

COVID-19 infection and the menstrual cycle, the aftermath of a pandemic

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Abstract

Objectives:

During the COVID-19 pandemic, the potential impact of vaccinations on menstrual cycle patterns was not initially a widely discussed side effect. However, as the global race to develop an effective vaccine intensified, a significant concern arose about the potential effects on menstrual disturbances, catapulting this issue to the forefront of health priorities.

Materials and Methods

Our study employed a unique descriptive cross-sectional design, using face-to-face interviews and a meticulously structured questionnaire to collect data. We focused on menstruating women aged 18 to 50 from May 31 to July 31, 2022, and specifically asked about their menstrual cycles in the first 12 cycles following either COVID-19 infection or vaccination.

Results

The survey was completed; 244 women who had confirmed COVID-19 infections and 305 women who had received at least two doses of the vaccine as recommended by health authorities. Among these, 80 (32%) reported changes in their menstrual cycle patterns post-infection, and 48 (15.74%) noted changes following vaccination.

Conclusion

Our findings highlight two critical, interrelated conclusions. Firstly, COVID-19 infection and vaccination can directly affect the menstrual cycle, notwithstanding momentarily. Secondly, most alterations dissipate within six months post-infection or after receiving the third vaccine dose.

Keywords: COVID-19, menstrual abnormalities, menstrual cycle, stress, vaccine, vaccination policy.

Introduction

In the bygone few years, our lives had been significantly pretentious by COVID-19 and the constraints the pandemic brought to each aspect of our everyday lives. On that pessimistic day, when the world became aware of the reality of the pandemic and its devastating impact on individuals and countries, health priorities were rearranged, and survival was considered an achievement, especially since the speed of the pandemic impact exceeded the ability of the health authorities to control it. Nevertheless, studying one specific aspect of it is difficult because of all the confounding factors that might be interlinked. It is challenging to construct an impeccable study in such circumstances. In the superseding time, scientific hard work succeeded in developing and registering the emergency use of the COVID-19 vaccine, where multiple spotlights from the media highlighted its wide range of effects on the menstrual cycle, the infection, and/or the vaccination. This vaccine was the hope that gave a renewed sparkle to human life after a long dark season in human history; it has nourished the tree of hope once again for a future that we hope will be fruitful. Nevertheless, it is already known that some viral infections correlate with changes in the female reproductive system, such as the duration of the menstrual cycle or the volume of menstruation [1]. Menstrual changes have also been reported following both. COVID-19 affection may be attributed to immunological processes [1, 2]. A decrease in stress and anxiety with the end of the pandemic may explain the return of the menstrual cycle to its normal pattern. There is considerable concern about the possibility of menstrual changes resulting from the pandemic rather than the virus itself. Those people who believed in this theory supported their view by believing in the direct impact of the pandemic on individuals, the economy, health, and the population level, and therefore, suggest this should be taken into consideration by governments, healthcare providers, and employers when developing pandemic recovery plans [2a].

The development of vaccines brought a ray of hope amid these trying times, marking a significant milestone in humanity's fight against the virus, and reported another outstanding victory for scientific progress for humanity. This breakthrough, achieved after extensive research and experimentation in laboratories, has been celebrated as a crucial victory, offering a path to recovery and healing for many who have suffered losses due to the pandemic. The dialogue surrounding the pandemic and its vaccines has been intense and multifaceted, with discussions often influenced by economic, material, and sometimes political factors. Amid concerns about vaccine side effects such as sore arms, lifestyle adjustments, fever, fatigue, and more serious health concerns, an unexpected issue has become known, considering future circumstances that we do not yet know. Women in their reproductive years, ranging from 18 to 50, began reporting changes in their menstrual cycles following COVID-19 infection or vaccination [3]. This development sparked concerns over a possible link between the COVID-19 infection, vaccination, and menstrual irregularities, which could potentially affect women's willingness to receive the vaccine. The menstrual cycle is a biological function and a symbol of health and fertility. While variations in the cycle are normal within limits, the observed changes prompted a need for careful examination to maintain public confidence in the vaccines' safety regarding women's reproductive health [4]. On the other hand, Akmaz et al. studied the impact of COVID-19-related mental health issues on the menstrual cycle characteristics of female healthcare providers and reported an association between the COVID-19 pandemic-induced anxiety, perceived

stress, depressive symptoms, and increased prevalence of menstrual cycle irregularity among healthcare providers [4a].

To address these concerns, our study set out to investigate the relationship between COVID-19 infection and / or vaccination and menstrual cycle changes among young women between May 31 and July 31, 2022, who attended our outpatient clinics. We focused on women aged 18 to 50 with a history of regular menstrual cycles, excluding those who were pregnant, suffering from amenorrhea, or had been on oral contraceptives for more than six months. Our goal was to provide a thoroughgoing analysis of the menstrual cycle parameters post-infection or vaccination to offer reassurance, and support informed decision-making regarding COVID-19 infection/ vaccination among women in this age group.

Materials and methods

This study, designed as a cross-sectional analysis, was conducted in the outpatient antenatal clinics of our hospital from May 31 to July 31, 2022. It involved adapting a meticulously designed questionnaire to collect data relevant to the research objectives. A cohort of 549 women attending the outpatient clinics was interviewed and deemed suitable for inclusion in the study. Of these, 305 women (Group 1) were part of the vaccinated cohort, while 244 women (Group 2) had been infected. The study aimed to compare the demographic data, assess any associated medical conditions, and evaluate the impact on the menstrual cycle post-infection or vaccination. Before participation, verbal consent was secured from each patient after a detailed briefing on the study's purpose, ensuring ethical compliance. This research protocol has been approved by the department council number 2023/15, dated 21/08/2023, the Ethics Committee, and the Scientific Research Committee at our institution in meeting number 7498/2023/37, dated 27/12/2023. The Institutional Review Board (IRB) number 1020248347. Data were collected, and the analysis was conducted using SPSS (Statistical Package for the Social Sciences), with Chi-square and Wallis tests applied for essential statistical evaluations.

Results

The analysis revealed the mean age of participants in both groups was 29.19 years, with an average gravidity and parity reported at 3.52 and 2.72, respectively. Of the total, 387 women (70.49%) were married, and the remainder, 162 (29.51%) were not. A noteworthy finding was the prevalence of associated medical conditions, such as chronic respiratory diseases and immunological and thyroid disorders, identified in 49, 27, and 44 patients, respectively, as detailed in Table I. Examination of menstrual cycle alterations showed that the majority in both groups reported no significant changes. However, within Group 1, notable variations were observed: 48 (15.74%) participants experienced shifts in cycle timing (either advancements or delays), 28 reported a change in cycle duration (shortening or lengthening), 38 observed alterations in menstrual flow (lightening or intensification), and 31 noted accompanying symptoms including stress and mood fluctuations, as depicted in Table II.

For Group 2, about 80 participants noted timing changes in their cycles, 53 reported duration alterations, 56 observed changes in flow, and 64 experienced additional symptoms like stress and mood changes, as outlined in Table III.

Discussion

In this analysis, we have observed a range of alterations in menstrual cycle characteristics —spanning cycle length, flow, discomfort, and irregularity— among subjects reporting menstrual inconsistencies after COVID-19 infection/ vaccination. After the pandemic stabilized, many concurrent health problems emerged, including menstrual cycle variables, the subject of this research. Notably, by September 2021, reports from over 30,000 women had surfaced detailing adverse menstrual effects following immunization. While initially overlooked due to the pressing life-threatening nature of the pandemic, these menstrual disturbances warrant attention. Among participants in this study who noted menstrual cycle modifications, a significant portion documented changes in cycle patterns, irregularities, and related symptoms. The COVID-19 pandemic has profoundly affected the lives of the global population. The menstrual cycle is the monthly phenomenon that indicates by simple words a failure of pregnancy, in which female hormones stimulate an ovary to release an egg under a direct effect of pituitary hormones via a complicated, well-organized process that leads to thickening the endometrial lining of the uterus to support a pregnancy, The regular menstrual cycle is complex, involving the response of the endometrial lining to the dynamic hormonal reflex from the hypothalamic-pituitary-ovarian axis [5]. Therefore, the menstrual cycle can be acutely sensitive to various inside or ecological variables. These may consider stress status quo willy-nilly, the nature of these conditions, weight fluctuations, diet, medications, inflammatory reactions, systemic illness, and some personal matters that are difficult to disclose [6, 7]. Such factors can potentially lead to changes in menstrual cyclicity and characteristics such as duration, flow intensity, and accompanying symptoms like pain [8]. Based on these non-controversial scientific facts, we know that the pandemic has interfered with the physiology of the menstrual cycle pattern. In addition, it is known that periods of stress and psychological distress can affect women's menstrual cycles [8]. However, these alterations typically resolved within six months following infection or three months post-vaccination, with no significant correlation found with demographic factors such as age or marital status. These observations support the advocacy for vaccination in comparable scenarios despite the limitations of this study's observational nature in establishing causality. Noteworthy is the finding that infected individuals experienced more prolonged menstrual changes than their vaccinated counterparts did. Of particular concern was the incidence of amenorrhea extending beyond twelve months in some cases. Based on well-known, scientifically proven facts, stress inhibits the hypothalamic-pituitary-gonadal axis (HPG). Accordingly, the stress and stress hormones inhibit GnRH release from the hypothalamus, and glucocorticoids inhibit luteinizing hormone (LH) release and estrogen and progesterone production by the ovary [1, 2].

The menstrual cycle is a critical indicator of female health. As a regular physiological occurrence, menstruation reflects a broader health status. The complexity of the menstrual process, governed by hormonal shifts, influences mood, energy, and overall physical condition. The International Federation of Gynecology and Obstetrics (FIGO) outlines standard criteria for assessing menstrual normalcy, encompassing frequency, duration, regularity, and volume. It is established that the hypothalamic-pituitary-ovarian axis, responsible for menstrual cycle regulation, is susceptible to disruptions by various stressors, both biological and environmental. The theory suggesting pandemic-related stress, as opposed to direct effects of the virus or vaccination as a potential cause of menstrual irregularities, remains unrefuted by current evidence [8, 9, 10].

The exact biological mechanisms through which COVID-19 infection or vaccination influences menstrual function are yet to be fully understood. It is well-documented that stress, particularly at high levels, can significantly disrupt menstrual cycles [11]. The impact of stress varies, affecting menstrual frequency, bleeding, and duration in different ways. One possible explanation for observed menstrual irregularities is immune-mediated, infection/ vaccine-induced thrombocytopenia. Historical data reveal that such menstrual changes and thrombocytopenia have been associated with various infections and vaccinations [12, 13]. Both might provoke an intense immune response, potentially impacting the hypothalamic-pituitary-ovarian axis temporarily. Since the advent of emergency-approved COVID-19 vaccines in December 2020, billions of doses have been administered globally [14]. To clarify matters realistically, the philosophy of all countries of the world and the World Health Organization recommendations have stressed the necessity of receiving the vaccine, which has become a requirement for work, travel, investment, and movement, but rather an indicator of the beginning of a return to normal life, even for people with special circumstances, such as pregnant women, for example [14^a].

Among participants in this study who noted menstrual cycle modifications, a significant portion documented changes in cycle patterns, irregularities, and related symptoms. However, these alterations typically resolved within six months following infection or three months post-vaccination, with no significant correlation found with demographic factors such as age or marital status. These observations support the advocacy for vaccination in comparable scenarios despite the limitations of this study's observational nature in establishing causality. Noteworthy is the finding that infected individuals experienced more prolonged menstrual changes than their vaccinated counterparts did. Of particular concern was the incidence of amenorrhea extending beyond twelve months in some cases. It was accompanied by unavoidable lifestyle changes, especially the negative role of the media and social media platforms, which gained the glory of viewing due to the factual circumstances [11, 15].

The necessity for further investigation is underscored by findings from other researchers, suggesting that COVID-19 vaccinations may lead to menstrual changes [16]. Unfortunately, despite its frequent reporting, this extensive study did not address the aspect of menstrual flow variation [17]. Proposed mechanisms range from immune system stress impacting hormonal regulation to direct effects on the

endometrial environment [18]. It has been observed that females elicit stronger immune responses to vaccines compared to males, which could explain the higher incidence of adverse effects among women following vaccination [19, 20]. This gender difference in vaccine response underscores the need for more targeted research to fully understand the implications of COVID-19 on women's menstrual health. Amidst ongoing discussions about the pandemic's origins and the possibility of laboratory involvement, the call for more comprehensive, prospective studies remains. Such research is crucial to unraveling the complex effects of COVID-19 infection and vaccination on menstrual health. One more important point to keep in mind is the effect of the COVID-19 pandemic revealed that menstruation in female medical workers was more affected by COVID-19. This topic mandates regular exercise and good physical condition to act as protective factors, while anxiety and insomnia were risk factors for menstrual abnormalities [21- 23].

Conclusions:

The menstrual cycle is a vital indicator of health in women. A consistent menstrual cycle suggests good health, whereas disturbances may reflect underlying health conditions. Our study highlights the association between COVID-19 and shifts in menstrual patterns among women of childbearing age, with more pronounced effects observed in those directly infected by the virus. In the long term, vaccination appears to serve as a protective measure. The link between COVID-19 infection and increased menstrual irregularity emphasizes the importance of vaccination and monitoring menstrual health in affected women. Constant readiness to deal with such pandemics requires us to review points of failure and success. The need for further research to delve into the causal relationships is evident.

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Conflicts of Interest

Following the ICMJE uniform disclosure protocol, the authors declare no conflicts of interest.

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Author Contributions

All authors contributed to the manuscript equally. Each author has reviewed and approved the final version of the manuscript.

Tables

Table 1: Demographic Data of both groups

Characteristic	Value
Age (years)	29.19 ± 4.70
Gravidity	3.52 ± 1.29
Parity	2.72 ± 1.06
Marital status	
Married	387 (70.49%)
Single	162 (29.51%)
ASSOCIATED MEDICAL DISORDER	
RESPIRATORY CHRONIC DISEASE	49 (9.94)
ANY IMMUNOLOGIC DISORDER	27 (5.22)
THYROID DISORDER	44 (9.40)
DIABETES MELLITUS	23 (4.91)
HYPERTENSION	21 (4.49)
OTHERS	19 (4.05)

Values are given as median ± standard deviation or as number (percentage %)

Table 2: Menstrual changes after COVID-19 vaccination

Parameter		
MENSTRUAL CYCLE	Number	Incidence (%)
NO CHANGE	257	84.26
SHORTENED	21	06.89
DELAYED	27	08.85
CYCLE DURATION		
NO CHANGE	277	90.82
SHORTER	08	02.62
LONGER	20	06.56
MENSTRUAL BLEEDING		
NO CHANGE	267	87.55
LIGHTER	11	03.60
HEAVIER	27	08.85
ASSOCIATED SYMPTOMS		
NO SYMPTOMS	274	89.84
STRESS	12	03.93
MOOD CHANGES	19	06.23
Total	305	100

Table 3: Menstrual changes after COVID-19 infection

Parameter		
MENSTRUAL CYCLE	Number	Incidence (%)
NO CHANGE	164	67.21
SHORTENED	28	11.48
DELAYED	52	21.31
CYCLE DURATION		
NO CHANGE	191	78.29
SHORTER	23	09.42
LONGER	30	12.29
MENSTRUAL BLEEDING		
NO CHANGE	188	77.04
LIGHTER	34	13.93
HEAVIER	22	09.01
ASSOCIATED SYMPTOMS		
NO ADDITIONAL SYMPTOMS	180	73.77
STRESS	10	04.10
MOOD CHANGES	54	22.13
Total	244	100

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