

# Menstrual cycle abnormalities in women vaccinated against COVID-19

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## ABSTRACT

As more reports of menstrual cycle abnormalities after COVID-19 vaccine inoculation are emerging in media and in clinical practice as well, it was deemed necessary to investigate these claims. This review aims to gather current scientific evidence on COVID vaccination's effect on menstrual cycle. Further and extensive research is undeniably needed to fully understand these phenomena, but current studies have demonstrated an undeniable link between some menstrual cycle abnormalities (especially heavy menstrual flow and variations in cycle length) and breakthrough bleeding in non-menstruating population and vaccination against SARS-CoV-2. Up to this point, these disturbances seem to be temporary, not lasting for more than a few cycles. The reported menstrual changes have appeared after inoculations of all brands of vaccines, and no particular technology (mRNA or adenovirus-vectored) was particularly associated with them. The greatest concerns raised were those regarding fertility. However, until now, there is no evidence of any of the COVID vaccines affecting fertility when comparing vaccinated and unvaccinated populations.

**Keywords:** menstruation cycle, abnormalities, Covid-19 vaccines

## INTRODUCTION

With the vaccines against COVID-19 being introduced at the end of the year 2020, health organizations as well as the media have informed the population about common side effects such as pain at the injection site, fatigue, myalgia or fever. But as the vaccine was available to more and more women of fertile age, many physicians have been approached by patients who reported menstrual cycle disturbances in different forms, including changes in menstrual duration, frequency, regularity, and volume (heavier bleeding and clotting), increased dysmenorrhea and worsened premenstrual syndrome. None of the clinical trials protocols of any of the current COVID-19 vaccines included any monitoring or information regarding menstrual cycle post-vaccination so the manufacturers could not address if menstrual changes were simply a coincidence or a side effect. Unfortunately, questions about menstru-

ations were excluded in most vaccine studies as well [1,2]. Additionally, increasing reports in social media raised concerns of menstrual cycle abnormalities occurring after COVID-19 vaccination, which further propagated vaccine hesitancy amongst the female population, as many women view menstrual cyclicity as proof of good health and fertility [3-5]. Given the probability of the population refusing a potentially life-saving vaccine due to inaccurate information and to the fact that menstrual abnormalities post-vaccination may affect patients' wellbeing, with clinicians needing to learn to address these problems, we conducted a review of current available literature regarding this topic.

## MATERIALS AND METHODS

For this review we aimed to evaluate current scientific literature on menstrual cycle abnormalities

linked to the COVID-19 vaccination. We conducted internet research using the databases of PubMed and ScienceDirect, as well as preprint servers (MedRxiv and SSRN). Search keywords used were “menstrual cycle”, “COVID-19”, “vaccine”.

## WHAT WE KNOW SO FAR – DISCUSSIONS

Menstrual cyclicity is regulated by the hypothalamic-pituitary-ovarian axis which can be easily and markedly influenced by the surrounding environment, diet, physical activity, weight fluctuations and psychological stress. We already know that the pandemic has caused significant changes in health behaviors and great amount of stress in the population [3,6-9].

Information on how vaccines might affect the menstrual cycle is still limited, even if first reports of menstrual disturbances following vaccination have been cited as early as 1913 for the prophylactic typhoid vaccine, with more than half of the persons citing at least one change in their menstrual cycle (including variations in bleeding volume, frequency of menstruation or dysmenorrhea [10]. Other menstrual abnormalities have been reported after the hepatitis vaccine in a 1982 Japanese study [11]. Regarding the HPV vaccine, recent research has shown mixed results, however there have been as well links between this vaccine and various changes in menstrual cycle [12,13]. Vaccines function by activating the immune system which, sometimes, may activate as well a cascade of inflammatory responses that in some individuals may target certain organs (e.g. the uterus). The mechanism of how vaccines influence menstruation is not clear, but biologically plausible theories include the immunological influence on hormones, or the effects mediated by the immune cells in the lining of the uterus [2,14,15].

Until the 23<sup>rd</sup> of February 2022 UK's Medicines and Healthcare products Regulatory Agency received more than 39.000 individual reports to its Yellow Card surveillance system claiming a variety of menstrual abnormalities for both mRNA and adenovirus-vectored COVID-19 vaccines, most of them including heavier than usual menstrual bleeding, delayed periods or unexpected vaginal bleeding. However, these changes were reported to be of short duration [16].

One study published by Edelman et al. analyzed menstrual cycle data of almost 4,000 subjects, both vaccinated and unvaccinated against COVID-19, over a period of 6 consecutive cycles [5]. This study excluded women whose cycle length was outside normal limits (of 24-38 days) and those who suffered from diseases such as endometriosis, polycystic ovarian syndrome, or thyroid disease. Firstly,

both vaccinated and unvaccinated cohorts were found to experience small variations of cycle length. Furthermore, they found that the COVID vaccine was associated with a change in cycle length of less than one day which was not considered to be clinically significant. Only a small subset of individuals who received both vaccine doses within a single cycle had a mean 2 day increase in their cycle length compared with unvaccinated women, with 10.6% of vaccinated individuals having 8 days or more increase in their cycle length compared with only 4.3% in the unvaccinated group. Nonetheless, this change was temporary and considerably lessened after two post-vaccine cycles. Regarding menses length, no changes were found in vaccinated cohorts when compared to the unvaccinated ones [5].

The Norwegian Institute of Public Health published a study finding associations between vaccination against COVID-19 and menstrual disturbances among young women (aged 18-30). Firstly, it was shown that, even prior to vaccination with the first dose, the rate of any menstrual disturbance was considerably high, estimated at 37.8%. Moreover, these abnormalities significantly increased following immunization. While 7.6% of participants in the study reported heavier than usual bleeding during the last period before vaccination, 13.6% stated that the first period after the first dose of the vaccine was heavier than normal. The prevalence of other menstrual abnormalities was as well higher after the first vaccine dose compared to prior vaccination: longer duration than normal (12.5% vs. 9.3%), shorter intervals between menstrual cycles (12% vs. 9.5%) and more painful menstruation than usual (14.6% vs 11.4%). There were no significant differences in the rates of prolonged intervals between menstrual cycles, breakthrough bleeding or period-like pains without bleeding after the first dose. These menstrual disturbances were short-lived, most women reporting that they returned to normal by the time of the second vaccine dose, which was given approximately two months after the first one. After the second dose, the incidence of the disturbances of menstrual cycle cited above was higher. The risk of heavier bleeding was elevated after the second dose for women who had previously experienced it after the first vaccination. Most of the participants in this study were vaccinated with either Comirnaty (Pfizer) or Spikevax (Moderna) vaccines, while an insignificant minority received the AstraZeneca or the Janssen variant. For both mRNA vaccines the rates of menstrual abnormalities described were similar. Another interesting finding of this study was that 92.3% of the women who had menstrual disturbances after the first dose of the COVID vaccine were also vaccinated with the second dose, while 94% of the women who did not report any

menstrual changes got the second dose. This suggests that these changes did not have such a significant impact on the women to refuse a second dose [17].

In a UK retrospective study on almost 5000 premenopausal vaccinated women, 80% of them did not report any menstrual cycle disturbances in the first four months after their first COVID-19 vaccine dose. In this study, as in the others previously presented, the menstrual changes were diverse, most of them being increased menstrual flow or changes in cycle length and regularity. The researchers investigated multiple variables trying to find risk factors for these changes and it was shown that smoking increased the chances by 44%, while a positive COVID history with more than 50% (reaching 70% in individuals with long-COVID). On the other hand, the usage of combined oral contraceptives was associated with far lower odds of reporting such disturbances, by up to 48% [18].

Lee et al. published a study regarding both abnormal menstrual bleeding and breakthrough bleeding (in people who do not normally menstruate) occurring after COVID vaccination [2]. It was found that 42% of people with regular menstrual cycles had a heavier menstrual bleeding after at least one of the vaccine doses, while 44% of those people reported no change. Approximately a third of the first subgroup experienced a longer duration of menstruation as well. The participants of this study were further segregated into categories, those with no diagnosed reproductive conditions (with 40.83% of them experiencing heavier menstrual flow) and those diagnosed with conditions such as endometriosis, menorrhagia, polycystic ovarian syndrome, or fibroids, who reported considerably more cases of heavy periods (52.35%, 44.56%, 46.51%, and 46.34% respectively). Among non-menstruating premenopausal women who use long-acting reversible contraceptives, a vast majority reported breakthrough bleeding (70.49% of them), while more than a third of the persons on gender-affirming hormones experienced it. Breakthrough bleeding was experienced by 65.97% of postmenopausal women who were not on any hormonal treatments. Most of the people participating in this study received either the Pfizer or the Moderna vaccine and there was no difference found regarding post-vaccination bleeding flow or rate of breakthrough bleeding between these two [2].

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One notable mention is that most of the studies relied on self-reported data from internet surveys. There is an increased probability for people directly affected by menstrual changes to be more responsive to such inquiries and report these anomalies. Additionally, the pandemic and the media coverage of this problem as well may have made women more aware of their health and menstrual cycle variations, even if they may have experienced similar episodes before vaccination [2,17]. While the International Federation of Gynecology and Obstetrics has defined a standardized system for defining abnormal uterine bleeding regarding menstrual frequency, duration, regularity and volume, women tend to be subjective as they usually report to their own experience. However, their concerns should not be easily dismissed if their symptoms do not meet those criteria [19].

As previously mentioned, claims that COVID vaccines affect fertility have made women reluctant to the vaccine, as well as parents of adolescent girls who were faced the dilemma of either protecting their children from a potential life-threatening disease or affecting their pubertal development and fertility. But these claims are beginning to be contradicted by some recent studies. In clinical trials, unintended pregnancies occurred at comparable rates in both vaccinated and unvaccinated cohorts. Likewise, miscarriage rates were similar for both groups [1,2,20]. Another researcher compared implantation rates for frozen embryo transfer in SARS-CoV-2 vaccine seropositive, infection seropositive and seronegative women. There was no difference found between these three groups regarding embryo implantation and early pregnancy development [21].

## CONCLUSIONS

While further research is certainly needed regarding how the COVID-19 vaccine affects menstrual cycle, especially in the long term, we may draw some conclusions from the information that has been gathered so far. Unquestionably there is a link between vaccination and abnormal uterine bleeding events, nevertheless, these changes do not appear to be severe and they are transient, without seemingly affecting women's fertility.

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