

#### ORIGINAL RESEARCH

# Short Term Effect of Corona Virus Diseases Vaccine on the Menstrual Cycles

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Background: The latest threat to world health is coronavirus disease-2019 (COVID-19), and the exact death rate of SARS-CoV-2 infection is still to be explored and varies widely throughout the world. Inactivated virus vaccines, recombinant viral vaccines, subunit vaccines, DNA vaccines, and attenuated vaccinations have all been investigated in the hunt for an optimal SARS-CoV vaccine. Some women had menstrual abnormalities after immunisation, including heavy menstrual bleeding (menorrhagia), frequent bleeding (metrorrhagia/polymenorrhag), and postmenopausal haemorrhage. Vaccine-induced thrombocytopenia might be one of the underlying reasons.

Purpose: The aim to carry out this study was to survey by recruiting the female participants who were vaccinated with one or two shots of the available vaccine and observe short-term menstrual changes.

Patients and Methods: This web-based survey cross-sectional study included women who were above 18 years, had the vaccine at least one month (one menstrual period) before participating in the study, had access to social media platforms and were willing to take part in the study. Women were excluded if, at the time of the study, they were pregnant or had amenorrhea of more than 6 months. **Results:** Analysing the menstrual flow more, we saw that 24.5% of the patients had increased flow, while 15.5% had reduced flow which for both changes in the flow, the p-value was 0.017. However, 23.65 showed delayed periods, and 51.6% showed no changes. The changes in the timing were significant, indicating a p-value of 0.008. The study will be a significant contribution to the literature as this pandemic is new, and the vaccination against COVID-19 is still in the trial phase.

Conclusion: We observed in our study that there was a change in the menstruation timings and flow after vaccination. However, further longitudinal studies are needed to conclude the impact of the COVID-19 vaccine on the menstruation cycle.

Keywords: COVID-19, menstrual abnormalities, menstrual changes, menstrual flow, short-term effect, vaccination

### Introduction

COVID-19, or coronavirus disease-2019 or Pneumonic Pneumonia of Unknown Origin, is the most recent threat to global health. There is a wide range of single-stranded, positive-sense, encapsulated RNA viruses in this collection, first discovered in Wuhan, China, in late December 2019. SARS-CoV, SARS-CoV-2, and MERS-CoV are all members of the Coronavirus family.<sup>2</sup> Legal authorities worldwide have taken several unusual measures to combat the COVID-19 outbreak. In addition to a smart lockdown, academic and commercial closures, stay-at-home orders, and rigorous travel restrictions. However, these initiatives have proven to be highly successful, they have come at a significant and broad socioeconomic cost.3 The exact death rate of SARS-CoV-2 infection is still to be explored and varies widely worldwide, ranging from 0.3 to 8.4%. The complications of COVID-19 involved respiratory complications, cardiovascular, neurological, liver and kidney complications, haematological involvement, electrolyte imbalance, GI tract involvement, endocrine complications and obstetric and gynaecological, skin, ocular and central nervous system issues.4 The mental health burden during the COVID-19 pandemic was also documented in the literature to have a high frequency of at least

mild generalised anxiety and depression symptoms, psychological distress, and COVID-19 related dread in 44.5% of the examined sample.4-6

To protect the whole global population from a pandemic, we must use all of the tools at our disposal, which means vaccine development is necessary Several effective vaccine approaches are undergoing clinical trials<sup>7</sup> In searching for the best SARS-CoV vaccine, researchers have looked into inactivated virus vaccines, recombinant viral vaccines, subunit vaccines, DNA vaccines, and attenuated vaccinations<sup>8</sup> Following vaccination against COVID-19, some women had menstrual irregularities such as excessive monthly bleeding, frequent bleeding, and postmenopausal haemorrhage One of the underlying causes might be vaccine-induced thrombocytopenia Females who have underlying platelet problems have previously had 'heavy menstrual bleeding Recent reports of increased menstrual bleeding among women in numerous countries following the COVID-19 vaccination may be due to vaccine-induced thrombocytopenia Significant blood loss can induce severe anaemia, aggravate thrombocytopenia, and increase the risk of haemorrhages and clots in many women.<sup>10</sup>

Some factors may impact a woman's menstrual cycle, including stress, weight gain, and hormones. According to research, women experience considerably more tension, anxiety, and depression than males during pandemics. 11,12 Women's menstrual health is affected by times of stress and psychological distress. Stressors can stimulate the hypothalamic-pituitary-gonadal (HPG) axis and change the neuro-modulatory cascade that controls GnRH regulation. This can induce functional hypothalamic amenorrhoea (FHA), which is persistent anovulation caused by something other than an organic reason. This amenorrhoea can be reversed with behavioural change, such as cognitive behavioural therapy<sup>13</sup> Missed periods are linked to psychological distress, as is the exacerbation of symptoms related to menstruation and psychosexual health High-stress levels, mental instability, and sadness have been linked to dysmenorrhoea Menorrhagia and premenstrual symptoms (PMS) are also linked to significant levels of psychological discomfort More perceived stress is linked to decreased libido<sup>13</sup> Following the widespread use of the vaccine, there are a lot of our patients visiting the Gynaecology clinics did mention a short-term change in their menstrual pattern and/or character.

Many people who reported a change to their immediate period after the vaccination had normal menstrual cycle character afterwards and there is no evidence that COVID-19 vaccination has harmful effects on fertility.<sup>14</sup> Moreover, in clinical trials, unintended pregnancies occurred at similar rates in vaccinated and unvaccinated groups. 15 Another study 16 evaluate whether COVID-19 vaccination is associated with changes in cycle or menses length in those receiving vaccination as compared with an unvaccinated cohort. The study includes 2403 vaccinated and 1556 unvaccinated. The vaccinated cohort received the Pfizer-BioNTech, Moderna and Johnson & Johnson/ Janssen. However, COVID-19 vaccine was associated with a less than 1-day change in cycle length for both vaccine-dose cycles compared with pre-vaccine cycles, whereas individuals who unvaccinated saw no significant changes compared with three baseline cycles. In models that were modified, the first dose's difference in change from the unvaccinated cohort's cycle length was 0.64 days, with a 98% confidence interval of 0.27 to 1.01; the second dose's difference in change was 0.79 days, with a 98% confidence interval of 0.40 to 1.18. The length of the menses did not change after immunisation.

Another study in the Middle East and North Africa region aims to examine the prevalence and impact of menstrual abnormalities after the COVID-19 vaccine among females living in that region. The study reported that 66.3% of participants stated menstrual symptoms post-vaccination, of which 46.7% experienced them after their first dose. On the other hand, the symptoms went away in 93.6% of the patients after 2 months. The kind of vaccine had no discernible impact on the prevalence of anomalies (p > 0.05).

### **Methods and Materials**

The aim to carry out this study was to survey by recruiting the female participants who were vaccinated with one or two shots of available vaccine and observing the menstrual changes. A web-based cross-sectional survey study was conducted from May to June 2021. The web-based approach was adopted because of women's restricted mobility related to the COVID-19 pandemic. Additionally, about 80% of Jordanian adults had internet access, and 94% were Dovepress M M Al-Mehaisen et al

active on social media. The sample size was calculated using the OpenEpi, Version 3, open-source calculator—SSPropor calculator, at 99.99%, the least sample size of 1338 was calculated.

We included women above 18 years of age because the vaccine at the time of the study was offered to adults above the age of 18. Women who had the vaccine at least one month (one menstrual period) before participating in the study and accessed social media platforms were included. Participants who were willing to participate were preceded by the survey. Women who were pregnant at the time of the study and had amenorrhea and used hormonal contraception for more than six months were excluded. Before commencing the study, all participants are informed about the purpose of the study in accordance with the Declaration of Helsinki. Ethical approval was granted by the Institutional Review Board of Al Balqa Applied University.

Data was collected in a prepared data collection sheet which was designed by the experts to make sure the face validity of the questionnaires. Data collected included women's age, age of menarche, information about the period regularity, duration, and volume before receiving the vaccine, number of periods since the last dose of vaccine, number of vaccine doses and types. Additionally, women were asked about changes in the timing of the first period after receiving the vaccine and changes in the menstrual cycle in terms of regularity, duration, and volume. Furthermore, women were asked if they had new-onset dysmenorrhea, intermenstrual bleeding (IMB), or postcoital bleeding (PCB). Participation in the study was voluntary, and no personal data was collected; and we considered that when women filled and sent the questionnaire as consent for participation in the study. The questionnaire was prepared online, and a link to the study questionnaire was posted on various social media platforms, study was left open for 8 weeks Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) for Windows, Version 22.0 Armonk, NY. SPSS Categorical data were presented as frequency and percentage. The Chi-square test was applied to observe the association between variables A P-value of <0.05 was considered to be significant.

### **Results**

During the study period, 1506 women responded to the questionnaire Table 1 summarises the characteristics of the study population. The results showed that 75.4% of the women who responded were in the age groups of 26–45 years, 59.8% had menarche before the age of 15 years, 85.8% reported having regular periods, 55.2% had a period duration between 21 and 28 days, 53.7% had menstruation duration between 3 and 8 days.71.9% described their menstrual flow as moderate, 72.9% had some dysmenorrhea. Data analysis showed that 43.5% had only one period after receiving the vaccine, and 24.4% reported that the first period was early. Table 2 shows that 76% reported no changes regarding the duration of menstrual cycle and 60% reported no changes in the menstrual flow. The majority of those who had regular

Table I Characteristic Data of the Study Population

Variable	Category	Numbers	Percentages	
Age groups (years)	18-25 years	112	7.4	
	26-35 years	458	30.4	
	36-45 years	677	45.0	
	46-55 years	259	17.2	
Age of menarche	Less than 15 years	901	59.8	
	≤15 years	605	40.2	
Period regularity before the vaccine	Regular	885	58.8	
	Irregular	449	29.8	
	Not sure	172	11.4	

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Table I (Continued).

Variable	Category	Numbers	Percentages
Duration of the period before the vaccine	Less than 21 days	211	14.0
	21-28 days	831	55.2
	29–35 days	359	23.8
	More than 35 days	105	7.0
Duration of menstruation before the vaccine	Less than 3 days	25	1.7
	3–5 days	491	32.6
	5–8 days	808	53.7
	8-10 days	182	12.1
Menstrual flow before the vaccine	Heavy	259	17.2
	Moderate	1083	71.9
	Light	164	10.9
Dysmenorrhea before the vaccine	Yes	1098	72.9
	No	408	27.1
Vaccine type	Pfizer's	691	45.9
	Sinopharm	591	39.2
	AstraZeneca	224	14.9
Number of vaccine doses received	One	526	34.9
	Two	980	65.1

Table 2 Menstrual Characteristics Post-Vaccine

Variable	Category	Percentage	Number
Number of months (menstrual periods)	One period	43.5	655
since last dose of vaccine	Two periods	46.9	707
	Three periods or more	9.6	144
Timing of the first period after the vaccine	Early	24.4	368
	Late	23.6	356
	No change	51.9	782
Duration of period after vaccine	Increased	19.5	294
	Decreased	4.5	68
	No change	76.0	1144

Table 2 (Continued).

Variable	Category	Percentage	Number
Menstrual flow after vaccine	Increased	24.5	369
	Decreased	15.5	233
	No change	60.0	904
New dysmenorrhea after vaccine	Yes	41.6	627
	No	41.5	625
	Not sure	16.9	254
New IMB/PCB after vaccine	Yes	9.9	149
	No	74.8	1126
	Not sure	15.3	231

Abbreviations: IMB, intermenstrual bleeding; PCB, postcoital bleeding.

periods before the vaccine reported no change in the period after the vaccine (P-value 0.000). Dysmenorrhea before the vaccine and after the vaccine was also found to be significantly associated. No new episodes of dysmenorrhea were found (P-value 0.002). The association between the date of the last dose of vaccine with period timings, period duration, period volume, and dysmenorrhea after vaccine and period timings and period volume was found to be statistically significant (Table 3). Table 4 shows the association of vaccine type with menstrual complaints, and it was found that there was no association, and only dysmenorrhea was found to be statistically significant. AstraZeneca was associated with new episodes or increased dysmenorrhea (P-value 0.035).

Table 3 Effect of Vaccine Administration on Postmenstrual Characteristics

Post Vaccine Change in Period Timing					P-value
		Late	Early	No Change	
Regularity of the period before	Yes	229	241	393	0.000
vaccine	No	81	69	280	
	Not sure	43	35	80	
Date of last vaccine dose	Less than I month I-3 months		155	295	0.002
			166	370	
	More than 3 months	26	24	90	
Post vaccine new or increase dysmenorrhea				P-value	
		Yes	No	Do not know	
Dysmenorrhea before vaccine Yes		311	284	97	0.002
	No	155	199	33	
	Sometimes	160	141	55	

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Table 3 (Continued).

Post Vaccine Change in Period Timing				P-value	
		Late	Early	No Change	
Post vaccine change in period duration					P-value
		Yes	No		
Date of last vaccine dose	Less than I month	311	284		0.911
	I–3 months	155	199		
	More than 3 months	160	141		
Post vaccine change in period volume					
		Increased	Decreased	No change	
Date of last vaccine dose	Less than I month	173	111	332	0.008
	I-3 months	172	104	405	
	More than 3 months	23	18	97	
Post vaccine new or increase dysmen	orrhea				P-value
		Yes	No	Do not know	
Date of last vaccine dose	Less than I month	296	250	76	0.084
	I–3 months	278	305	93	
	More than 3 months	52	69	18	

Table 4 Association of Type of Vaccine and Postmenstrual Characteristics

Type of Vaccine	Post Vaccine Change in Period Timing			P-value	
	Late	Early	No Change		
Pfizer	181	148	339	0.347	
Sinopharm	118	146	303		
AstraZeneca	52	49	98		
USSR	3	2	9		
Post vaccine change in p	P-value				
	Increased No change				
Pfizer	145	511	511		
Sinopharm	107	454	454		
AstraZeneca	42	155	155		
USSR	ı	13			

Table 4 (Continued).

Type of Vaccine	Post Vaccine Change in Period Timing			P-value
	Late	Early	No Change	
Post vaccine change in p	period volume			P-value
	Increased	Decreased	No change	
Pfizer	182	111	363	0.258
Sinopharm	131	84	342	
AstraZeneca	52	34	113	
USSR	I	2	11	
Post vaccine new or inc	rease dysmenorrhe	a	·	P-value
	Yes	No	Do not know	
Pfizer	283	284	89	0.035
Sinopharm	239	245	79	
AstraZeneca	98	79	18	
USSR	I	11	2	

### **Discussion**

The study was conducted to observe the impact of COVID-19 vaccination on the menstruation cycle through a survey As this is an emerging research topic, minimal studies are available to compare and contrast the findings of our study with the available data. The fast spread of SAR-CoV-2 infections has afflicted many nations, necessitating the development of a safe and effective SARCoV-2 vaccine Using information from SARS and MERS vaccine development techniques, many research organisations across the world have been able to begin SAR-CoV-2 vaccine development. The benefits of vaccination far outweigh the risk of a few rare side effects. The only contraindications to COVID-19 vaccination are severe or acute allergic reactions to the vaccine or its components. Several investigations observed a change in the menstrual cycle, worsening premenstrual symptoms, and menorrhagia in women with COVID-19 compared to before the pandemic. 13,19 It is also suggested by the study of Prado et al<sup>20</sup> as menstrual cycle investigators that researchers need to be aware and prepared to understand that in the near-future women may suffer a COVID-19 pandemic "post-traumatic" period that will make the irregularity of the menstrual cycle common between them. In addition to wearing masks, washing hands, ensuring sufficient ventilation indoors, and physically separating from and avoiding crowds, the World Health Organization (WHO) promotes safe and effective immunisations to eradicate COVID-19.

In our study, we attempted to determine if the vaccine was associated with menstrual changes, as noted by a few of our patients. A survey was conducted in which 1506 participants responded to our questionnaire We found two major significant changes related to two major changes in the period associated with the amount of blood flow and the timing (regularity) of the flow. In an international adverse event report, there were 958 occurrences of post-vaccination menstrual abnormalities, including vaginal haemorrhages, and similar to our findings, AstraZeneca was found to have twice the cases of menstrual irregularities than other vaccines. MHRA Recent reports of haemorrhage, blood clots, and thrombocytopenia after receiving COVID-19 vaccinations have raised concerns about the safety of genetic vaccines for persons with coagulation problems or who are taking specific medicines Thrombocytopenia appears to be a common side effect of mRNA COVID-19 vaccines like Pfizer or Moderna, according to pharmacovigilance data<sup>9</sup> A report from the MHRA, however, showed no evidence of a relationship between COVID-19 vaccinations and changes in menstrual cycles since the number of complaints is modest compared to both the number of persons vaccinated and the incidence of menstrual abnormalities in general<sup>21</sup> As both mRNA and adenovirus vectored COVID-19 vaccinations have been linked

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to menstrual abnormalities,<sup>22</sup> probably, the immunological response to immunisation rather than a particular vaccine component is responsible for these alterations Human papillomavirus (HPV) vaccination is linked to menstrual abnormalities<sup>23</sup> Although several stimuli, including viral infection can alter the menstrual cycle, roughly a quarter of individuals infected with SARS-CoV-2 had disrupted menstrual cycles in a study of menstruation women.<sup>24</sup> The current study showed that the majority of the women said that there was no change in duration and menstrual flow which is also in line with the study which enrolled participants retrospectively and was unable to identify strong signs to support the idea that COVID-19 vaccination is linked to menstrual changes.<sup>25</sup> However, some studies contradict with the findings of the study; for instance, a study reported that 35.3% of their participants had menstruation alterations prior to immunisation during the COVID-19 pandemic. On the other hand, abnormal periods followed vaccination in 66.3% of participants.<sup>17</sup> 42% of individuals in a recently published research with 39,129 participants in the USA reported heavier bleeding after vaccination.<sup>26</sup> In addition, only 20% of premenopausal vaccination recipients in the UK who participated in a retrospective trial with 4989 individuals reported no menstrual cycle problems up to four months after receiving their first COVID-19 vaccine injection.<sup>27</sup>

Furthermore, another study reported that 358 people who received both doses of the vaccination in the same cycle were most impacted, with a 2.32 day (98.75% CI 1.59 to 3.04) delay in the start of their following period. In contrast to the uninfected cohort's 4.3%, 10.6% of this group reported a shift in cycle duration of more than 8 days, which is regarded as clinically significant (P 0.001). Two cycles following immunisation, cycle durations were back to normal in all groups.<sup>28</sup>

Women's menstrual cycle may be influenced by immunological effects on hormones that control the menstrual cycle<sup>29</sup> or by uterine immune cells engaged in the cyclical build-up and destruction of this tissue.<sup>24</sup> Many women in different cultural contexts may have felt uncomfortable talking about it, may not have thought it was vaccine-related, or may not have been encouraged by their clinicians to make an official report to the adverse events reporting system, so the actual number of cases is expected to be much higher than the numbers recorded in the pharmacovigilance systems<sup>9</sup> As this debate continues, it is recommended that women be urged to report any changes in their menstrual cycles or unexpected vaginal bleeding Comprehensive data will allow for a more thorough study, as well as reassure patients that their vaccination safety concerns are being addressed seriously When it comes to treatment, the MHRA recommends that women who report changes in their menstrual cycles or fresh vaginal bleeding after menopause should be treated according to the typical clinical recommendations for these diseases, which include hormonal contraception.<sup>21</sup>

The study's main limitation is that it involves a short time after the vaccine, which is challenging to show essential results. Specifically, the women were only asked about their first period after the vaccine. Moreover, the study looks very broadly considering the characteristics of the menstrual period because it is not based on objective scientific data; instead, it is based on personal estimation of women. Therefore, future studies need to focus on assessing the amount of blood loss during menstruation to make the result accuracy completely subjective. In addition, the study has included women in the age group between 46 and 55 which can cause bias as they since premenopausal symptoms are started therefore the future studies should exclude age group between 46 and 55 to avoid bias in results.

Moreover, the results obtained from this study may not be generalised as it was a survey-based study and not all the confounders had been taken into consideration such as the history of COVID-19. However, this is the first study conducted in this context in Jordan. To the best of our search literature in our region and future, we hope to conduct a longitudinal study to observe the hormonal response attributed to the COVID-19 vaccine.

### Conclusion

The present study has observed the changes in the menstrual cycle after getting COVID-19 vaccination, which concluded a difference in menstrual characteristics post vaccine and observed the impact of the type of vaccine. However, further long-term research is needed to determine the effect of the COVID-19 vaccination on the menstrual cycle.

# **Data Sharing Statement**

The data will be available for review from the corresponding author on request.

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### **Disclosure**

The authors declare no competing interests.

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