

Research Article

# Abnormal Uterine Bleeding following by COVID-19 Vaccine

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## Abstract

**Background:** After the COVID-19 vaccination, concerns about side effects were risen globally. One of the reported side effects was changes in menstrual periods. In this study, we aimed to evaluate changes in the menstrual cycle, including frequency, length, abnormal bleeding, and pain after the COVID-19 vaccine.

**Methods:** In this retrospective cohort study we interviewed 700 women working in Kamali, Bahoner, Rajaei, and Madani hospitals who had normal menstrual periods before vaccination. Qualified researchers with a well-structured self-administered questionnaire collected data. statistical analysis was with the SPSS software (v. 26.0.0.0) frequency and percentage of variables described precisely to investigate the association between menstrual changes and its associated factors, we used the Chi-square test, A p-value <0.05 was considered statistically significant.

**Results:** After receiving responses from a total of 700 women, 82 were not fitting into the inclusion criteria. Thus, a total of 618 females were included. Overall, 16.7% of participants experienced AUB following Covid-19 vaccination; in the AUB group, 6.2% experienced two types of AUB. Oligomenorrhea was the most common type of AUB 37.9%, followed by menorrhagia 20.7% and polymenorrhea 18.1%. a higher percentage of women with AUB were nulliparous compared to their counterparts (92.3% vs. 7.6%, P-Value=0.042). AUB in 48.6% following the second dose of vaccine and 30(26.0%) of them experienced AUB after the third dose and 28 (24.3%) started it after the first dose. The AUB after both COVID-19 vaccine doses were observed among 48.6% followed by the third dose 26.0% and 24.3% started it after the first dose.

**Keywords:** Abnormal uterine bleeding; Covid-19; Covid vaccine.

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## Introduction

The COVID-19 disease has affected the whole world as a pandemic. This new coronavirus has caused many health problems such as pneumonia, ARDS (Acute Respiratory Distress Syndrome), kidney damage, myocardial function disorders, and digestive diseases [1]. This disease has also affected the health of sexual organs. A woman's menstrual period can be affected by various factors such as stress, being overweight, hormones, etc [2]. Some studies show changes in menstrual periods, such as worsening of premenstrual symptoms and menorrhagia, in women affected by COVID-19 compared to before the pandemic [3,4].

On the other hand, some of these problems continue even after the COVID-19 vaccination. Many women around the world have complaints of irregular menstrual periods after receiving the COVID-19 vaccine. Some complain of a high volume of bleeding (menorrhagia), some of them complain of bleeding before their period or disorder of their periods (polymenorrhea/metrorrhagia), and some complain of postmenopausal bleeding [5].

The Medicines and Healthcare Products Regulatory Agency (MHRA) is continuously monitoring reports of menstrual disorders (period problems) and unexpected vaginal bleeding following the injection of the COVID-19 vaccine in the UK. A range of menstrual disorders have been reported following the COVID-19 vaccination, including more vaginal bleeding than normal periods, delayed periods, and unexpected vaginal bleeding. The number of reports of menstrual disorders and vaginal bleeding is proportional to the number of vaccinations. has taken place and compared to the normal prevalence of menstrual disorders in society is low [6].

Since April 5, 2021, we have had 958 cases of menstrual disorders after receiving the vaccine, including vaginal bleeding, which have been registered by the MHRA [6].

Platelet disorders have been reported in the past as one of the causes of heavy menstrual bleeding [7]. There is a possibility that the thrombocytopenia caused by the vaccine can be an explanation for heavy menstrual bleeding in women after receiving the Covid-19 vaccine in different countries. It should be noted that heavy blood loss for women during menstruation can lead to severe anemia [5]. This can also be an early sign of prothrombotic thrombocytopenia induced by the vaccine for young women, which can lead to fatal events of CVST (Cerebral Sinus Venous Thrombosis) [5]. In addition, the vaccine activates the immune system and the activated immune system may attack immune cells and inflammatory molecules in the uterus. This phenomenon may be related to changes in menstrual cycle. So far, side effects include pain, skin redness, swelling, fatigue, headache, muscle pain, chills, fever, and nausea.

There are no covid-19 vaccines. However, changes in the menstrual cycle have not been recorded, so researchers should be aware of this issue and raise questions about the menstrual cycle in clinical studies for the Covid-19 vaccine [8].

Also, until today, limited studies have been done on this issue, and considering the importance of these disorders, we need more research in this field.

## Methods

This study is a retrospective cohort study, in this study the target population includes women working in Kamali, Bahoner, Rajaei, and Madani hospitals who received the covid-19 vaccine and had regular menstrual periods before receiving the vaccine. Demographic information and history of the selected people are registered in a questionnaire by trained people, also the complete medical history of patients is obtained, in the next stage, people are divided into two groups based on having menstrual disorders or not after receiving the vaccine, and then These groups are examined from different aspects such as the type of vaccine received, age, severity and types of AUB separately and incidence of dysmenorrhea and infertility.

Patients with regular menstruation before receiving the covid-19 vaccine, not being infected with COVID-19 after receiving the COVID-19 vaccine, and not being pregnant after receiving the COVID-19 corona vaccine. were included in the study. Other inclusion criteria were not having platelet disorders before receiving the COVID-19 vaccine, do not have infertility, and not being menopausal.

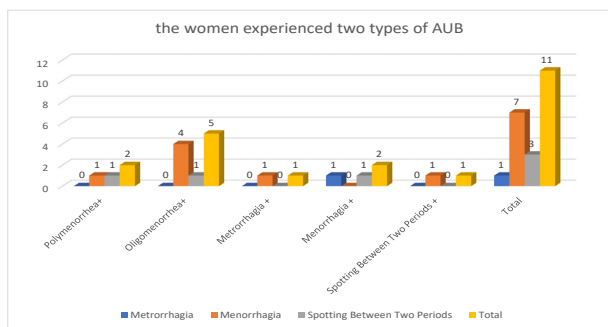
Exclusion criteria were the participant's lack of consent to participate in this research, the participant has left employment in the aforementioned hospitals, and during the follow-up process, the person has suffered from other ovarian or uterine diseases.

Individuals will be followed for 2 months after receiving each dose of the Covid-19 vaccine. The follow-up method of people was based on history and entering information in the questionnaire, after taking the history the first time and entering the information in the questionnaire, the symptoms of the investigated disorders were explained to the people and it was recommended to be informed if any of the symptoms occur and if symptoms occur, follow-up at the appointed time. history was taken again and the information was entered into the questionnaire. To describe the basic characteristics of the participants in this study (separated by groups), the mean and Standard Deviation (SD) was used for the quantitative variables, and frequency and percentage were used for the qualitative variables.

Chi-square analysis, independent t-test, and univariate and multivariate logistic regression will be used in data analysis. In all statistical analyses, a p-value <0.05 was considered statistically significant and the tests will be conducted two-sided. SPSS version 22.0.0.0 statistical software will be used for data analysis.

## Results

Of 700 eligible women, 618 persons consented to participate in our study (response rate: 88.2%). Regarding the number of doses and the type of vaccine, 97.1% (680) received at least two doses of an inactivated vaccine (mainly the BBIBP-CorV COVID-19 vaccine). Based on our findings 16.7% (177) of participants experienced one (166/177) or two (11/177) types of AUB following Covid-19 vaccination (Figure1); oligomenorrhea was the most common type of AUB 37.9(44), followed by menorrhagia 20.7% (24) and polymenorrhea 18.1% (21). Table 1 shows the basic characteristics of our participants, overall and by AUB status. The mean age (SD) of participants was 25.5(6.9) with a similar distribution between the two groups (24.8(6.2) vs 25.7



**Figure 1:** Information of the women experienced two types of AUB.

**Table 1:** Baseline characteristics of women with and without AUB after COVID-19 vaccination.

Parameters (no. of evaluated patients)	Total (n=700) Mean (SD)/ % (N)	With AUB (n=117)	Without AUB (n=583)	P-value
Age, y	25.5(6.9)	24.8(6.2)	25.7(7.1)	0.186
BMI (kg/m <sup>2</sup> )	23.1(3.4)	22.9(3.3)	23.1(3.4)	0.178
Married	158(22.6%)	22(%)	136(%)	0.285
Nullipara	605(86.4%)	108(92.3%)	497(85.2%)	
Primipara	38 (5.4%)	5(4.2%)	33(5.6%)	0.042
Multipara	57(8.1%)	4(3.4%)	53(9.0%)	0.029
Without relation	575(82.1%)			
None/Condom	110(10.1%)	17(77.2%)	91(90.1%)	0.12
Hormonal pills/hormonal IUD	15	5(22.7%)	10(9.9%)	
Thyroid diseases	24(3.9%)	4(3.8%)	20(3.9%)	
Any comorbidity	42(7.2%)	10(10.6%)	32(6.6%)	0.67

(7.1)). In terms of gravidity, 83.3% (583) of participants were nullipara with significant differences between the two groups; a higher percentage of women with AUB were nulliparous compared to their counterparts (108 (92.3%) vs. 9(7.6), P-Value=0.042). Non-single women constituted 22.6% (158) of our sample of whom, 12% (15) used a hormonal contraceptive (IUD or pills) at the time of vaccination and later; this percentage was non significantly more frequent in the AUB group than the non-AUB group (20.8% vs 10%, P-value: 0.180). Overall, comorbidities were in 47 (6.7%) of the women; thyroid problems were the most prevalent comorbidity. AUB in 56 (48.6%) following the second dose of vaccine and 30 (26.0%) of them experienced AUB after the third dose and 28 (24.3%) started it after the first dose. There wasn't any specific pattern of the affect of BMI on the AUB group.

## Discussion

We evaluated the side effects of the BBIBP-CorV (Sino-pharm BIBP COVID-19 vaccine), Oxford–AstraZeneca COVID-19 vaccine, and Sputnik V (Gam-COVID-Vac) on menstrual cycle changes. menstrual cycle changes were mainly oligomenorrhea followed by menorrhagia that occurred between the vaccination and the next menstrual period. Women who reported AUB were characterized by a history of greater use of hormonal IUDs and nulliparity compared to those who experienced no chang-

es. Instead distribute a large number of questionnaires we decide to use more precise and scientific questionnaires among healthcare workers. Indeed, in 60 days we interviewed 700 persons. The questionnaire was conducted in June 2021, 6 months after the beginning of the vaccination campaign in Iran and 3 months after it reached its third peak [9]. We reduced recall bias by asking women 3 to 6 months after their vaccinations, so the experience was still fresh in their memory, and at the same time enabled perspective of a periodic side effect. Interview of experts with hospital health workers reduced authenticity issues, such as anti-vaccine groups that might try to tamper with the results. We randomly select healthcare workers to reduce bias. Therefore, we were unable to conclude the exact incidence of AUB from this study. To date, we have inconsistent findings about AUB after vaccination or infection with COVID-19. These findings were overlooked by vaccine companies, but as reports accumulated, awareness increased. The concern of the impact of COVID-19 vaccination on the menstruation cycle was raised in the united states, where the National Institutes of Health allocated \$1.67 million for research to find the possible connection [10]. The Norwegian Institute of Public Health in a pre-existing cohort asked 5688 Norwegian women whether they had experienced menstrual changes before and after each vaccine dose they found that menstrual changes are generally common regardless of vaccination and the prevalence of any menstrual changes was 37.8% before vaccination [11]. In a digital survey from March 2021, which included 1031 participants, 46% had a change in the menstrual cycle since the beginning of the COVID-19 pandemic. About 18% reported menorrhagia and 9% reported missed periods [3]. Li et al. [10] reported on 177 participants with COVID-19, 25% of which presented mainly with decreased volume (20%), and 19% with prolonged menstrual cycle changes. These results were similar to our findings that 38% of women who reported AUB described it as oligomenorrhea. We had similar results in previous studies. For example, the MECOVAC study was an online survey that found that about 55% of women who received the first dose of the COVID-19 vaccine reported menstrual cycle changes, regardless of the type of vaccine. The occurrence of menstrual irregularities seems to be slightly higher (65%) after the second dose [11]. On the other hand, some studies had conflicting results with ours. For example, in an online survey among vaccinated Saadians, the abnormal menstrual cycle was reported in only 0.98% (18/1846) of Pfizer-BioNTech and 0.68% (7/1028) of ChAdOx1 vaccines [12]. The low rate of side effects in this study may be for the fact that the questionnaire was open to both genders, with no age limit, and inquired on up to the 7<sup>th</sup> day post-vaccination. In a prospective study, Edelman et al. [13] included 3959 women and found that the COVID-19 vaccine changed the length of the cycle less than 1 day, and no change in menses' length. we differ our study by examining several other menstrual characteristics such as types of AUB and inter-menstrual bleeding that were not in the study of Edelman et al.; moreover, we had more heterogenic population, including women who use contraceptives and with irregular menses. Age is an important parameter when addressing AUB. Most irregular bleeding occurs during quinquagenarian [14]. In addition, a woman's body mass index is known to greatly affect the regularity of menstruation [15,16] as well as the normalization of ovulation [17]. In our study, both groups had similar baseline characteristics in age and BMI. This further strengthens the relationship between AUB and the COVID-19 vaccination since these possible outliers were equally distributed between our study groups. In our study, most of the women in terms of regularity, frequency, duration, and volume

had normal menses. Among those who reported AUB after vaccination, there were significantly more women with a history of prolonged menstruation and more of them used hormonal IUDs [18]. Conversely, women who reported no change in their menstrual bleeding had a higher rate of non-hormonal contraceptive use and breastfeeding, which are associated with reduced menstrual volume [19]. Although we are awaiting definitive evidence about the association between COVID-19 and menstrual changes, physicians continue to encounter everyday women who have experienced these effects and need to be able to counsel them properly. This data will allow women to plan for potentially altered cycles and will be important for those who rely on being able to predict menstrual cycles to either achieve or avoid pregnancy [20].

### Conclusion

As a conclusion based on our findings, most of the women did not experience abnormal uterine bleeding after of COVID-19 vaccines but among them who had experienced AUB, oligomenorrhea is the most common followed by menorrhagia. Nulliparous women experienced AUB more.

This encourages women to receive booster doses. Further research is required to find the long-term effects of the COVID-19 vaccine on the menstrual cycle.

### Declarations

**Ethics approval and consent to participate:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethics committee of Alborz University of Medical Sciences (Reg. No: IR.ABZUMS.REC.1400.270).

**Consent for publication:** Not applicable.

**Availability of data and material:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** SSH and ABB contributed to interviewing and data curation MF, MH SB, and AH contributed to the conceptualization, supervision, and writing the original draft; MF, AH, and HR reviewed and edited the final manuscript. All authors read and approved the final manuscript.

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