

An investigative study of persistent symptoms and menstrual abnormalities in female students infected with COVID-19 at a university in Chongqing, China

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Abstract: In order to investigate the general conditions of female students infected with COVID-19 (2019 Novel Coronavirus) in a college in Chongqing, China, and the impacts of persistent symptoms on female menstruation, we conducted a questionnaire survey among female students in a college in Chongqing from February 1 to 28, 2022. We collect information from female students at a university in Chongqing after the first wave of COVID-19 infections following the loosened epidemic policies, including general information (age, height, weight, smoking and alcohol consumption history, medical history, and coronavirus vaccination states), general conditions of coronavirus infection, persistent symptoms after infection, and menstrual conditions (menstrual flow, menstrual cycle, menstrual duration, menstrual blood characteristics, dysmenorrhea, dysmenorrhea duration, and physical discomfort). SPSS26.0 statistical software was used to analyze menstrual conditions using the chi-square and rank-sum tests. The results showed that among the persistent symptoms after COVID-19 infection, the proportion of female students at a university in Chongqing who had dyspnea, cough, and chest tightness was 63.64%, generalized fatigue was 56.82%, and neurological and digestive symptoms were 55%. After infection, students with prolonged menstrual cycles significantly increased ($p < 0.05$), those with regular menstrual flow significantly decreased ($p < 0.05$), yet physical discomfort during menstruation significantly reduced ($p < 0.05$). There were no statistically significant differences between menstrual blood characteristics, menstrual duration, dysmenorrhea, and dysmenorrhea duration ($p > 0.05$) before and after infection. This study found that the persistent symptoms of COVID-19 infection include dyspnea, cough, chest tightness, generalized fatigue, and neurological and digestive symptoms. They caused changes in some menstrual conditions, such as menstrual cycle, menstrual flow, and physical discomfort. But whether there are long-term effects remains to be determined and further research is needed.

1. Introduction

Since the COVID-19 outbreak, it has become a global public health emergency due to its wide

range of infections and high mortality rates, seriously threatening people's health and lives[1]. With countries' continuous research on COVID-19, widespread use of vaccines, and various effective preventive and therapeutic measures in recent years, death rates have seen a remarkable decline compared to the severe damage caused early to the respiratory and immune systems of those infected. On December 7, 2022, a notice by the Comprehensive Team for Joint Prevention and Control Mechanism for COVID-19 under the Chinese State Council of "Further Optimizing the Prevention and Control of COVID-19" marked the full lift of prevention and control policy bans in China.

After infection, most patients recovered about 10 days after treatment. However, some patients still developed long-term clinical symptoms involving multiple systems and organs, among which persistent dyspnea was one of the most common persistent symptoms [2,3]. On March 1, 2022, the National Institute for Health and Care Excellence (NICE) published "COVID-19 Rapid Guideline: Managing the long-term effects of COVID-19," classifying long COVID into signs and symptoms from 4 to 12 weeks after infection or consistent for more than 3 months which is defined as "post-COVID-19 syndrome" by the World Health Organization [4]. According to the duration of symptoms, long COVID consists of two phases: (1) ongoing symptomatic COVID-19 (4-12 weeks) and (2) post-COVID-19 syndrome (>12 weeks).

In addition to persistent dyspnea, other persistent symptoms include sore throat, fever, nasal congestion, cough, and generalized body aches and pains [5]. Few patients develop severe illnesses inducing life-threatening dyspnea. Large numbers of previous studies have shown that persistent symptoms after infection (post-COVID-19 syndrome) can involve many human body systems, mainly characterized by varying degrees of physical, cognitive, and emotional disturbances [6] and manifested as persistent fatigue, weakness, taste or smell dysfunction, sleep disorders, anxiety, depression, headache, etc.,[7] with higher prevalence in females.[8]

Menstruation is an essential indicator of female health. [9] Menstrual disorders are the most common female endocrine diseases occurring in adolescence, also known as adolescent functional uterine bleeding, which seriously affects physical and mental health. [10] Observational studies have found that early menarche onset, dysmenorrhea, and abnormal cycles not only reduce quality of life but also increase non-suicidal self-harming behaviors. [9]

Many viruses impact the female reproductive endocrine system. [10,11] Previous studies verified that due to typical receptors, the reproductive system may be a target organ for viral infection in addition to respiratory, cardiovascular, and digestive manifestations in patients after COVID-19 infections. [12] Moreover, infection could elevate glucocorticoids, leading to abnormal ovulation and menstrual disorders. [13] Some females experience transient changes in menstruation during COVID-19 infection, noticing a decrease in menstrual flow and an abnormal color [12-15]. After infection, some see menstrual cycle changes, with a significant increase in menstrual disorders, amenorrhea, and changes in menstrual duration. [14]

The continuous virus mutation also changes the effects on female reproductive systems. We designed to collect menstrual information after COVID-19 infection from female students at a university in Chongqing to conduct a preliminary study and understand the current COVID-19 impacts on menstrual status.

2. Study Subjects and Methods

2.1 Data Source and Sample

From February 1 to 28, 2022, we delivered self-administered questionnaires to female students at a university in Chongqing. We collected menstrual information after the first wave of COVID-19 infection following the loosened prevention and control policies in China. We selected female students infected during this first wave as our study subjects, with 152 effective questionnaires

collected through class group chats. The inclusion criteria were (1) attending our target university in Chongqing, (2) female students, and (3) being infected during the first wave.

2.2 Questionnaire Content

Baseline Data: age, height, weight, smoking and alcohol history, medical history, and COVID-19 vaccination

COVID-19 Infection: general conditions during infection and persistent symptoms after infection.

Menstrual Information: menstrual flow, cycle, duration, physical discomfort, blood characteristics, dysmenorrhea, and dysmenorrhea duration. Menstrual cycle, menstrual flow, and dysmenorrhea are classified according to the 9th edition of the Clinical Medicine "Obstetrics and Gynecology" guidelines. Menstrual cycle: The average menstrual cycle is 21-35 days; less than 21 days are too short; more than 35 days are too long; no menstruation or repeated twice or more within one month is considered abnormal menstruation. Menstrual flow: It is mainly determined by the number of sanitary pads used; 20 or more are excessive menstrual flow; 5-20 are normal; 5 or less are too low. Dysmenorrhea: It is divided into four levels: Level 1 for no dysmenorrhea, level 2 for mild pain without medication, level 3 for improvement after medication, and level 4 for no gain after medication.

2.3 Statistical Analysis

We organized data using Excel and performed statistical analyses using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). We conducted the normality test to express continuous data conformed to a normal distribution as mean \pm standard deviation. Discrete count data was expressed as n (%). Comparisons before and after COVID-19 infection were performed by paired chi-square and rank-sum tests. Statistical significance was indicated by $p < 0.05$.

3. Results

3.1 Baseline Characteristics

Table 1: Baseline Characteristics of Study Subjects

| | |
|----------------------|-------------------|
| Basic Information | |
| Age (years) | 20.4 \pm 1.4 |
| Height (cm) | 161.66 \pm 5.38 |
| Weight (Kg) | 55.66 \pm 11.97 |
| Smoking | |
| Yes | 5(3.29%) |
| No | 147(96.71%) |
| Alcohol | |
| Yes | 25(16.45%) |
| No | 127(83.55%) |
| Medical History | |
| Yes | 13(8.55%) |
| No | 139(91.45%) |
| COVID-19 Vaccination | |
| Yes | 152(100%) |
| No | 0 |

The study subjects were female students from a university in Chongqing, totaling 152. Age

20.4±1.4 years, height 161.66±5.38 cm, weight 55.66±11.97 kg, 5 smoked, 25 alcohol consumption, 13 with medical histories, and all received COVID-19 vaccines. See Table 1.

3.2 COVID-19 Infection Status

3.2.1 Duration of acute symptoms

152 study participants, 42 (27.63%) had symptoms for 1-3 days, 54 (35.53%) had symptoms for 4-6 days, 35 (23.03%) had symptoms for 7-9 days, and 21 (14%) had symptoms for more than 7 days. See Table 2.

Table 2: Duration of Acute Symptoms

| Duration | Subjects (n) | Percentage |
|----------|--------------|------------|
| 1-3 days | 42 | 27.63% |
| 4-6 days | 54 | 35.53% |
| 7-9 days | 35 | 23.03% |
| >9 days | 21 | 14% |

3.2.2 Medications Intake

152 enrolled, 119 (85.61%) were taking antidotes and analgesics, 45 (32.37%) were taking cold and flu remedies, and 43 (30.94%) were taking expectorant and cough remedies. See Table 3.

Table 3: Medication Status

| Drug Type | Subjects (n) | Percentage |
|----------------------|--------------|------------|
| Antidotes&Analgesics | 119 | 85.61% |
| Cold&Flu | 45 | 32.37% |
| Expectorant&Cough | 43 | 30.94% |

3.2.3 Persistent symptoms (4-12 weeks after infection)

Generalized weakness in 25 (56.82%), dyspnea, cough, and chest tightness in 28 (63.64%), neurological symptoms and digestive symptoms in 27 (55%). See Table 4.

Table 4: Persistent Symptoms after COVID-19 Infection

| Symptoms | Subjects (n) | Percentage |
|---------------------------------|--------------|------------|
| Generalized Weakness | 25 | 56.82% |
| Dyspnea, Cough, Chest Tightness | 28 | 63.64% |
| Neurological&Digestive | 27 | 55% |

3.3 Menstrual Changes Before and After COVID-19 Infection

3.3.1 Menstrual flow

Table 5: Menstrual Flow Changes Before and After COVID-19 Infection (n=152)

| Flow | Before Infection | After Infection | p-value |
|----------|------------------|-----------------|---------|
| Too much | 7 | 12 | 0.125 |
| Normal | 143 | 134 | 0.022 |
| Too low | 2 | 6 | 0.219 |

Subjects with normal menstrual flow statistically decreased ($p < 0.05$). See Table 5.

3.3.2 Menstrual blood characteristics

Subjects with standard color without clots decreased by 4, dark color with clots decreased by 4, dark color without clots increased by 6, and standard color with clots increased by 2. The difference in menstrual blood characteristics before and after infection was insignificant ($p>0.05$). See Table 6.

Table 6: Blood Characteristics Changes Before and After COVID-19 Infection (n=152)

| Characteristics | Before | After | p-value |
|------------------------|--------|-------|---------|
| Standard without clots | 106 | 102 | 0.454 |
| Dark with clots | 11 | 7 | 0.388 |
| Dark without clots | 4 | 10 | 0.109 |
| Standard with clots | 31 | 33 | 0.791 |

3.3.3 Menstrual cycle

Subjects with regular menstrual cycles decreased by 11, short menstrual cycles increased by 5, prolonged menstrual cycles increased by 12 ($p<0.05$), and irregular cycles decreased by 6. There are statistically significant differences in menstrual cycles before and after infection ($p<0.05$). See Table 7.

Table 7: Menstrual Cycle Changes Before and After COVID-19 Infection (n=152)

| Cycle | Before Infection | After Infection | p-value |
|-----------|------------------|-----------------|---------|
| Normal | 119 | 108 | 0.072 |
| Short | 1 | 6 | 0.063 |
| Prolonged | 9 | 21 | 0.012 |
| Irregular | 23 | 17 | 0.286 |

3.3.4 Menstrual Duration

Subjects with standard menstrual duration decreased by 3, prolonged duration decreased by 1, and irregular duration increased by 3. The difference in menstrual duration before and after infection was insignificant ($p>0.05$). See Table 8.

Table 8: Menstrual Duration Changes Before and After COVID-19 Infection (n=152)

| Duration | Before Infection | After Infection | p-value |
|-----------|------------------|-----------------|---------|
| Normal | 139 | 136 | 0.607 |
| Too short | 1 | 2 | 1.000 |
| Prolonged | 8 | 7 | 1.000 |
| Irregular | 4 | 7 | 0.250 |

3.3.5 Dysmenorrhea and Duration

Table 9: Dysmenorrhea Changes Before and After COVID-19 Infection (n=152)

| Pain Level | Before Infection | After Infection | p-value |
|------------|------------------|-----------------|---------|
| No pain | 37 | 44 | 0.118 |
| Mild | 79 | 77 | 0.845 |
| Moderate | 33 | 29 | 0.424 |
| Severe | 3 | 2 | 1.000 |

Subjects without pain increased by 7, mid pain decreased by 2, moderate pain decreased by 4, and

severe pain decreased by 1. The difference in dysmenorrhea before and after infection was insignificant. ($p > 0.05$) See Table 9 and Table 10.

Table 10: Dysmenorrhea Duration Changes Before and After COVID-19 Infection (n=152)

| Dysmenorrhea Duration | Before Infection | After Infection | p-value |
|-----------------------|------------------|-----------------|---------|
| 1 day | 56 | 56 | 1.000 |
| 2 days | 34 | 31 | 0.549 |
| 3 days | 13 | 17 | 0.125 |
| 4 days and more | 1 | 0 | 1.000 |

3.3.6 Physical discomfort during menstruation

Subjects experienced physical discomfort decreased by 16 ($p < 0.05$) before and after infection. See Table 11.

Table 11: Physical Discomfort During Menstruation Changes Before and After COVID-19 Infection (n=152)

| Physical Discomfort | Before Infection | After Infection | p-value |
|---------------------|------------------|-----------------|---------|
| Yes | 23 | 7 | 0.002 |
| No | 129 | 145 | |

4. Discussion

Our study focuses on the impacts of persistent symptoms on female menstruation after the first wave of COVID-19 infection at the end of 2022 since the loosened prevention and control policies in China. The results of the duration of acute symptoms after infection showed that 42 (27.63%) had symptoms for 1-3 days, 54 (35.53%) had symptoms for 4-6 days, 35 (23.03%) had symptoms for 7-9 days, and 21 (14%) had symptoms for more than 7 days. The results of persistent symptoms (4-12 weeks after infection) manifested that 25 (56.82%) had generalized weakness, 28 (63.64%) had dyspnea, cough, and chest tightness, and 27 (55%) had neurological and digestive symptoms. Therefore, symptoms are primarily respiratory related, reminding us of respiratory protection, especially students with previous respiratory medical histories should protect themselves from deterioration by COVID-19 infections. Some studies have revealed that COVID-19 symptoms involve respiratory, circulatory, neurological, digestive, and psycho-cognitive systems with varying duration and severity. [7,16,17]

After infection, changes in some female menstrual indicators are statistically significant. Subjects with prolonged menstrual cycles significantly increased ($p < 0.05$), while regular menstrual flow significantly decreased ($p < 0.05$). Our results are consistent with Tingting Lu et al. [5] that some female patients experience prolonged or shorter menstrual cycles and menstrual blood characteristics change after COVID-19 infection. The study by K. Z. Li et al. [18] also illustrated transient changes in prolonged menstrual cycles and decreased menstrual flow in patients after infection. Li Rong et al. [19] indicated that SARS-CoV-2 can invade target host cells via ACE2 (angiotensin-converting enzyme 2) receptor and serine protease, which are abundantly expressed in the reproductive system. Therefore, the impacts of COVID-19 infection on female reproductive health are present. However, decreases in dysmenorrhea and physical discomfort ($p < 0.05$) may be due to three reasons: first, patients take medications after COVID-19 infection. Second, patients experience nerve paralysis, which decreases body perception and sensitivity after infection. Third, patients concurrently

experience other illnesses, diverting their attention from menstruation.

Besides COVID-19, there might be other risk factors for abnormal menstruation. Since the pandemic, significant increases have been observed in reported acute mental health problems. Research displays that up to 84% of females experienced at least one mental health symptom, with low mood, anxiety, and insomnia being the most common[20]. Furthermore, it has been discovered that the COVID-19 pandemic increases stress levels and tension to the extent that these symptoms impact the female menstrual cycles. The hypothalamic–pituitary–adrenal (HPA) axis is sensitive to stressors (e.g., war, dilemmas, and anxiety), leading to changes in hormonal pulsation mechanisms and affecting female menstrual cycles. [21] Moreover, decreases in exercise, irregular diets, and weight gain are associated with higher abnormal menstruation probabilities. [22,23] Daily physical activity is linked to increased insulin sensitivity and body weight maintenance, which can help regulate the menstrual cycle. There is growing evidence that healthy behaviors, including alterations in alcohol use, food, and physical exercise, might affect the menstrual cycle. Lockdowns and quarantines were designed to mitigate the COVID-19 pandemic that limited movement and caused annoyance for everyone. As a result, ordinary, moderate physical activity can contribute to regular menstruation, although there is a need to remain mindful of the importance of self-protection during this pandemic. Finally, female college students usually have irregular routines, poor sleeping habits and sleep quality, poor exercise habits, higher stress sensitivity, poor rest during menstruation, etc., all contributing to abnormal menstruation. [24-26]

There is no precise treatment for menstrual abnormalities after COVID-19 infection. Hence, female students must raise their awareness of self-health management, increase physical exercise, develop living habits, improve sleep quality, and reduce mental stress.

There are some limitations in this study. Firstly, the subject pool is small, which may cause some bias. Secondly, this study only collects data from female students in one university. If we want to know the menstrual abnormalities after COVID-19 infection among all female students in universities in Chongqing, we must expand our study population.

5. Conclusion

In this study, we found that among persistent COVID-19 symptoms experienced by female students at a university in Chongqing, the number of those who had respiratory distress, cough, and chest tightness was 63.64%, generalized fatigue was 56.82%, and neurological and digestive symptoms were 55%. There was an increase in prolonged menstrual cycles, a decrease in menstrual flow, and a decrease in physical discomfort during menstruation. This study provides primary data with a reference value to understand the impacts of COVID-19 infection on menstruation in female college students. It gives suggestions to help improve menstrual abnormalities and promote health in female college students. Further studies are needed to explore the long-term effects of COVID-19 on female menstruation.

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