Review Article

# Menstrual Dysfunction and COVID19 Vaccine

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**Abstract**

*Introduction*: There has been an increasing concern that the vaccination against the novel COVID19 disease is likely to provoke various side effects for the general population including menstrual cycle dysfunctions for women in the reproductive age. There are some risk factors that enhance the possibility for post-vaccine implications on the menstrual health. Such risk factors are smoking, past COVID19 infection and the lack of usage of oral estrogen-containing contraceptives.

*Aim*. The aim of this report is to clarify the relationship between the vaccines against the SARS-CoV-2 and the menstrual cycle dysfunction in the women of reproductive age.

*Materials and Methods*: an extend research was made via the PubMed database using the following keywords: "menstrual", "dysfunction", "COVID19", "vaccine". No further filters and eliminations were used.

*Conclusion*: There are several mechanisms through which vaccines are able to alter the menstruation cycles. The irregularities are not permanent and after a short period of time, menstrual cycles return to normal. Women of reproductive age are still encouraged to be vaccinated.

*KeyWords: menstrual, dysfunction, COVID19, vaccine*

## Introduction

Protective vaccines against SARS-CoV-2, that provokes the novel coronavirus disease (COVID19), have been recently developed in the early 2020. Various general adverse effects have been described, but only recent reports mention menstrual dysfunctions in women of reproductive age.

Multiple technologies were used for the development of the vaccines, such as the mRNA technology, the usage of vector and finally the usage of protein subunit. The vaccines of every type diminishes the possibility of infection in case of exposure, moderates the symptoms and the severity of the illness in case of infection and finally it reduces the likelihood of someone infected to transverse the virus to others (1). The great infectiousness of COVID-19 leads to the need of massive vaccinations for the general population. Of particular interest, among them, women of reproductive age, breastfeeding women and women currently pregnant or intending to be pregnant were encouraged to be vaccinated. Similar to every vaccine, there are some adverse effects. In the general population the main side effects of the COVID19 vaccine include fatigue, dizziness, nausea, muscle pain, fever and chills. Local inflammation at the sight of the injection was also common.

For women of reproductive age menstrual cycle irregularities provoked by the vaccine, might be a possible adverse effect.

As the COVID-19 pandemic insists, women of reproductive age, among the rest of population, continue being vaccinated to get the protection from the infection with SARS-CoV-2 virus. As such, it is of great significance to be clarified whether the vaccine schemes are safe enough as it comes to the sexual and menstrual health of women of reproductive age. The aim of this report is to examine whether the vaccine against COVID-19 is likely to give rise to menstrual dysfunction in young women of reproductive years.

## Materials and Methods

An extend research of the relatively published bibliography was conducted via the PubMed database. The keywords used for the search were:

"Menstrual Dysfunction" AND "COVID-19 vaccine". Data were extracted using a common data elicitation form, using the aforementioned keywords. The study was performed with respect to the PRISMA-ScR guidelines.

Specifically, as it concerns the PRISMA, the records that were identified through PubMed search were initially 5 and the additional ones that came up through the review of references were 4. So the records that were screened were 9. The articles excluded because of non-relevant title, abstract and full-text were 3. Finally, 6 references fulfilled the above-mentioned criteria and were used in the present review. *(Figure 1)*

## Results and Discussion

The menstrual cycle regulation is a physiological process of grave significance in the well-being of women of reproductive age, which is inextricably linked to the general health and fertility. A typical cycle consists of 26-35 days including approximately 5-7 days of menses. There are various factors that may provoke menstrual disorders including biological features (such as body weight, age, genetics), lifestyle factors (such as stress, emotional stress, alcohol, smocking, drugs, exercise), personal history (adrenarche, menarche, parity) and finally environmental factors (such as chemicals and toxins that affect the endocrine system).

The regulation of menstrual cycle depends on the hypothalamic-pituitary-gonadal axis (HPG axis) and the circulating hormones exceeded by this axis. The HPG axis arranges the endometrium thickening and shedding. The hypothalamus via the CRH and the pituitary gland via the ACTH hormone are also responsible for the release of cortisol from the adrenal glands. It is a hormone excreted in response to stress, immunization and inflammation. When exposed to a stressful stimuli, CRH stimulates an inflammatory pattern in the female reproductive system influencing the evaluation and the degeneration of the corpus luteum. In other words, CRH and cortisol upon exposure to stressful stimuli, lead to cycle abnormalities, because of low female sex hormone levels (1).

There are various factors, besides the vaccine, that correlate with COVID-19 and may cause menstrual dysfunction. As such, these confounding variables complicate the causal relationship between the vaccine and the menstrual dysfunction. To begin with, the radical change in the lifestyle because of the lockdown and the stress of the pandemic and the infection with SARS-CoV-2 themselves may have an impact on the HPG axis (2). Menses were reported longer and with larger volume than usual. Furthermore, a corticosteroid drug called dexamethasone was prescribed to treat hospitalized patients with a severe infection. The mechanism of the drug acts through the endometrial cortisol, influencing the maturation of the endometrial blood vessels. Thus, dexamethasone by definition affects the menstrual cycle function. However, these changes in the menstrual cycle are considered to be temporary and as the stimuli passes by, the normal function of the menstrual cycle returns with no-longer impacts (3).

There are two possible mechanism pathways that may explain the changes in the menstrual cycle because of the COVID-19 vaccine. Firstly, it is highly possible that the innate immune cells which are triggered by the vaccination, interfere with the reproductive hormones and may prolong the follicular phase, leading to an abnormal cycle. The second biological mechanism interferes with the breakdown and the regeneration of the endometrium by the macrophage and the natural killer cells.

It has been also noticed that women of reproductive age who consume estrogen-containing contraceptives per os have a reduced risk of post-vaccination adverse effects regarding their menses (4). This phenomenon can be explained by the fact that in these women the concentration of circulating progesterone and estrogen is higher, because of the drugs. These hormones are immunomodulators and they also have an anti-inflammatory action against severe COVID19 infection (5).

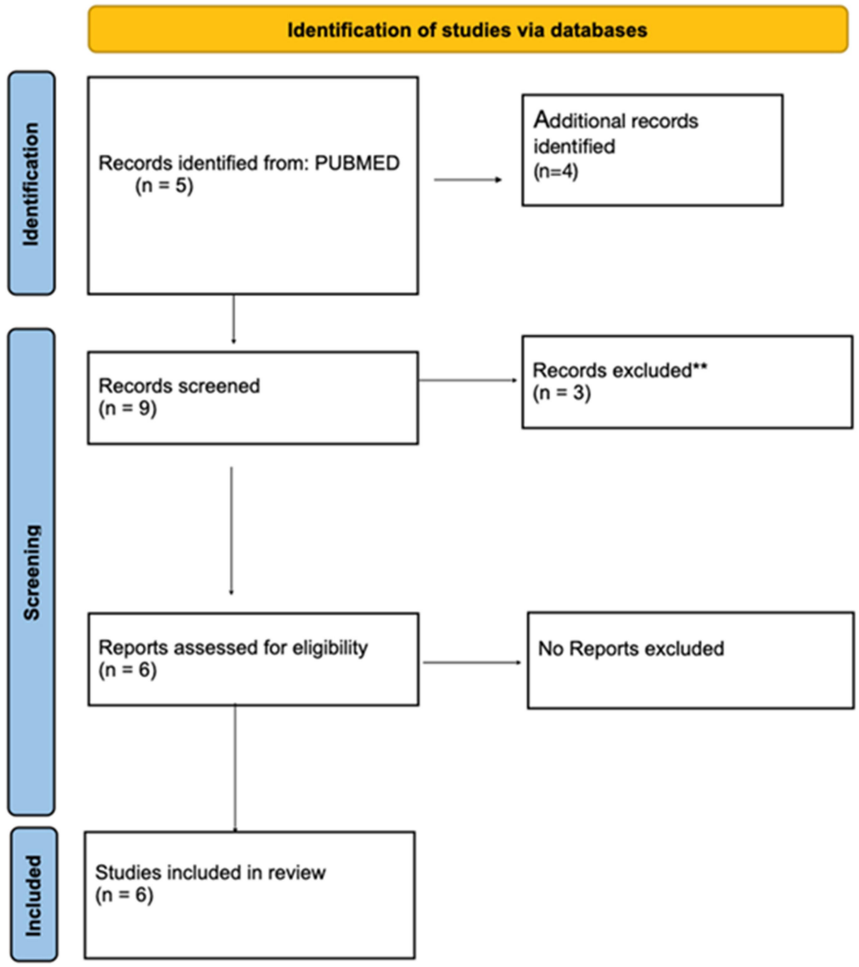


**Figure 1.** *Flow chart*

There was also evidence that women not using hormonal contraceptives had a delay of averaged 2.3 days on the post-vaccination menstrual period, compared to the pre-vaccination cycle. However the timing of the vaccination regarding to the menstrual cycle did not have any effects on the flow and the volume of the subsequent period. Finally, the type of the vaccine had not affected neither the timing nor the flow of the forthcoming menstrual period (6).

It has been reported that any irregularities in the menstrual cycle after the vaccination for the COVID-19 are related to past COVID-19 infection, smocking, contraceptive type and other menstrual changes over the past year. On the contrary, age, ethnicity, body mass index, physical activity, period length and flow, irregular cycle, vaccination type, vaccination timing, parity, medication use, supplements / vitamins consumption, endometriosis, polycystic ovarian syndrome, uterine polyps/fibroids, thyroid disease and eating disorders are not associated with the changes in the menstrual cycle in the post-vaccination period (4). The concern that the vaccination is likely to provoke menstrual cycle irregularity forms a source of vaccination hesitations and may also burst anti-vaccination campaigns.

In order to overcome the blurry scenery around

the impact of the vaccines against COVID19, future studies should observe and record the relationship between the vaccines and the menstrual cycle. To be accomplished that, it is important that the mechanism/type of the vaccine and the number of doses and boosters are considered. Moreover future studies should clarify the time needed for the menstrual cycle with irregularities to get back to normal. Additionally, it would be useful if future studies compared the menstrual dysfunction because of the vaccine to the one because of the infection with the SARS-CoV-2 virus. As so, there will be a spherical opinion around the impact on the menstrual and sexual health of the women of reproductive age (3).

## Conclusions

To conclude with, this was a systematic review that tried to highlight the concerns about the involvement of the vaccination for protection against the COVID19 disease to the women's menstrual cycle. There were discussed mechanisms with which the vaccines may provoke menstrual cycle dysfunctions in women of reproductive age. However there are no evidence that there are neither long term or permanent dysfunctions in the cycle. Irregularities may occur by numerous factors related to COVID19 including changes in the lifestyle, drugs treating an infection from the virus, vaccines and the virus itself. They may disturb reproductive women for a short period and then the run away and the menses get back to normal. Also, it is possible that a personalized diagnostic strategy might be needed in order that the menstrual homeostasis is reestablished. This strategy includes the evaluation of the thyroid gland function, the personalized hormonal status and social aspects (1). Thus, young women of reproductive age and women who are or intend to be pregnant are encouraged to be vaccinated. Further research needs to be fulfilled so as to make the things clear around the vaccination and its impact on the menstrual health.

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