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Research Article

JOURNAL OF WOMENS HEALTH AND DEVELOPMENT

ISSN: 2644-2884

COVID-19 Vaccine-Related Menstrual Disorders among Reproductive Age Women in the UAE

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Abstract

Objective: The menstrual cycle is regulated by a complex interaction between several factors. It serves as a vital part of a woman's reproductive health. Following the administration of the COVID-19 vaccines, several clinics globally saw an increase in women attendees concerning changes in their menstrual cycle, later several studies were also conducted in various countries to evaluate this association. Therefore, our study aims to investigate the impact of COVID-19 vaccination on the menstrual cycle, focusing on the prevalence and nature of menstrual abnormalities among vaccinated females of reproductive age living in the UAE.

Methods: Participants were surveyed regarding their menstrual history before and after COVID-19 vaccination. Data were collected anonymously through self-administered online surveys, including information on the menstrual cycle length, duration, flow, presence of clots, association of menstrual cramps, intermenstrual bleeding/spotting, and the impact of these changes on the quality of their life.

Results: Out of the participants, 35.9% reported variations in their menstrual cycle, notably after the second dose of vaccination. Symptoms included alterations in cycle length, cramp intensity, menstrual flow and intermenstrual bleeds. While menstrual irregularities were self-limiting in many cases, 8.6% reported a significant negative impact on quality of life, emphasizing the importance of considering psychological and physical well-being. Among those previously infected with COVID-19, 10.9% reported post-recovery menstrual changes.

Conclusion: While most menstrual irregularities were self-limiting, it is equally important to recognize the presence of menstrual changes after the administration of the vaccine. Proposed mechanisms for these disturbances encompass vaccine-induced thrombocytopenia and disruption of the hypothalamic-pituitary-ovarian axis. The study underscores the importance of understanding vaccine effects and emphasizes the need for education and pre-vaccination counseling to mitigate hesitancy.

Keywords: Covid-19; Covid-19 vaccination; Menstrual disorders; Women health; Menstrual cycle

Introduction

The menstrual cycle serves as an indicator of a woman's overall health, with any irregularities potentially signaling gynecological or other medical conditions. Disruptions in the menstrual pattern present a significant healthcare challenge, profoundly impacting women's quality of life. In 2019,

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Citation: Insha Nazeer, Fathima Muzeera M Musaffar, Fatima A Alsaadi, Maria Hasani, Ambreen Ansar, Tasneem Sandozi. COVID-19 Vaccine-Related Menstrual Disorders among Reproductive Age Women in the UAE. Journal of Women's Health and Development. 7 (2024): 23-28.

Received: April 03, 2024
Accepted: April 10, 2024
Published: April 25, 2024

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DOI:10.26502/fjwhd.2644-288400117

the emergence and rapid global spread of COVID-19 had detrimental effects on human life. Various vaccines were swiftly developed to address this pandemic, underwent clinical trials, and received expedited approval for emergency use [1,2]. As of March 2023, a staggering 13 billion vaccine doses have been administered worldwide, with 24.9 million in the United Arab Emirates [3,4,5]. However, clinical trials assessing vaccine-related adverse events did not adequately consider reproductive aspects. Following the widespread implementation of vaccination programs, numerous countries observed a rise in the number of women seeking medical attention for menstrual issues. According to the latest update in November 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom documented 41,919 cases of menstrual problems, including instances of heavier-than-usual periods, delayed menstruation, and unexpected vaginal bleeding [6]. Subsequent studies have reported a range of abnormal menstrual symptoms post-vaccination, encompassing pain, intermenstrual spotting, increased cycle length, and abnormal bleeding [1,7]. Factors such as age, pregnancy status, the COVID-19 vaccine dosage, and the severity of the infection were identified to influence these menstrual changes [2]. Against this backdrop, our study aims to investigate alterations and abnormalities in the menstrual cycles of women aged 15 to 45 residing in the United Arab Emirates following COVID-19 vaccination and infection.

Materials and Methods

Study Design and Participants

A cross-sectional study, based on an anonymous online questionnaire, was undertaken between July and October 2022, following approval from the Research and Ethics Committee of Dubai Medical College for Girls, Dubai, UAE. All participants provided informed consent before participating in the survey, clearly understanding the study's objectives, data confidentiality, and anonymity. The survey was disseminated through various social media platforms using the snowballing technique. Some questions in the questionnaire were adapted from previous studies. The inclusion criteria included women aged 15 to 45, residing in the UAE, who had received any type of COVID-19 vaccine, while the exclusion criteria were women aged 15 to 45 who did not receive the vaccine, as well as pregnant and lactating women.

Study Questionnaire

The self-administered online questionnaire was available in English and Arabic languages and comprised four main sections:

Section 1: Gathered participant demographics, including age, nationality, pregnancy/ lactation status, medical history (chronic illnesses, gynecological diseases, medication history), and details of COVID-19 vaccination (type, number of doses and experienced side effects).

Section 2: Focused on the participant's menstrual history, exploring various aspects of the menstrual cycle before COVID-19 vaccination.

Section 3: Examined Menstrual changes observed post-COVID-19 vaccination. This section delved into details such as menstrual cycle length, duration, flow, presence of clots, association of menstrual cramps, intermenstrual bleeding/ spotting, the cycle phase during vaccine administration, and the impact of these changes on the quality of life. The participants were allowed to choose more than one option of the menstrual changes they experienced, therefore making the sum of responses more than 100%.

Section 4: Investigated the resolution of menstrual changes and in addition, it explored any prior COVID-19 infections and associated menstrual changes.

Sampling Type, Sample Size & Statistical Analysis

The sample size was determined using Statulator [8], based on the results from a cross-sectional study conducted in the MENA region where the estimated prevalence of menstrual changes was around 66% [1]. The required sample size was determined to be a total of 176 with a 95% confidence interval and a 7% margin of error. The study utilized the convenience sampling method for collecting survey data. The statistical analysis was conducted using the IBM Statistical Package for Social Sciences (SPSS) version 23. Descriptive statistics, crosstabs, and chi-square test was applied to assess relationship of different categorical variables taking α at 0.05.

Results

A total of 202 females consented to participate in our survey out of which 192 were eligible. Most women belonged to the age range of 15-25 years and were non-GCC expatriates. The demographic characteristics of the participants have been described in Table 1. Of the 192 women, 35.9% reported experiencing menstrual disorders after receiving COVID-19 vaccination. A greater number of the participants reported taking the Pfizer BioNTech vaccine. Of the women who took Pfizer BioNTech alone, 25% reported changes in their menstrual cycle; 29.5% noted changes with Sinopharm alone and 26% taking the Pfizer and Sinopharm combination suffered changes in their menstrual cycle. No significant association was found between the menstrual cycle changes and type of vaccine taken by the respondents ($p=0.947$). Of the participants who noticed changes in their menstrual cycle, 47.8% experienced them after the second dose of the vaccine, while 21.7% noted the changes after the booster dose. The rest of the participants noticed changes immediately after the first dose (17.3%), while some experienced changes after every dose (13%).

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DOI:10.26502/fjwhd.2644-288400117

Table 1: Participant demographics.

Category	Variable	Frequency	Percent
Nationality	Non-GCC expat (Asian, European)	138	71.9
	GCC expats	13	6.8
	Local	41	21.4
Age	15-25 years	158	82.3
	26-35 years	14	7.3
	36-45 years	20	10.4
Type of vaccine	Pfizer BioNTech	109	58.3
	Sinopharm	44	23.5
	Oxford/AstraZeneca	8	4.3
	Pfizer BioNTech, Sinopharm	23	12.3
	Covishield	1	0.5
	Pfizer BioNTech, Sinopharm, Oxford/ AstraZeneca	1	0.5
	Pfizer BioNTech, Oxford/AstraZeneca	1	0.5
Gynecological diseases	No known illness	156	81.3
	Polycystic ovarian disease (PCOD)	29	15.1
	Infections	1	0.5
	Endometrial polyps	1	0.5
	Fibroids	3	1.6
	Menorrhagia	2	1
Hormone therapy	No	182	94.8
	Yes	10	5.2

Menstrual cycle abnormalities following COVID-19 vaccination

Among women experiencing menstrual irregularities post-vaccination, 49 noted a change in their cycle length, with their menses starting later or earlier than expected. The illustration of changes in cycle length in relation to gynecological diseases of affected participants is shown in Figure 1 and 2. Of the 49 women, 34 had a history of regular menstrual cycles and no gynecological diseases. Of these, 23 women reported having delayed cycles and the rest 11 experienced an earlier onset than expected. Table 2 shows a comparison of changes in cycle length before versus after COVID-19 vaccination in relation to history of gynecological diseases. There was no statistically significant difference in the length of menstrual cycle before versus after vaccination (p=0.442).

Alterations in the intensity of menstrual cramps were reported by 25.5% participants and the difference in the intensity of pain perceived before versus after vaccination and the difference are illustrated in Figure 3 as a box and whisker chart.

Few participants also noted changes in the duration of their menstruation with roughly 9.3% reporting their menses lasted for more than 7 days and 4.1% less than 3 days. Approximately 27.6% participants observed changes in the character of their menstrual flow with 15.6% reporting heavier and 11.9% lighter periods than usual. Roughly, 25.5% of the affected participants reported the presence of large clots during menstruation. Out of a total of 53 (27.6%) participants who experienced intermenstrual spotting and bleeding, 36 participants who had no spotting or bleeding problem before vaccination experienced it after the vaccination, but the observed differences seen in spotting/bleeding before and

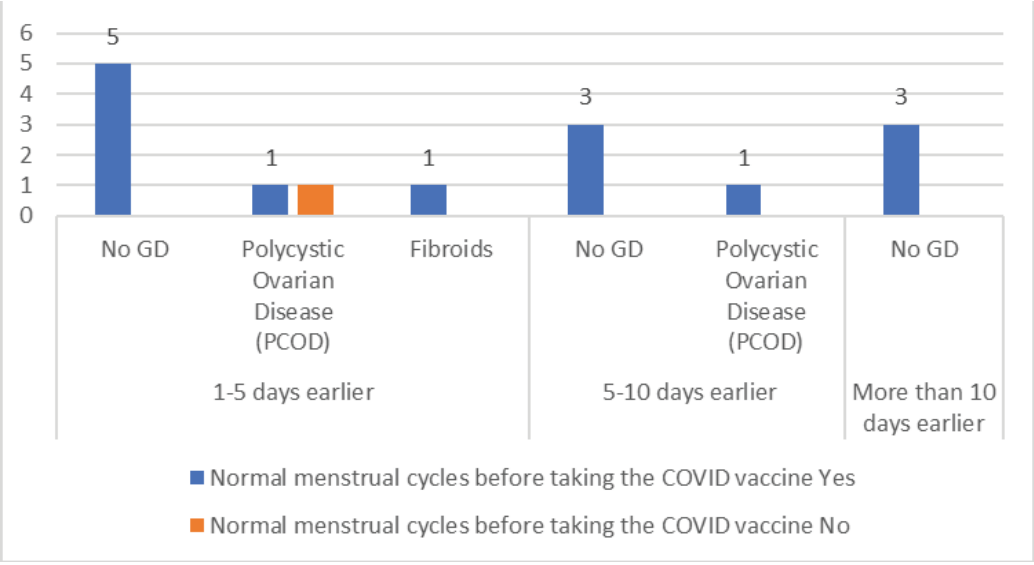

Figure 1: Changes in the menstrual cycle length in relation to gynecological diseases of affected participants (early cycle). (GD- Gynecological diseases)

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DOI:10.26502/fjwhd.2644-288400117

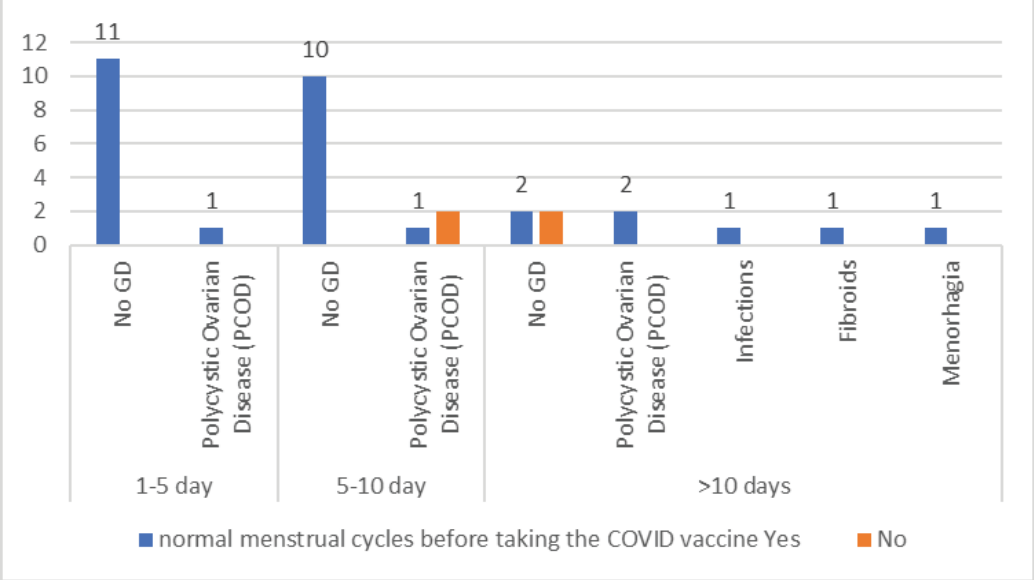

Figure 2: Changes in the menstrual cycle length in relation to gynecological diseases of affected participants (delayed cycle) (GD- Gynecological diseases)

Table 2: Comparison of changes in menstrual cycle length before versus after COVID-19 vaccination in relation to history of gynecological diseases

Changes in menstrual cycle after vaccination	Gynecological diseases	Normal menstrual cycles before taking the COVID-19 vaccine		Total
		Yes	No	
No	No Gynecological diseases	101	19	120
	Polycystic Ovarian Disease (PCOD)	9	11	20
	Endometrial Polyps	0	1	1
	Fibroids	1	0	1
	Menorrhagia	0	1	1
Yes	No Gynecological diseases	34	2	36
	Polycystic Ovarian Disease (PCOD)	6	3	9
	Infections	1	0	1
	Fibroids	2	0	2
	Menorrhagia	1	0	1
Total		44	5	49

after COVID vaccination was clinically significant though statistically insignificant (p=0.728).

Impact of menstrual cycle changes

Of the 69 participants who experienced menstrual changes after COVID-19 vaccination, around 8.6% of them reported significant negative impact on daily life, 49.2% faced occasional challenges, and 42% reported no significant effect on their quality of life.

Resolution of menstrual cycle changes

In this study, when comparing the resolution of menstrual changes in the affected females in relation to hormonal therapy, 12 women who had a history of normal menstrual cycle and were not on hormonal therapy reported their cycles to not have returned back to normal until the time of their participation in the survey. On comparing the resolution of menstrual cycle changes in relation to gynecological disease, among women who had no gynecological disease and normal menstrual cycle history before vaccination, nine of them experienced prolonged disturbances and 21 females said their cycles to have returned to normal in a duration of one to six months. Six women who were suffering from gynecological disease, reported resolution over a time period of one to six months which may be attributed to the treatment they may have been taking.

COVID-19 infection and menstrual cycle abnormalities

Among the 54.6 % of women who contracted COVID-19, 10.9% reported menstrual disturbances post-infection and 43.7% noticed no change in their cycles.

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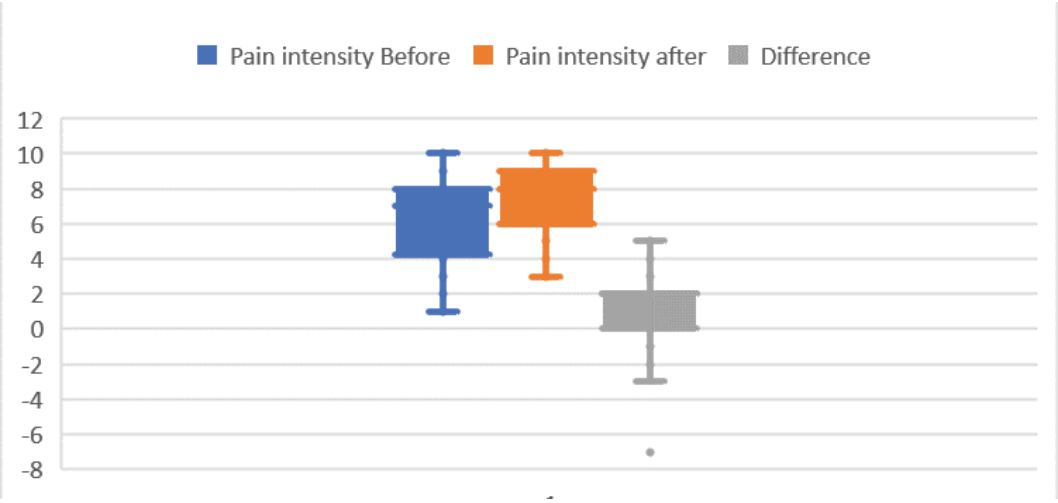

Figure 3: Changes in the intensity of menstrual cramps experienced by the participants.

Discussion

Various factors can impact the menstrual cycle, disrupting its normal pattern [1]. In this cross-sectional study, 35.9% of the participants noted changes in their menstrual cycle post COVID-19 vaccination, with a notable majority (47.8%) experiencing these after the second dose. This aligns with Taskaldiran and associates' study, emphasizing a higher prevalence of menstrual disturbances after the second dose of the vaccine [9]. The obtained data revealed many changes in the menstrual cycles of the study population. They included alterations in cramp intensity (25.5%), changes in character of menstrual flow (27.6%), variation in cycle length (25.5%), passage of clots (25.5%), altered duration of menstruation (13.4%) and intermenstrual bleeding (27.6%). Furthermore, our results align with multiple studies including a cross-sectional study in the MENA region where 66.3% reported abnormal menstrual symptoms post-vaccination [1]. Similarly, a recent preprint study in the USA reported experiencing heavier bleeding after vaccination (42%) [10]. It is believed that the COVID-19 vaccination could be linked to an augmentation in the mean duration of menstrual cycle length [1,11]. Many researchers have consistently reported delayed menstruation, heightened bleeding severity, and increased cramp intensity as the most frequent menstrual symptoms, aligning with the outcomes of our study [9,11,12]. The precise mechanism through which the vaccine impacts the menstrual cycle remains unclear, but several theories have been postulated. One hypothesis suggests vaccine-induced thrombocytopenia, as similar symptoms have been observed with other vaccines such as hepatitis A and B, MMR, DTaP, and HPV [1,13]. Another hypothesis involves the disturbance of the hypothalamic-pituitary-ovarian axis due to the immune response triggered by the vaccine [13,14]. A potential explanation for heavy menstrual bleeding after COVID-19 vaccination is the secretion of vasodilator substances following an increased expression of macrophages and endometrial leukocytes [7]. Lagana et al. have documented that vaccine-related menstrual irregularities are self-limiting, with resolution confirmed in 50% of affected women in less than two months, aligning with our findings and several other studies [12,13].

Similarly, numerous studies exploring the relationship between the COVID-19 infection and the menstrual changes have revealed that a significant number of females reported menstrual disturbances as a long-term effect of COVID-19, as evident in our study. The frequency of menstrual changes after COVID-19 infection appears to be directly proportional to the severity of the illness, with higher rates reported among those who were hospitalized [9]. The prevailing theory for these changes points to the cytokine storm induced by the virus, disrupting the regular release of sex hormones and contributing to a procoagulant state [7,9,15]. Moreover, evidence suggests that the virus interacts with ACE-2 receptors in various body sites, including the ovary, uterus, and vagina, potentially indicating alterations in female reproductive functions leading to menstrual disorders [16]. Some studies have also linked these changes to vitamin deficiencies (C, D, and B6) during infection, positing a role in regulating the menstrual cycle [17]. A study by Costeira et al. suggested the involvement of the COVID-19 virus's spike protein in the pathogenesis of menstrual irregularities observed after infection and vaccination [18]. Additionally, the potential contribution of pandemic-related stress, anxiety, and similar factors in causing menstrual abnormalities are a crucial consideration [12,19]. In this study, 8.6% of participants experiencing menstrual changes reported a noteworthy negative impact on their quality of life. It is essential to recognise that alterations in the menstrual cycle can significantly affect a woman's psychological and physical health, potentially leading to constraints in work and school, influencing social relationships, and exacerbating stress [1]. Our study exhibited strengths, including acquiring each

participant's menstrual cycle history as a baseline. Utilizing self-administered surveys enabled participants to express themselves freely while maintaining anonymity, which was particularly crucial given the sensitive nature of our study topic. Considering the pandemic situation, online surveys were chosen as the safest method for conducting our research. This study's limitations include using a self-administered online survey, which introduces a high likelihood of recall bias. The data collection method, employing a snowballing technique, led to an overwhelmingly large number of responses from females aged 15-25, resulting in a non-uniform age distribution pattern and potential selection bias. Additionally, the reliance on online platforms for questionnaire distribution limited access to females with internet connectivity. Furthermore, the exceptionally small sample size renders the study results non-generalizable to each Emirate in the UAE.

Conclusion

In conclusion, our motivation to comprehend the potential impacts of the vaccine on female reproductive health and well-being prompted an investigation into the menstrual irregularities following COVID-19 vaccination or infection. This study serves as a valuable resource for education, raising awareness, and addressing concerns related to this matter, ultimately enhancing the quality of patient care. Pre-vaccination counseling by healthcare professionals can shed light on the benign nature of vaccine-related menstrual side effects and mitigate vaccine hesitancy. Despite various theories, the precise mechanism underlying menstrual changes remains unclear, emphasizing the need for further research to establish the exact correlation between the COVID-19 vaccine and menstrual disturbances.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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