ORIGINAL RESEARCH

Effect of COVID-19 Infection on Menstruation: A Retrospective Study

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Abstract

Background: The global coronavirus disease-2019 (COVID-19) pandemic has infected a large subset of women in the reproductive age-group, but the effect of COVID-19 infection on menstruation is still unclear. This study outlines the influence of COVID-19 infection on the menstrual cycle.

Methods: Women in the reproductive age-group, admitted with COVID-19 infection were followed up with a structured telephonic interview. Women with previously regular menstrual cycles were included in the study. The questions included severity of COVID-19 infection, details of menstrual cycle before and after the infection, and COVID-related stress recorded by Perceived Stress Scale-10.

Results: Data from 350 women with COVID-19 infection were presented. Moreover, 59.1% (n = 207) of women reported a change in their menstrual cycles. About 43.7% (n = 153) noted changes in the volume of flow with 78.4% (n = 120/153) experiencing less flow. Irregular menstrual cycles were reported by 37.1% (n = 130) women, 50.8% (n = 66/130), experienced infrequent menstruation, with delay varying from 45 to 90 days, and 13.8% (n = 18/130) of these women also experienced intermenstrual spotting. Most of these women recovered, and only 17.1% continue to have irregular menstrual cycles even after 1 year of COVID infection. Moreover, 34.28% (n = 120) reported worsening of premenstrual symptoms, and 22.44% (n = 55) reported worsening of dysmenorrhea after the COVID-19 infection. The stress score was not significantly associated with the severity of COVID-19 infection (p >0.05). Social factors like concern about health of other family members, quarantine, and isolation were the biggest contributors to stress.

Conclusion: COVID-19 infection and associated stress can influence normal menstruation.

Clinical significance: The findings of this study outline the short- and long-term effects of COVID-19 infection on menstruation. This information can be used to reassure the patients and will be helpful in counseling to allay their fears related to altered menstrual cycles after the COVID-19 infection.

Keywords: Coronavirus disease-2019, Menstruation, Severe acute respiratory syndrome coronavirus 2, Stress.

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Introduction

The coronavirus disease-2019 novel virus infection outbreak was first noted in Wuhan, China, in December 2019, which later spread throughout the world. The causative pathogen is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which has been responsible for the ongoing global pandemic. The first case reported in India was on January 27, 2020, from Thrissur, Kerala,[1] and later spread to infect 3.52 crore Indians, and resulted in the mortality of 4.8 lakh Indians by January 10, 2022.[2]

The COVID-19 pandemic can affect multiple organ systems in the body and has the potential to cause enormous psychological stress due to prolonged quarantine, isolation, and the real risk of death. Glucocorticoids are used in the treatment protocol of moderate and severe COVID-19 infection, and the associated stress can alter the functioning of the hypothalamic–pituitary–ovarian axis, leading to disturbance in the menstrual cycle.[3–5]

The global COVID-19 infection has affected a large subset of women in the reproductive age-group, and the effects of this infection on pregnancy, including ectopic pregnancies have been well documented, however, its effect on menstruation is still not clearly defined.[6,7] Hence, this observational study was performed to study the influence of COVID-19 infection on the menstrual cycle in Bengaluru, India.

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Materials and Methods

Women in the reproductive age-group, who were admitted with COVID-19 infection in our hospital during the first wave of pandemic, in the year 2020, and the second wave of the pandemic, in the year 2021, were followed up with a telephonic interview. Telephonic interview was conducted for 422 women, between October and December 2021. A total of 350 women met our study criteria and were included in the statistical analysis. Data of 72 women were excluded because either they had irregular menstrual cycles before the COVID-19 infection, or their data were incomplete.

Inclusion Criteria

- Women between the ages of 18 and 45 years who had COVID-19 infection.
- Women with previously regular menstrual cycles before the COVID-19 infection.

Exclusion Criteria

- Pregnant or lactating women.
- Women using oral contraceptive pills.

The structured interview was modeled on a simplified questionnaire that was devised and validated by conducting a pilot test on 30 participants. The questions included the demographic characteristics of the study participants such as age, education level, place of residence, and obstetric information. The next part included questions related to COVID-19 infection and its severity. Respondents were asked details of three menstrual cycles before and three menstrual cycles after the COVID-19 infection. They were also asked about associated premenstrual syndrome (PMS), which is a cluster of bothersome symptoms, like fatigue, backache, breast tenderness, and irritability, that usually develops a few days before the onset of menstruation and subsides when menstruation starts.

The remaining questions were related to perceived stress score due to COVID-19 infection. The "Perceived Stress Scale" (PSS)-10 is an objective way to assess the degree of stress, caused by a life event, as perceived by the respondent. Ten questions are designed to evaluate how helpless or overwhelming the respondents feel during the stressful event. The scale also includes direct questions about the current stressful situations. The questions are of general nature and ask about the feelings of the respondents about their current situation, and responses are marked on a Likert scale. The PSS score is attained by reversing the responses for the positively stated questions and adding the scores across all the responses. Scores of 0–13 indicate low stress and 14–26 are indicative of moderate stress, and scores from 27 to 40 are considered high perceived stress.[8]

Management of COVID-19 infected patients was based on the COVID clinical categories given in Table 1.

Table 1: COVID-19 clinical categories

Clinical category	*Description*	*Parameters*
Asymptomatic	No symptoms	SpO_2: ≥94% in room air RR: ≤24/minute No evidence of hypoxemia or breathlessness
Mild	Patients with uncomplicated upper respiratory tract infection	SpO_2: ≥94% in room air RR: ≤24/minute No evidence of hypoxemia or breathlessness
Moderate	Pneumonia with no signs of severe disease	SpO_2: 94–90% on room air RR: 24–30/minute
Severe	Severe pneumonia	SpO_2: <90% on room air RR: >30/minute

RR, respiratory rate

Statistical Analysis

Data were entered into Microsoft Excel for analysis. Output measures were reported as frequency (*n*), percentage (%), and means. The Pearson Chi-square test and paired sample *t*-test were used to compare the percentages and means. Statistically significant differences were considered when *p*-value was <0.05.

Results

A total of 422 women responded to the telephonic interview for this study. The final analysis included data related to 350 women who reported regular menstrual cycles before the COVID-19 infection. Of these 350 women, 76.9% ($n = 269$) women had contracted COVID-19 infection in the first wave in 2020 and 23.1% ($n = 81$) women had the COVID-19 infection in the second wave in 2021. Among our study group, 67.7% ($n = 237$) respondents suffered from "mild" COVID-19 infection, and 32.3% ($n = 113$) had "moderate" or "severe" infection.

Demographic Characteristics of Participants

The mean age of our 350 respondents was 31.2 years. Forty percent ($n = 139$) of the women were in the age-group of 25–34 years. Most of the women were homemakers 60.3% ($n = 211$), rest of them were students or working women from factories. Moreover, 89.2% ($n = 313$) of the study population was married, and 86% ($n = 301$) were multiparous women with at least one child. Most of the women 60% ($n = 210$) belonged to social economic scale (SES) "Lower" and "upper lower" as per modified Kuppuswamy classification, the rest 40% belonged to SES "upper" and "upper middle." Moreover, 72.57% ($n = 254$) participants had completed secondary schooling, and 27.42% ($n = 96$) were graduates (Table 2).

Impact of COVID-19 on Menstruation

More than half the respondents 59.1% ($n = 207$) reported a change in their menstrual cycles, after the COVID-19 infection, and included a change in the volume of flow, duration, frequency, or regularity of menstruation.

A paired *t*-test was used to compare the menstrual data from before and after the COVID-19 infection. Changes in the volume of menstrual flow were perceived by 43.7% ($n = 153$) respondents, 78.4% ($n = 120$) of these women, experienced less flow, whereas increased flow was reported by 9.4% ($n = 33$) women. Decreased flow was experienced by 48.7% ($n = 55$) women with moderate or severe infection and 27.4% ($n = 55$) women with mild infection. A Chi-square test of independence showed that there was a significant association between the severity of the infection and the patients' perceived volume of menstrual flow, χ^2 (2, $N = 350$) = 20.54, $p < 0.001$ (Table 3).

Table 2: Demographic data of participants

Parameters	*Number (n = 350)*	*Percentages*
Age (25–34 years)	139	40%
Homemaker	211	60.3%
Students and professionals	139	39.7%
Married women	313	89.2%
Multiparous	301	86%
Socioeconomic status		
Lower and upper lower	210	60%
Upper and upper middle	140	40%
Educational status		
Secondary schooling	254	72.57%
Graduates and postgraduates	96	27.43%

Table 3: Impact of COVID-19 infection on menstruation

Severity of the infection and volume of flow				
	Post-COVID flow volume			
Severity	*Decreased*	*Increased*	*Normal*	*Total*
Mild	65	19	153	237
	27.4%	8.0%	64.6%	100.0%
Moderate or severe	55	14	44	113
	48.7%	12.4%	38.9%	100.0%
Total	120	33	197	350
	34.3%	9.4%	56.3%	100.0%

Paired *t*-test for the effect of COVID-19 infection on volume of menstrual flow: The value of t is 13.135423, $p < 0.00001$.[10,11] The result is significant at $p < 0.05$.

Chi-square test for effect of severity of infection on volume of menstrual flow: Chi-square statistic is 20.5483, $p = 0.000035$. The result is significant at $p < 0.05$.

Severity of infection and regularity of menstrual cycle			
	Post-COVID		
Severity	*Irregular*	*Regular*	*Total*
Mild	85	152	237
	35.9%	64.1%	100.0%
Moderate or severe	45	68	113
	39.8%	60.2%	100.0%
Total	130	220	350
	37.1%	62.9%	100.0%

Paired *t*-test for effect of COVID-19 infection on menstrual regularity: The value of t is 14.360615, $p < 0.00001$. The result is significant at $p < 0.05$.

Chi-square test for effect of severity of infection on menstrual regularity: Chi-square statistics is 0.5134, $p = 0.473655$. The result is not significant at $p < 0.05$.

Menstrual cycles were considered irregular when there was a difference of more than 9 days from the previous regular menstrual cycles. Overall, 37.1% ($n = 130$) experienced irregular menstrual cycles. Statistically, the COVID-19 infection significantly effects the regularity of menstrual cycles ($p < 0.001$). Moreover, 35.9% ($n = 85$) women in the mild infection group and 39.8% ($n = 45$) women in moderate and severe infection group experienced irregular menstrual cycles; however, the association between the severity of infection and regularity of menstrual cycle was statistically not significant χ^2 (1, $N = 350$) = 0.51, $p = 0.47$.

Half of these women 50.8% ($n = 66/130$), with irregular cycles, experienced infrequent menstruation with delay varying from 45 to 90 days, 13.8% ($n = 18/130$) of these women also experienced intermenstrual spotting.

Among the women infected in the first wave of COVID infection, 34.9% ($n = 94/269$) experienced irregular menstrual cycles. When asked about the regularity of menstrual cycle, most of these women had recovered and started regular menses within 6 months of recovering from COVID-19 infection, and only 17.1% ($n = 46/269$) of patients from the first wave of COVID-19 pandemic continued to have irregular menstrual cycles even after 1 year of COVID infection. Eleven of these 46 women had suffered from moderate or severe infection; the rest had only mild infection.

Table 4: Severity of COVID-19 infection and duration of menstrual flow

		Duration of flow (days)				
Severity		*N*	*Mean*	*Std. deviation*	*t value*	*p value*
Mild	Pre-COVID	237	4.28	0.98	2.215	0.28
	Post-COVID	237	4.17	0.97		
Moderate or severe	Pre-COVID	95	4.46	1.04	2.470	0.015
	Post-COVID	95	4.16	1.01		
Total	Pre-COVID	350	4.34	1.00	3.310	0.001
	Post-COVID	350	4.17	0.98		

Table 5: Severity of COVID-19 infection and perceived stress score

	Mild stress	*Moderate stress*	*Severe stress*	*Total*
Mild	62 (64.33) [0.08]	171 (167.25) [0.08]	4 (5.42) [0.37]	237
Moderate or severe	33 (30.67) [0.18]	76 (79.75) [0.18]	4 (2.58) [0.78]	113
Total	95	247	8	350

Chi-square statistics is 1.6692, $p = 0.434053$. The result is not significant at $p < 0.05$

Factors contributing to stress			
COVID-19 infection	*Mild*	*Moderate or severe*	*Total*
Financial	1	3	4
Social	197	88	285
Excessive hair fall	110	40	150
Skin lesions	14	10	24
Generalized tiredness	48	26	74
Sleep disturbance	29	18	47
Persistent cough	26	15	41
Persistent pain	22	14	36

The mean duration of flow before the COVID-19 infection was 4.34 days, which decreased to 4.17 days post-COVID-19 infection, this change was statistically significant ($p < 0.001$). Among the moderately and severely infected women, the mean duration of flow was 4.46 days before COVID-19 infection, which decreased to 4.16 days post-COVID-19 infection, this too was statistically significant ($p = 0.015$) (Table 4).

Among the respondents, 34.28% ($n = 120$) reported worsening of PMS, and 22.44% ($n = 55$) reported worsening of dysmenorrhea after their COVID-19 infection.

The perceived stress score for patients was evaluated based on the patients' responses. All respondents reported some degree of stress during the pandemic. Moreover, 27.1% ($n = 95$) has mild stress, 70.6% ($n = 247$) has moderate stress, and 2.3% ($n = 8$) reported severe stress. However, the stress score was not significantly associated with the severity of COVID-19 infection ($p > 0.05$) (Table 5).

Discussion

There is a paucity of literature on the effect of the COVID-19 infection on menstruation. The purpose of this cross-sectional study was to

examine whether the menstrual cycles of women with previously regular menstrual cycles were adversely influenced by the COVID-19 infection.

In our study, more than half (59.1%) of the normally menstruating women reported a change in their menstrual cycles after their COVID-19 infection. These changes included a change in the volume of flow or duration of flow or the regularity of menstrual cycle. Li et al., from China, also reported 25% of COVID-19 infected women had disruption of their menstrual cycles.[4] Phelan et al. reported that 46% of women in the study had noted a change in their menstrual cycle. Their study included not just women with COVID-19 infection, but all women affected during the pandemic.[9] Alice McNamara, a sports medicine physician, reported that 24.7% of women athletes, experienced a change in their menstrual cycle during COVID-19 lockdowns, and they attributed this change to the stress induced due to disruption of athlete schedules and training.

One possible explanation could be that the SARS-CoV-2 enters cells through angiotensin-converting enzyme-2 (ACE2) receptor. Organs with high expression of ACE2 are vulnerable to attack by this virus. Reis et al. confirmed the existence of ACE2 markers in all stages of follicle maturation in the human ovary. ACE2 expression has also been reported in ovarian granulosa cells, which means the ovary might also become the target of SARS-CoV-2.[10,11] ACE2 is also expressed in the endometrium, and its expression changes with the phases of menstrual cycle. It is expressed more in the secretory phase compared to the proliferative phase, and this may adversely affect the endometrial regeneration.[12] However, Li et al. compared the average anti-mullerian hormone (AMH) concentration and other sex steroid hormones in COVID-19 patients. The results were no different from matched controls, hence, they concluded that SARS-CoV-2 infection may have little impact on ovarian reserve and only show transient menstrual changes. In their study, 84% returned to having a normal menstrual volume, and 99% of patients returned to their normal menstrual cycle within 1–2 months after discharge.[4] In our study, most respondents returned to normal regular cycles within 6 months of recovering from COVID-19 infection.

More than a third of our respondents (34.28%) reported worsening of their PMS, and 22.44% reported worsening of dysmenorrhea after the COVID-19 infection. In the study by Phelan et al., 53% of women reported worsening of PMS.[9] Singh et al., from Bhopal, India, also reported a strong association between stress and premenstrual symptoms in their study.[13]

In our study, 43.7% of respondents noted change in the "patients' perceived" volume of menstrual flow, with 78.4% of these women experiencing a decrease in flow volume. The mean duration of flow before the COVID-19 infection, decreased significantly after the COVID-19 infection. The volume of flow and duration of flow were found to have a significant association with the severity of COVID infection. Li et al. reported that patients had only transient menstrual changes, manifesting mainly as prolonged cycles and decreased volume. They reported that among COVID-19 infected women, 18% mildly ill patients, and 21% severely ill patients showed prolonged menstrual cycles.[4] Demir et al., from Turkey, also reported duration of menstrual flow and pads used per day significantly decreased, when compared to their experience before the COVID-19 pandemic. However, only 4 of their 263 participants had tested COVID-19 positive and other participants were normal women adversely affected by the stress and disruption of their lifestyle due to COVID-19 restrictions during the pandemic. The author concluded that this effect on menstrual cycle was probably the effect of psychological stress during the pandemic.[5] In another study, Singh et al. attributed decreased menstrual flow to increased stress levels in medical students. Their study was unrelated to COVID-19 pandemic.[13]

The physiological increase in sympathetic activity during any acute stress results in an increased neural activity in different areas of the brain (including the amygdala). These increased stress levels result in fluctuations in the pregnenolone levels in the body, causing anovulation, luteal phase defects, and menstrual irregularities.[14] Another explanation for significant association with the severity of COVID infection could be an effect of the glucocorticoids used in the treatment of moderate and severe COVID-19 infection.

In our study, the perceived stress score did not correlate with the severity of COVID-19 infection. This evidently points to the fact that many other factors, other than the severity of infection, contribute to the stress of the patient. Social factors like concern about the health of other family members, quarantine, and isolation were the biggest contributors to stress. Excessive hair fall added to the stress, other contributors included generalized tiredness, sleep disturbance, and persistent cough and pain. These factors were not specifically related to the severity of infection and were common even with mild infection.

Strengths and Limitations

This study adds to the body of evidence, describing the effects of COVID-19 infection on the menstrual cycle. This will be helpful in counseling the patients and thus allay their fears related to altered menstrual cycles after the COVID-19 infection. This study also provides reassurance that these changes are transient and are likely to recover within a few months. This information when shared with doctors providing telemedicine services can help to improve the overall satisfaction with the telemedicine services in resource-poor settings.[15] Limitations of this study include a recall bias by the patients due to the retrospective and descriptive study design. However, as this study was conducted by a telephonic interview, the patients were more forthcoming with their menstrual history, as they spoke to doctors from the same hospital where they had received treatment during the COVID-19 pandemic.

Conclusion

The global COVID-19 infection and associated stress adversely affect normal menstruation in more than half the women. Most of these women will experience a delay in menstruation cycle and decrease in volume and days of menstrual flow. However, these menstrual changes are transient and reversible within a short period of time.

Clinical Significance

The findings of this study outline the short- and long-term effects of COVID-19 infection on menstruation. This information can be used to reassure the patients and will be helpful in counseling, to allay their fears related to altered menstrual cycles after the COVID-19 infection.

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