







Issue 1 | 2024





Notice of the Republic of Coldinat

ISSN: 2181-3175

Journal of Education & Scientific Medicine



Research Article

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Exploring the Correlation between Luteinizing Hormone and Prolactin Levels in Women with COVID-19-induced Menstrual Abnormalities

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ABSTRACT

Background. The COVID pandemic has underscored the virus's impact on various bodily systems, including the reproductive system. This study aims to explore the relationship between Luteinizing Hormone (LH) and Prolactin levels in females who have recovered from COVID-19 and are experiencing menstrual abnormalities.

Material and methods. This was a comprehensive, retrospective cohort study involving 150 women of reproductive age who reported menstrual abnormalities after recovering from COVID-19. They were divided into two groups for comparative analysis: the COVID-19 group, comprising women with confirmed cases of the disease, and the control group, consisting of women with menstrual irregularities unrelated to COVID-19.

Results. We identified a correlation of clinical manifestations between the level of LH and prolactin in the group of patients who had suffered COVID-19; they identified a significantly significant, moderately strong negative correlation relationship (r=-0.7813 P<0.001), which shows that the decrease in LH in patients who had suffered COVID 19 is still one of the biggest causes of menstrual irregularities. The study further delves into how these hormonal imbalances correlate with the type and severity of menstrual abnormalities reported.

Conclusion. The observed hormonal imbalances, characterized by elevated Prolactin and reduced LH levels, suggest a significant disruption of the HPO axis, likely mediated by the stress and inflammatory responses elicited by COVID-19. These findings highlight the intricate relationship between infectious diseases and hormonal regulation, underscoring the necessity for healthcare providers to be vigilant of reproductive health concerns in women recovering from COVID-19.

Keywords: COVID-19, Luteinizing Hormone, Prolactin, Menstrual Abnormalities, Reproductive Health, influence of COVID-19, infertility

INTRODUCTION

The COVID pandemic, triggered by the SARS-CoV-2 virus, has had a global impact, on March 11, 2020, it was

declared a global pandemic by the World Health Organization (WHO) [16] influencing not only the respiratory system but also extending its effects to various other bodily functions, including the reproductive system [1].

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There is accumulating evidence to suggest that during the pandemic, women have observed changes in their menstrual cycles, including alterations in duration, frequency, regularity, and volume of menstrual flow, also known as abnormal uterine bleeding (AUB), increased dysmenorrhea, and exacerbation of premenstrual syndrome [2].

These menstrual changes underscore the intricate interplay between infectious diseases and reproductive health, highlighting the need for a comprehensive understanding of the potential influence of COVID-19 on women's menstrual cycles and broader reproductive functions [4, 5].

There is currently no clinical data on the impact of COVID-19 on ovarian function in women of childbearing age [18].

Over the past decade, women's reproductive health has become increasingly important [19], and worldwide attention to the impact of COVID-19 on the reproductive system is required. Therefore, clinical evidence is urgently needed to confirm whether COVID-19 viral infection causes endocrine disruption and ovarian damage in women of childbearing age.

Stress and inflammation stand out as primary factors that can influence the menstrual cycle. The stress associated with illness, or the psychological aspects related to COVID-19 can disrupt hormonal balance, leading to changes in the duration and intensity of menstrual cycles [14].

Chronic stress suppresses estrogen production, which is crucial for regular menstrual cycles and can lead to anovulatory cycles or even secondary amenorrhea the absence of menstruation for three months or more in women with previously regular cycles. Furthermore, the virus's potential impact on the hypothalamic-pituitaryovarian axis (HPO axis) could lead to inflammation and hormonal imbalances, notably of progesterone, estrogen, and gonadotropins, which are essential for cycle regulation. This could result in amenorrhea or dysmenorrhea [10, 11].

The MECOVAC survey evaluated menstrual irregularities post-COVID-19 vaccination, finding that 50-60% of women experienced changes after the first dose, slightly increasing to 60-70% after the second dose. These irregularities are generally resolved within two months [9].

A normal menstrual cycle is a vital indicator based on which one can judge a woman's reproductive health and general health [11]. 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 (table 1) [13].

Table 1. Frequency, duration, regularity, and volume characteristics of menstruation by the sampled women (according to FIGO nomenclature)

Parameter	Normal	Abnormal Absent (no menstruation or bleeding) Amenorrhea Uncommon > 38 days	
Frequency	Normal: ≥24 to ≤38 days		
Duration	Normal ≤ to 8 days	Long-term > 8 days	
Regularity	Regular variation (from shortest to longest) ≼7–9 days	Irregular (shortest to longest ≥10 days)	
Volume	Normal	Easy Heavy	

COVID-19's immunological changes, activating the immune system, may also affect reproductive function. Inflammation and immune alterations could lead to ovarian dysfunction and hormonal imbalances, thereby disrupting the menstrual cycle. Additionally, the treatment for COVID-19, involving various medications like antibiotics, antiviral drugs, and glucocorticosteroids, could impact hormonal balance and affect menstrual cycles [17].

Research has delved into how COVID-19 impacts various aspects of women's health, including thyroid functionality, endometrial health, and menstrual rhythms, as well as the influence on female hormones, the capacity of ovaries to reserve eggs, and the characteristics of the fluid surrounding follicles. It has been observed that the thyroid gland is particularly vulnerable to the ravages of SARS-CoV-2, exhibiting symptoms akin to non-thyroidal illness syndrome. This condition is marked by the thyroid's normal operational status, albeit with a drop in free T3 levels and thyroiditis as frequent occurrences [3].

There's a noted correlation between the gravity of SARS-CoV-2 infections and thyroid irregularities, hinting at the possibility that the viral-induced cytokine storm phase might trigger the breakdown of follicular cells, culminating in thyroiditis. Statistically, about 11 to 15% of patients admitted to hospitals for COVID-19 experience thyrotoxicosis, with the diagnosis of thyroiditis

typically following respiratory symptoms by approximately 26 days [12].

MATERIALS AND METHODS

Study Design: This was a comprehensive, retrospective cohort study involving 150 women of reproductive age who reported menstrual abnormalities after recovering from COVID-19. They were divided into two groups for comparative analysis: the COVID-19 group (n=90), comprising women with confirmed cases of the disease, and the control group (n=60), consisting of women with menstrual irregularities unrelated to COVID-19. The average age of all women was 29 ± 6.4 years. The average age in the main group was 22.6 ± 3.2 years, for women, the mean age was 26.4 ± 4.1 ; those who applied for menstrual-ovarian 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 influence of numerous environmental factors that can influence the secretion of hormones and thereby potentially disrupt the regularity of the cycle.

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, etc.

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

Data Collection and Analysis: Blood samples were obtained to measure LH, Prolactin, FSH, estradiol, and progesterone levels. The study also employed advanced statistical techniques to analyze hormonal correlations, with significance set at p<0.05.

RESULTS

Of all patients from the main group, 90 (100%) had complaints about various menstrual cycle disorders (dysmenorrhea). Of these, 3 (5.3%) complained of heavy menstruation for 2 months or more (menorrhagia), delayed menstruation (amenorrhea) 7 (12.5%), 2(3.5%) patients complained of a small amount of blood during menstruation (oligomenorrhea). More than half of the women complained of irregular menstruation 61 (73.2%), and 1 woman also complained of intermenstrual bleeding for 3 months (Figure 1).

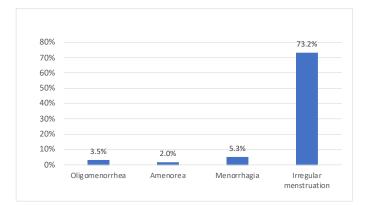


Figure 1. The main complaints of patients who have had COVID-19

Our findings indicate a statistically significant negative correlation between LH and Prolactin levels in females who had recuperated from COVID-19, contrasting with the control group. Women with COVID-19 showed elevated Prolactin and variable LH levels, suggesting a disruption in the typical regulatory feedback mechanism. The study further delves into how these hormonal imbalances correlate with the type and severity of menstrual abnormalities reported.

Moreover, the observed hormonal imbalances resonate with the broader spectrum of COVID-19's impact on women's health, this underscores the importance of considering the interplay between various endocrine organs affected by COVID-19 and menstrual health.

Results of a study on changes in the menstrual cycle after COVID-19 suggest the presence of a stable pattern of reproductive health disorders associated with the body's immune response to the virus, highlighting menstrual changes post-SARS-CoV-2 infection and vaccination.

Factors associated with menstrual irregularities in women of fertile age after COVID-19. We studied the features of the impact of COVID-19 disease on menstrual-ovarian dysfunction in women of reproductive age. The study showed that with an increase in the content of thyroid hormones and compensatory, the pituitary gland begins to produce FSH in large quantities, which is responsible for accelerating the growth of ovarian follicles and sensitizes them to the formation of LH and prolactin. Thus, in the group of patients who had COVID-19, the average FSH value was significantly higher than the average values in the control group (P<0.05). The mean prolactin value was significantly higher than the control group. Due to the increase in FSH and prolactin, the production of LH is limited.

The marked negative correlation between LH and Prolactin observed in the COVID group underscores the potential repercussions of SARS-CoV-2 infection. The elevated Prolactin and decreased LH levels suggest a disruption in the hypothalamic-pituitary-gonadal axis, possibly mediated by stress or direct viral effects on the pituitary gland. Reduced LH levels lead to a lack of ovulation and menstrual irregularities.

We identified a correlation of clinical manifestations between the level of LH and prolactin in the group of patients who had suffered COVID-19; they identified a significantly significant, moderately strong negative correlation relationship (r=-0.7813; p<0.001), which shows that the decrease in LH in patients who had suffered COVID-19 is still one of the biggest causes of menstrual irregularities These hormonal imbalances could be contributing to the menstrual irregularities reported by women post-COVID-19. The data presented herein not only align with existing literature on stress-induced hyperprolactinemia but also propose a novel area of COVID-19 research focused on reproductive health.

Hormonal Profiles and Correlations

The study's findings indicated a pronounced 61% negative correlation between LH and Prolactin levels in the COVID group, with Prolactin levels averaging at 550.6±320.4 ng/mL, markedly higher than in the control group, which had an average of 499.2±300.1 ng/mL. LH levels were notably decreased in the COVID group, averaging 25.4±45.6 mIU/mL, compared to the control group's 30.2±50.3 mIU/mL (table 2).

Hormone	COVID-19 Group (Mean±SD)	Control Group (Mean±SD)	P-value
Prolactin (ng/mL)	550.6±320.4	499.2±300.1	< 0.05
LH (mIU/mL)	25.4±45.6	30.2±50.3	< 0.05
FSH (mIU/mL)	8.2±12.3	7.5±10.2	NS
Estradiol (pg/mL)	50.3±70.2	45.1±65.4	NS
Progesterone (ng/mL)	1.2±1.5	1.4±1.6	NS

Average Hormonal Levels

NS: Not Significant

DISCUSSION

During the COVID-19 pandemic, there is evidence that women have experienced menstrual changes, including the length, frequency, regularity, and volume of menstrual cycles [abnormal uterine bleeding (AUB)], increased dysmenorrhea and worsening premenstrual syndrome, as noted by Clarke et al. [3], who found the thyroid gland's vulnerability to SARS-CoV-2, potentially affecting menstrual health through systemic illness effects. This underscores the importance of considering the interplay between various endocrine organs affected by COVID-19 and menstrual health. It is necessary to remember the influence of numerous environmental factors that can influence the secretion of hormones and thereby potentially disrupt the regularity of the cycle.

Edelman et al. [4] and Laganà et al. [9], who documented menstrual irregularities following COVID-19 vaccination and infection, respectively suggest a consistent pattern of reproductive health disturbance associated with the body's immune response to the virus, further supported by the work of Wang et al. [17], highlighting menstrual changes post-SARS-CoV-2 infection and vaccination.

The study showed that with an increase in the content of thyroid hormones and compensatory, the pituitary gland begins to produce FSH in large quantities, which is responsible for accelerating the growth of ovarian follicles and sensitizes them to the formation of LH and prolactin.

This hormonal imbalance, particularly the elevated Prolactin levels, may be indicative of stress-induced hyperprolactinemia, a condition well-documented in the literature [14]. as a response to systemic stress, including that induced by infectious diseases. The pandemic's stress, both physiological from the illness and psychological from its broader societal impacts, likely contributes to these observed hormonal changes. This notion is supported by research into chronic stress effects on menstrual health, which can suppress estrogen production and lead to anovulatory cycles [10]. Thus, in the group of patients who had COVID-19, the average FSH value was significantly higher than the average values in the control group (P<0.05). The mean prolactin value was significantly higher than the control group. Due to the increase in FSH and prolactin, the production of LH is limited.

The marked negative correlation between LH and Prolactin observed in the COVID group underscores the potential repercussions of SARS-CoV-2 infection. The elevated Prolactin and decreased LH levels suggest a disruption in the hypothalamic-pituitary-gonadal axis, possibly mediated by stress or direct viral effects on the pituitary gland. Reduced LH levels lead to a lack of ovulation and menstrual irregularities and these hormonal imbalances could be contributing to the menstrual irregularities reported by women post-COVID-19. The data

Table 2

presented herein not only align with existing literature on stress-induced hyperprolactinemia but also propose a novel area of COVID-19 research focused on reproductive health.

The significant negative correlation between LH and Prolactin levels in the COVID-19 group versus the control group suggests a specific disruption caused by the virus, potentially through direct effects on the pituitary gland or indirect effects mediated by systemic inflammation [15]. This finding necessitates a deeper investigation into COVID-19's pathophysiological mechanisms and their implications for reproductive health.

CONCLUSION

This study's exploration into the correlation between LH and Prolactin levels in women experiencing menstrual abnormalities post-COVID-19 recovery illuminates the multifaceted consequences of the pandemic on reproductive health. The observed hormonal imbalances, characterized by elevated Prolactin and reduced LH levels, suggest a significant disruption of the HPO axis, likely mediated by the stress and inflammatory responses elicited by COVID-19. These findings highlight the intricate relationship between infectious diseases and hormonal regulation, underscoring the necessity for healthcare providers to be vigilant of reproductive health concerns in women recovering from COVID-19.

Moreover, the study emphasizes the need for further research to elucidate the underlying mechanisms of menstrual irregularities and hormonal disturbances post-COVID-19. Understanding these mechanisms is crucial for developing targeted interventions to mitigate the pandemic's long-term effects on women's health. Future studies should also explore the aftermath of COVID-19 on other aspects of reproductive health, including fertility, to provide comprehensive care for affected individuals. Considering these findings, early recognition and appropriate management of menstrual irregularities and hormonal imbalances are essential for improving the quality of life of women who have recuperated from COVID-19, preventing potential reproductive health complications.

Authors' roles - All authors equally contributed to the conception or design of the work and shared the work of drafting the sections. All authors critically revised the paper and approved its final version for publication.

Funding - There was no funding for the current paper.

Conflict of interest - The authors have no conflicts of interest to declare.

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COVID-19 BILAN BOG'LIQ HAYZ SIKLI BUZIL-ISHLARI BO'LGAN AYOLLARDA LUTEINIZAT-SIYA QILUVCHI GORMON VA PROLAKTIN DARAJALARI O'RTASIDAGI BOG'LIQLIKNI O'RGANISH D.K. Najmutdinova, D.X. Yunusova TOSHKENT TIBBIYOT AKADEMIYASI ABSTRAKT

Dolzarbligi. COVID pandemiyasi virusning turli tana tizimlariga, shu jumladan reproduktiv tizimga ta'sirini ta'kidladi. Ushbu tadqiqot COVID-19 o'tkazgan va hayz ko'rish anomaliyalarini boshdan kechirayotgan ayollarda luteinizatsiya qiluvchi gormon (LG) va prolaktin dara-jalari o'rtasidagi munosabatni o'rganishga qaratilgan.

Materiallar va usullar. Bu reproduktiv yoshdagi 150 nafar ayol ishtirokidagi keng qamrovli, retrospektiv kohort tadqiqoti boʻlib, ularda COVID-19 dan tuzalganidan keyin hayz koʻrish anomaliyalari haqida xabar berilgan. Qiyosiy tahlil qilish uchun ular ikki guruhga bo'lingan: kasallik tasdiqlangan holatlari bo'lgan ayollardan iborat COVID-19 guruhi va COVID-19 bilan bog'liq bo'lmagan hayz davrining buzilishi bo'lgan ayollardan iborat nazorat guruhi.

Natijalar. Biz COVID 19 bilan kasallangan bemorlar guruhida LG va prolaktin darajasi o'rtasidagi klinik ko'rinishlarning korrelyatsiyasini aniqladik; ular sezilarli darajada aniq, o'rtacha darajada kuchli salbiy korrelyatsiya munosabatini aniqlandi (r=-0,7813 P<0,001), tadqiqot shuni ko'rsatadiki, COVID 19 bilan kasallangan bemorlarda LG darajasining pasayishi hali ham hayz davrining buzilishining eng katta sabablaridan biri hisoblanadi.

Xulosa. Prolaktinning ko'tarilishi va LG darajasining pasayishi bilan tavsiflangan kuzatilgan gormonal o'zgarishlar, ehtimol, COVID-19 tomonidan qo'zg'atilgan stress va yallig'lanish reaktsiyalari bilan bog'liq bo'lgan gipotalamo-gipofizar o'qining sezilarli darajada buzilishini ko'rsatadi. Ushbu aniqlangan natijalar yuqumli kasalliklar va gormonal regulyatsiya o'rtasidagi murakkab bog'liqlikni ta'kidlab, tibbiyot xodimlarining COVID-19 dan tuzalgan ayollarning reproduktiv salomatligi bilan bog'liq muammolaridan hushyor bo'lishlari zarurligini ta'kidlaydi

Kalit so'zlar: COVID-19, LG, prolaktin, hayz davrining anomaliyalari, reproduktiv salomatlik, COVID-19 ta'siri, bepushtlik

ИЗУЧЕНИЕ КОРРЕЛЯЦИИ МЕЖДУ УРОВНЯМИ ЛГ И ПРОЛАКТИНА У ЖЕНЩИН С НАРУШЕНИЯМИ МЕНСТРУАЛЬНОГО ЦИКЛА, ВЫЗВАННЫМИ COVID-19 Д.К. Нажмутдинова, Д.Х. Юнусова ТАШКЕНТСКАЯ МЕДИЦИНСКАЯ АКАДЕМИЯ АБСТРАКТ

Актуальность: Пандемия COVID подчеркнула влияние вируса на различные системы организма, включая репродуктивную систему. Целью является изучение взаимосвязи между уровнями ЛГ и пролактина у женщин, перенесших COVID-19 с нарушениями менструального цикла.

Материал и методы. Проведено комплексное ретроспективное когортное исследование с участием 150 женщин репродуктивного возраста, которые сообщили о нарушениях менструального цикла после выздоровления от COVID-19. Для сравнительного анализа их разделили на две группы: группу с COVID-19, в которую вошли женщины с подтвержденными случаями заболевания, и контрольную.

Результаты. Выявлена корреляция клинических проявлений между уровнем ЛГ и пролактином в группе пациентов, перенесших COVID-19; они выявили значимо значимую, умеренно сильную отрицательную корреляционную связь (r=-0,7813 P<0,001), которая показывает, что снижение уровня ЛГ у пациенток, перенесших COVID 19, по-прежнему является одной из основных причин нарушений менструального цикла.

Заключение. Наблюдаемые гормональные нарушения, характеризующиеся повышенным уровнем пролактина и снижением уровня ЛГ, предполагают значительное нарушение гипоталамогипофизарной оси, вероятно, опосредованное стрессовыми и воспалительными реакциями, вызванными COVID-19. Эти результаты подчеркивают сложную взаимосвязь между инфекционными заболеваниями и гормональной регуляцией, подчеркивая необходимость того, чтобы медицинские работники должны быть бдительны.

Ключевые слова: COVID-19, ЛГ, Пролактин, нарушения менструального цикла, репродуктивное здоровье, влияние COVID-19, бесплодие.