

Evaluation of the menstrual cycle of female infected with SARS-CoV-2 in women aged 36 to 45 years in Iranian society

Evaluación del ciclo menstrual de mujeres infectadas con SARS-CoV-2 en mujeres de 36 a 45 años en la sociedad iraní

Faegeh Miryousefiata¹, Ruhollah Khalil Arjmandi² 

1. Medical Student, Osmangazi University, Eskisehir, Turkey

2. Department of Medicine (M.D), Qom Branch, Islamic Azad University, Qom, Iran

Corresponding author

Ruhollah Khalil Arjmandi

E-mail: ruholla.arjmandi@yahoo.com

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Abstract

Introduction: The menstrual cycle's effects on illness susceptibility, development, and severity of acute respiratory syndrome coronavirus 2 (SARSCoV2) infection are poorly understood. It is estimated that more than a third of regularly menstruating women developed irregular cycles during the pandemic, with associated depression, anxiety, and stress. Another study indicates that among patients with confirmed COVID-19, a quarter have altered bleeding.

Methods: The results of real-time reverse transcriptase polymerase chain reaction (RTPCR) tests and symptoms in two women infected with SARSCoV2 are described in this paper.

Results: After being discharged from the hospital, the first patient experienced a fever on the first day of her menstrual period and again on the first day of her following menstrual period. The findings of the RTPCR test were positive during the first menstrual period before to admission, then went negative during hospitalization, and then were positive again during the second menstrual period following release. After being released from the hospital, another woman experienced a fever on the first day of her monthly period. Before admission and during hospitalization, the RTPCR test was negative, but it became positive during the first menstrual period after discharge.

Conclusions: According to the cases, SARSCoV2 infection may be aided by sex hormones. The menstrual status of women who have been exposed to SARSCoV2 should be assessed as part of the care procedure.

Key words: COVID-19, fever, menstrual cycle, SARS-CoV-2.

Resumen

Introducción: Los efectos del ciclo menstrual sobre la susceptibilidad, el desarrollo y la gravedad de la infección por coronavirus 2 del síndrome respiratorio agudo (SARSCoV2) son poco conocidos. Se estima que más de un tercio de las mujeres que menstrúan regularmente desarrollaron ciclos irregulares durante la pandemia, con depresión, ansiedad y estrés asociados. Otro estudio indica que entre los pacientes con COVID-19 confirmado, una cuarta parte tiene sangrado alterado.

Metodología: En este artículo se describen los resultados de las pruebas y los síntomas de la reacción en cadena de la polimerasa con transcriptasa inversa en tiempo real (RTPCR) en dos mujeres infectadas con SARSCoV2.

Resultados: Después de ser dada de alta del hospital, la primera paciente experimentó fiebre el primer día de su período menstrual y nuevamente el primer día de su siguiente período menstrual. Los resultados de la prueba RTPCR fueron positivos durante el primer período menstrual antes de la admisión, luego fueron negativos durante la hospitalización y luego fueron positivos nuevamente durante el segundo período menstrual después del alta. Después de ser dada de alta del hospital, otra mujer experimentó fiebre el primer día de su período menstrual. Antes del ingreso y durante la hospitalización, la prueba RTPCR fue negativa, pero se volvió positiva durante el primer período menstrual después del alta.

Conclusiones: Según los casos, las hormonas sexuales pueden ayudar a la infección por SARSCoV2. El estado menstrual de las mujeres que han estado expuestas al SARSCoV2 debe evaluarse como parte del procedimiento de atención.

Palabras clave: COVID-9, fiebre, ciclo menstrual, SARS-CoV-2.

Introduction

The COVID-19 epidemic is already in its seventh month over the world. Infections with the novel SARS-CoV-2 virus are on the rise globally, with increasing numbers of mortality. International and local public health reactions came almost simultaneously, imposing limits to prevent the virus from spreading, overburdening health systems, and a lack of personal protective equipment.

Since December 2019, the 2019 new coronavirus infection (COVID19), caused by the severe acute respiratory syndrome coronavirus 2 (SARSCoV2), has become a major worldwide health issue. The pandemic had resulted in 9 473 214 illnesses and 484 249 fatalities as of June 27, 2020. ⁵ A population-level observational investigation by Sun et al ⁶ found a substantial increase in COVID19 among adults aged 30 to 50 years, with 40% of the patients being female, indicating that women of childbearing age are at high risk of infection. Female immunity appears to alter throughout the menstrual cycle, according to growing research. The menstrual cycle's effects on illness susceptibility, development, and severity of COVID19, on the other hand, remain mainly unclear. We provide the epidemiologic and clinical characteristics of two female SARSCoV2 infected individuals, as well as the infection's relationship to the menstrual cycle.¹

On January 12, 2020, a 37-year-old lady who had previously been healthy (gravida 2, para 2, regular menstrual cycle, and no history of hormonal therapy) had supper with a relative. Her relative developed a fever five days later and was diagnosed with SARSCoV2. Until the first day of her menstrual period on January 28, 2020, the woman experienced no fever or other gastrointestinal or respiratory symptoms. She had a mild and sporadic fever at initially. She experienced a high fever, fatigue, and a lack of appetite the next day afternoon.

A community physician prescribed ibuprofen, oseltamivir (75 mg every 12 hours orally), arbidol (0.2 g every 8 hours orally), and moxifloxacin (0.4 g every day orally) due to the likelihood of SARSCoV2 infection. Her antiviral regimen was supplemented two days later with lopinavir and ritonavir tablets (200 mg/50 mg every 12 hours orally). Her symptoms persisted, prompting her to visit the emergency department on February 2, 2020. Despite the fact that chest auscultation was normal, chest CT scans revealed bilateral lower lobe infiltrates .

She was recommended ibuprofen, oseltamivir (75 mg every 12 hours orally), arbidol (0.2 g every 8 hours orally), and moxifloxacin (0.4 g every day orally) by a community physician due to the likelihood of infection with SARSCoV2. Her antiviral regimen was supplemented 2 days later with lopinavir and ritonavir tablets (200 mg/50 mg orally every 12 hours). Her symptoms persisted, prompting her to seek medical help on February 2, 2020.

Chest computerized tomography (CT) scans revealed bilateral lower lobe infiltrates, despite the fact that chest auscultation was normal .

The patient was admitted to the hospital with COVID19 on February 4, 2020. On admission, the physical examination revealed a body temperature of 97.5 degrees Fahrenheit (36.4 degrees Celsius), blood pressure of 98/61 millimeters of mercury, pulse rate of 78 beats per minute, respiration rate of 20 breaths per minute, and oxygen saturation of 95 percent on room air. Her laboratory tests revealed a Creative protein count of 12.3 mg/L (low risk of cardiovascular disease: 1 mg/L; medium risk of cardiovascular disease: 13 mg/L; high risk of cardiovascular disease: >3 mg/L; and infection or inflammation: >10 mg/L) and an erythrocyte sedimentation rate of 30 mm/H (normal range: 10-30 mm/H).

Complete blood count, coagulation tests, liver function tests, kidney function tests, metabolic panel testing, and high-sensitivity cardiac troponin tests did not yield any clinically relevant results. On February 8, 2020, a follow-up chest CT scan revealed that the shadow on both lungs had partially disappeared (Figure 2B). As a result, she was taken off all of her antiviral and antibacterial drugs. Three- and six-days following admission, RTPCR testing for SARSCoV2 nucleic acid on oropharyngeal swabs were done, and the findings were positive.²

The oropharyngeal swab RTPCR tests were repeated 10- and 12-days following hospitalization, and both times the results were negative. A subsequent chest CT scan on February 14, 2020, revealed that groundglass opacification had improved even more. During her stay in the hospital, her temperature stayed normal. This patient was discharged on February 18, 2020, based on Iranian hospital discharge criteria, which included (a) a normal temperature for at least three days, (b) resolution of respiratory symptoms, (c) significantly improved radiological signs, and (d) negative results in two consecutive RTPCR tests performed more than or equal to 24 hours apart.³

The patient was asked to stay in quarantine at home for another 14 days after being released from the hospital. She felt fine till the first day of her monthly cycle on February 24, 2020. The patient did not report any other interaction, although he did develop a fever, which peaked at 100.2°F (37.9°C). She had no additional symptoms at the time save exhaustion. For three days, she took arbidol (0.2 g orally every 8 hours) and moxifloxacin (0.4 g orally every day). A RTPCR test on February 25, 2020, and a follow-up test on oropharyngeal swabs four days later both came back positive. Chest CT scans, on the other hand, revealed no alterations from the previous results. Until the last day of her menstrual period on February 29, 2020, the patient experienced a minor and intermittent

fever. Her temperature had stayed normal since then. On 10 oropharyngeal swabs, the RTPCR test was done.

A 45-year-old lady working as a nurse in a hospital in Qom, Iran, was previously healthy (gravida 1, para 1, regular menstrual cycle, and no history of hormonal therapy). She developed a mild fever on January 24th, with a high of 100.4°F (38°C) at night. She was prescribed arbidol (0.2 g every 8 hours orally) by a physician due to the likelihood of infection with SARSCoV2 due to occupational contact history. She suffered weariness, muscle discomfort, palpitation, and a lack of appetite on January 26, 2020, the first day of her menstrual period. During her menstrual month, she continued to take arbidol, but her symptoms did not improve. The patient was admitted to a hospital's outpatient department on February 2nd.

Multiple infiltration was seen in the bilateral lung view on chest CT images. A blood test revealed a white blood cell count of 3.88 10⁹/L and a lymphocyte count of 0.94 10⁹/L. Despite the fact that an oropharyngeal swab RTPCR test came back negative, the woman was diagnosed with COVID19 based on her occupational exposure history, symptoms, and chest CT findings. The patient was admitted to the hospital with COVID19 on February 3, 2020. On admission, the physical examination revealed a body temperature of 99.5 degrees Fahrenheit (37.5 degrees Celsius), blood pressure of 105/85 millimeters of mercury, pulse rate of 110 beats per minute, respiration rate of 20 breaths per minute, and oxygen saturation of 94 percent on room air. Her lab tests revealed a Creactive protein concentration of 14.8 mg/L and an erythrocyte sedimentation rate of 40 mm/H. The serum specific IgM antibodies to eight respiratory pathogens, including respiratory syncytial virus, adenovirus, type A and type B influenza virus, parainfluenza virus, Legionella pneumophila, Mycoplasma pneumoniae, and Chlamydia pneumoniae, were found to be negative. After her admission, her temperature returned to normal the next day.

All of her antibacterial meds had been revoked. On February 8, 2020, a follow-up chest CT scan revealed decreasing infiltration in both the left and right lungs. Three, seven, nine-, and eleven-days following admission, RTPCR testing for SARSCoV2 nucleic acid on oropharyngeal swabs were done, and the results were negative. A repeat chest CT scan on February 14, 2020, revealed considerable improvement in infiltration in all lesions. During her stay in the hospital, her temperature stayed normal. The patient was ordered to stay at home for 14 days after being discharged from the hospital on February 18, 2020. She felt fine till the first day of her monthly cycle on February 21, 2020. Her fever returned, this time with weariness and dizziness, reaching 99.3°F (37.4°C). For 5 days, she took arbidol (0.2 g orally every 8 hours) and moxifloxacin (0.4 g orally every day). On February 23, 2020, an RTPCR test for SARSCoV2 nucleic

acid on oropharyngeal swabs yielded positive results. Both IgG and IgM antibodies against SARSCoV2 were found in her blood. Chest CT scans, on the other hand, revealed no signs of increasing invasion. The patient had a mild and intermittent fever till February 25, 2020, the day before her menstrual period ended. Her temperature had stayed normal since then. On February 28, 2020, an oropharyngeal swab was tested for RTPCR, and the results were negative.

Discussion and Conclusions

There have been reports of sex variations in infectious illness susceptibility and outcomes. 9 and 10 SARSCoV2 may have a longer incubation period and less apparent symptoms in women than in men, according to a recent epidemiological investigation of the COVID19 outbreak. 11 The mechanism behind these distinctions, however, is unknown. In this paper, we describe two SARSCoV2 infected women whose RTPCR test findings and symptoms altered during their menstrual cycle. After being discharged from the hospital, the first patient experienced a fever on the first day of her menstrual period and again on the first day of her following menstrual period. The RTPCR test was positive during the first menstrual period before admission, turned negative during hospitalization, and then returned to positive during the second menstrual period following release.⁴

After being discharged from the hospital, another woman got a fever on the first day of her menstrual period. Before admission and during hospitalization, the RTPCR test was negative, but it became positive during the first menstrual period after discharge. These findings suggest that sex hormones may play a role in SARSCoV2 infection.

The levels of sex hormones, primarily estrogens and progesterone, fluctuate over the menstrual cycle in female humans and drop rapidly before menstruation. 12 Changes in immunological function and response to respiratory virus infections are linked to substantial fluctuations in sex hormone levels. 13 Estrogen has been shown to be a strong anti-inflammatory hormone that reduces adaptive immune responses and protects hosts from influenza A virus-mediated pathogenesis in an animal model of influenza A virus infection.⁵

Treatment with an oestrogen receptor antagonist or ovariectomy can increase mortality in females in another animal model of SARSCoV infection, demonstrating that oestrogen receptor signaling is important in shielding females against severe SARSCoV infection. 15 in line with earlier research, our findings in this case revealed a strong link between symptoms, positive RTPCR test results, and menstruation. The observations of Chadchan et al. may help to explain this phenomenon. 16 They discovered that in human endometrial stroma,

the expression of angiotensin converting enzyme 2 (ACE2), which allows SARSCoV2 to enter human cells, is high and increases throughout the secretory phase^{6&7}. Progesterone also promotes ACE2 expression in the human endometrial stroma. Future research should focus on the role and mechanism of sex hormones in the pathogenesis of SARSCoV2 infection. In the first example, the fever started on the first day of her period and went away on the last day. When menstruation began in the second case, symptoms intensified. These findings show that the menstrual state should be taken into account during the observation period. Rather than symptoms, the findings of RTPCR testing or CT scans should be used to identify potentially infected patients throughout the observation period.^{8&9}

During their first menstrual period after being discharged from the hospital, the patients in this study experienced a return of fever and had positive RTPCR test results. Despite the possibility that negative RTPCR test findings during hospitalization are false negatives, 17 there are an increasing number of reports of positive RTPCR test results among COVID convalescent patients 19. 18, 19, 20 These findings show that some of the rehabilitated patients may still be viral carriers. The hospital discharge management strategy may need to be reevaluated, and female patients' menstruation status should be assessed during the 14-day home quarantine period.

Conflict of Interest

The authors declare that they have no conflict of interest.

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