Original Article

Covid 19 Vaccine And Menstrual Symptoms In Egyptian Adolescent Female Cross Sectional Study

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Abstract

Objectives The study's goal is to look into the effect of COVID-19 vaccines on adolescent female menstrual cycles. **Methods** From October 2021 to May 2022, a cross-sectional online self-administered survey was used for the study. Adolescent females above the menarche who had received the vaccine, were single, and without a previous history of primary ovarian insufficiency were the target population (language secondary school and first year student at faculty of physical therapy Kafrelsheikh university). Regional distribution of the survey was done through social media. **Results** a total of (270) female with mean age ranged from 16 to 18 years, with a mean of (16.98± 1.796). Overall, 66.6% of female didn't feel any changes in the period after vaccination, (10.7%) had Menstrual Cramps, (9.6%) irregular menstruation, (5.9%) increase the duration of the menstruation, (7.8%) Increased amount/abundance of bleeding, (4%) Increased period frequency and (5.19%) Worsening of premenstrual symptoms, (1.4%) intermenstrual bleeding, (37%) post menstrual bleeding. there was a significant relationship between duration of menstrual cycle in days and covid -19 vaccination p = 0.014, symptoms appearance in relation to dose p = .001, severity of vaccine side effect p= .023. **Conclusion** The study described a bearable link between the COVID-19 vaccine and the menstrual irregularities that have negatively impacted the women's quality of life.

Key words: COVID-19, menstrual cycle, vaccine, menstrual abnormalities

INTRODUCTION

The SARS-CoV-2 virus and COVID-19, the illness it causes, first emerged in Wuhan, China, infected a significant number of people, and then quickly spread all over the world. Worldwide cases were estimated to be 224 million as of September 14, 2021, and 4.6 million people perished. [1] Recent studies have revealed that the novel virus can have an impact on a variety of bodily systems, including the respiratory, nervous, musculoskeletal, cardiovascular, and reproductive systems. Even though COVID-19 has been the subject of extensive research, many questions and concerns remain unanswered. [2-4] High levels of expectation anxiety have also been heightened by the COVID-19 pandemic. People frequently seem to be more afraid of the future than the past, given the timeline for the anticipated course and spread of this virus. Even though the vast majority of people are unaffected, the intense media coverage and the potential for infection tend to be very stressful and anxious. [5].

The International Federation of Gynecology and Obstetrics (FIGO) has established standard criteria for prototypical menstruation with regard to menstrual waver, period, regularity, and volume; deflection from these may result in abnormal uterine bleeding.[6] The menstrual cycle's appearance is also referred to as one of life's "vital signs, and can

both indicate and possibly predict a person's general health and wellbeing [7]. For instance: protracted and irregular menstrual cycles have been linked to an increased risk of premature death and irregular or nonexistent menstruation may be a sign of decreased fertility, which in turn may be linked to a number of chronic diseases. [8]. Discussions about how women's menstrual cycles have changed, including menstrual duration, frequency, regularity, and volume (heavier bleeding and clotting), increased dysmenorrhea, and worsened premenstrual syndrome, have increased on social media and blogs since the start of the COVID-19 pandemic (PMS). [9]

Material and Methods

This study, which ran from October 2021 to May 2022, used a descriptive cross-sectional design. targeted to look into how COVID-19 vaccinations affected adolescent girls' menstrual periods, ages 16 to 18, (language secondary school and first-year student at faculty of physical therapy Kafrelsheikh university). Estimated sample power was calculated before starting the study using the G*power program upon a pilot study conducted over 12 subjects (3 had zero doses, 3 had one dose, 3 had 2 doses, 3 had 3 doses) with the primary outcome is the duration of the menstrual cycle after vaccination in days and using chi square test with the power of 80% and error of 0.05 and effect size of 0.201; the resultant sample was 270. It involved the distribution of an anonymous survey on a Google form through Facebook and WhatsApp, among other social media sites. To avoid the COVID-19 virus spreading, to make data collection simple to use, and to avoid influencing participants' opinions, no direct contact with participants was made during the data collection process. The study looked into the key relationships. the relationship between the COVID-19 vaccine, menstrual irregularities, and related factors.

Being between the ages of 16 and 18 years old, a single female, having a body mass index (BMI) of less than 30, having had regular periods in the six months prior to the pandemic, and agreeing to participate in the study were the inclusion criteria. Married women, those with thyroid issues, or those with polycystic ovary syndrome were not included in the study.

A web-based questionnaire[10] for the study was produced using Google Forms® online survey creation software. There are 27 detailed self-report questions in the questionnaire, which can be found in the supplemental materials, and they cover six key domains. The first is demographics, which includes age, nationality, and marital status (3questions). Questions about pre-existing medical conditions, smoking, and the menstrual cycle are asked in the second section (8 questions). The third group focuses on the number of doses, the type of vaccine received, and the objective evaluation of the COVID-19 vaccination side effects' severity (3 questions). The fourth faction discusses the most recent COVID-19 infection, the NIH-estimated severity of the infection's symptoms, and menstrual irregularities during the pandemic (3 questions). The fifth faction includes inquiries into the duration of side effects, their connection to dosage, and the impact they have on daily life (6 questions). The sixth category includes an open-ended inquiry about the length of the menstrual cycle and menstruation between the baseline and post-vaccination periods (4 questions). The Kafrelsheikh university's Ethics Research Committee granted permission for the study (P.T/WH/8/2021/17).
At the beginning of the questionnaire, each participant read and electronically signed the informed consent form.

Data analysis

The statistician was blinded about grouping, Data were analyzed using SPSS 26. Mean and Standard deviation was calculated and presented for age variables while other variables were treated as nominal data, Chi-square test was used to investigate possible associations between the different variables when classifying the data into 4 categories according to the number of vaccine doses. ANOVA tests were conducted to test the mean difference between different groups regarding age.

Results

Demographics

350 participants were asked to fill Out the questionnaire; only (300) participants completed the questionnaire, of which (25) were excluded because they failed to meet the eligibility requirements, also there were (5) participants who were excluded as they were not in the specified age range for the current study. Finally, this analysis included (270) female respondents. The mean age of the participants ranged between 16 and 18 years (mean= 16.98 1.796). Participants were first-year physical therapy students at Kafrelsheikh University.

Sinopharm, AstraZeneca, Pfizer-BioNTech, and Johnson & Johnson were given to the majority of participants (58.52%, 20%, 5.93%, and 3.7%, respectively). 15% of participants had a confirmed COVID-19 infection, 30% of participants reported symptoms similar to COVID-19, and 54% of participants had symptoms without a diagnosis. (Table 1-4)

Table (1) Types of vaccines

Vaccine type	Count	Percent
AstraZeneca	54	20%
I didn't receive the vaccine	4	1.48%
Johnson & Johnson	10	3.7%
Moderna	3	1.11%
More than one type of vaccine	16	5.93%
Novavax	3	1.11%
Pfizer-Biontech	16	5.93%
Sinopharm	158	58.52%
Sputnik	6	2.22%

Table (2) Number and percentage of responses regarding history in pre-vaccination period

Question	Answer	N(%)
Clotting abnormalities history	Yes	19(7)
	No	251(93)
Allergy history	Yes	43(15)
	No	227(84)
Smoking history	Yes	0
	No	270(100)
Previous COVID-19 infection	Symptoms without diagnosis	82(30)
	No symptoms	145(54)
	Diagnosed	43(15)
Severity of previous COVID-19 symptoms	No symptoms	143(53)
	Mild symptoms	111(41)
	Moderate symptoms	14(5)
	Sever symptoms	2(0)
Regularity of menstrual cycle in the past year	Regular	197(73)
	Irregular	73(27)
	Menopause	0(0)
Previous diagnosis of the menstrual diseases	No	270(100)
	Yes	0
Experiencing new symptoms before taking the vaccine	No	191(70)
	Yes	79(30)
Menstrual abnormalities effect on QOL	No	49(18)
	Yes	54(20)

Clinical Characteristics

Menstrual Cycle Abnormalities and COVID-19 Infection

Most participants who had COVID-19 infection (63.2%) didn't feel any changes in the period, (10.4%) had Menstrual Cramps, (9.1%) irregular menstruation, (5.5%) increase the duration of the menstruation, (3.9%) Increased amount/abundance of bleeding, (2.3%) Increased period frequency and (2.9%) Worsening of premenstrual symptoms, (.9%) intermenstrual bleeding, (.3%) post menstrual bleeding. (Table 5)

Menstrual Cycle Abnormalities After COVID-19 Vaccination

There was relation between menstrual cycle duration in days and covid -19 vaccination p = 0.014, symptoms appearance in relation to dose p = .001, severity of vaccine side effect p= .023 Overall, 66.6% of female didn't feel any changes in the period after vaccination, (10.7%) had Menstrual Cramps, (9.6%) irregular menstruation, (5.9%) increase the duration of the menstruation, (7.8%) Increased amount/abundance of bleeding, (4%) Increased period frequency and (5.19%) Worsening of premenstrual symptoms, (1.4%) intermenstrual bleeding, (.37%) post menstrual bleeding .(table 5)

According to our findings, there was no correlation between the type of vaccination, prior COVID-19 infection, prior diagnoses of PCOS, thyroid disorders, uterine fibroids, endometriosis, or adenomyosis, stopping or starting any form of contraception, previous coagulation abnormalities (such as thrombocytopenia, bleeding or administration of anticoagulant medications) ($p > 0.05$). However, there was a significant association between the covid-19 dose and the duration of the menstrual cycle ($p = 0.014$), the onset of symptoms and dose ($p = .001$), and the severity of vaccine side effects ($p = .023$).

Table (3) Chi-square test P-value to test the association between the number of vaccine doses and other factors related to the menstrual cycle.

Variable name	**Category**	**No dose**		**One dose**		**Two Doses**		**Three doses**		**Chi-Square P-value**
Experiencing new symptoms after taking the vaccine	No	1	0%	24	9%	142	53%	11	4%	0.344
	Yes	2	1%	15	6%	66	24%	9	3%	
Symptom appearance dose	First Dose	0	0%	12	4%	48	18%	4	1%	0.001
	Second Dose	0	0%	0	0%	21	8%	6	2%	
	Third Dose	0	0%	0	0%	2	1%	3	1%	
The severity of vaccine side effects	Mild	0	0%	11	4%	73	27%	5	2%	0.023
	Moderate	0	0%	7	3%	47	17%	4	1%	
	Severe	0	0%	4	1%	16	6%	7	3%	

Table (4) Chi-square test P-value to test the association between the number of vaccine doses and other factors related to the menstrual cycle.

Variable	Chi-square P-value
Timing of menstrual cycle before vaccination in days	0.959
Duration of menstrual cycle before vaccination in days	0.253
Timing of menstrual cycle after vaccination in days	0.157
Duration of the menstrual cycle after vaccination in days	0.014

Table (5) Menstrual symptoms and vaccination among groups

Menstrual symptoms and vaccination	During COVID	After Vaccination				Chi-Square	P-value
		One-Dose	Two Doses	Three Doses	Total		
Increased amount/abundance of bleeding	12(3.93)	5(1.85)	11(4.07)	3(1.11)	19(7.04)	4.545576	0.871989
Increase the duration of the menstruation	17(5.57)	5(1.85)	10(3.7)	1(0.37)	16(5.93)		
Increased period frequency	7(2.3)	2(0.74)	8(2.96)	1(0.37)	11(4.07)		
Menstrual Cramps	32(10.49)	3(1.11)	22(8.15)	4(1.48)	29(10.74)		
Irregular menstruation	28(9.18)	4(1.48)	19(7.04)	3(1.11)	26(9.63)		
Intermenstrual bleeding	3(0.98)	0(0)	3(1.11)	1(0.37)	4(1.48)		
Postmenopausal bleeding	1(0.33)	0(0)	1(0.37)	0(0)	1(0.37)		
Worsening of premenstrual symptoms	9(2.95)	1(0.37)	9(3.33)	4(1.48)	14(5.19)		

Menstruation has stopped since the vaccination	3(0.98)	1(0.37)	2(0.74)	1(0.37)	4(1.48)		
Didn't feel any changes in my period	193(63.28)	25(9.26)	143(52.96)	11(4.07)	180(66.67)		

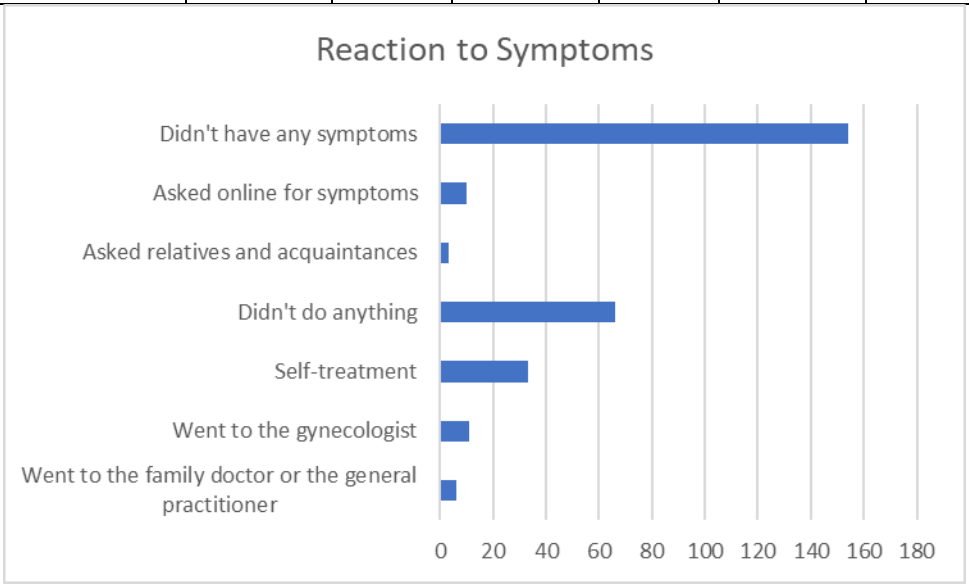

Figure (1) reaction to symptoms in the whole sample

Discussion

Our research showed that regardless of the vaccine type, the incidence of menstrual abnormalities among the participants did not change after receiving the COVID-19 vaccine, particularly after the first dose. However, women who experienced pronounced side effects from the COVID-19 vaccine had significantly higher rates of abnormal menstruation. In comparison to their pre-vaccine status, females reported significantly longer mean menstrual periods and menstrual cycles after receiving the vaccine, as well as worsening premenstrual symptoms. Twenty percent of the participants said that post-vaccination menstrual irregularities had affected their quality of life. Menstrual abnormalities and the severity of vaccine side effects were significantly correlated, p =.023.

Although there have been thousands of clinical studies on COVID-19 disease and the SARS-CoV-2 virus is still spreading throughout the world, the impact of COVID-19 on female reproductive function is still unknown. As a result, the findings of the current study will function as a necessary input to lowering anxiety and fear. The results of this study showed a significant link between the number of the menstrual cycle days and the covid-19 vaccination (p = 0.014), the appearance of symptoms in relation to dose (p =.001), and the severity of vaccine side effects (p =.023). Up to their most recent update on November 17, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom reported 41,919 cases of menstrual abnormalities, which include heavier or delayed periods, and unexpected vaginal bleeding. Weekly summary of yellow card reporting for the coronavirus vaccine. GOV.UK; 2021. This underlines how crucial it is to look into menstrual abnormalities following COVID-19 vaccination[11].

The study's findings are consistent with those of (Ding et al., 2021) who claimed that some of the frequent side effects of the covid-19 vaccination listed by the MHRA include a sore arm, fever, fatigue, and myalgia. Period changes and unexpected vaginal bleeding are not listed, but patients who have experienced these symptoms soon after vaccination are increasingly approaching primary care physicians and reproductive health professionals[12].

The menstrual cycles of the women during the epidemic also show other strange effects on their health. Stress and psychological problems, such as the recent flu pandemic, can affect women's menstrual cycles. Future research should examine the effects of this on long-term health, which are still unknown. In September 2020, 1,031 women of reproductive age were invited to participate in a study by Phelan et al.7 in Dublin, Ireland, by means of social media.

Four hundred and eighty-three percent (53%) of respondents reported that the pandemic had worsened their premenstrual symptoms, while four hundred and sixty-five percent (45%) reported losing their libido[13].

After a COVID-19 illness, the proportion of women who have irregular periods and amenorrhea slightly increased, but the menstrual volume among the study participants significantly decreased in the three months after the illness. On the opposite hand, three months after the illness, nearly all menstrual changes stopped. Another investigation into the impact of COVID-19 on menstrual status revealed amenorrhea to be more prevalent, menstrual volume to be lower, and cycles to be longer[14].

In a retrospective, cross-sectional study, sex hormones and anti-Müllerian hormone were measured in blood samples from the early follicular phase. The severity of the disease appears to be correlated with greater menstrual changes. In addition to having comorbid conditions like diabetes, liver disease, and malignant tumors, patients with confirmed severe cases of COVID-19 (34% versus 8% of mild or asymptomatic cases) also had more menstrual cycle changes, primarily lengthened cycles or a reduction in volume. [15] The average sex hormone levels and ovarian reserve in women of childbearing age with COVID-19, however, did not change significantly. From a biological perspective, it is conceivable that patients with the severe form of COVID-19 experience hormonal changes brought on by a suppression in ovarian function that result in menstrual disorders.[16]. The socioeconomic burden of menstrual irregularities is significant on women, their families, the healthcare system, and society at large. It can lead to anemia, significantly lower quality of life, and other health and lifestyle issues. [17]

We anticipate any effects to be short-lived given the widespread use of vaccinations. According to these studies, vaccinations (generally) affect menstrual symptoms. Investigation continues, but it is still unclear how vaccinations affect menstrual cycle characteristics. [18]

The COVID-19 infection and SARS-CoV-2 illness may alter the hypothalamic-pituitary-ovarian-endometrial axis. Acute hypothalamic hypogonadism, which can result in transient amenorrhea or irregular menstrual cycles, can be brought on by any severe illness, including COVID-19. This defense mechanism enables the immune response to be powered instead of reproduction. This could also be the reason why some individuals with Post Ebola Syndrome, which is similar to Long Covid, have reported irregular or stopped menstrual cycles [19].

SARS-CoV-2 infection and the reproductive system may additionally or alternatively interact in more specific ways. Endometrial/ovarian level may be impacted. Ovarian hormone progesterone has a potent anti-inflammatory effect. Prior to menstruation, progesterone levels drop significantly. Due to the influx of inflammatory cells caused by this into the nearby endometrial environment, the functional endometrium eventually sheds during menstruation. Intense vasoconstriction of the specialized endometrial spiral arterioles and activation of the local coagulation system regulate menstrual blood loss. SARS-CoV-2 infection may have an impact on ovarian hormone production as well as the endometrial response to menstruation because both ovarian and endometrial tissue contain ACE2 receptors. For instance, changes in endometrial leukocyte quantity or phenotype during or following SARS-CoV-2 infection may affect menstrual blood loss. According to earlier research, viral infections that disrupt the immune system can cause premenstrual symptoms related to progesterone to worsen. [20].

Stress can have an effect on a process like the menstrual cycle. Menstrual frequency, menstrual bleeding amount, and menstrual cycle duration can all be affected to varying degrees by the kind and level of stress factors 19. Therefore, pain or stress may be the cause of the changes.

Acute stress has an impact on the brain regions in charge of emotion regulation in the luteal phase, according to a 2010 study that examined changes in menstrual cycles in relation to stress-related neural mechanisms. It also made a comparison between these results and those from the late follicular phase. They showed that elevated stress, particularly in the late luteal phase, alters the body's pregnanolone levels and results in irregular menstruation. Additionally, they showed that elevated sympathetic activity during[21].

In order to better understand the menstrual cycle abnormalities in adolescent females and how they relate to the various COVID-19 vaccines as well as how it affects their quality of life, this study is looking into these issues. Through easing their worries and assisting them in managing their symptoms, this investigation will help us deliver better medical care to these patients and achieve a satisfactory outcome by enhancing their quality of life.

Conclusion

The study described a bearable link between the COVID-19 vaccine and the menstrual irregularities that have negatively impacted the women's quality of life.

Limitation

This study isn't without limitations; absence of objective assessment is major limitation beside lack of evidence of such effects on menstrual symptoms at different ages.

Conflict of Interests

The authors have no conflict of interests to declare.

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