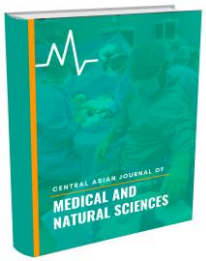


CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 05 Issue: 01 | Jan 2024 ISSN: 2660-4159

Article

Assessment of Changes in Hormonal Levels in Women with Menstrual Dysfunction Who Suffer from COVID-19

Najmutdinova D.K.[1], Yunusova D. X.[2], Axmedova G.A.[3]

1 Dsc in Medical Sciences, Professor of Department Obstetrics and Gynecology in Family Medicine of Tashkent Medical Academy
2 Phd Researcher Professor of Department Obstetrics and Gynecology in Family Medicine of Tashkent Medical Academy
3 Phd In Medical Sciences, Assistant Professor of Department Obstetrics and Gynecology in Family Medicine of Tashkent Medical Academy
* Correspondence: dilshoda.gadoyevared.knight@mail.ru

Abstract: According to the World Health Organization, the COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused over 620 million infections and 6.5 million deaths worldwide as of September 2022 [1]. Over the past few years, the COVID-19 pandemic has had a significant impact on the health and lives of people around the world. Numerous retrospective studies have shown that age is a critical factor affecting the prognosis of patients with COVID-19 (Guan et al., 2020). Additionally, gender is believed to play an important role in the progression of COVID-19, as female patients have a better prognosis (Chen et al., 2020). Similarly, some infectious diseases, such as MERS and SARS, have mild clinical symptoms and better outcomes in women of childbearing age (Alghamdi et al., 2014; Karlberg et al., 2004). Researchers have been studying COVID-19 since day one, and there is already robust data on the effects of infection with the SARS-CoV-2 virus on the respiratory [2], circulatory [3] and nervous systems [4]. However, little is known about the impact of COVID-19 on the reproductive system, especially the female reproductive system. The impact of the COVID-19 pandemic on the female reproductive system and changes in the menstrual cycle have been widely reported anecdotally and in the media [5]. However, the available data to date are not robust enough to draw firm conclusions on this issue.

Keywords: COVID-19, fertility, menstrual cycle, menstrual bleeding, reproductive system

Citation: Najmutdinova D.K., Yunusova D. X., Axmedova G.A. Assessment of Changes in Hormonal Levels in Women with Menstrual Dysfunction Who Suffer from COVID-19. Central Asian Journal of Medical and Natural Science 2024, 5, 617-623.

Received: 14th Dec 2023
Revised: 16th Dec 2023
Accepted: 28th Dec 2023
Published: 30th Jan 2024

1. Introduction

A normal and regular menstrual cycle is a vital indicator on the basis of which one can judge a woman's reproductive health and her general health. Menstrual bleeding has dynamic and cyclical characteristics, and its monthly variability is a clear sign of health and fertility. The International Federation of Gynecology and Obstetrics (FIGO) proposes a nomenclature for assessing normal menstrual bleeding and diagnosing abnormalities, establishing four assessment parameters: frequency, regularity, duration and volume [6].

Table 1. Characteristics of the normal menstrual cycle (FIGO 2011)

Index	Descriptive Terms	Anomal
Interval between menstruation	Short	<24 (> 4 episodes in 90 days)
	Normal	24-38 days
	Long	>38 (1-2 episodes in 90 days)
Duration of menstrual bleeding	Long-term	>8
	Normal	3-8
	Short	<3
Regularity	Regular variation (from shortest to longes t⩽7–9 days)	Irregular (from shortest to longest ⩾10 days)
	Abundant	>80
	Normal	5-80
Duration of menstrual bleeding	Meager	>5

The effect of COVID-19 on thyroid function, the endometrium and the menstrual cycle, as well as the effect on female hormones, ovarian reserve and follicular fluid parameters, was studied. The thyroid gland appears to be particularly susceptible to damage by SARS-CoV-2, with a nonthyroid disease syndrome characterized by normal thyroid function, decreased free T3, and thyroiditis as the most common clinical manifestations. Thyroid dysfunction appears to be associated with the severity of SARS-CoV-2 infection (Lui et al., 2021). It is hypothesized that destruction of thyroid follicular cells during the cytokine storm of the acute phase of SARS-CoV-2 infection may lead to thyroiditis. Between 11 and 15% of hospitalized patients have thyrotoxicosis (Lania et al., 2020; Muller et al., 2020). The period between respiratory symptoms and diagnosis of thyroiditis varies, with an average of 26 days (Christensen et al., 2022). Therefore, the aim of this work is to study the impact of COVID 19 on menstrual-ovarian dysfunction in women of reproductive age.

2. Materials and Methods

2.1. Materials

104 women with menstrual irregularities were examined. The average age of all women was 29±6.4 years. All women were divided into the main and control groups. The main group consisted of 56 (53.8%) women who had COVID 19. The average age in the

main group was 22.6±3.2 years. And the control group was 48(46.1%) women, mean age 26.4±4.1; who applied for menstrual-ovarian cycle disorders who had not had COVID 19. The average age at menarche was 13±2.3 years (Median 12(11;15); A special questionnaire was created that included criteria for selecting patients for the study. It is necessary to remember the impact numerous environmental factors that can influence the secretion of hormones and thereby potentially disrupt the regularity of the cycle.

2.2. Inclusion Criteria For The Study

The main selection criteria were patients' complaints about irregular menstruation, the nature of the disorders, pregnancy planning, the presence or absence of a history of coronavirus infection, the reproductive age of the patients, pregnancy planning, obstetric-gynecological and endocrinological history.

2.3. Exclusion Criteria

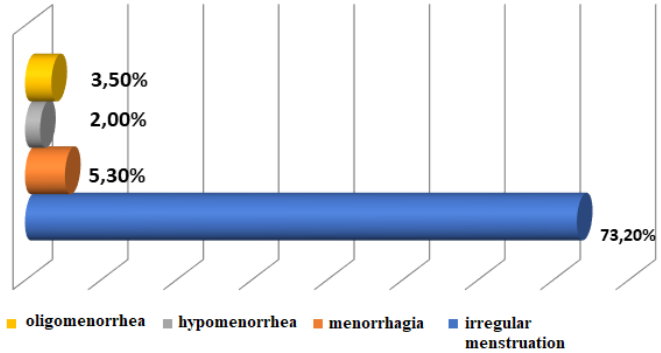
Menstrual dysfunction before COVID-19 disease, a history of chronic somatic pathology, gynecological structural pathologies of the uterus and appendages, grade 2-3 obesity.

2.4. Methods

Clinical - study of somatic and endocrine status, hormonal studies - using the ICL method of levels of LH, FSH, testosterone (free), TSH, Free T4, T3, ATPO on demand, ultrasound examination of the uterus, ovaries, thyroid gland, statistical research methods.

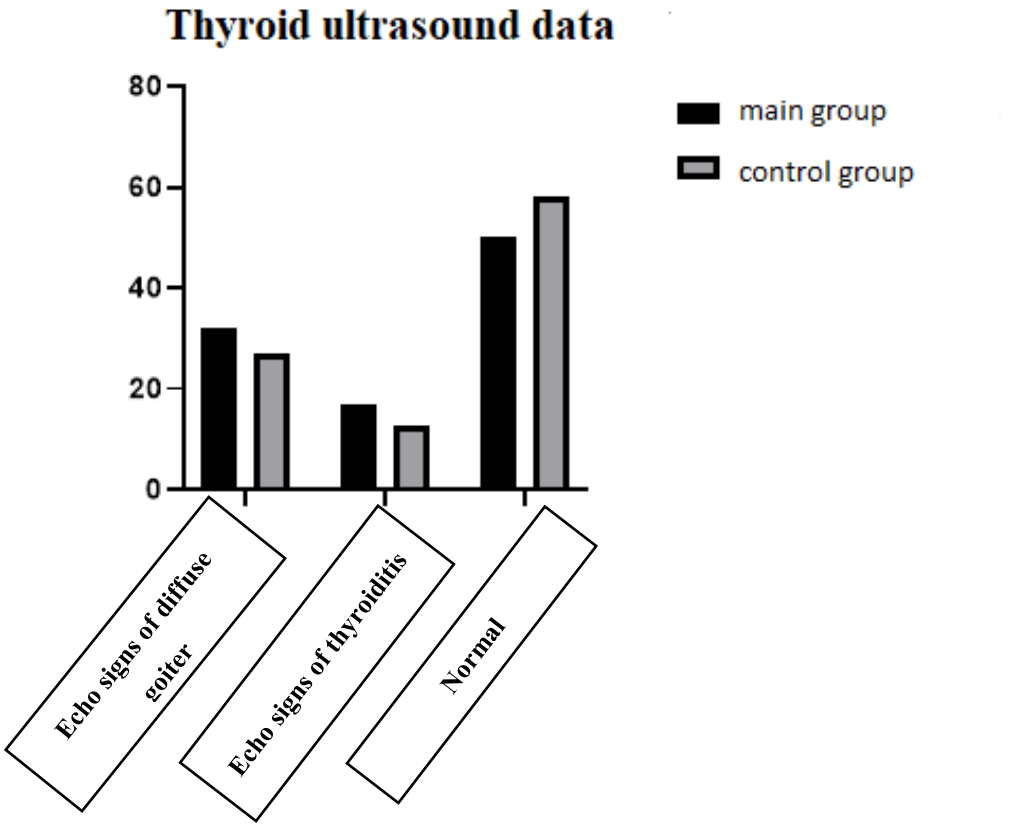
3. Results and Discussion

All patients from the main group, 56 (100%) had complaints of various menstrual irregularities. Of these, 3(5.3%) complained to heavy menstruation with monthly blood loss of more than 80 ml (menorrhagia), 7(12.5%) complained about the absence of menstruation for at least 3 menstrual cycles (amenorrhea), 2(3.5%) complained about a small amount of blood during menstruation (hypomenorrhea). More than half of the women complained of irregular menstruation 41 (73.2%), and also 1 woman complained of intermenstrual bleeding for 3 months (picture No. 1). In the main group, compared to the control group, there was a statistically significant increase in the frequency of NMC from 47.4% to 73.4% ($p = 0.05$; $\chi2 = 9.627$). On average, in the main group there was an increase in both the cycle duration - from 24.4 ± 3.6 days to 33.6 ± 10.6 days ($p = 0.432$; $\chi2 = 0.366$), and the duration of menstruation - from 4.6 ± 1.8 days to 5.7 ± 2.4 days ($p = 0.011$; $\chi2 = 6.276$). At the same time, an increase in the frequency of oligomenorrhea was also recorded - from 7 (26.8%) to 12 (40%) cases ($p = 0.274$; $\chi2 = 1.200$).



Picture 1. The main complaints of patients who have had COVID 19

Menstrual irregularities and infertility in women of reproductive age after COVID 19 are often associated with pathology of the pituitary-ovarian system and dysfunction of the thyroid gland (thyroid gland), especially hypothyroidism. The most common cause of hypothyroidism in women of reproductive age is autoimmune thyroiditis (AIT), characterized by increasing lymphoplasmacytic infiltration, destruction and subsequent sclerosis of thyroid tissue. In many women, thyroid dysfunction is often combined with menstrual irregularities, infertility, and increased morbidity during pregnancy. Thus, in the main group we studied, 18 (32.1%) women with ultrasound examination of the thyroid gland revealed echo signs of diffuse goiter, 28 (50%) revealed echo signs of thyroiditis, and 10 (17%) had normal thyroid findings. In the control group, thyroid gland pathology was less common, so 13 (27%) had normative indicators, more than half of the patients (28 (58.3%)) had echo signs of diffuse goiter, and 6 (12.5%) were diagnosed with signs of thyroiditis.



Picture 2. Tyroid Ultrasound Data

Normal levels of thyroid hormones provide sufficient concentrations of estrogen and progesterone, which promote oocyte maturation and improve uterine receptivity.

Table 2. Indicators of thyroid hormones

Index	Reference values	Main group (n=56)		Control group (n=48)	
		M±m	Медиана	M±m	Медиана
TTH	0,3-4,0 μME/ml	6,66±1,86*	2,2(0,24;10)	2,807±5,82*	1,73(0,1;40,62)
T_3	2,5-4,3 nmol//l	2,66±1,028	2,8(0,84;6,)	2,958±1,396	2,84(0,98;11,4)
T_4 free	8,9-17,2 nmol/l	11,952±8,9	10,5(1,79;7)	13,391±7,084**	13,4(1,5;54,4)

Anti-TPO	Upto	35ME/ml	43,6±106,1*	6,3(1;502,5)	8,847±15,081	4,12(1,03;64,8)

Note: * - data reliability P<0.05; ** - P<0.01; *** - P<0.001

Thus, in the group of patients who had COVID 19, the average TSH value was 6.66±1.865 (P<0.05), which is significantly higher than the average values of the control group and laboratory reference values. (Table No. 2). The average T3 value practically did not differ from the control group and were equal to the laboratory reference data of 2.66±1.028.

The free fraction of thyroxine T4 most adequately characterizes the hormonal function of the thyroid gland; its average value in the main group of patients was 11.952±8.887. A marker for antibodies to TG that allows identifying autoimmune lesions of the thyroid gland, the average value of antibodies to TPO was significantly higher than the control group 43.6±106.1 (P<0.05)

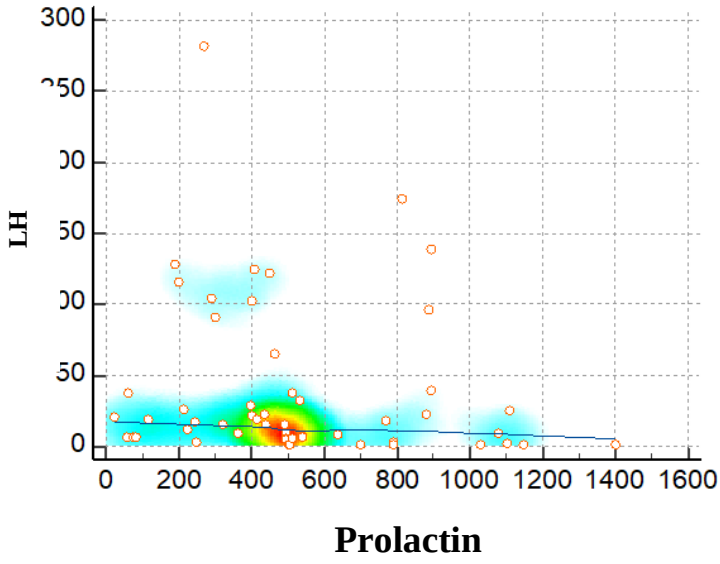
Thus, menstrual irregularities in patients who have had COVID 19 may be associated with disruption of the endocrine system. AIT is the most common cause of hypothyroidism in women of reproductive age.

Table 3. Sex hormone levels

Index	**Reference values**	**Main group (n=56)**		**Control group (n=48)**	
		M±m	**Медиана**	**M±m**	**Медиана**
Prolactin	66-490нг\мл	521,4±313,3*	495,5(24,3;1402)	629,8±398,1	488(0;1950)
FSH	3,5-12,5 мЕД/мл	16,752±25,3	10,37(1,5;114,2)	7,24±16,3**	4,1(0,6;116)
LH	14,0-95,6 мЕД/мл	37,3±54,9**	15,23(0,86;281,7)	42,8±51,6	20,45(0,8;226,5)
Testosterone free	0,29-1,67 пг/мл	1,58±1,011	1,325(0,12;58)	1,7±1,7*	1,225(0,87;9,7)

Note: * - data reliability P<0.05; ** - P<0.01; *** - P<0.001

With an increase in the concentration of thyroid hormones and antibodies to TPO, the pituitary gland begins to produce compensatory FSH in large quantities, which is responsible for accelerating the growth of ovarian follicles, and also sensitizes them to the action of LH, and prolactin. Thus, in the group of patients who had suffered COVID 19, the average FSH value was significantly higher than the average values of the control group 16.752±25.3 (P<0.05). The average prolactin value was 521.4±313.3 (P<0.05), which was also significantly higher than the control group. Due to an increase in FSH and prolactin, the production of LH is suppressed, so in the main group the average LH value was 37.3 ± 54.9 (Table No. 3). Reduced LH levels lead to lack of ovulation and menstrual irregularities. Thus, between the level of LH and prolactin in the group of patients who suffered from COVID 19, a significantly significant negative correlation relationship of average strength was revealed (r=-0.7813 P<0.001), (Pic. 3), which shows that the decrease in LH in patients who suffered from COVID 19 is still one significant cause of menstrual irregularities.



Picture 3. Dispersion diagram of the correlation between LH levels and prolactin

4. Conclusion

As a result of the above study, the following conclusion can be noted that dysfunction of the thyroid gland and thyroid hormones leads to an imbalance of sex hormones, which in turn leads to disruption of the menstrual cycle in patients who have had COVID 19. As a result, early detection and treatment of dysfunction of the thyroid gland will be able prevent complications from the reproductive system, improve the quality of life of women who have had COVID 19.

References

1. Информационная панель ВОЗ по коронавирусу (COVID-19). [(по состоянию на 21 февраля 2022 г.)]. *Доступно онлайн:* https://covid19.who.int/
2. Lovato A., De Filippis C. Clinical presentation of COVID-19: A systematic review focusing on upper airway symptoms. *Ear Nose Throat J.* 2020;99:569–576. doi: 10.1177/0145561320920762. [PubMed] [CrossRef] [Google Scholar]
3. Xie Y., Xu E., Bowe B., Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat. Med.* 2022;28:583–590. doi: 10.1038/s41591-022-01689-3. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
4. Spudich S., Nath A. Nervous system consequences of COVID-19. *Science.* 2022;375:267–269. doi: 10.1126/science.abm2052. [PubMed] [CrossRef] [Google Scholar]
5. Morgan E. Pandemic Periods: Why Women's Menstrual Cycles Have Gone Haywire. [(accessed on 21 February 2022)]. Available online: https://www.theguardian.com/society/2021/mar/25/pandemic-periods-why-womens-menstrual-cycles-have-gone-haywire
6. Munro MG, Critchley HOD, Fraser IS. Corrigendum to "The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions" [Int J Gynecol Obstet 143(2018) 393–408]. *Int J Gynaecol Obstet* 2019; 144(2): 237 (таблица)
7. Morgan E.P. Periods: why women's menstrual cycles have gone haywire. Guardian. 2021; 25
8. Wang H., Mao Y., Ju L. et al. Detection and monitoring of SARS coronavirus in the plasma and peripheral blood lymphocytes of patients with severe acute respiratory syndrome. Clin Chem. 2004;50(7):1237–1240. DOI: 10.1373/ clinchem.2004.031237.
9. Milla M., Harcourt B.H., Hickman C.J. et al. SARS-coronavirus replication in human peripheral monocytes/macrophages. Virus Res. 2005;107(1):93–101. DOI: 16/j.virusres.2004.09.004.

10. Guan W., Ni Z., Hu Y. et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708–1720. DOI: 10.1056/NEJMoa2002032
11. American Association of Blood Banks. Update: impact of 2019 novel coronavirus and blood safety. (Electronic resource.) URL: http://www.aabb.org/advocacy/ regulatorygovernment/Documents/Impact-of-2019-Novel-Coronavirus-on-Blood-Donation.pdf. (access date: 16.08.2021).
12. European Centre for Disease Prevention and Control. Rapid Risk Assessment: Outbreak of acute respiratory syndrome associated with a novel coronavirus, Wuhan, China; first update — 22 January 2020. ECDC: Stockholm; 2020.
13. CDC. Coronavirus Disease 2019 (COVID-19). 2020. (Electronic resource.) URL: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical- criteria.html (access date: 16.08.2021).
14. Devaux C.A., Rolain J.M., Colson P., Raoult D. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19? Int J Antimicrob Agents. 2020;55(5):105938. DOI: 2020.10593810.1016/j.ijantimicag..
15. AbdAlla S, Lother H, Abdel-tawab AM, Quitterer U. The angiotensin II AT2 receptor is an AT1 receptor antagonist. J Biol Chem 2001;276:39721-39726.
16. Acosta TJ, Ozawa T, Kobayashi S, Hayashi K, Ohtani M, Kraetzl WD, Sato K, Schams D, Miyamoto A. Periovulatory changes in the local release of vasoactive peptides, prostaglandin f(2alpha), and steroid hormones from bovine mature follicles in vivo. Biol Reprod 2000;63:1253-1261.
17. Ahmed A, Li XF, Shams M, Gregory J, Rollason T, Barnes NM, Newton JR. Localization of the angiotensin II and its receptor subtype expression in human endometrium and identification of a novel high-affinity angiotensin II binding site. J Clin Invest 1995;96:848-857.
18. Anton L, Merrill DC, Neves LA, Diz DI, Corthorn J, Valdes G, Stovall K, Gallagher PE, Moorefield C, Gruver C et al. The uterine placental bed Renin-Angiotensin system in normal and preeclamptic pregnancy. Endocrinology 2009;150:4316-4325.