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# The Impact of Covid-19 Infection and Vaccinations on the Menstrual Cycle

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**ABSTRACT**

**Background:** Coronavirus disease-19 (COVID-19 infection) might present with no clinical symptoms or with mild to severe clinical symptoms. Menstrual cycle issues are one of the long-term clinical characteristics of COVID-19. The menstrual cycle is a biologically important cycle for females, regulated closely by endocrine, autocrine, and paracrine mechanisms, with substantial fluctuation in length (21-35 days) and hormone levels during the cycle. Inactivated viral vaccine, recombinant viral vaccine, subunit vaccine, DNA vaccine, and attenuated vaccine have all been tested for Co-V-19 vaccine efficacy. Few females suffered menstrual problems after immunization, such as Menorrhagia, Metrorrhagia, Polymenorrhea, and Postmenopausal bleeding. Vaccine-associated thrombocytopenia could be one of the causes.

**Aim:** To document menstrual changes in female participants following COVID-19 infection and Covid-19 vaccination with one to two doses and to study the impact of the Corona vaccine on the cycle.

**Methods:** This retrospective investigation occurred in two phases. The first phase recruited 547 females, with an average age of 35 years and who were infected with COVID-19 to complete a questionnaire to record menstrual changes in women after COVID-19 infection without vaccination, while phase two enrolled 673 females with an average age of 33 years (21-49) and who received the vaccine before the study to record menstrual disturbances after vaccination for COVID-19 , at Prince Rashid military hospital, Irbid, JORDAN, during the period March 2020-Apr 2022.

A questionnaire with 6 sections was constructed to determine the influence of COVID-19 infection and Covid-19 vaccination on the menstrual cycle.

**Results:** In phase one: 46.98% (257/547) had changes in the number of days between two following periods and in the volume of blood loss. 42.41% of subjects (232/547) had an increase or reduction in the length of menses.

In phase two: 24.96% (168/673) of subjects experienced higher volume and 15.6% (105/673) experienced decreased volume. 23.03% (155/673) experienced delayed periods and 53.2% (358/673) experienced no changes.

**Conclusion:** COVID-19 infection might influence the menstrual cycle. There was a discrepancy in menstrual profile after vaccination, irrespective of vaccine type or the number of doses given.

However, our study is cross-sectional, and these findings need further investigations or clinical trials to demonstrate the effect of Covid -19 infection or vaccinations on menstrual cycle.

## Introduction

This infection may be without clinical features or with mild to very intense clinical features. Some of these clinical features may persist for weeks or months following primary recovery. These clinical features are termed long term COVID-19 effects or post COVID-19 syndrome [(1)]. Not only the admitted subjects could have these clinical features but also those with mild infection. One of the long term clinical features of COVID-19 are problems in the menstrual cycle [(2-3)]. Menstrual cycle is a biologically crucial cycle for females regulated strictly by endocrine, autocrine and paracrine factors, with high variability in length (21–35 days) and variations in hormones levels during the cycle [(4)]. It is necessary for reproduction and correlated with three symptoms; pain, heaviness of blood volume and premenstrual syndrome [(4-5)]. The association between COVID-19 infection and menstrual problems in women was investigated [(2)]. Most of women had changes in the menstrual cycle and might consider these changes as post COVID-19 effects.

COVID-19(Coronavirus disease-2019) is the newest worldwide infection. These are single-stranded, positive-sense, encapsulated RNA viruses. SARS-CoV, SARS-CoV-2 and MERS-CoV are Coronavirus family. The hazards of COVID-19 include liver and hematological [(6)]. Vaccine trials were evaluated for the proper SARS-CoV vaccine, including inactivated virus vaccine, recombinant viral vaccine, subunit vaccine, DNA vaccine and attenuated vaccination. After vaccination, few females experienced menstrual disturbances such as heavy, frequent cycles or postmenopausal bleeding. A possible cause could be vaccine-related thrombocytopenia [(7)]. Subjects with platelet pathologies experienced heavy menstrual bleeding. Remarkable bleeding might cause intense anemia, exacerbate thrombocytopenia and increase the risk of bleeding and clots [(8).]

Stressors activate the hypothalamic-pituitary-gonadal axis and modify the neuro-modulatory cascade which regulate GnRH, causing functional hypothalamic amenorrhea of continuous anovulation. After vaccination, there were changes in our subject's menstrual features. Subjects with changes in instant time following the vaccination experienced normal menstrual cycle later with no side effects on fertility. Unplanned pregnancies happened at comparable incidences in vaccinated and unvaccinated subjects [(9)].

## Methodology

This retrospective investigation occurred in two phases at Prince Rashid military hospital, Irbid, JORDAN, during the period March 2020-Apr 2022, after obtaining written informed consent from all subjects and approval from our local ethical and research board review committee of the Jordanian Royal medical services. Phase one recruited 547 females, with an average age of 35 years old and who were infected with COVID-19 to complete the questionnaire to record menstrual changes in women after COVID-19 infection without vaccination and phase two recorded menstrual changes after vaccination for COVID-19. A questionnaire was constructed to determine the influence of COVID-19 infection and Covid-19 vaccination on the menstrual cycle. The questionnaire includes six sections: the first section includes the demographics; the second section includes the medical data; the third section includes the menstrual cycle profile before Covid-19 infection or vaccination; the fourth section includes Covid-19 infection and vaccination; the fifth section includes menstrual cycle changes following COVID-19 infection and the sixth section includes menstrual changes after vaccination

Phase two enrolled 673 females with an average age of 33 years (21-49) who got the vaccine prior to the study. Females who were pregnant or had amenorrhea and had been using hormonal contraception for more than 6 months were excluded. The same questionnaire was used to collect information. The data included period regularity, the number of periods since the last dose of vaccine, and the number of vaccine doses and types. Changes in the time of the first period after

the immunization, as well as the menstrual cycle in terms of regularity, period, and volume were observed. A history of recent onset dysmenorrhea, intermenstrual or postcoital bleeding was collected.

**Statistics**

For continuous variables, the description was rated as an average, while categorical variables were evaluated as incidence with percentages. The Chi-square test was employed to evaluate the relationship between parameters. A P-value less than 0.05 was judged significant.

**Results**

In phase one, 46.98% (257/547) had changes in the number of days between two subsequent periods as well as the volume of blood lost. 42.41% of participants (232/547) showed an increase or decrease in menstrual length. In phase two, 28.3% (155/547) of patients had higher volume and 17.7% (97/547) had lower volume. 21.9% (120/547) had delayed periods, whereas 78.1% (427/547) had no alterations.

**In phase one:** the questionnaire addressed 713 subjects but 166 refused to participate and 547 infected subjects participated before vaccination. Mild infection was reported in 238 subjects (43.5%), moderate infection was recorded in 295 subjects (53.9%) and severe infection with hospital admission was found in 14 subjects (2.6%).285/547 (52.1%) were married. 56.7% of women (310/547) had a medical degree. Table I. 12.8% of them (70/547) had chronic diseases.

**Table I. Subjects characteristics (n = 547)**

| Variable | Class | No. (%) |
|---|---|---|
| **Age (years)** | **20-30** | 50(9.1) |
| | **31-35** | 160(29.3) |
| | **36-40** | 245(44.8) |
| | **41-50** | 92(16.8) |
| **Marital** | **Married** | 285(52.1) |
| | **Single** | 262(47.9) |
| **Medical education** | **Yes** | 310(56.7) |
| | **No** | 237(43.3) |
| **Chronic illnesses** | **Yes** | 70(12.8) |
| | **No** | 477(87.2) |
| **Covid-19 infection** | **Mild** | 238(43.5) |
| | **Moderate** | 295(53.9) |
| | **Severe with admission** | 14(2.6) |

There was a change in the number of days between two subsequent periods in 53.01% of individuals (290/547). 42.41% of participants (232/547) showed an increase or decrease in menstrual length. There were fewer participants who experienced pain before or during menstruation (240/547, 43.9%), missed periods or period cessation as a result of infection (120/547, 21.9%), and bleeding between periods (105/547, 19.2%). Table No. 2.

**Table II. Menstrual cycle changes following COVID-19 infection (n = 547).**

| Variable | No.(%) |
|---|---|
| **Number of days between two following periods** | |
| **No change** | 290(53.01) |
| **Closer and shorter** | 150(27.4) |
| **Longer** | 107(19.6) |
| **Length of periods** | |

| | |
|---|---|
| **No change** | 315(57.6) |
| **Increase** | 115(21.02) |
| **Reduction** | 117(21.4) |
| **Volume of bleeding** | |
| **No change** | 295(53.9) |
| **Increase** | 155(28.3) |
| **Reduction** | 97(17.7) |
| **Bleeding between periods** | |
| **Yes** | 105(19.2) |
| **No** | 442(80.8) |
| **Missed period or cessation** | |
| **Yes** | 120(21.9) |
| **No** | 427(78.1) |
| **Change in pain before or during menstruation** | |
| **Yes** | 240(43.9) |
| **No** | 307(56.1) |

**In phase two:** the questionnaire addressed 713 subjects of whom 673(94.5%) received the vaccine, 33(4.6%) refused to take the vaccine and 7(0.9%) refused to participate in the investigation. Table III. 43.1 %( 290/673) had only one period following last dose of vaccination and 23.8 %( 160/673) had early first period after the vaccine. Table IV. 77.3 %( 520/673) had no changes of duration of menstrual cycle and 59.4 %( 400/673) had no changes in the menstrual volume. Most subjects had no changes in the time following vaccination **(P>0.05)**. New dysmenorrhea was recorded **(P = 0.038)**.

**Table III. Characteristics of Pre-vaccination investigated subjects (n=673).**

| Parameter | Class | No. (%) |
|---|---|---|
| **Age (yrs.)** | **21-25** | 50(7.4) |
| | **26-30** | 200(29.7) |
| | **31-40** | 300(44.6) |
| | **41-49** | 123(18.3) |
| **Marital** | **Married** | 340(50.5) |
| | **Single** | 333(49.5) |
| **Medical education** | **Yes** | 400(59.4) |
| | **No** | 273(40.6) |
| **Chronic illnesses** | **Yes** | 75(11.1) |
| | **No** | 598(88.9) |

The relationship between the last dosage of vaccine and period date, duration and volume, as well as dysmenorrhea after vaccination was striking. V. Table. There was no link found between the type of immunization and menstrual diseases **(P>0.05)**. V. Table.

**Table IV. Menstrual Cycle After vaccination (n=673).**

| Parameter | Class | No. (%) | p-value |
|---|---|---|---|
| **Vaccine** | **Pfizer** | 391(58.1) | **(P>0.05)** |
| | **Sino pharm** | 177(26.3) | |
| | **AstraZeneca** | 99(14.7) | |
| | **Sputnik USSR** | 6(0.9) | |
| **Number of vaccine doses** | **1** | 240(35.7) | **(P>0.05)** |

| | | | |
|---|---|---|---|
| | **2** | 433(64.3) | |
| **Number of menstrual periods after last dose of vaccine(months)** | **1**<br>**2**<br>**>3** | 290(43.1)<br>315(46.8)<br>68(10.1) | **(P>0.05)** |
| **Dating of the first period following the vaccine** | **Early**<br>**Delayed**<br>**No change** | 160(23.8)<br>155(23.03)<br>358(53.2) | **0.091** |
| **Duration of period** | **Increased**<br>**Reduced**<br>**No change** | 113(16.8)<br>40(5.9)<br>520(77.3) | **0.104** |
| **Menstrual volume** | **Increased**<br>**Reduced**<br>**No change** | 168(24.96)<br>105(15.6)<br>400(59.4) | **0.331** |
| **New dysmenorrhea** | **Present**<br>**Absent**<br>**Unknowncc** | 280(41.6)<br>275(40.9)<br>118(17.5) | **0.038** |
| **New intermenstrual and postcoital bleeding** | **Present**<br>**Absent**<br>**Unknown** | 55(8.2)<br>495(73.5)<br>123(18.3) | **0.375** |

**Table V. Correlation between Type of Vaccine and menstrual profile.**

| **Vaccine** | **Change in Period dating after vaccination** | | | **p-value** |
|---|---|---|---|---|
| | **Delayed** | **early** | **No change** | |
| **Pfizer** | 80 | 67 | **244** | **0.104** |
| **Sino pharm** | 51 | 67 | 59 | |
| **AstraZeneca** | 21 | 24 | 54 | |
| **USSR** | 3 | 2 | 1 | |
| **Change in period duration following vaccination** | | | | |
| | **Increased** | **No change** | **Reduced** | |
| **Pfizer** | 50 | 318 | 23 | **0.144** |
| **Sino pharm** | 40 | 126 | 11 | |
| **AstraZeneca** | 20 | 73 | 6 | |
| **USSR** | 3 | 3 | 0 | |
| **Change in period volume after vaccination** | | | | |
| | **Increased** | **reduced** | **No change** | |
| **Pfizer** | 82 | 46 | 263 | **0.909** |
| **Sino pharm** | 62 | 41 | 74 | |
| **AstraZeneca** | 22 | 17 | 60 | |
| **USSR** | 2 | 1 | 3 | |
| **Recent or increased dysmenorrhea following vaccination** | | | | |
| | **Present** | **absent** | **Unknown** | |
| **Pfizer** | 144 | 134 | 113 | **0.58** |
| **Sino pharm** | 87 | 87 | 3 | |
| **AstraZeneca** | 48 | 50 | 1 | |
| **USSR** | 1 | 4 | 1 | |

## Discussion

After COVID-19 infection, there is a large number of women with changes in the menstrual cycle [2,3]. The menstrual cycle is an interactions between the hypothalamus, pituitary, ovaries,

uterus, prostaglandins and neuroendocrine factors. The menstrual problems are induced by the disruption of these interactions [10]. Vitamins (vitamins C, D & B6) regulate these problems. As COVID-19 is a systemic inflammation, it reduces the circulation of 25 (OH)D leading to vitamin D deficiency. Decreased levels of vitamin D may induce irregular menstrual cycle as amenorrhea and oligomenorrhea [11,12], because of the direct action of vitamin D on the circulating androgens. Reduced level of vitamin D may worsen the premenstrual clinical features such as the pain, which might be stronger before or during menstrual cycle. The diminution of vitamin B6 during the COVID-19 infection in women, increases level of estrogen in the blood causing heavy and painful menstrual bleeding. Vitamin C may influence menstrual cycle indirectly, by disturbing absorption of other fat-soluble vitamins which regulate the cycle [5]. Vitamin C is an enhancing factor on the production of estrogen and progesterone and enhances hormonal levels, increasing the thickness of endometrium, so its deficiency could cause heavy bleeding during the menstruation [13-14].

The rapid spread of SAR-CoV-2 infections required a safe and efficient SAR-CoV-2 vaccine. There was a change in the menstrual cycle, worsening premenstrual features, and menorrhagia in females with COVID-19 [15]. Females could have a COVID-19 pandemic "post-traumatic" period with frequent irregularities in the menstrual cycle (16). In this investigation, two remarkable changes were noted in the period correlated with the blood volume and the timing (regularity). There were 958 menstrual disturbances after vaccination, such as vaginal bleeding (6). AstraZeneca had twice as many menstrual irregularities as other vaccines (6). Bleeding, blood clots, and thrombocytopenia following COVID-19 vaccination raised questions about the safety of genetic vaccines for subjects with coagulation problems. Thrombocytopenia is a frequent side effect of mRNA COVID-19 vaccines as Pfizer or Moderna [7]. There is no association between COVID-19 vaccinations and changes in menstrual cycles because the number of symptoms is modest compared to the number of subjects vaccinated and the frequency of menstrual pathologies [17]. mRNA and adenovirus COVID-19 vaccinations were related to menstrual disturbances [18]. The immunological reaction to immunization rather than a vaccine component causes these disturbances. Human papillomavirus vaccination is related to menstrual pathologies [2]. Stimuli like viral infections may modify the menstrual cycle. 25% of subjects infected with SARS-CoV-2 had disrupted menstrual cycles [19].

Our investigation demonstrated that most females had no changes in duration or menstrual volume, as in a study that couldn't relate COVID-19 vaccination to menstrual irregularities [20]. 35.3% of subjects had menstruation problems before immunization. Pathological periods followed vaccination in 66.3% of subjects [21]. 42% of subjects had heavier bleeding following vaccination (22). 20% of premenopausal vaccination recipients had no menstrual cycle issues four months following the first COVID-19 vaccine injection. 358 subjects with two doses of the vaccination in the same cycle were most influenced, with a 2.32-day delay in the beginning of the following period. Compared to the uninfected cohort's 4.3%, 10.6% of this group had a remarkable shift in cycle duration of more than 8 days. Two cycles after immunization, cycle durations were normalized in all groups [23]. A female's menstrual cycle could be affected by immunological influences on hormones that regulate the menstrual cycle [24] or by uterine immune cells [19].

Females with changes in menstrual cycles or postmenopausal bleeding must be managed, including hormonal contraception [25]. The COVID-19 vaccine (Pfizer-Biotech, Moderna, and Johnson & Johnson/Janssen) was correlated with a less than 1-day change in cycle length for both vaccine-dose cycles compared with pre-vaccine cycles. Unvaccinated subjects had no remarkable disturbances compared with three baseline cycles. The first dose's discrepancy in change from the unvaccinated cohort's cycle length was 0.64 days; the second dose's discrepancy in change was 0.79 days. The length of the menses did not change following

immunization. 66.3% of subjects had menstrual features after vaccination, of which 46.7% had them following the first dose. The features disappeared in 93.6% of subjects after 2 months. The type of vaccine had no influence on the incidence of pathologies [(21)].

The investigations important limitation is that it takes a brief period following the vaccine. The subjects were only asked about the first period following the vaccine. The investigation is not based on objective information but is based on personal estimation. The investigation recruited females aged 46- 55 which may lead to bias as premenopausal features are begun.

**Conclusion**

COVID-19 infection might influence the menstrual cycle. There was a discrepancy in menstrual profile after vaccination, irrespective of vaccine type or the number of doses given.

However, our study is cross-sectional, and these findings need further investigations or clinical trials to demonstrate the effect of Covid -19 infection or vaccinations on menstrual cycle.

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