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Research Article

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Impact of COVID-19 Vaccine on the Menstrual Health

Sarah Muafaq Al-Azawi[1], Raida Al-Wazzan[2]*

[1]Ninevah Health Directorate, Mosul, Iraq; [2]Department of Obstetrics and Gynecology, College of Medicine, University of Mosul, Mosul, Iraq

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Abstract

Background: The implementation of vaccines is a major step in saving humanity from the consequences of COVID-19, and there has become hope for everyone in the world. Menstruation is a key indicator of overall women's health. The COVID-19 vaccination has been associated with changes in the menstrual cycle. ***Objective***: To evaluate the effects of COVID-19 vaccines on the menstrual cycle. ***Methods***: This is a face-to-face interview-based cross-sectional study that recruited 403 vaccinated women with the COVID-19 vaccine who had normal MC before receiving the vaccine for at least six months in Mosul, Iraq, from February 1 to July 31, 2022. We asked the women about their menstrual cycle parameters before and after the vaccination. The results were analyzed statistically. ***Results***: The most frequent age group among study participants was 20–34 years (52.9%). About half of women (58.3%) had received the Pfizer vaccine. 12.2% and 13.65% of women reported significant changes in their menstrual cycle following the first and second doses, respectively. These changes included irregularities in the cycle and modifications in the amount and duration of menses, and the Pfizer vaccine was significantly responsible for these changes. ***Conclusions***: In a small number of women who had a normal menstrual cycle before vaccination, post-Covid-19 vaccination menstrual cycle changes occurred, and the reported changes were not critical. This result can reassure the community about the vaccine's impact on the menstrual cycle.

Keywords: COVID-19 infection, COVID-19 vaccine, Menstrual cycle (MC), Pfizer, AstraZeneca, Sinopharm.

تأثير لقاح كوفيد -19 على الدورة الشهرية

الخلاصة

الخلفية: ان تطبيق التطعيم خطوة عظيمة في حفظ حياة البشرية من عواقب عدوى كورونا-19 واصبح املا للجميع. يعتبر الحيض مؤشرا لصحة المرأة. عدد من التغييرات سجلت في الدورة الشهرية بعد التطعيم بلقاح كورونا-19 وعزي سببها الى اللقاح. **الهدف**: تقييم آثار لقاحات الكوفيد-19 المختلفة على الدورة الشهرية. **الطريقة:** دراسة مقطعية تعتمد على مقابلة النساء وجها لوجه والتي شملت (403) امرأة ملقحة بلقاح كورونا من اللواتي لديهن دورة شهرية طبيعية قبل اخذ اللقاح بمدة لاتقل عن ستة اشهر في مدينة الموصل، العراق من فبراير 2022 إلى يوليو 2022. سئلت النساء عن دوراتهن من ناحية الانتظام، ومدة الدورة، كمية ومدة الطمث قبل وبعد التطعيم. تم دراسة النتائج احصائيا. **النتائج:** اكثر النساء الملقحات المشاركات بالدراسة تتراوح اعمارهن بين 20-34سنة (52.9%). نصف عدد النساء تقريبا (58.3%) تطعموا بلقاح فايزر. عدد من النساء (12.2% و 13.65%) سجلن تغييرات في دوراتهن الشهرية بعد التطعيم بالجرعة الاولى والثانية على التوالي مشتملة عدم الانتظام في الدورة, تغيير في كمية وفترة الطمث. كانت اكثر هذه التغييرات في النساء المطعمات بلقاح فايزر. **الاستنتاجات**: بعد التطعيم بلقاح كورونا-19 حدثت تغييرات بسيطة لدى عدد قليل من النساء اللواتي لديهن دورة شهرية طبيعية قبل التطعيم. هذه النتيجة من الممكن ان تطمأن المجتمع حول اللقاح بما يخص الدورة الشهرية.

* ***Corresponding author***: Raida Al-Wazzan, Department of Obstetrics and Gynecology, College of Medicine, University of Mosul, Mosul, Iraq; Email: rmw@uomosul.edu.iq

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INTRODUCTION

The SARS-CoV-2 virus, which started in China (Wuhan), causes Covid-19, an infectious disorder that affects all organs [1]. According to the latest statistics from the World Health Organization (WHO), at the end of April 2024, there were over 775 million confirmed cases and over 7 million deaths worldwide. However, many countries have either changed their reporting frequency or stopped reporting new cases and deaths related to COVID-19 [2]. The menstrual cycle (MC) is a physiological process that involves complex hormonal integration [3]. Standardized parameters for normal menstruation (regularity, frequency, duration, and amount) have been defined by the "International Federation of Gynecology and Obstetrics (FIGO)." [4]. Various factors affecting the MC include medications, lifestyle, and stress [3]. Additionally, COVID-19 has emerged as a stressful condition, stemming from the infection itself, the fear of contracting it, and the quarantine period [5]. The release of numerous SARS-CoV-2 vaccines for emergency use began in December 2020, which significantly reduced mortality and the severity of the disease [6]. Three main groups divide the 18 vaccines worldwide, including diverse technologies [7]. The first group consists of mRNA-based vaccines (Pfizer and Moderna). The other groups include inactivated whole virus vaccines (Sinovac and Sinopharm) and re-combinant adenoviral vector vaccines (AstraZeneca, Johnson &Johnson and Sputnik) [8] . Globally, over 13 billion vaccine doses have been distributed until 2023 [7]. Iraq uses three vaccines (Pfizer, AstraZeneca, and Sinopharm) to vaccinate people [9]. Following administration, these vaccines caused mild side effects such as fever and headache, as well as severe, long-lasting events such as stroke and myocardial infarction [8, 10]. Previous studies [3] reported changes in MC following the human papillomavirus vaccine, while published research [11–13] reported a range of MC changes following the COVID-19 vaccination. The exact cause of these changes is unknown, but many theoretical explanations have been proposed, such as an alteration of hormonal balance caused by the acute illness caused by the vaccine, an immune response and its interaction with endometrial tissue [14], or stress associated with the vaccine [15]. When counseling women for vaccination administration, it is important to mention that the COVID-19 infection itself is associated with MC changes [16]. Till May 2024, WHO said that “COVID-19 remains a major threat," and administration of the vaccine to high-risk groups is one of its recommendations [2]. We performed this study to clarify the effect of the vaccine on MC in our community, as its results may assist clinicians in counseling women and decrease their hesitancy to administer the vaccine.

METHODS

Study design and setting

This is a face-to-face interview-based cross-sectional study conducted in Mosul, Iraq, from February 1 to July 31, 2022. Four hundred and three healthy menstruating women were recruited for the study.

Inclusion and exclusion criteria

The study included menstruating women aged 18 years and older who were non-pregnant and non-lactating, received two doses of the same vaccine brand in Iraq and had normal MC for the six cycles before receiving the first dose of the vaccine from February 1 to July 31, 2022, in Mosul, Iraq. We excluded any woman with a gynecological disease or other medical illness.

Data collection and outcome measurements

The interview was conducted by the same researcher among participants, with clarification of any question that seemed unclear to make the answer more accurate. The researcher asked the women about their socio-demographic, obstetrical, gynecological, medical history, vaccine brands, date of administration, and menstrual cycle (MC) before, after, and during the first three menstrual cycles following the second dose of the vaccine. We analyzed women's menstrual cycle (MC) from four perspectives: cycle rhythm, cycle length, flow amount, and menstrual length. The MC is considered normal if all the parameters defined by “the International Federation of Gynecologists and Obstetricians (FIGO)” [4] are within the normal range. We recorded and tabulated any change in one of the recorded parameters that occurred after vaccination.

Ethical consideration

The Medical Research Ethics Committee at the College of Medicine/University of Mosul obtained ethical approval. We solely used the data for the purposes of this study. We obtained written informed consent from the participants.

Statistical analysis

Descriptive and analytical statistics were performed using the SPSS software statistical program (V. 25). The descriptive statistics include the mean ± standard deviation (SD) for measurable variables, as well as frequencies and percentages for categorical variables. The chi-square test and the Fisher-Exact test were performed for comparison between categorical variables. Statistical significance was defined as a p-value< 0.05.

RESULTS

The study included 403 vaccinated women. Table 1 displays the characteristics of the study sample. The age range was 18 to 51 years, and 73% of women aged

less than 35 had a significant statistical difference (p=0.000) from older women.

Table 1: The characteristics and brand of vaccine among the study sample

Variables (n=403)		Results n(%)	p-value*
Age (year)	18–34	294(73)	0.000
	35-51	109(27)	
Marital status	Single	196(48.6)	0.000
	Married	188(46.7)	
	Widow	5(1.2)	
	Divorce	14(3.5)	
Education	below University	80(19.85)	0.000
	University level	308(76.43)	
	Post graduate and Higher education	15(3.72)	
Parity	Nulliparous	215(53.35)	0.057
	Parous	188(46.65)	
Brand of vaccine	Pfizer	235(58.3)	0.000
	AstraZeneca	154(28.2)	
	Sinopharm	14(3.5)	

* Chi-square (Goodness of Fit) test has been used.

About half (48.6%) of the study sample was single. Three-quarters (76.5%) of participants were at the university level, with a significant statistical difference (p=0.000). Among women, nulliparous women reported 53.35%, with a significant statistical difference (p=0.000). 58.3% of women reported receiving the Pfizer vaccination, with AstraZeneca and Sinopharm following behind with a significant statistical difference (p=0.000). There were changes in MC after the first dose in 49 women (12.2%) and after the second dose in 55 women (13.65%), with a significant statistical difference from those who had no changes (p=0.000), as shown in Figure 1.

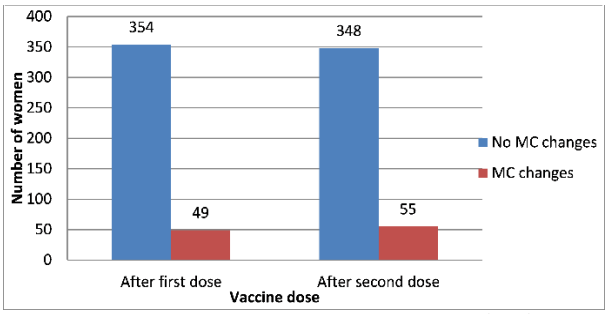

Figure 1: Post Covid-19 vaccination MC changes after first and second dose among study sample.

A higher number of women had MC changes that started after the first dose (89.09%) and increased by 10.9% after the second dose. As shown in Figure 2, 60 changes were reported in MC after vaccination, with three women experiencing more than one change. These changes included changes in flow amount (n=40), cycle rhythm (n=13), cycle length (n=4), and menses length (n=3).

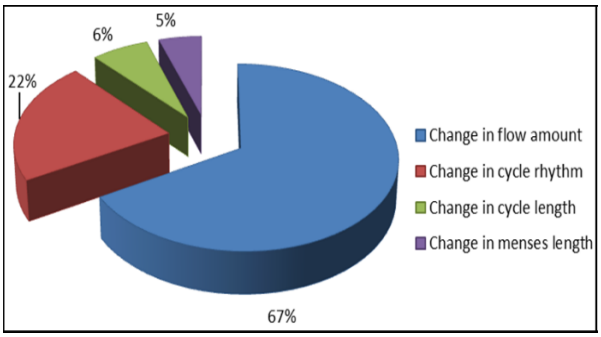

Figure 2: Pattern of Post COVID-19 vaccination MC changes among study sample.

The change in length of the menses reported at 1.5% after the first dose dropped back to 0.7% after the second dose, indicating a statistically significant difference (p=0.015), as demonstrated in Table 2.

Table 2: Effect of vaccine on MC among study sample

MC parameters (n=403)		Before vaccine	After 1st dose	After 2nd dose	p-value
Cycle rhythm	Regular	403(100)	395(98)	390(96.8)	0.002**
	Irregular	0(0.0)	8(2)	13(3.2)	
Cycle length	Same length	403(100)	398(98.8)	399(99)	0.086
	Changed length	0(0.0)	5(1.2)	4(1)	
	Increase	0(0.0)	4(80)	2(50)	0.524
	Decrease	0(0.0)	1(20)	2(50)	
Flow amount	Same amount	403(100)	373992.6)	363(90.1)	0.000**
	Change in amount	0(0.0)	30(7.4)	40(9.9)	
	Increase	0(0.0)	28(93.3)	38(95)	0.766
	Decrease	0(0.0)	2(6.7)	2(5)	
Menses length	Same amount	403(100)	397(98.5)	400(99.3)	0.015
	Change in length	0(0.0)	6(1.5)	3(0.7)	
	Increase	0(0.0)	5(83.3)	3(100)	1.000
	Decrease	0(0.0)	1(16.7)	0(0.0)	

Values were expressed as frequencies and percentages. ** Chi-square test.

The cycle rhythm became irregular in 2% and 3.2% of women after the 1st and 2nd doses, respectively, with a significant statistical difference (p=0.002). There was no significant statistical difference in the cycle length changes after both doses (p=0.086). There was a significant statistical difference in the amount of flow after vaccination (p=0.000), with a tendency to become heavier in 38 women and lighter in 2 women. Figure 3 shows that MC changes happened in 15.32% of women who got the Pfizer vaccine, 12.99% of women who got the AstraZeneca vaccine, and 28.57% of women who got the Sinopharm vaccine. The difference between the groups was not statistically significant (p=0.281). Studying the pattern of MC changes in relation to vaccine brands revealed that a higher number of changes occurred with Pfizer with a significant statistical difference than the other two brands (p=0.000), as shown in Table 3.

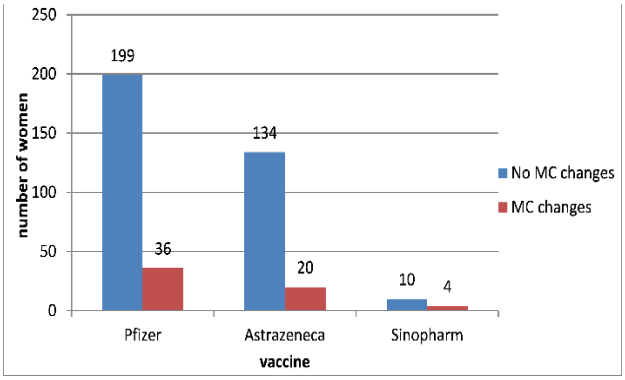

Figure 3: Post vaccination MC changes with Vaccine brands among study sample.

Table 3: Menstrual cycle changes according to vaccine brands among study sample

Changes in MC (n=60)	Pfizer	AstraZeneca	Sinopharm	p-value*
Change in cycle rhythm (n=13)	10(76.92)	3(23.08)	0(0.0)	0.000
Change in cycle length (n=4)	4(100)	0(0.0)	0(0.0)	0.006
Change in flow amount (n=40)	19(57.5)	17(42.5)	4(10)	0.001
Change in menses length (n=3)	3(100)	0(0.0)	0(0.0)	0.036

Values were expressed as frequencies and percentages. * Fisher Exact test.

DISCUSSION

Studies began evaluating the impact of COVID-19 vaccinations on human health to address the reluctance to receive them [16]. This study aimed to assess the impact of these vaccinations on menstruating women in Mosul, Iraq. This study included women of reproductive age, aged 18 to 51 years. The Muhaidat *et al*. study [17] reported a range of 14 to 54 years among their participants. Younger than 35 years comprised three-quarters of this study sample, which was between 60.5% and 80.08%, respectively [3,18]. Three-quarters of study participants were at the university level, which differs from a previous study [20], which found that 87.9% had a university education. Similar to the findings of the Amer *et al*. [20], half of the participants in this study were single. The present study found that nulliparous was 53.35%, which was lower than other studies [15,21] (60.1% and 79.2%, respectively). The available vaccines in Iraq were Sinopharm, AstraZeneca, and Pfizer, with the Pfizer vaccine being the preferred one [9], administered to 57.8% of the study sample. Other studies [21,17,22,20,11] reported that about 50%–82.3% of their vaccinated people received the Pfizer COVID-19 vaccine. In this study, 38.2% of participants received AstraZeneca, falling within the range of 1.7%–53% [5,22]. In this study, 3.4% of participants received Sinopharm, falling within a range of 8.8%–39.1% [5,20]. Other studies [12,13,24] reported the use of other brands of the vaccine. For inclusion in the study, women should receive both doses of the same brand of vaccine, unlike other studies [11] that included women receiving two different brands. This study included participants who received two doses of the vaccine, as administering the third dose was not common in Iraq. This is in contrast to other studies [19] that examined changes after the third and fourth doses of vaccine, as well as some studies [14,17] that included participants who received both one and two doses. Analyzing post-vaccination MC in the literature [12,13,3], which was done in different countries showed that it varied between 0.5% and 78%, which could be attributed to differences in vaccine types and brands, study design, countries and race. This study reported MC changes of 12.2% and 13.65% after the first and second doses, similar to a Turkish study [11] that reported 15.1% changes. However, it differs from another study [13], which reported MC changes of 2.1% and 1.0% after the first and second doses. This could be attributed to the study sample of Chinese healthcare workers, all of whom receive inactivated virus-containing vaccines. In the study of Anjorin *et al*. [12], which focused on African individuals, found that 0.5% of the female participants reported MC changes. Variations in the study design, including the use of a web-based questionnaire, the inclusion of menopausal women, a range of countries, ten different vaccine brands, and racial differences, could explain this result. Another study [3] showed that 78% of people who participated in a retrospective online survey used different vaccine brands (Pfizer, AstraZeneca, Moderna, and Johnson & Johnson), and higher number of women aged 35 -55 years. A higher number of women had MC changes after the first dose, similar to other studies [14,17,23]. Another study [24] also reported a slight increase in changes after the second dose. The most reported changes in MC post-vaccination in this study were the change in amount of flow, irregularity of the MC, change in cycle length, and change in menses length. Other studies [14,5]

reported changes in different order, as Fallatah *et al*. [14], documented changes in cycle length, menses length, and flow amount. Abu-Lubada *et al*. [5] observed an irregular cycle, followed by change in the flow amount. In this study, 3.2% of women's MC changed to become irregular after vaccination, which is lower than other studies [5,25,26] that reported 13.1%, 20.4%, and 35.26%, respectively. Similar to previous studies [15,21], this study found no significant changes in cycle length after vaccination. However, other studies [7,16,11] reported changes in cycle length following COVID-19 vaccinations, potentially due to differences in the study's design and vaccine type. Other studies [23,14,3,5,11,24] declared alterations in the amount of menstrual flow after vaccination, ranging from 6.3% to 55.6%. The current study reported 9.9% (9.42% heavier and 0.49 % lighter menses), slightly higher than the 6.3% (heavier 3.7% and lighter 2.6%) reported in another study [23]. However, in another study [26], this figure is significantly lower than that of the Lagana *et al*. study [24], which reported 55.6% of heavy menstrual bleeding. The study design, the diverse age groups in the study population, and the use of a larger number of vaccine brands (8 brands) may account for this difference. Other studies [1,16,27] failed to show this change. There was a significant change in the length of menses post-vaccination, mainly after the first dose, similar to other studies [3,11,17,20]. While other researchers [7,21] failed to show any effect on menstrual length, Taşkaldiran *et al*. [11] reported a change in menstrual length in 5.3% of cases, which was 1.5% higher than this study's findings. Additionally, this study did not report amenorrhea (0.5%) or intermenstrual bleeding (1.2%), as reported in other studies [5,7]. Unlike other studies [10,11,24] that reported differences in MC changes with brands of vaccine, this study is in line with other studies [5,14,16,17] that failed to report this difference. This study evaluated post-vaccination MC changes based on vaccine brands and found that 28.57%, 15.32%, and 12.99% of women received Pfizer, AstraZeneca, and Sinopharm, respectively. Another study [11] reported that the percentage of women who received Pfizer and Sinovac, Pfizer alone, and Sinovac was 23.5%, 15.2%, and 5.1%, respectively. Another study [24] reported that 64.3%, 62.5%, and 46.9% of women who received Moderna, AstraZeneca, and Pfizer, respectively, reported alterations in their MCs. We compared the MC change pattern after vaccination with different vaccine brands, and we found that the Pfizer brand was statistically different from other brands similar to other studies [5,6,26]. Another study [14] reported a similar change in flow amount after using the AstraZeneca vaccine. The accepted explanation for the small number of post-vaccination MC changes reported in this study was a decreased stress state among people in the Iraqi community at the time of vaccination, as they hoped to rid themselves of the COVID-19 infection and its consequences, take precautionary measures and quarantine, and return to their lives before the pandemic. This is because stress can directly affect the hormonal balance that regulates MC [23]. like other study's conclusion [27], this study's participants were all of one race, so the results may not apply to other communities. Country-specific vaccine types, brands, and administration schedules can cause different effects even when using the same vaccine. The other study's strengths, including the use of a face-to-face interview and the exclusion of abnormal MC prior to vaccination and any gynecological or medical illness, are also noteworthy.

Study limitations

The limitations of the study include the lack of follow-up by women to determine the time needed for MC changes to return to normal and the relationship between the time of receiving the vaccine and the menstrual phase was not taken into consideration.

Conclusion

Women with normal MC after receiving the first and second doses of COVID-19 vaccinations showed minor changes in rhythm, amount of menstrual flow, and menstrual length. All vaccine brands produced changes in MC. When examining the changes in MC related to vaccines, Pfizer's vaccine was responsible for the majority of these changes. It is wise to recommend examining any new vaccine for women of reproductive age in terms of its effect on MC.

Conflict of interests

No conflict of interests was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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