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COVID-19 vaccine and menstruation cycle changes

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ABSTRACT

Background: Over 474 million cases and almost 6 million fatalities caused by COVID-19 have been reported globally. The case fatality rate was 0.5-2.8%, but it was 3.7-14.8% for people aged 80 to 89. Given how dangerous this infection is, prevention is essential. As a result, the number of COVID-19 cases significantly decreased (> 75% protection) when immunisations were introduced. On the other side, it has also been noted that individuals have sought treatment for severe respiratory, cardiovascular, neurological, and gynaecological symptoms. **Method:** A group from king saud medical city in the Kingdom of Saudi Arabia used a semi-structured questionnaire to perform an online cross-sectional survey on females in the reproductive age range (15-49 years) between Dec 2022 and Jul 2023. SPSS Statistics version 24.0 was used to analyse the data, which was then displayed as frequency and percentage. The link was tested using the chi-square method, and a p-value of 0.05 was deemed significant. **Results:** 46.5% of the individuals in our study were between the ages of 21 and 30, and 87.7% reported menarche between the ages of 11 and 15. 1474 (71%) of the participants reported changes to their menstrual cycle after COVID-19 vaccination. 320 (21.7%) reported changes after the first dosage, 831 (56.4%) after the second dose, and 12 (0.8%) after the booster, according to these statistically significant results (p value 0.002). **Conclusion:** Females of reproductive age, particularly those who received the new vaccines, reported menstruation irregularities following vaccination. Prospective investigations are required for comparable findings.

Keywords: Menstrual changes, COVID-19, vaccination side effects

1. INTRODUCTION

The respiratory infection COVID-19, which is brought on by the SARS-CoV-2 agent, has a high transmissibility and spreads by droplets. A variety of clinical signs are seen in COVID-19 infected patients. The majority of patients (80%) often experience mild to moderate respiratory symptoms; in 15% of instances, symptoms are severe; and in 5% of cases, various organ dysfunctions that are critically life-threatening result. The WHO has confirmed more than 474 million cases worldwide as of March 24, 2022, with around 6 million deaths attributed to COVID-19. In addition, the global case fatality rate, which fell from 1.7% to 39.0% in 2020, varies from 0.3% to 2.8%

(Zhu et al., 2020; Horita et al., 2023).

Treatment is essential because of how terrible this condition is, and the healthcare system is under a lot of strain. The few medicines with proven advantages are very expensive and not widely accessible, and appropriate therapeutic approaches are still lacking. Non-pharmaceutical interventions such as mask use, hand hygiene compliance, cough and respiratory etiquette practise, social distancing (restricting movement, avoiding crowds, working from home), closure of academic/educational institutions, contact tracing, home isolation, and lockdowns were the main strategies used in most regions of the world to try to contain the infection (Nicola et al., 2020). The role of antiviral medications and preventative vaccines cannot be overlooked, despite the fact that the implementation of NPIs considerably flattened the case curve.

It is more crucial than ever that medical technology be able to test both novel and existing antiviral medications and produce affordable, safe, and effective vaccinations. Vaccines have emerged as the more dependable and economical public health intervention of the two, especially for containing and mitigating the virus while also protecting the economy and social fibre of society (Hajj et al., 2015; Ehreth, 2003). The prevalence of clinically important coronavirus illness cases, the number of asymptomatic infections, and the associated infectivity have all significantly decreased as a result of the introduction of vaccinations (WHO, 2023). Numerous vaccinations that are currently in use around the world have received approval from WHO. While a few vaccinations are single doses, the majority are developed for two-dose regimens.

Vaccines are created using a variety of technologies in order to activate the immune system to generate the proper response to combat the disease. Many vaccines, including Sinopharm, Sinovac, and CanSino, use weakened or inactivated viruses to start the immune system's response, but more recent vaccines from Pfizer and Moderna use mRNA to tell the immune system to make antibodies against the "spike protein," which is a protein found on the surface of SARS-CoV-2. The "spike protein" and immune response are produced using a modified virus (sometimes called an adenovirus or a vector virus) that is used by AstraZeneca and Sputnik (WHO, 2023).

2. METHOD

A team from the King Saud Medical City in the Kingdom of Saudi Arabia conducted an online cross-sectional survey on females between the ages of 15 and 49 between Dec 2022 and July 2023. The poll involved respondents from different nations and was performed in a global context. The poll included women from the Kingdom of Saudi Arabia and other nations. The varied collection of nations represents a vast range of topographical regions, cultural heritages, and socioeconomic environments. The technique utilized was non-probability convenient sampling which include 2076 participants. Women between the ages of 15 and 49 who had a regular menstrual cycle (25 to 35 days prior to vaccination), had received at least one dose of the COVID-19 vaccine at least one month prior to participating in this survey, and had access to the Internet and social media platforms on their mobile phones meet our inclusion criteria.

Additionally, females with known geographic locations and at least three cycles after childbirth or pregnancy were included. We did not include pregnant women amenorrheic, using oral contraceptives for longer than five months, or who had polycystic ovary syndrome. The core team and subject matter specialists created the questionnaire. The questionnaire contained 42 variables, including the respondent's age, menarche age, the number of doses of the COVID-19 vaccination they had received, how long it had been between doses, and information about their menstrual cycle's regularity, length, duration, and volume before the vaccination. Additionally, questions about changes in cycle duration following immunization (even after the first dose) were asked of females. haemorrhage during menstruation, dysmenorrhea, variations in its severity, and bleeding between periods.

By sending the questionnaire to six to eight specialists in the field, the questionnaire's construct validity and content were evaluated. Each question received a score from the experts based on its clarity and relevance. While questions earning a score of less than 80% were edited and finalised for the survey, variables receiving a score of more than 80% for content and construct validity were included. King Saud University Medical City's Research Ethics Committee granted approval for the study (approval number H1R1-28-Sep22-01). A consent form was provided at the beginning of the questionnaire because this was an online survey. It outlined the study's goals in detail, emphasised that participation was optional and there were no financial incentives, and provided assurances to participants that their personal data would be kept private and used exclusively for research purposes.

All participants in the study were literate, so only those who understood and concurred with the ethical statement were allowed to continue with the lengthy survey. In addition to English, the questionnaire was also available in Urdu and Arabic, and participants could fill it out in whatever language they liked. The validated questionnaire was completed using Google Forms, and the link was shared with females of reproductive age groups on social media, especially through WhatsApp. To increase the number of responses, the questionnaire was further distributed by volunteer data collectors. Version 24 of SPSS Statistics for

Windows was used to analyse and process the data. Frequency and percentage were used to depict categorical data. To determine whether there is a relationship between variables and a p-value of less than 0.05, the chi-square test was used.

3. RESULTS

A total of 2076 replies were included in the study out of 2300 participants after excluding those who provided less than 60% of the questionnaire's information. 1511 (72.8%) of the participants were from the Kingdom of Saudi Arabia, followed by 420 (20.2%) from Pakistan, 56 (2%), and 4% from other nations. A total of 1944 participants, or 93.6%, lived in cities. The average age of the participants in our research was 24.8 years, and 966 (46.5%) of them were between the ages of 21 and 30. 87.7% reported menarche between the ages of 11 and 15. The bulk of the ladies, 1510 (72.7%), were unmarried, while 490 (23.6%) were married. Before receiving any vaccinations, the females' menstrual cycles were regular.

Table 1 Socio-Demographic Data

Variable		Number	Percentage %
Nationality	Saudi nationality	1511	72.8%
	Pakistan	420	20.2%
	Bahrain	49	2.36%
	Others	96	4.62%
Living area	Urban	1944	93.6%
	Rural	132	6.36%
Age	15 to 20 yrs	811	39.1%
	21 to 30 yrs	966	46.5%
	31 to 40 yrs	260	12.5%
	41 to 49 yrs	39	1.88%
Menarche age	6 to 10 yrs	176	8.48%
	11 to 15 yrs	1821	87.7%
	16 ≥ yrs	79	3.81%
Marital status	Single	1510	72.7%
	Married	490	23.6%
	Widow	55	2.65%
	Divorced	21	1.01%
Any medical problem	Yes	210	10.1%
	No	1866	89.9%
	Anemia	89	4.29%
	Neurological disease	21	1.01%
	Blood pressure abnormalities	17	0.82%
	Allergic disease	11	0.53%
	Depression	11	0.53%
	Diabetes	9	0.43%
	Kidney disease	10	0.48%
	Gastrointestinal tract problems disease	8	0.39%
	Heart disease	10	0.48%
	Arthritis	7	0.34%
	Asthma	7	0.34%
	Vitamin deficiency	5	0.24%
	Blood disorders	5	0.24%
Vaccination	Single dose	45	2.17%
	2 doses	1211	58.3%
	3 doses	820	39.5%

In terms of vaccination status, 1211 (58.3%) study participants had gotten two doses of the vaccine, whereas 820 (39.5%) had also had the booster injection, and 45 (2.1%) had only received one. From most to least, the individuals got several vaccinations from Pfizer-BioNTech, AstraZeneca/Oxford, Sinopharm, Moderna, and Sputnik. The time between the first and second doses was on average 47.2 days. The subjects had been immunised on average 185.7 days ago. Following their COVID-19 vaccines, 1474 (71%) trial participants reported alterations to their menstrual cycle. These results were statistically significant ($p=0.002$) (Table 2) and showed that 320 (21.7%) study participants reported alterations after the first dosage, 831 (56.4%) after the second dose, and 12 (0.8%) females after the booster (Figure 1).

Table 2 change in menstrual cycle after vaccination

No of doses	Change in the menstrual cycle			p-value
	No n (%)	Yes n (%)	Total n (%)	
No menstrual change	401 (66.6)	81 (5.5)	541 (26.1)	0.002
Change after first dose	2 (0.33)	320 (21.7)	311 (15)	
Change after second dose	21 (3.4)	831 (56.4)	856 (41.2)	
Change after booster dose	0 (0)	12 (0.8)	11 (0.53)	
Could not recall	178 (29.6)	230 (15.6)	357 (17.2)	
Total	602 (100)	1474 (100)	2076 (100)	

The type of vaccine and the reported alterations in the menstrual cycle by the participants who had only received one dose of the vaccine were significantly associated ($p=0.007$). According to the findings, female participants who took AstraZeneca reported the biggest alterations, with 10 (35.7%), followed by Pfizer with 8 (28.6%), and Sinovac with 6 (21.4%). Participants who received booster doses also showed a substantial correlation ($p=0.003$) between the type of vaccine and menstruation alterations, with Pfizer leading the way with 501 (84.2%) participants (Table 3).

Table 3 Type of vaccine and the reported alterations in the menstrual cycle

Number of doses	Vaccine	Menstrual cycle changes						p-value
		No number	%	Yes number	%	Total number	%	
First dose	Sinovac	1	5.88	6	21.4	7	15.6	0.007
	Pfizer	9	52.9	8	28.6	17	37.8	
	AstraZeneca	1	5.88	10	35.7	11	24.4	
	Sinopharm	2	11.8	2	7.14	4	8.89	
	Moderna	4	23.5	2	7.14	6	13.3	
Second dose	Sinovac	108	28.2	209	26.5	317	27.1	0.089
	Pfizer	180	47	422	53.6	602	51.4	
	Astrazenica	54	14.1	98	12.4	152	13	
	Sinopharm	19	4.96	23	2.92	42	3.59	
	Moderna	22	5.74	30	3.81	52	4.44	
	Sputnik	0	0	6	0.76	6	0.51	
Booster dose	Sinovac	9	3.4	28	4.71	37	4.3	0.003
	Pfizer	201	75.8	501	84.2	702	81.6	
	AstraZeneca	4	1.51	2	0.34	6	0.7	
	Sinopharm	49	18.5	61	10.3	110	12.8	
	Moderna	2	0.75	3	0.5	5	0.58	
Total		665	-	1411	-	2076	-	-

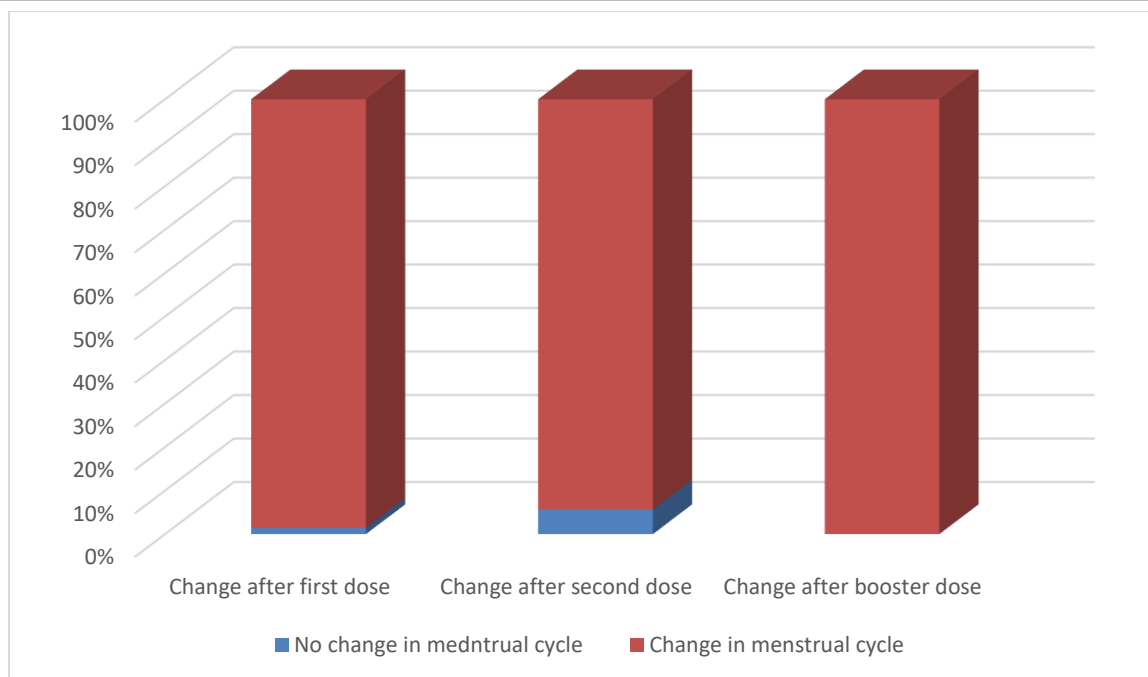


Figure 1 change in menstrual cycle after COVID 19 vaccination

4. DISCUSSION

This study's goal was to determine how COVID-19 vaccination affected women between the ages of 15 and 49 who were in menstrual cycles. We found that more than 60% of those taking part in the study reported menstrual cycle changes following the COVID-19 immunisation. Despite the fact that data suggest the incidence of menstrual abnormalities was already relatively high in various parts of the world before the COVID-19 pandemic and vaccination initiation, a recent study from Japan published in 2021 reported an incidence of menstrual abnormalities of 34% among women of reproductive age in 2017, when there was no pandemic (Shimamoto et al., 2021).

Our results are consistent with previous data, which indicates that the incidence of menstrual alterations after COVID-19 vaccination ranges from 21% to 68%. According to biological theory, numerous stimuli, such as vaccination, might cause the menstrual cycle to be activated (Muhaidat et al., 2022; Dabbousi et al., 2023). A number of studies have revealed evidence for this connection, including recent prospective research done in the US that discovered a substantial correlation between menstrual cycle irregularities and COVID-19 immunization (Edelman et al., 2022). Another theory is that the powerful immunological response and stress experienced after receiving the COVID-19 vaccine may have an impact on the hypothalamic-pituitary-ovarian axis, causing irregular menstruation (Edelman et al., 2022).

One major conclusion of our study is that the incidence of post-vaccination menstrual irregularities is strongly influenced by the type of vaccine. Although Lagana et al. observed no menstruation issues with various types of immunisations among their study participants Lagana et al., (2022), Kareem et al., (2022) reported similar findings. Our research demonstrates that all vaccines affected monthly cycles, however the majority of women received either the Pfizer (mRNA design/technology based) or AstraZeneca (adenovirus vectored design/technology based) vaccine. Further studies are required to determine the degree of these anomalies and their possible effects because other studies have found considerably greater frequencies of irregularities in monthly cycles after injections of these vaccines (Baena et al., 2022; Pezzaioli et al., 2022).

The lengthening of the menstrual cycle in 469 (34%) of the study subjects, in addition to abnormalities, was another notable anomaly in menstruation following COVID-19 vaccination. This is in line with the findings of a sizable prospective cohort research carried out in the US, which revealed a non-persistent rise in the average menstrual cycle length among females who received the COVID-19 vaccine (Alghamdi et al., 2021). This study discovered a significant correlation between age and post-vaccination alterations in the menstrual cycle. Women in the 21–30 age range reported similar changes in a sizable amount. Our findings are in line with those of Alghamdi et al., (2021), who noted menstruation abnormalities in females in the same age range following Covid-19 vaccination. The results of this study also support those reported by Alahamdi et al., (2021) who found that post-COVID-19 immunisation irregularities in menstrual cycles were reported by most of Saudi women of reproductive age who had finished secondary school (Alghamdi et al., 2021).

5. CONCLUSION

After getting the COVID-19 immunisation, females frequently experience irregular menstrual cycles. The uneven length of the cycle following two doses of the COVID-19 vaccination is the most common aberration. To investigate the long-term effects of COVID-19 vaccination on the reproductive health of females, prospective studies with larger sample sizes are required. This is true in light of the newly recognised phenomenon known as "long haul COVID-19", in which patients have been reported to visit hospitals with different infections even after recovering from COVID-19 and testing negative.

Ethical issues

No ethical issues in the study, approval was obtained from the specialized committee as declared in the method section as well as participants consent.

Authors contribution

Wesam Abd Saeed Al-Mekhalafy: Participated in all steps of the research from the proposal to the submission

Mufareh Asiri: Participated in writing discussion and results

Tahani AL-Hazza: Participated in collecting literature and discussion

Saad Alonze: Participated in the discussion, results, and submission

Mona Abdulrahman Alhagbani: Participated in writing proposal and submission

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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