.0%	
Period arrived >10 days later	1 1.7%	2 3.1%	3 4.7%	1 2.4%	2 5.7%	0 0.0%	
Duration of the cycle							
Variation in length of cycle	1 1.7%	6 9.4%	8 12.5%	3 8.6%	3 8.6%	1 12.5%	
Spotting	2 3.3%	0 0.0%	7 10.9%	1 2.4%	1 2.9%	0 0.0%	
Menstruation lasted >7 days	0 0.0%	1 1.6%	7 10.9%	2 4.8%	1 2.9%	0 0.0%	<0.001
Menstruation lasted <3 days	1 1.7%	4 6.3%	2 3.1%	0 0.0%	2 5.7%	0 0.0%	
Quantity of menstrual blood							
Became heavier	1 1.7%	8 12.5%	10 15.6%	1 2.4%	4 11.4%	0 0.0%	
Became less	4 6.7%	4 6.3%	8 12.5%	2 4.8%	0 0.0%	2 25.0%	<0.001

Table (2) shows that, regarding changes in frequency of menstrual cycles of participants, the most frequent were variation in frequency and 1-5 days earlier arrival of the period, after receiving the second dose of Pfizer vaccine (14, 21.9% and 12, 18.8%, respectively). Regarding changes in duration of the cycle, the most frequent was variation in length of cycle, which occurred mainly after the third doses of Pfizer and AstraZeneca (12.5% for both). The most frequent changes in quantity of menstrual blood among participants were variation in its quantity and having heavier menstruation (17.2% and 15.6%, respectively), which occurred after receiving the third dose of Pfizer vaccine, while menstrual blood became less among 25% of participants after receiving the third dose of AstraZeneca.

Table 3: Pattern and impact of menstrual changes among participating women (n=49)

Characteristics	No.	%
Menstrual changes		
• Irregularity	25	51.0
• Heavier menstrual bleeding	24	49.0
• Lighter menstrual bleeding /amenorrhea	20	40.8
• Prolonged duration of menstrual cycle	11	22.4
• Shorter duration of menstrual cycle	9	18.4
Disturbing personal life	22	44.9
Need to visit a doctor	19	38.8
Undergoing investigations	13	26.5
Taking medication	16	32.7
Return to normal		
• Within the next 1-2 menstrual cycles	25	51.0
• After more than 2 menstrual cycles	24	49.0

Table (3) shows that among participants who experienced menstrual changes, 51% had menstrual irregularities, 49% had heavier menstrual bleeding, 40.8% had lighter menstrual bleeding, 22.4% had prolonged menstrual cycles, and 18.4% had shorter menstrual cycles. Disturbance of personal life occurred in 44.9%, while 38.8% needed to visit a doctor, 26.5% underwent investigations and 32.7% took medications. Menstrual cycles of 51% returned to normal within 1-2 cycles, while those of 49% returned after more than two cycles.

Discussion

Several studies have been conducted worldwide to investigate the potential impact of COVID-19 vaccination on menstruation, including the longitudinal study by the NIH (17). It has been emphasized that the menstrual cycle is a vital reproductive sign among females during their reproductive period, which provides important insight into hormonal balance and pregnancy. Menstrual disorders may range from mild (not affecting life and daily activities) to severe, affecting life, productivity, psychological status, and even sexual life (13,14).

The present study aimed to investigate the incidence and impact of menstrual abnormalities among 102 women after receiving COVID-19 vaccines (Pfizer-BioNTech or Oxford-AstraZeneca).

The present study indicated that 48% of participants had menstrual abnormalities after receiving COVID-19 vaccinations, manifested as changes in frequency (51%), quantity, being heavier (49%), or lighter (40.8%), and length, being longer (22.4%), or shorter (18.4%). These changes affected almost half of those who experienced menstrual abnormalities. These abnormalities disturbed the personal life of almost half of participating women, while 38.8% had to visit a doctor and 32.7% received

medications. However, these changes were short-term. Menstrual cycles of more than half of participants returned to normal within 1-2 menstrual cycles. Moreover, our study showed that changes in frequency and quantity of menstrual blood were significantly higher after receiving the third dose, especially that of Pfizer-BioNTech vaccine as compared to those after the first or second doses and those who received AstraZeneca vaccine.

Findings of our study are in accordance with those reported by several studies. Male (18) noted that short-term changes in the menstrual cycle have been reported for both mRNA and adenovirus-vectored COVID-19 vaccines. Moreover, the cross-sectional study of Muhaidat et al. (16) in the MENA Region reported that 34% of women had to seek medical help to alleviate their menstrual disturbances. Notably, only 17.3% who sought medical help required medications to alter their cycle, and fortunately, all the participants had their abnormalities resolved within one or two cycles. This finding is in line with other reports.

Several studies reported short-term and transient menstrual disturbances after receiving COVID-19 vaccinations, such as menstrual irregularities, heavier bleeding, delayed periods, unexpected vaginal bleeding, or altered duration (9-12).

The incidence rate of menstruation irregularity in our study is in agreement with those reported in other similar studies. In Italy, Laganà et al. (15) reported that the majority of the women had their menstruation arrive 1-5 days earlier than the expected date after their vaccination.

Pfizer-BioNTech vaccine has been widely available and accepted in the Gulf region, because of which we see the majority of women had this vaccine for their first, second and third or booster dose, reportedly based on its efficacy reports in combating the coronavirus (19).

Similarly, higher occurrences of heavy bleeding were also reported in some other studies. Moreover, alterations in the length of the menstrual cycle (e.g., more than seven days) were also in line with other studies (4; 15-18).

Male (18) argued that, although reported menstrual cycle changes after COVID-19 vaccination are usually short-term, research into these common adverse reactions is important for the overall success of vaccination programs. Moreover, research may also help understand the mechanism between COVID-19 vaccines and menstrual changes.

Alvergne et al. (20) explained that the hypothalamo-pituitary-ovarian axis may mediate the effects of COVID-19 vaccination on the menstrual cycle. They proposed that the possible mechanism for disturbances of menstrual cycle after receiving COVID-19 might be mediated by perturbations to ovarian hormones. However, their study was unable to detect a clear association between the timing of vaccination within the menstrual cycle and reports of menstrual changes. Their study also looked at the impact of vaccine types on menstrual timing or flow but found no noticeable differences. Therefore, they suggested that vaccine effects on menstrual periods are probably not mediated by a specific approach or ingredient, but rather by the immune response.

Biologically plausible mechanisms linking immune stimulation with menstrual changes include immunological influences on the hormones driving the menstrual cycle or effects mediated by immune cells in the lining of the uterus, which are involved in the cyclical build-up and breakdown of this tissue (21).

In terms of management, the Royal College of Obstetricians and Gynaecologists and the Medicines and Healthcare Products Regulatory Agency (MHRA) recommend that anyone reporting a change in periods persisting over several cycles, or new vaginal bleeding after the menopause, should be managed according to the usual clinical guidelines for these conditions. Clear and trusted information should be provided to all women before being vaccinated against COVID-19, especially those who rely on being able to predict their menstrual cycles to either achieve or avoid pregnancy. Moreover, Alvergne et al. (20) suggested the use of combined hormonal contraception to protect against vaccination-associated menstrual changes.

Conclusions

Women who receive COVID-19 vaccinations may have menstrual abnormalities, at least for one or two of their following menstrual cycles. This change mainly occurs after the third dose, regardless of the brand of received vaccine. It is recommended that women be clearly informed after vaccination of the possibility of short-term menstrual abnormality and to seek proper medical advice in such conditions. Further studies are required to investigate the possible mechanisms behind these COVID-19 vaccines' adverse events.

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