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Alterations in menstrual characteristics and associated factors in Chinese women post SARS-CoV-2 infection: a cross-sectional study

Yumin Jiang[1], Yunqing Li[1] and Yuhua Huang[1*]

Abstract

Objective Following a significant relaxation of restrictions in China on December 7, 2022, after a surge in SARS-CoV-2 infections, an uptick in women presenting with menstrual disorders was observed in clinics. This study aimed to explore the alterations in menstrual characteristics and associated factors post SARS-CoV-2 infection.

Methods A cross-sectional online survey was conducted among 869 non-amenorrheic adult Chinese females (aged 18–53) to study the changes in menstrual characteristics and other infection-related factors post initial SARS-CoV-2 infection. The reported menstrual changes (group A) were compared to the reported no menstrual changes (group B). Data collected included basic individual-level information such as age, height, weight, menstrual history, reproductive and menstrual disorders, chronic diseases, SARS-CoV-2 vaccination status, COVID-19 symptoms, and changes in menstrual characteristics (regularity, period volume, and degree of dysmenorrhea) post SARS-CoV-2 infection.

Results Of the 869 participants, 442 (50.9%, group A) reported alterations in at least one menstrual characteristic; 171 (19.7%) experienced an extended menstrual cycle, and 122 (14.0%) reported a decrease in menstrual volume. Participants who reported menstrual changes (group A) were more likely to have pre-existing chronic diseases (7.7% vs. 3.0%, $P=0.003$) and exhibit more symptoms of COVID-19 during the acute (4.94 vs. 4.03, $P<0.001$) and recovery (4.37 vs. 3.41, $P<0.001$) phases. These participants were also more likely to report fever as a COVID-19 symptom (93.4% vs. 86.9%, $P=0.001$) and experienced a longer duration of fever (2.25 vs. 1.96 days, $P=0.001$) as compared to group B. Notably, group A with chronic diseases, fewer vaccine doses, and more COVID-19-related symptoms experienced more frequent menstrual changes post COVID-19 ($P<0.05$) than group B.

Conclusion Participants with chronic diseases, fewer vaccination doses, and more COVID-19-related symptoms may experience more frequent menstrual changes post COVID-19 infection according to the self-report results in this study.

Keywords Alterations in menstrual, Post SARS-CoV-2 infection, SARS-CoV-2 vaccination, COVID-19 symptom

*Correspondence:
Yuhua Huang
yuhua_huang1228@163.com
[1]Gynecology department, Beijing Traditional Chinese Medicine Hospital Affiliated to Capital Medical University, No.23 Art Museum Back St, Dongcheng District, Beijing 100010, China

Introduction

Over the past three years, COVID-19 has exerted severe impacts on various organs and organ systems [1]. Hypothalamic hypogonadism may occur in severe COVID-19, which can cause temporary amenorrhea and infrequent menstruation [2]. The angiotensin converting enzyme 2-receptor, which is the cellular receptor for SARS-CoV-2, is widely expressed in the ovaries and endometrium [3]. This suggests that the virus could directly affect these tissues.

Previous studies indicated that the impact of COVID-19 infection [4–7] or COVID-19 vaccination [8–11] on menstrual cycles. The most commonly reported changes were irregular menstruation, an increase in premenstrual syndrome symptoms, the amount of blood loss, and infrequent menstruation [4–7]. Additionally, COVID-19 vaccination is also reported to be associated with temporary changes in menstrual characteristics, such as cycle length, flow, and menstrual pain [8]. A systematic review and meta-analysis quantified and characterized menstrual irregularities associated with COVID-19 vaccination, showing statistically significant associations between vaccination and menstrual irregularities among women of reproductive age [9]. Additionally, a study suggested that women who experienced high levels of stress during the early months of the pandemic were more likely to experience heavier menstrual bleeding and a longer duration of their period compared to those with moderate stress levels [10]. Yi et al., investigated a total of 1016 Chinese women, with 530 in the menstrual change group and 486 in the no menstrual change group. They found that the menstrual change group was significantly younger (32.55 ± 7.00 vs. 33.67 ± 7.39, $p = 0.013$) and reported more severe symptoms (32.1% vs. 21.1%). Additionally, the menstrual change group experienced higher rates of mental health issues, including nervousness (22.6% vs. 17.3%, $p = 0$ 0.009), anxiety (34.9% vs. 24.5%, $p < 0$ 0.001), depression (14.7% vs. 8.2%, $p = 0.003$), and fear (10.8% vs. 6.4%, $p = 0$ 0.011) [12]. In addition, anxiety for COVID-19 panic may affect menstrual cycles and may cause menstrual irregularities [12, 13]. However, there is a dearth of reports specifically addressing the effects of COVID-19 infection among Chinese women.

This study aims to identify associated factors for alterations in menstrual characteristics post-COVID-19 infection among Chinese women in Beijing.

Methods

Study design and participants

The study subjects were non-amenorrheic adult Chinese females who had been infected with COVID-19 for the first time. This study adhered to the guidelines of the World Medical Association Declaration of Helsinki and received approval from the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University (approval number: 2023BL02-026-01). The survey was anonymous, and no personally identifiable data were collected. Participants who selected "agree" in the online survey were considered to have given informed consent.

The cross-sectional survey employed a convenience sampling method to collect data from March 20 to April 10, 2023, using self-administered questionnaires (Supplementary Table 1) based on the Menstrual Distress Questionnaire (MEDI-Q) [14] and the PALM-COEIN classification system for causes of abnormal uterine bleeding (AUB) [15, 16], were distributed through social networks to adult Chinese women who had been infected with SARS-CoV-2. The data of the questionnaires and the answers were saved on *Wenjuanxing platform (Website*: https://www.wjx.cn/*)*. The data for this study was retrieved from the Wenjuanxing platform on April 11, 2023, before being organized in an Excel spreadsheet. A pilot study was conducted to evaluate the questionnaire's validity and clarity, with feedback used to enhance its content and structure. Reliability analysis indicated a Cronbach's Alpha coefficient of 0.85, demonstrating good internal consistency and reliability across the questionnaire's sections. Participation in this survey was voluntary, and data were collected anonymously without offering any material incentives for participation. All participants were diagnosed with COVID-19 through antigen or nucleic acid testing, and the survey was conducted 30 to 90 days post-infection. Participants self-reported menstrual changes and, if they had regular cycles, provided records of menstrual dates and durations for the three months before infection for comparison with post-infection data. Standards for reporting included: cycles advanced or delayed by 7 days or more were considered early or late; a reduction of 3 days or more in cycle length was recorded as shortened; a menstrual duration of 8 days or more post-infection was recorded as prolonged. For participants reporting significant changes in menstrual volume, the Menstrual Blood Loss Chart calculated pre- and post-infection volume: an increase of 50% or a pre-infection score of less than 100 with a post-infection score of 100 or more indicated increased volume; a decrease of 50% or a pre-infection score of 25 or more with a post-infection score of less than 25 indicated decreased volume.

The PALM-COEIN system is a standardized method for classifying causes of abnormal uterine bleeding in non-pregnant women of reproductive age. It stands for Polyp, Adenomyosis, Leiomyoma (fibroids), Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not otherwise classified. This system aids in the classification of AUB. AUB refers to the abnormalities in the frequency and regularity of the cycle, the length of the menstrual period, and the amount of menstrual bleeding in relation to normal menstruation, with PALM denoting structural causes and COEIN denoting non-structural causes. It signifies a move towards cause-based diagnosis and focused patient management [16].

Inclusion criteria: (1) Due to the significant decline in ovarian function after the age of 45, only women aged 18–45 years were included. (2) At least one positive test for SARS-CoV-2 pathogen between October 1, 2022 and March 1, 2023. Exclusion criteria: (1) Women who are lactating or pregnant. (2) Participants treated with hyperhormonal drugs for abnormal menstruation within 6 cycles prior to infection. (3) Participants without menstruation in the 6 months prior to infection. (4) Participants who had been treated with glucocorticoids after infection. (5) Failed to complete the questionnaire. Questionnaires with less than 3 min or more than 30 min of answering time and inconsistent answers were excluded, too; (6) patients with reproductive cancer.

Questionnaires and grouping

The first part of the questionnaire clarified the evidence for the participants being diagnosed with COVID-19 infection (including antigen and nucleic acid tests; patients with only symptoms or contact history stopped answering the rest of the questionnaire). The second part collected basic information including age (divided into four groups: < 20 years old, 21–30 years old, 31–40 years old and 41 + years old.), height, body weight, menstruation history, and history of reproductive disorders: Polycystic ovary syndrome ((PCOS), premature ovarian insufficiency (POI), adenomyosis), thyroid dysfunction, menstrual bleeding, and other chronic diseases (hypertension, hyperlipidemia, type 1 or type 2 diabetes, cardiovascular disease, cerebrovascular disease, tumor). The number of SARS-CoV-2 vaccine doses received before the SARS-CoV-2 infection and COVID-19 symptoms such as fever (axillary temperature greater than 37.2 ℃), cough, sore-throat, were collected. Participants were asked if they noticed any changes in their menstruation characteristics after infection with COVID-19. Those who chose "no" were included in the group without changes in menstruation characteristics (group B). Those who chose "yes" were included in the group with changes in menstruation characteristics (group A). Participants were asked to further describe the specific changes in menstruation characteristics. Based on the self-reported menstrual differences before and after infection with COVID-19, we determined whether menstruation was delayed or advanced, whether the menstrual period had been prolonged or shortened, whether menstrual volume had increased or decreased, and whether the degree of dysmenorrhea had become worse or better. Participants who selected both "since COVID-19 infection, menstruation has not yet occurred" and "menstruation has not been delayed (< 3 months)" were assigned to the group with no changes in menstruation (group B).

Sample size

Based on the preliminary literature, the sample size calculation method was used to determine the required sample size. The calculation ensured that the sample size was large enough to acheive the main effect of the study target at a 95% confidence level. The main conclusions of this study were binary categorical variables (i.e., whether menstrual changes were reported). The sample size "n" is calculated by the formula: $n=(Z_{0.05/2}/\delta)^2 \times p \times (1-p)$. In this formula, "n" represents the sample size; $Z_{0.05/2}$ is the critical point at the confidence level, which is 1.96 in the bilateral test; δ is the allowable error, and its value is 0.04; and p is the proportion of reported "menstrual changes" in the previous study, and the value is 0.46. The expected response rate is 80%, so the actual sample size required is 746. The current study meets the required sample size.

Statistical analysis

Both descriptive and inferential statistics were performed using SPSS 25.0 software. Data measurements were expressed as mean ± standard deviation for normally or near-normally distributed data, while median and interquartile range were used for non-normally distributed data. An independent-sample t-test was utilized to compare measurement data, and count data was represented as quantity (percentage) [n (%)]. Depending on the characteristics of the sample, count data comparisons were made using a χ^2-test, χ^2-correction test, or Fisher's exact probability method. We separately evaluated the correlations between vaccine doses, acute-phase symptoms, recovery-phase symptoms, and changes in menstrual characteristics using the Spearman rank correlation coefficient (rho). The 95% confidence interval (CI) for the Spearman rank correlation coefficient was estimated using a bootstrap resampling method. A multi-factor analysis was conducted using the Logit regression model. A *p*-value of less than 0.05 was considered statistically significant.

Results

Following 21 days of data collection, summarization, and data cleaning, we obtained 1010 questionnaires, of which 869 (86.13%) were valid. The participants' mean age was 32.38 ± 8.52 years, with an age range of 18 to 53 years.

Distribution of changes in menstruation characteristics after infection with COVID-19

Among the 869 participants, delayed menstruation was the most common type of menstrual change. In group A,

Table 1 Examining the impact of age on menstrual changes: a comparative analysis of reported alterations in menstrual characteristics across different age groups [*n*(%)]

Age (y)	Group A, *n* = 442							Group B [a], *n* = 427	Total
	Menstruation[a]		Period[a]		Volume[a]		Dysmenorrhe[b]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
18–20	11(21.2)	3(5.8)	6(11.5)	1(1.9)	6(11.5)	10(19.2)	9(17.3)[c]	22(42.3)	52
21–30	64(19.4)	13(3.9)	24(7.3)	8(2.4)	35(10.6)	42(12.7)	28(8.5)	158(47.9)	330
31–40	70(22.3)	12(3.8)	23(7.3)	13(4.1)	20(6.4)	51(16.2)	17(5.4)	151(48.1)	314
41+	26(15.0)	11(6.4)	14(8.1)	6(3.5)	22(12.7)	19(11.0)	9(5.2)	96(55.5)	173
Total	171(19.7)	39(4.5)	67(7.7)	28(3.2)	83(9.6)	122(14.0)	63(7.2)	427(49.1)	869
χ2	5.549		3.053		9.775		11.224	9.775	
P	0.476		0.802		0.134		0.011	0.134	

[a] Chi-square test showed no significant variation among different age groups. [b] Chi-square test showed significant variation among different age groups (χ2 = 11.224, *P* = 0.011). [c] Chi-square test showed significance variation compared with other age groups (χ2 = 8.321, *P* = 0.009)

Table 2 The influence of BMI on menstrual characteristics: a comprehensive analysis of reported changes in menstruation, period, volume, and Dysmenorrhea Across different BMI categories [*n*(%)]

BMI (kg/m²)	Group A, *n* = 442							Group B[a], *n* = 427	Total
	Menstruation [a]		Period [a]		Volume [a]		Dysmenorrhea[a]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
<18.5	19(16.1)	5(4.2)	13(11.0)	3(2.5)	17(14.4)	13(11.0)	13(11.0)	56(47.5)	118
18.5–24.9	112(19.5)	27(4.7)	38(6.6)	21(3.7)	53(9.2)	86(15)	40(7.0)	280(48.8)	574
25.0–29.9	22(21.2)	6(5.8)	8(7.7)	1(1.0)	9(8.7)	17(16.3)	6(5.8)	52(50.0)	104
30.0–39.9	8(19.0)	1(2.4)	3(7.1)	3(7.1)	3(7.1)	4(9.5)	2(4.8)	22(52.4)	42
≥ 40	10(32.3)	0(0.0)	5(16.1)	0(0.0)	1(3.2)	2(6.5)	2(6.5)	17(54.8)	31
Total	171(19.7)	39(4.5)	67(7.7)	28(3.2)	83(9.6)	122(14.0)	63(7.2)	427(49.1)	869
χ2	6.297		-		9.179		3.070	0.773	
P	0.614		0.214		0.327		0.546	0.942	

[a] Chi-square test showed no significant variation among different BMI groups

shortened periods in the 41 + age group show a significant variation compared to other age groups (χ^2 = 11.224, *P* = 0.011). Additionally, worsened dysmenorrhea in the 18–20 age group (17.3%) has significant variation compared with other age groups (χ^2 = 8.321, *P* = 0.009). The chi-square test indicates no significant variation among different age groups for menstruation, period, and volume (Table 1).

Table 2 examines the correlation between Body Mass Index (BMI) and reported menstrual characteristics, presenting percentages within different BMI categories. Noteworthy trends include delayed menstruation (16.1%) and increased dysmenorrhea (47.5%) in BMI < 18.5, prolonged periods (6.6%) and increased menstrual volume (9.2%) in BMI 18.5–24.9, and varied patterns in higher BMI categories. However, the chi-square test indicates no statistically significant variation among different BMI groups for all examined menstrual traits (menstruation, period, volume, dysmenorrhea). (Table 2).

Among the 869 participants, 620 (71.3%) had normal menstruation, whereas 249 (28.7%) had abnormal menstruation in the past. There were no statistically significant differences in the changes in menstruation characteristics between the two groups (*P* > 0.05). In addition, 778 of the participants (89.5%) had not been diagnosed with menstrual bleeding or reproductive system disorders, 63 (7.5%) had been diagnosed with polycystic ovary syndrome, and 28 (3.2%) had been diagnosed with other related diseases. There were no significant differences in the changes in other menstruation characteristics among the groups (*P* > 0.05). Compared with the group with chronic diseases, the proportion of menstrual changes in the group without chronic diseases was lower (χ2 = 9.171, *P* = 0.003) (Table 3).

Significant variations in menstrual period (prolonged, shortened and not changed period, χ2 = 16.591, *P* = 0.045) was observed among the group with different vaccination status. Participants who received no vaccination or one vaccination dose reported more menstrual changes (Table 4).

Among the 869 participants, 784 experienced fever (90.2%) during COVID-19. In addition, the proportion of delayed menstruation in the fever group was significantly higher than in the non-fever group (χ2 = 11.175, *P* = 0.004). The proportions of participants who experienced worse dysmenorrhea in those who experienced fever (χ2 = 5.215, *P* = 0.023), body aches and pains (χ2 = 5.285, *P* = 0.022), and headache (χ2 = 6.755, *P* = 0.009) were higher compared with participants who did not develop these symptoms during acute phase.

Table 3 Exploring relationships between menstrual characteristics and pre-existing menstrual history or diagnosed Diseases—A Comprehensive analysis of reported changes in menstruation, period, volume, and dysmenorrhea [*n*(%)]

History	Group A, *n* = 442							Group B[a, b,d], *n* = 427	Total
	Menstruation[a, b,c]		Period[a, b,c]		Volume[a, b,c]		Dysmen-orrhea[a, b,c]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
Abnormal menstruation	49(19.7)	5(2.0)	19(7.6)	12(4.8)	22(8.8)	38(15.3)	20(8.0)	122(49.0)	249
χ2	5.065		2.856		0.570		0.319	0.003	
P	0.079		0.240		0.752		0.573	0.958	
Diseases related to menstrual change	15(16.5)	3(3.3)	9(9.9)	5(5.5)	4(4.4)	17(18.7)	4(4.4)	42(46.3)	91
χ2	1.106		2.482		4.392		1.231	0.902	
P	0.575		0.289		0.111		0.267	0.342	
Chronic disease	11(23.4)	4(8.5)	7(14.9)	3(6.4)	6(12.8)	5(10.6)	5(10.6)	13(27.7) [d]	47
χ2	2.536		5.463		0.947		0.399	9.171	
P	0.281		0.065		0.623		0.385	0.002	

[a] Chi-square test showed no significant variation between groups with or without abnormal menstruation before SARS-CoV-2 infection. [b] Chi-square test showed no significant variation between groups with or without diagnosis of diseases related to the menstrual bleeding patterns and reproductive system before SARS-CoV-2 infection. [c] Chi-square test showed no significant variation between groups with or without diagnosis of chronic diseases before SARS-CoV-2 infection. [d] Chi-square test showed compared with the group without chronic diseases, the proportion of no menstrual changes in the group with chronic diseases was lower (χ2 = 9.171, *P* = 0.002)

Table 4 Rho analysis of relationships between menstrual characteristics and vaccination status before Infection—A comprehensive study of reported changes in menstruation, period, volume, and dysmenorrhea [*n*(%)]

Vaccination status	Group A, *n* = 442							Group B[b, c], *n* = 427	Total
	Menstruation [a]		Period [b]		Volume [a]		Dysmeno-rrhea[a]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
No data	1(5.6)	0(0.0)	0(0.0)	1(5.6)	1(5.6)	0(0.0)	1(5.6)	13(72.2)	18
Not vaccinated	19(33.3)	4(7.0)	3(5.3)	0(0.0)	6(10.5)	11(19.3)	5(8.8)	19(33.3)	57
1 dose	5(33.3)	1(6.7)	0(0.0)	0(0.0)	2(13.3)	4(26.7)	0(0.0)	5(33.3)	15
2 doses	29(21.2)	8(5.8)	14(10.2)	11(8)	14(10.2)	11(8.0)	11(8.0)	66(48.2)	137
3 doses	114(18.3)	25(4)	47(7.5)	16(2.6)	59(9.5)	91(14.6)	45(7.2)	315(50.5)	624
4 doses	3(16.7)	1(5.6)	3(16.7)	0(0.0)	1(5.6)	5(27.8)	1(5.6)	9(50.0)	18
Total	171(19.7)	39(4.5)	67(7.7)	28(3.2)	83(9.6)	122(14.0)	63(7.2)	427(49.1)	869
Rho	-0.084*	-0.042	0.013	-0.057	-0.022	0.032	-0.010	-0.070*	
Rho 95%CI	-0.158 to -0.016	-0.113 to 0.032	-0.062 to 0.083	-0.122 to 0.008	-0.091 to 0.049	-0.041 to 0.097	-0.079 to 0.052	-0.134 to -0.006	
P^d	0.014	0.221	0.710	0.099	0.525	0.349	0.779	0.041	

Rho: Spearman rank correlation coefficient. [a] Chi-square test or Fisher test showed no significant variation among different vaccination status groups. [b] Chi-square test showed significant variation among different vaccination status groups in terms of menstrual period (χ2 = 16.591, *P* = 0.045) and menstrual change (χ2 = 11.540, *P* = 0.042). [c] The' reported no change' is coded as' 0 ', and the rest is coded as' 1'. [d] For spearman rank correlation coefficient

Compared with patients who did not report menstrual changes, participants who reported menstrual changes after COVID-19 were more likely to experience fever (χ2 = 10.571, *P* = 0.001), sore throat (χ2 = 9.697, *P* = 0.002), and headache (χ2 = 9.276, *P* = 0.002) during the acute phase (Table 5).

The average fever duration of the 784 participants was 2.33 ± 1.05 d. The fever duration of participants who experienced shortened menstrual after infection was 2.77 ± 1.31 d, indicating a statistically significant difference (excluding participants who had no fever; t = 2.112, *P* = 0.035).

Participants reporting menstrual changes and worsening dysmenorrhea after COVID-19 were more likely to undergo fatigue (χ2 = 6.225, *P* = 0.013 and χ2 = 11.175, *P* = 0.001), body weakness (χ2 = 5.016, *P* = 0.025 and χ2 = 3.988, *P* = 0.046), memory decline (χ2 = 14.404, *P* < 0.001 and χ2 = 18.925, *P* < 0.001), and insomnia (χ2 = 4.500, *P* = 0.034 and χ2 = 6.313, *P* = 0.012) after the acute phase (Table 6).

Factors related to changes in menstruation after infection with SARS-CoV-2

Participants reporting menstrual changes after SARS-CoV-2 infection (*n* = 442, 50.9%-group A) were compared to those reporting no change (*n* = 427, 49.1%- group B). The mean age was slightly lower in the - group A (31.85 ± 8.37 years) compared to the group B (32.93 ± 8.66 years), with a marginal difference (t = 1.856, *p* = 0.064).

Table 5 Rho analysis of relationships between menstrual characteristics and the most common symptoms in the Acute Phase—A Comprehensive Study of reported changes in menstruation, period, volume, and dysmenorrhea [*n*(%)]

Symptom, *n*(%)	Group A, *n* = 442							Group B[a, d,e], *n* = 427	Total
	Menstruation[a]		Period[b]		Volume[c]		Dysmenorrhea[c, e]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
Fever	164(20.9)[a]	37(4.7)	61(7.8)	26(3.3)	74(9.4)	113(14.4)	62(7.9)	371(47.3)[a]	784
Rho	0.095**	0.034	0.008	0.016	-0.012	0.033	0.077*	0.110**	
Rho 95%CI	0.046 to 0.14	-0.022 to 0.076	-0.059 to 0.066	-0.049 to 0.062	-0.081 to 0.056	-0.037 to 0.087	0.044 to 0.102	0.045 to 0.173	
P^c	0.005	0.317	0.813	0.633	0.732	0.336	0.023	0.001	
Cough	136(20.6)	32(4.8)	52(7.9)	20(3.0)	67(10.1)	95(14.37)	48(7.3)	313(47.4)	661
Rho	0.04	0.03	0.01	-0.02	0.035	0.017	0.001	0.064	
Rho 95%CI	-0.032 to 0.102	-0.039 to 0.084	-0.058 to 0.077	-0.091 to 0.045	-0.028 to 0.097	-0.05 to 0.081	-0.068 to 0.06	-0.006 to 0.127	
P^c	0.236	0.371	0.758	0.559	0.296	0.615	0.981	0.061	
Body aches and pains	113(19.7)	30(5.2)	48(8.3)	20(3.5)	65(11.3)[c]	86(15.0)	50(8.7)[c]	274(47.7)	575
Rho	-0.001	0.049	0.033	0.02	0.083*	0.037	0.078*	0.042	
Rho 95%CI	-0.076 to 0.061	-0.013 to 0.109	-0.035 to 0.099	-0.05 to 0.081	0.023 to 0.140	-0.029 to 0.100	0.015 to 0.131	-0.028 to 0.103	
P^c	0.979	0.147	0.325	0.550	0.014	0.277	0.022	0.221	
Sore throat	112(22.13)	22(4.3)	36(7.1)	14(2.8)	53(10.5	72(14.2)	41(8.1)	226(44.7)d	506
Rho	0.073*	-0.008	-0.026	-0.03	0.037	0.006	0.039	0.106**	
Rho 95%CI	0.002 to 0.14	-0.068 to 0.059	-0.092 to 0.04	-0.095 to 0.034	-0.029 to 0.101	-0.063 to 0.08	-0.03 to 0.102	0.04 to 0.177	
P^c	0.032	0.814	0.438	0.37	0.275	0.849	0.253	0.002	
Headache	103(20.6)	27(5.4)	45(9.0)	13(2.6)	55(11.0)	78(15.6)	46(9.2)[e]	223(44.7)[e]	499
Rho	0.028	0.052	0.057	-0.041	0.058	0.053	0.088**	0.103**	
Rho 95%CI	-0.043 to 0.095	-0.013 to 0.113	-0.007 to 0.122	-0.107 to 0.027	-0.008 to 0.122	-0.011 to 0.12	0.025 to 0.148	0.036 to 0.167	
P^c	0.407	0.127	0.093	0.232	0.087	0.117	0.009	0.002	

Rho: Spearman rank correlation coefficient. [a] Chi-square test showed the proportions of women with delayed menstruation (χ2 = 11.175, *P* = 0.004) and menstrual change (χ2 = 10.571, *P* = 0.001) were higher in the fever group than in the non-fever group. [b] Chi-square test showed no significant variation among groups with different symptoms. [c] Chi-square test showed that the proportions of women with increased menstrual volume (χ2 = 8.074, *P* = 0.018) and worse dysmenorrhea (χ2 = 5.285, *P* = 0.022) were higher in the group with body aches and pains than in the group with no body aches and pains. [d] Chi-square test showed the proportion of menstrual change (χ2 = 9.697, *P* = 0.002) in the sore throat group was higher in the no sore throat group. [e] Chi-square test showed that the proportions of worsen with dysmenorrhea (χ2 = 6.755, *P* = 0.009) and menstrual change (χ2 = 9.276, *P* = 0.002) were greater in the headache group than in the no-headache group

Body Mass Index (BMI) showed minimal variation between the two groups (t = 0.262, $p = 0.794$).

Significant disparities were observed in the prevalence of chronic diseases, with 72.3% in the group A compared to 27.7% in the group B (χ2 = 9.171, $p = 0.002$). Participants reporting menstrual changes had a higher mean number of vaccinations before infection (2.70 ± 0.74) compared to those without changes (2.55 ± 0.93) (t = 2.593, $p = 0.010$).

Moreover, the group A exhibited higher mean numbers of symptoms in both the acute (t = 6.304, $p < 0.001$) and recovery phases (t = 5.433, $p < 0.001$). The duration of fever was also significantly longer in the group A (2.25 ± 1.22 days) compared to the group B (1.96 ± 1.20 days) (t = 3.484, $p = 0.001$). These findings suggest that certain demographic and health-related factors may contribute to the likelihood of experiencing menstrual changes following SARS-CoV-2 infection (Table 7).

In Table 8, the multivariate logistic regression analysis explores factors associated with changes in menstruation after SARS-CoV-2 infection. Age demonstrated a non-significant negative association (Beta = -0.012, $p = 0.153$, OR = 0.988, 95% CI: 0.972–1.005). Chronic diseases exhibited a significant positive association (Beta = 0.954, $p = 0.005$, OR = 2.595, 95% CI: 1.327–5.075), indicating that participants with chronic diseases were more likely to experience menstrual changes. The number of vaccinations before infection showed a significant negative association (Beta = -0.197, $p = 0.022$, OR = 0.821, 95% CI: 0.694–0.972), suggesting that with each additional vaccine dose, the likelihood of menstrual changes decreased. The number of symptoms in the acute had a positive association (Beta = 0.139, $p = 0.001$, OR = 1.149, 95% CI: 1.062–1.243), indicating that a higher number of symptoms during the acute phase was associated with an increased likelihood of menstrual changes. Fever

Table 6 Rho Assessment of relationships between menstrual characteristics and the most common symptoms in the Post-acute Phase—A Comprehensive Study of reported changes in menstruation, period, volume, and dysmenorrhea [*n*(%)]

Symptom	Group A, *n* = 442							Group B[b], *n* = 427	Total
	Menstruation		Period		Volume		Dysmenorrhea[a]		
	Delayed	Advanced	Prolonged	Shortened	Increased	Decreased	Worsen		
Fatigue	118(21.5)	27(4.9)	41(7.5)	14(2.6)	62(11.3)	80(14.6)	49(8.9)[a]	246(44.8)[b]	549
Rho	0.060	0.027	-0.012	-0.050	0.078*	0.02	0.085*	0.113**	
Rho 95%CI	-0.006 to 0.128	-0.038 to 0.087	-0.083 to 0.053	-0.123 to 0.022	0.013 to 0.134	-0.043 to 0.087	0.023 to 0.141	0.044 to 0.18	
P	0.078	0.423	0.727	0.142	0.022	0.554	0.013	0.001	
Cough	93(19.7)	22(4.7)	32(6.8)	14(3)	46(9.8)	67(14.2)	39(8.3)	228(48.4)	471
Rho	0.002	0.01	-0.037	-0.015	0.008	0.006	0.043	0.016	
Rho 95%CI	-0.066 to 0.07	-0.058 to 0.077	-0.106 to 0.033	-0.083 to 0.053	-0.059 to 0.073	-0.068 to 0.074	-0.019 to 0.105	-0.049 to 0.086	
P	0.957	0.777	0.271	0.651	0.815	0.864	0.203	0.64	
Body weakness	74(21.0)	17(4.8)	21(5.9)	10(2.8)	40(11.3)	51(14.4)	34(9.6)[a]	159(45)[b]	353
Rho	0.027	0.013	-0.055	-0.018	0.05	0.01	-0.076*	0.068*	
Rho 95%CI	-0.037 to 0.094	-0.056 to 0.078	-0.122 to 0.011	-0.082 to 0.048	-0.018 to 0.119	-0.056 to 0.077	-0.142 to -0.008	0.001 to 0.132	
P	0.431	0.7	0.108	0.591	0.14	0.775	0.025	0.046	
Phlegm	69(21.9)	13(4.1)	21(6.7)	9(2.9)	34(10.8)	39(12.4)	28(8.9)	158(50.2)	315
Rho	0.042	-0.013	-0.029	-0.016	0.032	-0.036	0.048	-0.015	
Rho 95%CI	-0.022 to 0.109	-0.076 to 0.053	-0.095 to 0.034	-0.08 to 0.053	-0.034 to 0.1	-0.1 to 0.033	-0.019 to 0.125	-0.077 to 0.05	
P	0.214	0.699	0.385	0.646	0.348	0.289	0.16	0.65	
Memory decline	61(22.6)	14(5.2)	21(7.8)	7(2.6)	35(13.0)	45(16.7)	33(12.2)[a]	103(38.1)[b]	270
Rho	0.049	0.023	0.002	-0.024	0.078*	0.051	0.129**	0.148**	
Rho 95%CI	-0.015 to 0.113	-0.045 to 0.085	-0.061 to 0.066	-0.087 to 0.041	0.004 to 0.148	-0.017 to 0.121	0.056 to 0.199	0.079 to 0.21	
P	0.147	0.506	0.96	0.481	0.022	0.135	<0.001	<0.001	
Insomnia	49(22.3)	7(3.2)	13(5.9)	7(3.2)	20(9.1)	38(17.3)	23(10.5)[a]	92(41.8)[b]	220
Rho	0.038	-0.037	-0.039	-0.001	-0.009	0.054	0.072*	0.085*	
Rho 95%CI	-0.023 to 0.105	-0.093 to 0.03	-0.1 to 0.019	-0.064 to 0.072	-0.073 to 0.062	-0.015 to 0.118	0.003 to 0.144	0.019 to 0.151	
P	0.263	0.279	0.247	0.969	0.788	0.11	0.034	0.012	

Rho: Spearman rank correlation coefficient. [a, b] Chi-square test showed that the proportions of women with worsening dysmenorrhea and menstrual changes were more in participants who experienced fatigue ($\chi2 = 6.225$, $P = 0.013$ and $\chi2 = 11.175$, $P = 0.001$), weakness ($\chi2 = 5.016$, $P = 0.025$ and $\chi2 = 3.988$, $P = 0.046$), memory decline ($\chi2 = 14.404$, $P < 0.001$ and $\chi2 = 18.925$, $P < 0.001$), and insomnia ($\chi2 = 4.500$, $P = 0.034$ and $\chi2 = 6.313$, $P = 0.012$) compared to those who did not report these symptoms

duration exhibited a non-significant positive association (Beta = 0.089, $p = 0.148$, OR = 1.093, 95% CI: 0.969–1.234). The number of symptoms in the recovery phase showed a positive association (Beta = 0.071, $p = 0.032$, OR = 1.073, 95% CI: 1.006–1.144), suggesting that a greater number of symptoms during the recovery phase correlated with a higher likelihood of experiencing menstrual changes. These findings highlight the significance of various factors in influencing the occurrence of menstrual changes post SARS-CoV-2 infection.

Discussion

Since 2019, COVID-19 has had a significant impact on the health of those infected, including lingering symptoms post-infection. Following the COVID-19 epidemic, numerous women reported changes in their menstrual cycle via social networks. As a normal menstrual history is an integral part of a woman's healthy life, these changes can affect their quality of life. This system is still under study. Some studies suggest that the SARS-CoV-2 may damage ovarian tissue, reduce egg quality, and make it more difficult to fertilize [17]. In addition, other research has found that women infected with the SARS-CoV-2 may experience endocrine level disorders, menstrual disorders, and a decrease in ovarian reserve [18]. However, there are also some studies that show that the SARS-CoV-2 has no significant negative impact on human oocytes and early embryonic development [6]. These research results indicate that infection with SARS-CoV-2 before fertilization has no significant negative impact on

Table 7 Characteristics of participants stratified by whether they reported menstrual changes after SARS-CoV-2

Characteristics	Group A, *n* = 442, 50.9%	Group B, *n* = 427, 49.1%	t-value / χ2	*P*-value
Age (y), mean ± SD	31.85 ± 8.37	32.93 ± 8.66	1.856	0.064
BMI (kg/m^2), mean ± SD	22.96 ± 5.70	23.06 ± 6.05	0.262	0.794
Chronic diseases, *n*(%)	34(72.3)	13(27.7)	9.171	0.002
Number of vaccinations before infection, mean ± SD	2.70 ± 0.74	2.55 ± 0.93	2.593	0.010
Number of symptoms in the acute phase, mean ± SD	4.94 ± 2.16	4.03 ± 2.12	6.304	< 0.001
Fever duration (d), mean ± SD	2.25 ± 1.22	1.96 ± 1.20	3.484	0.001
Number of symptoms in the recovery phase, mean ± SD	4.37 ± 2.76	3.41 ± 2.44	5.433	< 0.001

oocytes and early embryonic development, but we still need to be vigilant about the impact during the acute infection period in women [6].

Further research is needed to fully understand these relationships and their implications for women's health. Some studies suggest that receiving the COVID-19 vaccine may affect menstrual cycle. These changes may include an increase in the length of menstrual cycle, as well as changes in bleeding. However, these changes are usually temporary and within normal ranges [19, 20]. There are two main hypotheses to explain this phenomenon: 1. The COVID-19 vaccine may affect the signaling between the hypothalamus, pituitary, and ovaries, causing the hypothalamus to release more estrogen, thereby prolonging the menstrual period. The COVID-19 vaccine may also affect macrophages and natural killer cells in the endometrium, affecting tissue repair, leading to an increase in menstrual bleeding [21, 22].

The dependent variable in the logistic regression analysis presented in Table 8 is "changes in menstruation after infection with SARS-CoV-2." The study found that individuals with chronic diseases were 2.595 times more likely to experience menstrual changes compared to those without chronic diseases. Conversely, with each additional vaccine dose, the likelihood of experiencing menstrual changes decreased by approximately 0.821 times. Chronic diseases can indeed have an impact on menstruation. For instance, hypothyroidism, or an underactive thyroid, can make menstrual cycles irregular, heavier, and less frequent [23]. Conditions that put long-term stress on the body can also cause fluctuations in the menstrual cycle [23]. In some cases, like with Crohn's disease, periods may become irregular and symptoms such as pain and diarrhea may increase during menstruation [24]. Other factors, such as the number of symptoms in the acute and recovery phases, were also significantly associated with menstrual changes. However, the impact of factors like age and the number of days with fever may not be significant in this study. It's important to note that all results are based on observational research, and other factors, such as the number of symptoms in the acute and recovery phases, were also significantly associated with menstrual changes. However, the impact of factors like age and the number of days with fever may not be significant in this study. It's important to note that all results are based on observational research, and there may be potential biases and unknown confounding variables. Menstruation is regulated by the hypothalamic–pituitary–ovarian axis and can be affected by external factors such as stress, infection, and medication.

On the other hand, age and fever duration did not demonstrate significant associations with menstrual changes in this study. The lack of significant findings regarding age may be surprising, as menstrual health is often affected by hormonal changes related to aging. Similarly, the non-significant association with fever duration raises questions about the specific impact of acute illness on menstrual cycles. Changes in menstruation characteristics after infection with SARS-CoV-2 may be related to several factors:

Firstly, SARS-CoV-2 infection might influence menstrual cycle by inducing acute stress. In states of acute disease, the reproductive system could be temporarily suppressed, leading to delayed menstruation or even amenorrhea [25]. A single-center retrospective study involving 117 hospitalized women of childbearing age with COVID-19 pneumonia found that these patients experienced short-term reversible changes in menstrual characteristics more frequently than the control group.

Table 8 Factors related to changes in menstruation after infection with SARS-CoV-2

Independent variables	Beta	SE	Wald	*P*-value	OR	95% CI
Age (Y)	−0.012	0.008	2.045	0.153	0.988	0.972–1.005
Chronic diseases	0.954	0.342	7.769	0.005	2.595	1.327–5.075
Number of vaccinations before infection	−0.197	0.086	5.239	0.022	0.821	0.694–0.972
Number of symptoms in the acute phase	0.139	0.040	11.917	0.001	1.149	1.062–1.243
Fever duration	0.089	0.062	2.092	0.148	1.093	0.969–1.234
Number of symptoms in the recovery phase	0.071	0.033	4.617	0.032	1.073	1.006–1.144

SE: Standard Error; OR: Odds ratio; CI: Confidence Interval

The presence of systemic complications in these women was strongly associated with changes in menstrual characteristics. Some patients experienced an increase in early follicular FSH and LH concentrations, suggesting possible ovarian suppression [6]. Although the menstrual cycle returned to normal within six months in most patients, the direct impact of viral clearance still needs to be considered.

Secondly, SARS-CoV-2 infection itself might cause menstrual changes. Many studies have suggested that women may experience abnormal menstruation after COVID-19 vaccination, but most of these changes are short-term and reversible [26, 27]. The ability of SARS-CoV-2 to damage a tissue depends on its ability to enter and infect cells in the tissue [28]. The entry point of SARS-CoV-2 into cells is angiotensin-converting enzyme 2 (ACE2) [28]. ACE2 expression in human ovaries [29] and endometrium [30] may be involved in the regulation of follicular development and endometrial regeneration. In a cross-sectional survey targeting 956 females infected with COVID-19, 6.4% of the patients had changes in menstrual characteristics that persisted for more than six months from the time of infection [31]. These prolonged changes in menstrual characteristics may be caused by COVID-19 rather than by transient stress.

Lastly, changes in psychological state, lifestyle, and diet may also cause changes in menstruation characteristics. The average scores in various psychological symptoms and the detection rate of positive symptoms in the population during the epidemic period were significantly higher than the reference level during non-epidemic periods [32–34]. Psychological stress is known to be one of the risk factors for hypothalamic amenorrhea, which may lead to dysfunction in GnRH pulses in the hypothalamus, leading to delayed menstruation or even amenorrhea [35–37]. A survey involving 1031 women found a significant increase in excessive menstruation, dysmenorrhea, and worsening premenstrual symptoms after the pandemic [37, 38]. The period before samples were collected in this study was the transitional period of the epidemic; this period may have affected the psychological state of women, leading to changes in menstruation characteristics [33]. Anxiety was not included as an independent variable in the analysis, but symptomatological features (such as insomnia, fatigue, etc.) indirectly reflected the effects of anxiety and stress, and the results showed that patients with insomnia had a higher rate of abnormal menstruation, although multivariate analysis did not show statistical significance. Given that the effects of anxiety on the menstrual cycle can be complex and individual, more precise assessment tools are needed to shed more light on its specific role.

Although several studies have explored the impact of COVID-19 on the female reproductive system, there is a lack of extensive investigations specifically focused on menstrual changes, COVID-19 symptoms, and vaccination status among the Chinese female population. Our study addresses this gap by providing a preliminary investigation into these factors within this specific group. This study addresses this gap by providing a sufficiently large sample size during March 2023, a period marked by a sharp increase in COVID-19 cases in China between the winter of 2022 and spring 2023. Furthermore, the study ensured that participants had relatively accurate recollections of their recent COVID-19 experiences and menstrual changes, thereby minimizing potential biases. These efforts contribute valuable data for further exploration of the effects of COVID-19 and its vaccination on the reproductive health of Chinese women.

While the study on COVID-19's impact on Chinese women's menstrual cycle provides valuable insights, several areas warrant improvement. The research primarily focuses on short-term effects, neglecting potential long-term consequences. Causation remains unclear, and a more rigorous design is needed to establish direct relationships. The participant pool lacks diversity in terms of geography and socio-economic backgrounds, limiting the generalizability of findings. The influence of psychological factors on menstrual changes is briefly discussed but could benefit from more in-depth exploration. Details on vaccine types are minimal, and a nuanced discussion on the ethical considerations of the study is absent. Furthermore, the bootstrap did not account for the BMI differences when calculating subgroup results. In future studies, we plan to further explore the relationship between different BMI groups (especially overweight and obese women) and menstrual changes. Finally, the self-report sample collection method may introduce bias itself. Addressing these aspects would enhance the study's reliability, depth, and applicability to a broader population, contributing to a more comprehensive understanding of the interplay between COVID-19, vaccination, and menstrual health in women.

Conclusion

Individuals with pre-existing chronic conditions, a lower number of vaccination doses, and a higher occurrence of COVID-19 symptoms may encounter more frequent fluctuations in their menstrual patterns according to the self-reported results in this survey. A more comprehensive understanding of the interplay between COVID-19, vaccination, and menstrual health in women is needed with a full consideration of psychological factors, long COVID, BMI differences, details on vaccine types, data collection method, and the diversity in terms of geography and socio-economic backgrounds.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-025-03592-8.

Supplementary Material 1

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Author contributions

1. Conception and design: YJ, YH; 2. Acquisition of data: YJ, YL; 3. Analysis and interpretation of data: YJ, YH, YL; 4. Drafting of the manuscript: YJ, YL; 5. Critical revision of the manuscript: YJ, YL; 6. Final approval of the manuscript: YJ, YL, YH.

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Data availability

The dataset analysed during the current study is not publicly available but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study subjects were non-amenorrheic adult Chinese females who had been infected with COVID-19 for the first time. This study adhered to the guidelines of the World Medical Association Declaration of Helsinki and received approval from the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University (approval number: 2023BL02-026-01). The survey was anonymous, and no personally identifiable data were collected. Participants who selected "agree" in the online survey were considered to have given informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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