SciMedCentral

Medical Journal of Obstetrics and Gynecology

Research Article

The Association between COVID-19 Vaccine and Changes in Menstruation among Reproductive Women Jeddah, Saudi Arabia

Samera AlBasri[1]*, Abeer Alahmadi[2], Abeer AL Suwaidi[3], Renad Abualsaud[3], Zakeiah Alsulaimani[3], Hamidah Alkhalaf[3], and Osama Alariany[3]

[1]Department of Obstetrics & Gynecology, King Abdulaziz University, Saudi Arabia
[2]Department of Family Medicine, Ministry of health, Saudi Arabia
[3]Faculty of Medicine, King Abdulaziz University, Saudi Arabia

*Corresponding author
Samera AlBasri, Department of Obstetrics & Gynecology, King Abdulaziz University, Jeddah, Saudi Arabia.

Submitted: 06 September 2023
Accepted: 11 October 2023
Published: 14 October 2023
ISSN: 2333-6439

Copyright
© 2023 AlBasri S, et al.

OPEN ACCESS

Keywords
• COVID-19
• COVID-19 vaccine
• Menstrual cycle
• Immunization
• Menstruation

Abstract

Objective: The present study aims to address the association of COVID-19 vaccines on the menstrual cycle among reproductive women in Jeddah, Saudi Arabia, 2022.

Methods: This is a cross-sectional study that was carried out in Jeddah, Saudi Arabia which included a total of 676 female individuals of reproductive age. Data was collected through questionnaire that was distributed and filled out by the participants, which then were analyzed using SPSS.

Results: Approximately 52% of all 676 total number of participants, reported having their menstrual cycle affected and having some disturbances that were not present prior to receiving COVID-19 vaccines, knowing that more than 80% of all participants had already received three doses of COVID-19 vaccine. The most common reported menstrual abnormalities in the present study were irregular menses (16%) followed by dysmenorrhea (14%),

Conclusion: COVID-19 had major effects on our lives that required the development of a vaccine against it, however it had some side effects associated with it, such as causing changes in the menstrual cycle in form of getting more irregular, having more pain or bleeding, or having the cycle get shorter or longer.

INTRODUCTION

The world is affected by a new viral outbreak, known as Coronavirus Disease 2019 (COVID-19), as it spreads rapidly all over the globe, it was declared a pandemic by the World Health Organization (WHO) on 11th of March 2020 [1,2]. In order to contain and eradicate this COVID-19 wave, WHO recommended effective vaccines alongside wearing masks, washing hands, maintaining a social distance, and avoiding crowds [3].

Consequently, the vaccine was approved by the Saudi Food and Drug Authority (FDA) and was successfully released to be given to people safely [4]. Although the vaccine was approved, there has been growing concerns among women that it may disrupt the menstrual cycle and have an impact on fertility [5,6].

According to the Medicines and Healthcare products Regulatory Agency (MHRA's) surveillance scheme, Yellow card, there are a lot of reports from women who complained of menstrual irregularities such as heavy menstrual bleeding (menorrhagia), frequent bleeding (metrorrhagia/polymenorrhea), or postmenopausal bleeding following vaccination [5,7]. This may suggest that vaccines disturb the menstrual cycle by activating the immune system that might attack cytokines and immune cells in the uterus [1].

Furthermore, the menstrual cycle could be influenced by many situations during a pandemic such as weight gain, hormonal changes, sleep deprivation affecting the hypothalamus, physical and psychological stress [8,9]. The role of the pulsatile hormones is essential for maintaining a regular menstrual cycle, Therefore, disturbance of the regularity in hormone release may impact menstruation [10].

There is evidence that inoculation with the Human Papillomavirus (HPV) vaccine can cause some menstrual disturbances [8]. Infection with a virus, such as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) itself, is

evidenced to have some effect on the menstrual cycle [9,10]. Moreover, the study showed that there is no change in the menstrual cycle length with COVID-19 vaccination, on the other hand, the women who received two COVID-19 vaccine doses in a single cycle do appear to experience a longer but temporary cycle length change [11].

There is insufficient data to determine whether COVID-19 vaccinations impact the menstrual cycle [5,12]. It is critical to look into the possible link between COVID-19 immunization and menstrual disturbances to retain public trust in the vaccination program. This study aims to assess the association between COVID-19 vaccine and the change in menstruation among females of reproductive age group in Jeddah, Saudi Arabia, 2022.

METHODS

An online survey was used in this analytical cross-sectional investigation to collect data from the respondents, the survey was distributed from 16th of January 2023 to 7th of February 2023. The main city in the west region of the Kingdom of Saudi Arabia, Jeddah, where the study was conducted. Sample size was estimated to be 323 as calculated using the STATA software, version 13.0 (Stata Corp, College Station, TX, USA). However, the collected sample was 676 which is more than double the calculated sample and this was used to increase the quality and credibility of the research.

The study Invited participants based on the inclusion criteria which included: female individuals aged 18–55 years, living in Jeddah, were at least three cycles post pregnancy, and received at least one dose of a COVID-19 vaccine since December of 2020 to February 2023. Individuals who are taking any hormonal therapy or hypothyroid medications or had an established clinical diagnosis of medical conditions that may influence cycle regularity such as, polycystic ovarian syndrome, endometriosis, thyroid disorders, eating disorders, uterine polyps, and uterine fibroids were excluded from the study.

In order to include participants from the target population who are female adults currently residing in Jeddah and satisfy the inclusion criteria, this study employed a non- probability convenient sampling technique. Social media channels were used to disseminate the self-administered online questionnaire and gather responses from the participants. The study investigators created the questionnaire after carefully reviewing the relevant literature, and it was then face-validated by experts in the field. The questionnaire included the following variables: 1) Demographic data such as, age, marital status, and socioeconomic status; 2) menstruation related data such as, patterns, history of irregularities, number of parities, and use of contraception; 3) COVID-19 vaccinations data such as, number of doses received, type of vaccine, and changes of menstruation after the vaccination.

Data were analyzed using the IBM statistical package for the social sciences (SPSS) Statistics for MacOS, version 29 (IBM Corp., Armonk, N.Y., USA). Proportions and frequencies were used to summarize and describe the data. Moreover, inferential statistics using Chi-square test ($\chi 2$) and the extension of Fisher-Freeman-Halton Exact test were applied to test for significance. Moreover, P values <0.05 were considered statistically significant.

Before data collection, the Institutional Review Board (IRB) of King Abdulaziz University in Jeddah city granted its ethical approval to the study (1-23). On the opening page of the questionnaire, an explanation of the study's nature and goals was included to secure participants' consent. The care participants received was not affected by their voluntary participation in the study. All data was handled in an anonymous manner, stored safely in the office of the principal investigator, and only utilized for study purposes.

RESULTS

A total of 676 female individuals met the inclusion criteria and were included in the study analysis. The majority of the participants (66.1%) aged 18 – 19 years old. Saudi respondents represent most of the total study sample (88.9%), and 62.9% of the total number were single female individuals. Furthermore, 40.1% of the included participants have completed their high school education, while 47.2% of the participants hold a bachelor's degree. Among the study sample, 87% reported no use of contraception currently, and among those who used contraception 12.1% of them used contraceptive methods for more than 3 months. Only 14.6% indicated using fertility awareness methods, 94.9% of which used them for more than three months. Among the included participants, the maximum number of reported parities was four. Moreover, 33.7% of the respondents were using vitamins, and 21% of the total sample were on medications at the time of data collection. Detailed demographic data are illustrated in [Table 1].

The study participants self-reported their COVID-19 vaccination status as illustrated in Table 2. In terms of coverage, 80.2% of the respondents received three doses of the COVID-19 vaccine. Furthermore, the study investigated menstruation patterns and irregularities among the participants and 13.5% reported excessive bleeding before the vaccine. In addition, 74.9% of the female participants described their menstruation before the vaccine as regular.

Moreover, more than half (51.9%) of the respondents believe that their menstruation changed after they received COVID-19 vaccination [Table 2]. Details about type of vaccine at each dose are demonstrated in [Figure 1].

As for the reported menstrual abnormalities after the 1st dose of COVID-19 vaccine, the most commonly reported abnormality is irregular menses (16%), followed by dysmenorrhea (13.9%). Other reported abnormalities were infrequent menses >38 days (5.5%), frequent menses <24 days (4.6%), menorrhagia (1.6%). See menstrual changes after COVID-19 vaccines demonstrated in Figure 2-4.

The current study investigated certain factors including demographic factors such as age, marital status, and smoking

Table 1: Participants' demographic data

n=676		N	%
Age (years)	18-29	447	66.10%
	30-39	89	13.20%
	40-49	108	16.00%
	50-55	32	4.70%
Nationality	Saudi	601	88.90%
	Non-Saudi	75	11.10%
Marital status	Single	425	62.90%
	Married	224	33.10%
	Divorced or widow	27	4.00%
Educational level	Less than high school	18	2.70%
	Highschool	271	40.10%
	Diploma	24	3.60%
	Bachelor	319	47.20%
	Master or PhD	44	6.50%
Where do you live?	Urban	663	98.10%
	Rural	13	1.90%
Do you smoke?	Yes	61	9.00%
	No	615	91.00%
BMI	Underweight	84	12.50%
	Normal	309	45.80%
	Overweight	171	25.40%
	Obese	110	16.30%
Are you using any contraceptives currently?	Sterilization	1	0.10%
	Copper IUD	27	4.00%
	Progestin pills, electronic, injection, hormone IUD	9	1.30%
	Estrogen & progestin pills, pads, vaginal ring	29	4.30%
	Others	22	3.30%
	I don't use	588	87.00%
Are you lactating currently?	Yes	21	3.10%
	No	655	96.90%
Are you pregnant currently?	Yes	12	1.80%
	No	664	98.20%

in addition to the type of COVID-19 vaccine received by the respondents for possible association with the menstruation changes reported by the study participants. Although variations of prevalence among participants were observed, these differences did not achieve statistical significance [Table 3].

DISCUSSION

The menstrual cycle is affected by a complex interplay of factors throughout a woman's lifetime such as physiological, pathological, and environmental factors which all exert their effects on the menstrual cycle by causing changes in the hypothalamic-pituitary- ovarian axis [11].

In the present study, 676 female individuals of reproductive age were included to evaluate the association between COVID-19 vaccine and menstrual cycle changes.

Approximately, 52% of all participants reported that their menstrual cycles were affected in a way or another following the receipt of COVID-19 vaccine. In fact, more than 80% of the participants have already received three doses of COVID-19 vaccine at the time of conducting this study. Which is in line with other studies as well, for example, a study done by Luisa et al. about menstrual cycle disturbances following COVID-19 vaccination involving around 950 women in the study, around 184 (20%) of participants reported changes in their menstruation after the vaccine [13]. These reported disturbances included the cycle becoming less frequent (<38 days) in around 25% of the affected individuals, while 22% reported that the cycle is getting more frequent (>24 days) [13]. While in the current study, frequent and infrequent menstrual cycles were each reported by approximately 5% of participants. Furthermore, 42.93% of participants in the aforementioned study reported having their cycles irregular following the vaccine, and as per the International

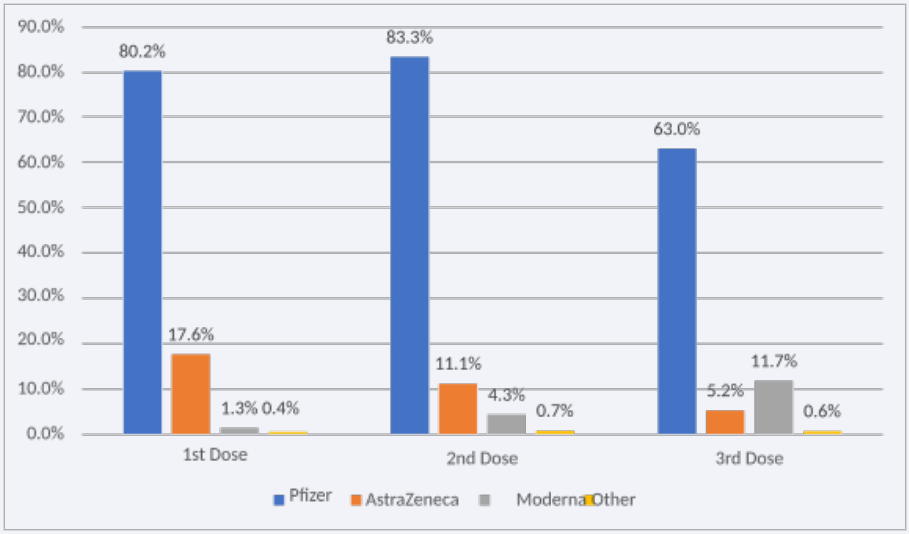

Figure 1 Participants' COVID-19 type of vaccination

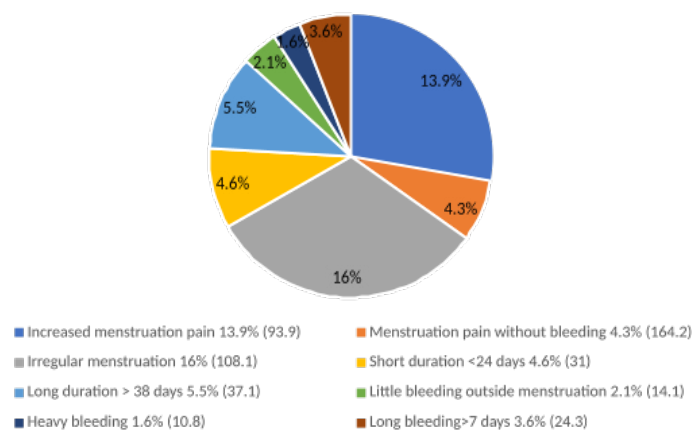

Figure 2 Menstrual changes after the first dose of COVID-19 vaccination

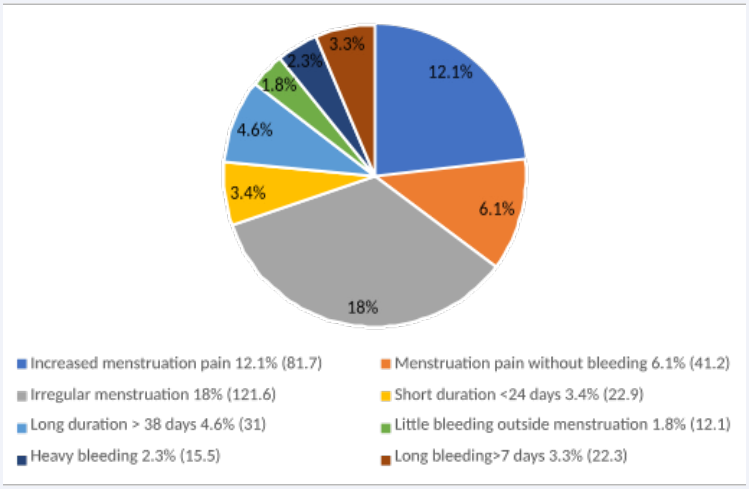

Figure 3 Menstrual changes after the second dose of COVID-19 vaccination

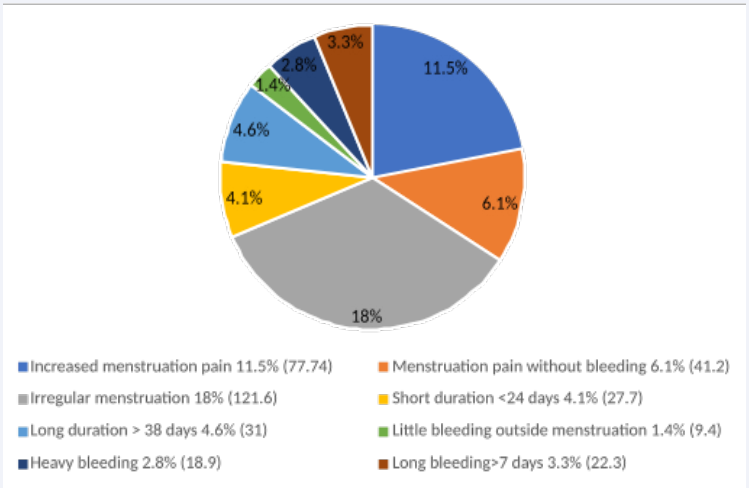

Figure 4 Menstrual changes after the third dose of COVID-19 vaccination

Table 2: Participants' COVID-19 and menstruation

n=676		N	%
Did you get vaccinated against COVID-19	No	0	0.00%
	One dose	4	0.60%
	Two doses	130	19.20%
	Three doses	542	80.20%
Were you having excessive bleeding before the vaccine?	Yes	91	13.50%
	No	585	86.50%
Was your menstruation regular before the vaccine?	Regular	506	74.90%
	Irregular	170	25.10%
What was the duration between your menstruation cycles?	Less than 24 days	218	32.20%
	24-38 days	398	58.90%
	More than 38 days	60	8.90%
How many days you used to have your menstruation before vaccine?	Less than 4 days	22	3.30%
	4 days	69	10.20%
	6 days	253	37.40%
	7 days	253	37.40%
	More than 7 days	79	11.70%
Do you think your menstruation changed after COVID-19 vaccine?	Yes	351	51.90%
	No	325	48.10%

Table 3: Associated factors with menstruation changes

n=676			Menstruation changes after first dose?	Menstruation changes after second dose?	Menstruation changes after third dose?
Age (years)		*NA*	0.57	0.67	0.46
	18-29	n	222	224	183
		%	65.70%	65.50%	65.40%
	30-39	n	40	44	35
		%	11.80%	12.90%	12.50%
	40-49	n	60	60	49
		%	17.80%	17.50%	17.50%
	50-55	n	16	14	13
		%	4.70%	4.10%	4.60%
Marital status	Single	*NA*	0.58	0.85	0.48
		n	213	215	176
		%	63.00%	62.90%	62.90%
	Married	n	114	115	90
		%	33.70%	33.60%	32.10%
	Divorced or widow	n	11	12	14
		%	3.30%	3.50%	5.00%
		NA	0.28	0.23	0.25
Smoking	Yes	n	35	36	32
		%	10.40%	10.50%	11.40%
	No	n	303	306	248

Pearson Chi-square test, *Fisher-Freeman-HaltonExact test. NA: Not Applicable.

Federation of Gynecology and Obstetrics, variation in the menstrual cycle of less than eight days is considered normal, however more than that is deemed to be irregular [13,14]. Which is consistent with the results of the present study since the most commonly reported menstrual cycle abnormality reported after the 1st dose of COVID-19 vaccine was irregular cycles which was reported by 16% of participants. The theorized pathophysiology behind the menstrual cycle becoming irregular after COVID-19 vaccine is the fact that any stressful event physiologically or psychologically can alter the hypothalamic-pituitary-ovarian axis which is the main regulator of the menstrual cycle, moreover, an exaggerated response or activity of the immune system as a result of COVID-19 vaccine will also affect the hypothalamic-pituitary-ovarian axis [15,16].

According to a cohort study that included 4000 women, the most commonly reported menstrual disturbances after COVID-19 immunization were, shortened menstrual cycle, worse menstrual pain and bleeding [17]. On the other hand, a cross-sectional study conducted by Nadia et al. in the Middle East and North Africa (MENA) region involving 2269 women reported an increase in menstrual cycle length rather than shortening, and menstrual cycle abnormalities were reported by 66% of participants of this study, and fortunately >90% of these affected reported having their menstrual cycle irregularities alleviated within a period of two months with no residual or longstanding disturbances [18]. As for our study, dysmenorrhea was reported by around 14% of women included in the study and it is the 2nd most commonly reported menstrual cycle abnormality. Additionally, a systematic review conducted by Maheen Nazir et al., about menstrual irregularities following COVID-19 vaccine, in which approximately 78000 vaccinated females participated, concluded in their results that around 52% of the participants reported menstrual abnormalities such as oligomenorrhea, menorrhagia and dysmenorrhea [19].

CONCLUSION

The pandemic that happened as a result of COVID-19 has led to numerous catastrophic effects on people's lives in terms of health, environment, economic and many other factors. This has led to the development of a vaccine to reduce the morbidity and mortality of the infection; however, it was associated with some adverse events. Women, for example, have been affected physiologically and psychologically eventually even affecting their menstrual cycle. In this study, we aimed to assess the association between menses and COVID-19 vaccine and through our results and literature review, we concluded that around half of women receiving the vaccine reported some menstrual cycle changes following immunization against COVID-19. For example, it was associated with menstrual cycle irregularities, increasing menstrual pain, and changes in the length of the menstrual cycle.

In summary, COVID-19 vaccine has been reported to cause menstrual abnormalities in some women, however menstrual cycle can generally be affected by various reasons, and it is difficult to clearly identify a specific cause for these changes, and since information about COVID-19 virus and its vaccine are continuously evolving and progressing, higher powered studies involving a variety of female populations are required.

REFERENCES

1. Kurdoğlu Z. Do the COVID-19 Vaccines Cause Menstrual Irregularities? Int J Women's Heal Reprod Sci. 2021; 9: 158-159.

2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020; 91: 157-160.

3. Mauvais-Jarvis F, Klein SL, Levin ER. Estradiol, Progesterone, Immunomodulation, and COVID-19 Outcomes. Endocrinol. 2020; 161: 1-8.

4. Arab News. Saudi Arabia Ready to Launch Vaccine Campaign. 2020.

5. Alvergne A, Kountourides G, Argentieri MA, Agyen L, Rogers N, Knight D, et al. COVID-19 vaccination and menstrual cycle changes: A United Kingdom (UK) retrospective case-control study. medRxiv. 2021.

6. Shanes ED, Otero S, Mithal LB, Mupanomunda CA, Miller ES, Goldstein JA. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy. Obstet Gynecol. 2021; 281-283.

7. Hunter PR. Thrombosis after covid-19 vaccination. BMJ. 2021; n958.

8. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate Psychological responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. Int J Environ Res Public Health. 2020; 17: 1729.

9. Stanton R, To QG, Khalesi S, Williams SL, Alley SJ, Thwaite TL, et al. Depression, Anxiety and Stress during COVID-19: Associations with Changes in Physical Activity, Sleep, Tobacco and Alcohol Use in Australian Adults. Int J Environ Res Public Health. 2020; 17.

10. Prado RCR, Silveira R, Asano RY. SARS-CoV -2 (COVID -19) pandemic and a possible impact in the future of menstrual cycle research. Heal Sci Reports. 2021; 4.

11. Edelman A, Boniface ER, Benhar E, Han L, Matteson KA, Favaro C, et al. Association Between Menstrual Cycle Length and Coronavirus Disease 2019 (COVID-19) Vaccination. Obstet Gynecol. 2022; 139: 481-489.

12. Sharp GC, Fraser A, Sawyer G, Kountourides G, Easey KE, Ford G, et al. The COVID-19 pandemic and the menstrual cycle: research gaps and opportunities. Int J Epidemiol. 2022; 51: 691-700.

13. Rodríguez Quejada L, Toro Wills MF, Martínez-Ávila MC, Patiño-Aldana AF. Menstrual cycle disturbances after COVID-19 vaccination. Women's Heal. 2022; 18: 174550572211093.

14. Munro MG, Critchley HOD, Fraser IS. 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 Gynecol Obstet. 2018; 143: 393-408.

15. Taylor HS, Pal L SE. Speroff's clinical gynecologic endocrinology and infertility. Lippincott Williams & Wilkins; 2019.

16. Suzuki S, Hosono A. No association between HPV vaccine and reported post- vaccination symptoms in Japanese young women: Results of the Nagoya study. Papillomavirus Res. 2018; 5: 96-103.

17. Trogstad L. Increased Occurrence of Menstrual Disturbances in 18- to 30-Year-Old Women after COVID-19 Vaccination. SSRN Electron J. 2022.

18. Muhaidat N, Alshrouf MA, Azzam MI, Karam AM, Al-Nazer M, Al-Ani A. Menstrual Symptoms After COVID-19 Vaccine: A Cross-Sectional Investigation in the MENA Region. Int J Womens Health. 2022: 395-404.

19. Nazir M, Asghar S, Rathore MA, Shahzad A, Shahid A, Ashraf Khan A, et al. Menstrual abnormalities after COVID-19 vaccines: A systematic review. Vacunas. 2022; 23: S77-87.