

(RESEARCH ARTICLE)



Impact of COVID-19 vaccine on menstrual cycle: A cross-sectional study

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Abstract

Background: According to recent reports, many women who received COVID-19 vaccine reported symptoms of menstrual irregularity. However, this finding is still unclear. Therefore, this study aimed to determine the prevalence of women with menstrual cycle changes following receiving COVID-19 vaccines and identify the risk factors associated with menstrual cycle changes during the pandemic.

Material and methods: A cross-sectional descriptive study was conducted among women aged 20-40 years attending the outpatient clinics, general gynecology and reproductive and endocrine and infertility medicine department (REIMD) at King Fahad Medical City (KFMC) hospital in Riyadh, Saudi Arabia. Demographic data, medical and COVID-19 vaccination history, detailed menstrual cycle duration and frequency were obtained.

Results: A total of 1117 women participated in this study. The age of 35.2% of them ranged between 24 and 29 years. Most (72.6%) of regular cycles before uptaking of COVID-19 vaccine became irregular. On the other hand, 17% of irregular cycles before uptaking the vaccine became regular, $p < 0.001$. Vast majority of the participants (98.6%) had received COVID-19 vaccine. More than half of them (51.4%) had taken three doses. The most frequently reported vaccine was Pfizer-BioNTech (70.4% -83.5%). Frequency of menstrual cycles have increased from 29.64 ± 16.29 days before uptaking of COVID-19 vaccine to 62.11 ± 173.12 after uptaking it, $p < 0.001$. In addition, rate of heavy bleeding increased from 12.4% before uptaking of the vaccine to 24.9%, $p < 0.001$.

Conclusion: Frequency and amount of menstrual bleeding were affected after intake of COVID-19 vaccine. However, number of doses and vaccine type were not associated with menstrual changes.

Keywords: COVID-19; Vaccine; Menstrual irregularity; Incidence

1 Introduction

Since the beginning of 2020 almost all the world was affected by COVID-19 pandemic ⁽¹⁾. COVID-19 was described as a pandemic by the world health organization 2020 since there were over a hundred thousand cases around the globe ⁽²⁾.

This new virus can cause various health problems. The reported complications were pneumonia, acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), myocardial infarction, and gastrointestinal diseases ⁽³⁾. COVID-19 infection leads to an increase in inflammatory response and impaired immune system with alteration in hypothalamic pituitary gland access ⁽⁴⁾.

In a new study was done by Phelan N, et al and another study done by Jing Y, et al have reported a change in menstrual cycle function after getting infected by COVID-19 virus compared to before the pandemic ^(5, 6).

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According to United Kingdom government reports they found that many women who received COVID-19 vaccine reported symptoms of menstrual irregularity such as heavy menstrual bleeding, frequent bleeding, or post-menopausal bleeding⁽⁷⁾. Many theories suggested that the cause may be either due to thrombocytopenic disorders or possible activate the immune system to attack immune cell and inflammatory molecule in the uterus that will lead to alteration in menstrual cycle induced by vaccine⁽⁸⁾.

There are also other risk factors that have been reported for irregular cycles during the pandemic such as stress, anxiety, and depression^(9, 10). More studies are needed on this topic in order to be able to understand whether a link exists between the COVID -19 vaccine and menstrual cycle disturbances. The aim of our study is to determine the prevalence of women with menstrual cycle changes after receiving COVID-19 vaccine.

Specific objectives

- To determine the prevalence of women with menstrual cycle changes following receiving COVID-19 vaccines among women attending the outpatients clinics, general gynecology and reproductive and endocrine and infertility medicine department (REIMD).
- To identify if there is direct association between vaccination and menstrual cycle changes.
- To identify the duration and the outcomes of menstrual cycle changes during the pandemic in our sample.
- To propose recommendations for early preventive measures for menstrual cycle irregularity during and after the pandemic.

2 Material and methods

2.1 Study design

This was a cross-sectional descriptive study

2.2 Study area

The study was conducted at outpatient clinics, general gynecology and reproductive and endocrine and infertility medicine department (REIMD) at King Fahad Medical City (KFMC) hospital in Riyadh, Saudi Arabia.

2.3 Study population

Women attending the outpatient clinics, general gynecology and reproductive and endocrine and infertility medicine department (REIMD) at King Fahad Medical City (KFMC) hospital in Riyadh, Saudi Arabia constituted the target population in the study

2.4 Inclusion criteria

- -Adult females between the age of 20 to 40 years old
- -living in Riyadh, Saudi Arabia.

2.5 Exclusion criteria

- -Women with irregular menstrual cycles before having COVID-19 vaccine
- -Women who did not receive COVID-19 vaccine

2.6 Sample size

A total of 323 participants were needed for this cross-sectional study to determine the prevalence of women with menstrual cycle changes after receiving COVID-19 vaccines in Riyadh city. The sample size was calculated with a confidence interval of 95%, and a margin of error of 5% and a power of 80%. The following formula was used to calculate sample size $= Z_{1-\alpha/2} \cdot 2 \cdot SD / d^2$, where $Z_{1-\alpha/2}$ is standard normal variance (5% type 1 error). SD standard deviation of variable, d = absolute error.

2.7 Sampling technique

A non-probability convenience sampling technique was adopted to recruit eligible women in the present study. The process of recruitment was continued till the required sample size has been achieved.

2.8 Study tool and technique of data collection:

Demographic data, medical and vaccination history, detailed menstrual cycle duration and frequency were obtained and summarized in excel data collection sheet. Variables that were assessed are the menstrual cycle changes before the pandemic, during and after the pandemic, premenstrual symptoms, menorrhagia, dysmenorrhea missed periods and a decrease or increase in self-reported weight, and the presence or absence of anemia.

2.9 Statistical analysis:

The collected data were analyzed by using the Statistical Package of Social Sciences software (SPSS) version 26. A descriptive analysis was carried out and continuous variables were expressed as means \pm standard deviation (SD) or median (interquartile range "IQR") while categorical variables were expressed as frequency and percentage. McNemar and paired t-tests were used to assess impact of COVID-19 vaccine on menstrual cycle parameters. P-values less than 0.05 were chosen for statistical significance critical level.

2.10 Ethical consideration:

Verbal consent for asking direct open questions was obtained from the research participants and confidentiality was maintained. All personal data were anonymous and secured to maintain confidentiality. Approval of the Institutional Research Board (IRB) of King Fahad Medical City was solicited.

3 Results

3.1 Personal characteristics of the participants

A total of 1117 women participated in this study. Table 1 summarizes their personal characteristics. The age of 35.2% of them ranged between 24 and 29 years whereas that of 29.7% ranged between 30 and 35 years. Majority of them (82.5%) were Saudi nationals and almost two-thirds (63.6%) were married. More than half (51.9%) had no children whereas 14.4% had more than three children. Majority of them were either governmental employed/self-employed (42.2%) or housewife/not working (40.7%). Most of them (71.4%) were university graduated. Almost one-fifth of them (21.8%) had previous history of abortion while 7.1% reported current history of breastfeeding. About two-thirds of them (63.2%) had all of their previous deliveries normal spontaneous vaginal while 23.3% had all of their previous deliveries' cesarean sections.

Table 1 Personal characteristics of the participants (n=1117)

	Frequency	Percentage
Age (years)		
18-23	155	13.9
24-29	393	35.2
30-35	332	29.7
36-42	237	21.2
Nationality		
Saudi	921	82.5
Non-Saudi	196	17.5
Marital status		
Single	367	32.9
Married	711	63.6
Divorced/widowed	39	3.5
Number of children		
None	579	51.9

One	139	12.4
Two	143	12.8
Three	95	8.5
More than three	161	14.4
Job status		
Housewife/not working	456	40.7
Governmental employed/self employed	471	42.2
Student	186	16.7
Retired	4	0.4
Educational level		
Below secondary school	17	1.5
Secondary school	146	13.1
University	798	71.4
Postgraduate	156	14.0
Number of previous abortions		
None	873	78.2
Once	157	14.1
Twice	53	4.7
More than twice	34	3.0
Current history of breastfeeding		
No	1038	92.9
Yes	79	7.1
Mode of delivery (n=541)		
All normal spontaneous vaginal	342	63.2
All cesarean section	126	23.3
Both	73	13.5

3.2 Medical and social characteristics of the participants

More than half of the participants were either overweight (31.4%) or obese (27.2%) as illustrated in Figure 1

Prevalence of current smoking was 4.5% whereas that of ex-smoking was 2.1% as seen in Figure 2.

History of chronic diseases was reported by 27.8% of the participants (Figure 3). Among them, the most frequently reported were endocrine diseases (25.1%), gynecological diseases (19.9%), respiratory diseases (15.1%) and diabetes (10%). Figure 4

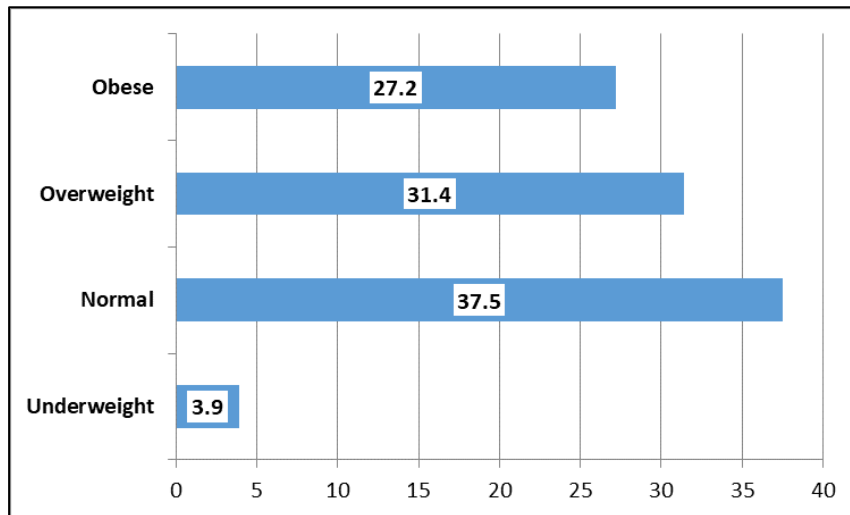


Figure 1 Body mass index of the participants (n=1115)

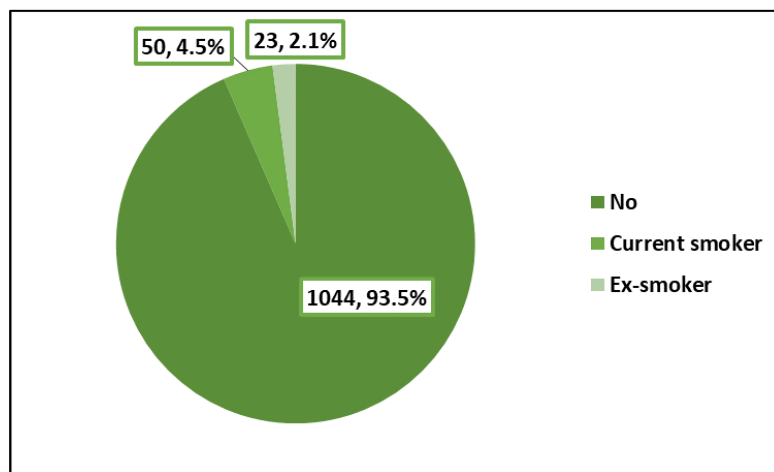


Figure 2 Smoking history among the participants

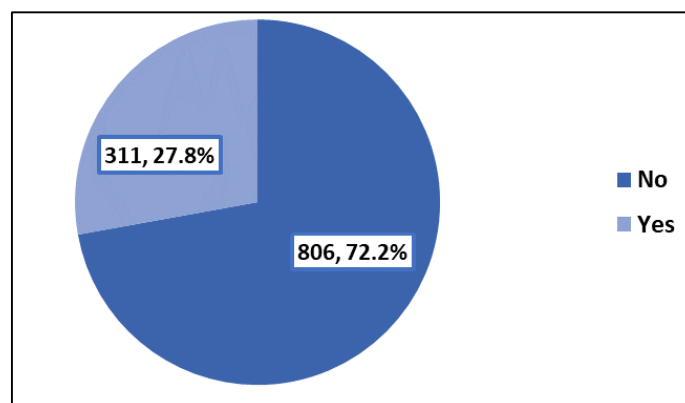


Figure 3 History of chronic diseases among the participants

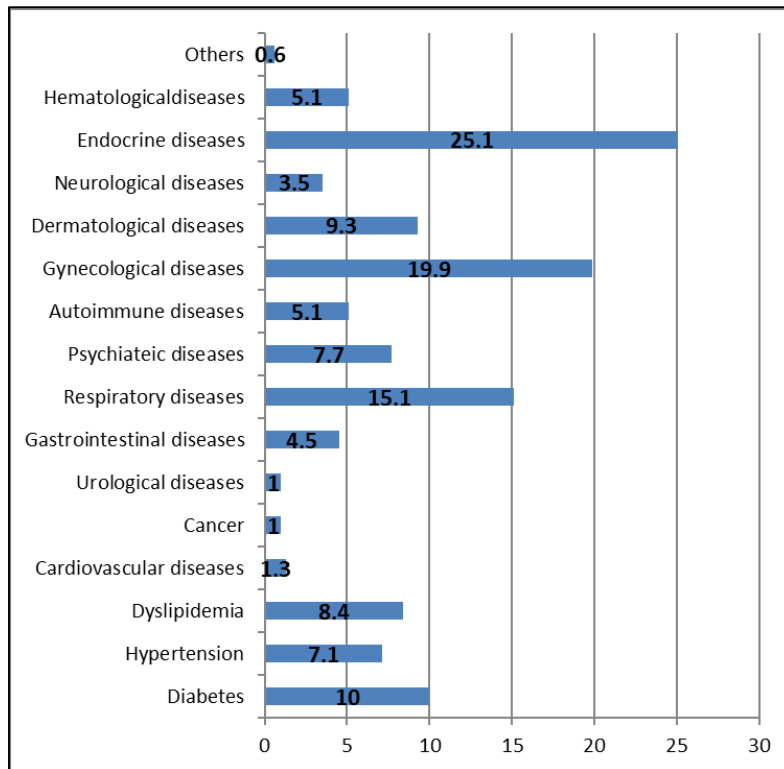


Figure 4 Frequency of individual chronic diseases among the participants (n=311)

3.3 Menstrual regularity

As illustrated from Figure 5, irregular menstruation was reported by 15.8% of the participants before uptaking the COVID-19 vaccine while after receiving of the vaccine, the rate of irregular menstrual cycles was 57.2% as illustrated in Figure 6.

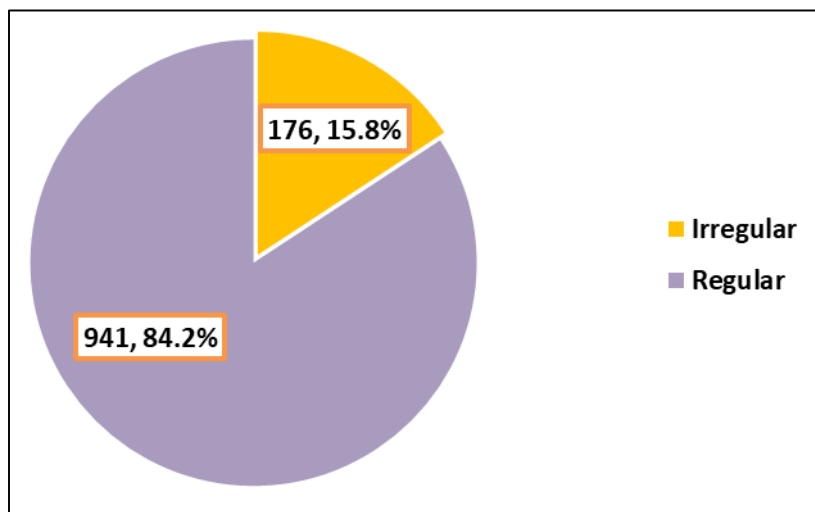


Figure 5 Description of the menstrual cycles before uptaking of COVID-19 vaccine among the participants

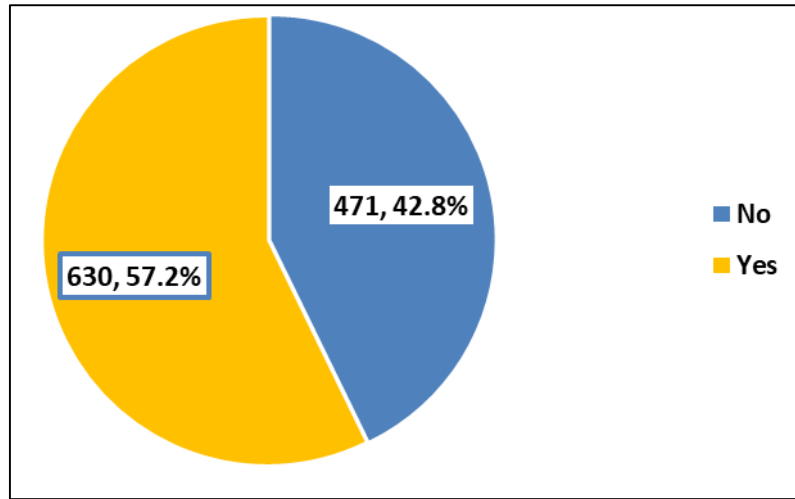


Figure 6 Prevalence of changes in menstrual cycle following receiving COVID-19 vaccines among the participants

From Table 2, it is shown that 72.6% of regular cycles before uptaking of COVID-19 vaccine became irregular. On the other hand, 17% of irregular cycles before uptaking the vaccine became regular, $p < 0.001$.

Table 2 Comparison of regularity of menstrual cycles before and after uptaking of the COVID-19 vaccine

Before uptaking of COVID-19 vaccine	After uptaking of COVID-19 vaccine		p-value*
	Regular N=162 N (%)	Irregular N=468 N (%)	
Regular (n=530)	145 (27.4)	385 (72.6)	<0.001
Irregular (n=100)	17 (17.0)	83 (83.0)	

3.4 COVID-19 vaccine uptake

As illustrated in Figure 7, vast majority of the participants (98.6%) had received COVID-19 vaccine. More than half of them (51.4%) had taken three doses of the vaccine as evident from Figure 8. The most frequently reported vaccine was Pfizer-BioNTech in a rate ranged between 70.4% for the first dose and 83.5% for the third dose, followed by AstraZeneca Oxford for the first (25.5%) and second (17.8%) and Moderna for the third dose (15.3%). Table 3.

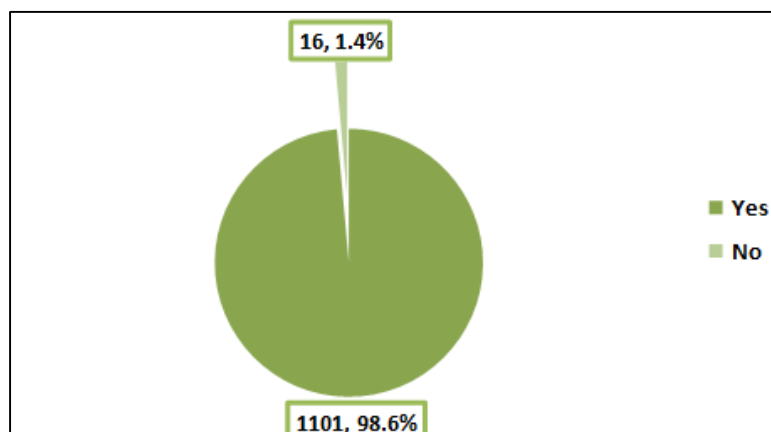


Figure 7 History of receiving COVID-19 vaccine among the participants

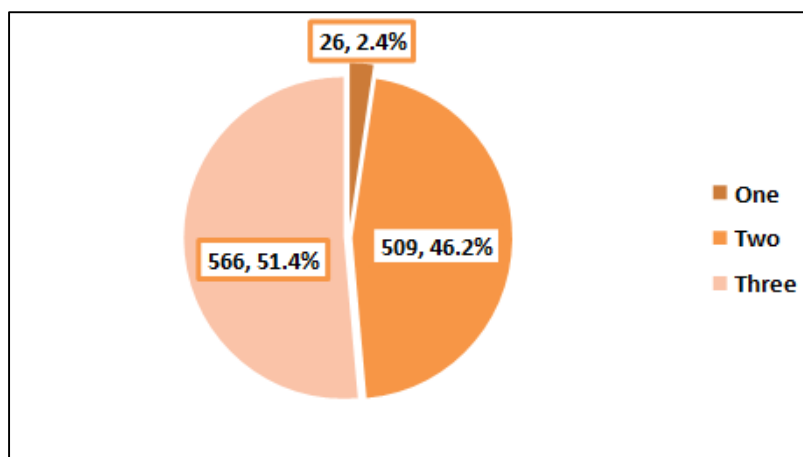


Figure 8 Number of COVID-19 vaccine doses taken by the participants

Table 3 Type of the COVID-19 vaccine received by the participants

Type of vaccine	Frequency	Percentage
First shot (n=1101)		
Pfizer-BioNTech	775	70.4
AstraZeneca Oxford	281	25.5
Moderna	20	1.8
Johnson & Johnson`s	4	0.4
Sinopharm	19	1.7
Sinovac	2	0.2
Second shot (n=1071)		
Pfizer-BioNTech	818	76.4
AstraZeneca Oxford	191	17.8
Moderna	42	3.9
Johnson & Johnson`s	1	0.1
Sinopharm	17	1.6
Sinovac	2	0.2
Third shot (n=589)		
Pfizer-BioNTech	492	83.5
AstraZeneca Oxford	4	0.7
Moderna	90	15.3
Johnson & Johnson`s	1	0.2
Sinopharm	2	0.3
Sinovac	0	0.0

3.5 Comparison of menstrual cycles before and after up-taking of COVID-19 vaccine

Frequency of menstrual cycles have increased from 29.64 ± 16.29 days before uptaking of COVID-19 vaccine to 62.11 ± 173.12 after uptaking it, $p < 0.001$. Also, severity of cramps has increased from median (IQR) of 5 (4-6) to 6 (4-8), $p < 0.001$. In addition, rate of heavy bleeding increased from 12.4% before uptaking of the vaccine to 24.9%, $p < 0.001$. Premenstrual tension syndrome and duration of the menstrual cycle were not significantly associated with uptaking of COVID vaccine.

3.6 Number and type of COVID-19 vaccine and existence of menstrual irregularity

As demonstrated in Table 5, there were no statistically significant association between number and type of COVID-19 vaccine from one side and menstrual irregularity from the other side among the participants

Table 4 Comparison of menstrual cycles before and after up-taking of COVID-19 vaccine among the participants

	Before uptake COVID-19 vaccine	After uptake of COVID-19 vaccine	p-value
Duration in days Mean \pm SD	5.99 \pm 1.68	6.29 \pm 4.67	0.058*
Frequency in days Mean \pm SD	29.64 \pm 16.29	62.11 \pm 173.12	<0.001*
Amount (F; %)	N=1117	N=630	<0.001**
Absent	27 (2.4)	48 (7.6)	
Light	138 (12.4)	253 (40.2)	
Moderate	813 (72.8)	172 (27.3)	
Heavy	139 (12.4)	157 (24.9)	
Severity of cramp (0-10)			
Median	5	6	<0.001°
IQR	4-6	4-8	
Premenstrual syndrome	N=630 568 (90.2)	N=227 201 (88.5)	>0.05

SD: Standard deviation; IQR: Interquartile range; F: Frequency; **McNemar test; °Wilcoxon matched-pairs signed rank test; * Paired t-test

Table 5 Association between number and type of COVID-19 vaccine and existence of menstrual irregularity among the participants

	Menstrual irregularity		p-value
	No N=471 N (%)	Yes N=630 N (%)	
Number of doses			
One (n=26)	8 (30.8)	18 (69.2)	0.445
Two (n=509)	221 (43.4)	288 (56.6)	
Three (n=566)	242 (42.8)	324 (57.2)	
Type of vaccine first shot (n=1101)			
Pfizer-BioNTech (n=775)	335 (43.2)	440 (56.8)	

AstraZeneca Oxford (n=281)	119 (42.3)	162 (57.7)	0.762
Others (n=45)	17 (37.8)	28 (62.2)	
Type of vaccine second shot (n=1071)	460	611	0.437
Pfizer-BioNTech (n=818)	349 (42.7)	469 (57.3)	
AstraZeneca Oxford (n=191)	88 (46.1)	103 (53.9)	
Others (n=62)	23 (37.1)	39 (62.9)	
Type of vaccine third shot (n=589)	250	339	
Pfizer-BioNTech (n=492)	205 (41.7)	287 (58.3)	0.578
Moderna (n=90)	41 (45.6)	49 (54.4)	
Others (n=7)	4 (57.1)	3 (42.9)	

4 Discussion

Many studies have demonstrated that women might experience menstrual changes after receiving COVID-19 vaccination ⁽¹¹⁻¹⁵⁾. However, this finding was not well documented yet understudied. It is hypothesized that menstrual changes are related to alterations in clotting or inflammation, induced by COVID-infection or vaccination on normal menstrual period ⁽¹⁵⁾.

In the present study, the overall prevalence of changes in menstrual cycle following receiving COVID-19 vaccines was 57.2% where amount of bleeding and frequency of menstrual cycles increased after uptaking of the COVID-19 vaccine while no changes were observed regarding duration of the bleeding as well as the rate of premenstrual syndrome. Interestingly, in the present study, neither number of COVID-19 vaccine doses nor their types were significantly associated with menstrual irregularities. Various findings were observed in other international studies. Phelan et al have found significant changes on several variables such as premenstrual symptoms, menorrhagia, dysmenorrhea missed periods and a decrease or increase in self-reported weight, and the presence or absence of anemia after uptaking of COVID-19 vaccine ⁽⁵⁾. In China (2021), Li K, et al found that 25% of reproductive women had menstrual volume changes and 28% had menstrual cycle changes, mainly a decreased volume (20%) and a prolonged cycle (19%) after receiving COVID-19 vaccine ⁽¹¹⁾. A study carried out in the Middle East and North Africa Region (MENA) revealed a rate of 66.3% as regards menstrual symptoms post-COVID-19 vaccination; mainly after the first dose (46.7%). However, the symptoms resolved within two months among majority of women (93.6%). In that study and in accordance with our findings, vaccine type did not significantly affect the rate of menstrual changes ⁽¹⁶⁾. In United Kingdom (2021), 42% of women with regular menstrual cycles had heavier bleeding than usual, while 44% had no change. ⁽¹²⁾ In United States (2021), more than half of the women received the Pfizer-BioNTech vaccine were associated with a less than one-day change in cycle length for both vaccine-dose cycles compared with pre-vaccine cycles while in unvaccinated women, no significant changes were reported ⁽¹³⁾. In Ghana (2021), a case series included three women developed abnormal uterine bleeding following COVID-19 vaccination; two had heavy menstrual bleeding and one inter-menstrual bleeding ⁽¹⁴⁾. In Norway (2021), a rate of 37.8% of any menstrual disturbance has been observed among women aged between 18 and 30 years. The relative risk of heavier bleeding than usual during the exposed compared to unexposed period for first dose vaccination was 1.90 while it was 1.84 for the second dose. The risk of heavy bleeding after the second dose, given that it had occurred after the first, was 65.7% ⁽¹⁵⁾.

None of the aforementioned studies reported adverse complications of irregular menstrual bleeding. However, this issue was not investigated in this study. The difference in the rates and forms of menstrual irregularities between various studies could be explained mainly by both variation in the demographic characteristics of the participants as well as perception and accurate definition of menstrual changes.

Main limitations of this study including being a single center study which could affect the generalizability of study's findings over other centers and the cross-sectional design of the study which proves only association and not causality between associated factors and the outcome. Despite of those two important limitations, the findings of this study could add to the literature investigating the possible association between receiving COVID-19 and occurrence of menstrual changes which may have importance for both healthcare professionals as well as women regarding awareness of possible side effects of the COVID-19 vaccine.

List of abbreviations

- Acute respiratory distress syndrome (ARDS)
- Acute kidney injury (AKI)
- Reproductive and endocrine and infertility medicine department (REIMD)
- King Fahad Medical City (KFMC)
- Statistical Package of Social Sciences software (SPSS)
- Interquartile range (IQR)
- Standard deviation (SD)
- Institutional Research Board (IRB)
- Frequency (F)
- Middle East and North Africa Region (MENA)

5 Conclusion

Menstrual changes; particularly changes in frequency, severity of cramps and menstrual amount are commonly reported by women after receiving COVID-19 vaccine. Number of doses and type of the vaccine were not associated with such changes. Although, these changes are not dangerous, awareness of both healthcare professionals as well as women regarding these changes is essential through their education.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans' subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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