International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2024; 8(4): 38-41
Received: 26-05-2024
Accepted: 30-06-2024

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Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age

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DOI: https://doi.org/10.33545/gynae.2024.v8.i4a.1493

Abstract
Background: People are worried about how the coronavirus outbreak will affect women's reproductive systems, especially their ability to get pregnant and have regular periods. Menstrual cycles can be changed by things like stress, endocrine problems, gynaecological conditions, autoimmune diseases, genetics, infections, and changes in living.
Objectives: This study aimed to analyze menstrual pattern changes in reproductive-aged women post-COVID-19 infection and determine changes in sex hormones during the pandemic.
Patients and Methods: 125 women ages 16 to 45 who had a COVID-19 infection in the last 3 to 6 months took part in a pro-retrospective study from May 1, 2020, to November 1, 2022. People who used hormonal treatment, had polycystic ovary syndrome, endometriosis, uterine fibroids or polyps, pelvic adhesions, pelvic inflammatory disease, or main ovarian failure were not allowed to participate. There was also a comparison group of 90 healthy women who did not have COVID-19. Hormone levels and menstrual history were checked for 90 women who were affected.
Results: Out of 135 subjects (median age 34±2 years) with COVID-19 infection, 76 had mild and 59 had moderate to severe infection. Moderate-severe individuals had 28 comorbidities compared to 6 in mild ones. Of the 88 individuals, 43 were overweight, 37 obese, and 8 severely obese. Diabetes, hypertension, and heart disease differed between mild and moderate-severe patients. Moderate-severe patients were hospitalised more. More than half of subjects reported menstruation alterations during the pandemic, with 27% of mild and 41% of moderate-severe groups reporting higher volume.
Conclusion: COVID-19 did not substantially influence average sex hormone concentrations or ovarian reserve in childbearing women. During ovarian suppression, sex hormone variations may cause menstrual alterations, which normalise following recovery. COVID-19 severity did not affect menstrual cycle.

Keywords: COVID-19, menstruation, sex hormones, women

Introduction

During a woman's monthly cycle, which lasts between 26 and 35 days, hormone levels change and are controlled by a complex web of endocrine, autocrine, and paracrine factors. This cycle has a big effect on women's minds, moods, and actions, showing up as differences in how much pain they feel, how well they can control their emotions, and physical, mental, and speech problems [1]. Having regular periods is a sign of good reproductive health, while irregular periods are often a sign of problems in the ovarian, thyroid, or pituitary axes [2]. Weight gain, bad health habits, and worry can also cause changes in hormone levels. Problems with ovulation can cause problems with uterine bleeding, ranging from not having any periods to having large periods at odd times. Some of these problems are natural in the early years after menarche, but they can also be caused by endocrinopathies, which are problems in the hypothalamic-pituitary-ovarian axis. These problems include polycystic ovary syndrome, thyroid disease, mental stress, and eating disorders [3]. In December 2019, people in Wuhan, China, were the first to get pneumonia from the SARS-CoV-2 virus. Coronavirus disease (COVID-19) was given the name by the World Health Organisation (WHO) on February 11, 2020. Fever, a dry cough, and tiredness are common signs, and the lungs are often affected [4]. There is a lot of information about how COVID-19 affects the nervous, breathing, and cardiac systems, but not much is known about how it affects the reproductive system of women. During the first COVID-19 vaccination programs, there were worries that the shots might mess up women's periods. This worry grew as more women said their periods changed in ways they didn't expect after getting vaccinated [5]. The study's goals are to look at how women of childbearing age's monthly patterns changed after getting COVID-19 and how sex hormones changed during the pandemic.

Methods

The cross-sectional survey-based study that looked at the past took place from May 1, 2020, to November 1, 2022. It was cleared by the Ethical Committee for Arabic Board for Medical Specialisation. 125 women between the ages of 16 and 45 who had been infected with COVID-19 in the last 3 to 6 months were asked to take part. People who wanted to take part had to not be pregnant. People who were currently taking hormones, had a reproductive problem (like polycystic ovary syndrome or endometriosis), were pregnant or nursing within the last year, or had gynaecological surgery in the past were not allowed to. The comparison group had 90 healthy women who had never had COVID-19. Their ages were the same as those in the sick group. The same rules were used to include and exclude both groups. The New Coronavirus Pneumonia Prevention and Control Program (5th version) says that participants were proven to have COVID-19 by RT-PCR or CT scans showing typical signs of viral pneumonia. Patients were put into two groups: mild and severe. Mild cases had mild symptoms with or without CT proof, while severe cases had multiple factors, such as oxygen saturation ≤95% at rest, breathing problems, or needed assisted ventilation. Serum samples from fifty women were taken on any of the first four days of their period and kept so that sex hormones and AMH could be tested. After three to six months, blood tests were taken during the first five days of the woman's period. For people who had two or more periods while they were in the hospital, samples were taken in the first cycle after the first symptoms went away. The sex hormone levels of fifty comparison cases were also checked. Simple linear regression was used to find factors that affected how subjects thought COVID-19 affected their menstrual cycles. In single analysis, variables with a P-value of less than 0.25 were added to multiple linear regression analysis. A P-value of less than 0.05 was thought to be statistically significant.

Results

A median age of 34+2 years was used to find female subjects (N=135) who had been infected with COVID-19 before. Most of the people who took part (42.2%) were married. Three-quarters of them couldn't read or write, and four-two percent had finished primary school. Nine of the women were vaping. Table 1 shows that most of the people who took part were from low social groups.

Table 1: Socio-demographic characteristics of the study sample (N=125)

Parameter	Mild (N=76)	Moderate (N=53)	Severe (N=6)	P-Value
Age	34+2	32+4	36+2	0.2
Parity	4	3	4	0.1
Social class				
Low	57(75)	33(62)	4(28)	0.2
High	15(19)	20(37)	2(18)	
Educational level				
Illiterate	25(32%)	17(34)	3(50)	0.01
Primary	32(42%)	21(42)	2(75)	
Secondary	11(8%)	9(18)	0	
High level	12(9.6%)	8(16)	0	
Marital status				
Married	53(42.4%)	41(82)	5(80)	0.4
Non-married	22 (17.6%)	14(24)	0	
Smoker	2(1.5)	5(10)	2(4)	0.4

This is about the clinical and medical data of the subjects. There were 76 people (56% of the total) in the mild COVID-19 infection group and 59 people (44% of the total) in the moderate to serious disease group. The group of moderate to serious cases had a higher rate of comorbid diseases than the group of light cases. Here is a list of the unusually high body weights of about 88 of the 135 women who took part in the study: People who were overweight or obese made up 43 (32%), people who were obese or overweight 37 (27%), and women who were extremely obese 8 (6%). Among moderate to serious COVID-19 cases, there is a big difference in the number of medical problems (like high blood pressure, diabetes, and heart disease) compared to the mild infection group (Table 2).

Table 2: Clinical characteristic of females with COVID–19

Clinical features	Mild (N:76)	Moderate-Severe (N=59)	P-value
Comorbidities			
Hypertension	4	11	0.02
Diabetes	2	8	0.01
Cardiac disease	0	6	0.01
Malignancies	0	1	0.02
Other diseases		2	
Previous COVID vaccination	4	3	O.2
Death	0	0	
BMI			
Normal weight	36 (47%)	12(6%)	
Over weight	22(29%)	21(35%)	
Obese	17(21%)	20(34%)	
Morbid obesity	2(2.6)	6(10%)	
Hospital admission	0	79	

The women who took part talked about the changes in their periods that happened after they got COVID-19. Over half of the people who took part said that their monthly cycle had changed in at least one way. This table showed that the magnitude of the menstrual flow changed a lot in the mild and moderate-severe groups. About 27% of those in the mild group and 41% of those in the moderate-severe group had a rise in blood volume. On the other hand, the light and moderate-severe groups' menstrual volumes stayed the same at 59% and 48%, respectively. 59% of those with the mild type had dysmenorrhea, and 34% of those with the moderate to severe type did too. In contrast, the length of the menstrual cycle stayed the same in 85% of the mild group and 39% of the severe group. In 15% of the mild group and 61% of the severe group, it got longer (Table 3).

Table 3: Menstrual changes of women with COVID-19

Menstrual character	Mild (76)	Moderate –Severe (59)	P value
Volume of period			
Unchanged	43(56%)	27(45%)	0.02
Increase	21(27%)	23(38%)	0.04
Decrease	12(15%)	9(15%)	0.01
Mensis duration			
Unchanged	37(48%)	41(69%)	0.01
Increase	25(32%)	13(22%)	0.01
Decrease	14(18%)	5(8%)	0.01
Duration of cycle			
Unchanged	65(85%)	25(42%)	0.01
Prolonged	11(14%)	34(57%)	0.01
Amenorrhea	0	2(6%)	
Intermenstrual bleeding	0	4(10%)	0.01
Dysmenorrhea	43(56%)	19(32%)	0.01

The levels of sex hormones and AMH in the early follicular stage of 91 COVID-19 patients and 91 controls are shown in Table 4. Some sex hormones, like FSH, LH, oestradiol,

progesterone, testosterone, and AMH, were slightly higher in patients who were either weakly or seriously sick than in the control group. Still, it was impossible to tell the difference between COVID-19 patients and the control group, or between mild and severe cases.

Table 4: Sex hormone and AMH concentration in disease and control groups

Hormone	Mild COVID Infection (N=15)	Moderate-severe COVID infection (N=10)	Control (N=25)	P- value
AMH ng/ml	3.3 (5-1.4)	2.5(4.9-2)	3.7(4-2.4)	0.4
FSH mIu/ml	15(12-4)	6(12-5)	7 (11-3)	0.1
LH mIu/ml	11(6-26)	8 (4.5-23)	7 (5-25)	0.1
E2 pg/ml	78(97-20)	66(95-215)	74(30-32)	0.3
Progestrone ng/ml	13(5-15)	10(20-5)	12(25-10)	0.2

Discussion

The COVID-19 plague has caused a lot of problems around the world for the past three years, killing millions of people and having long-lasting effects on their health. As people try to heal from COVID-19, they often worry about losing their sense of smell and taste, their hunger, and other symptoms. A lot of women who have been affected with COVID-19 have recently been said to have had changes in their periods. The hypothalamus, pituitary, ovaries, uterus, prostaglandins, and neuroendocrine factors all work together in a complicated way during the monthly cycle. Problems can happen if any of these interactions are disrupted [6]. There are a lot of things that can throw off the results of a study on a single feature of menstrual changes. This is especially true during the stressful COVID-19 pandemic, when people are also dealing with stress, vaccinations, COVID-19 treatment, and the disease itself [7]. Menstrual problems can be caused by a lot of stress, and the pandemic has changed a lot of people's lives, which may have caused stress that can affect menstrual cycles. In a recent study, people who reported high perceived stress levels (PSS) had periods that lasted longer and were heavier than people who reported mild PSS [8]. In this study, subjects talked about short-term changes in their periods, mostly longer cycles and less blood flow. About half of the women who got COVID-19 had changes to their menstrual cycle afterward. These changes included changes in the length, volume, and length of their periods. Some people also had shorter or messed up cycles and more volume, which was not common in the control group. These changes are often connected to mental health problems like anxiety and sadness, which are long-term signs of COVID-19 [10]. A study from the U.S. found that women with high PSS also had big changes in their periods during the pandemic [11]. It is known that having a higher body mass index (BMI) can make your periods less regular. COVID-19 might make this affect worse, but this study did not find a link between the two [11]. Women with more education were less likely to think that COVID-19 caused problems with their periods. This might be because they knew more about the virus and how it works [12]. On the other hand, women who were not married and smoked thought COVID-19 was more likely to affect their periods. Women who aren't married may be more aware of problems with their periods, while smokers may think that health problems are caused by things other than smoking [13]. Thomson *et al*. [14] study of COVID-19 patients who were hospitalised showed that being admitted to the hospital, which is a stressful event, could change the menstrual cycle. Patients in hospitals, who were often sicker and more likely to be overweight or have metabolic syndrome, were more likely to have problems with their periods. Some other things that might put someone at risk include their age, the seriousness of their illness, having other illnesses, heart problems, and taking glucocorticoids [14, 15]. A study found that about 20% of sick patients had a large drop in the amount of blood in their periods. There was no significant difference between mild and severe cases. Some patients had bigger periods or shorter cycles, but there was no real difference between them and the control group in terms of irregularities. Women who tested positive for COVID-19 had much bigger changes in their menstrual flow and cycle length. The only thing that put women at risk for having their periods last longer was problems in other systems. Most patients went back to having regular periods and cycles within one to two months of being discharged, which suggests that these changes were short-term [16]. In a study of 78 patients in Wuhan, China [17], 21.79% were very sick, 48% had recently been diagnosed with a mental problem, 12% had a history of a mild gynaecological disease, and 36% had had gynaecological surgery. Patients who were very sick had more cases of amenorrhoea, changes in menstrual volume, unpredictable periods, and monthly pain than patients who were not very sick, but the differences were not significant [15]. Dexamethasone, which is used to treat COVID-19 patients in hospitals, may increase the chance of monthly changes [18]. There were no big changes in the amounts of sex hormones found between COVID-19 patients and controls in this study. This means that the ovary endocrine system wasn't really affected. But some patients had strange hormone levels, like high FSH and LH during the early follicular phase, which pointed to the ovaries being turned off. More prospective continuous studies are needed to support these results and find out how long menstrual irregularities last. Also, the mental health of women during the COVID-19 outbreak was not checked, which is an important thing to think about.

Conclusion

Through COVID-19, there were no big changes in the average levels of sex hormones or ovarian reserve in women of fertile age. The changes in these patients' periods may be due to temporary changes in sex hormones that happen when the ovaries stop working properly. These changes will go away quickly once the patients get better. In addition, they say that changes in the menstrual cycle are not affected by how bad COVID-19.

Conflict of Interest: Not available.

Financial Support: Not available.

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How to Cite This Article
Issa LS, Sharief M. Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age. International Journal of Clinical Obstetrics and Gynaecology. 2024;8(4):38-41.