

Investigation of Alterations in Hormone Levels in Saudi Patients Affected by COVID-19

<https://doi.org/10.62940/als.v13i3.3838>

Issue: Volume 13, Issue 3

Received: 23-02-2025

Revised: 15-08-2026

Accepted: 24-08-2026

Published online: 27-09-2026

Keywords: COVID-19, SARS-CoV-2, Hormones, Patient cohort

Saleh N. Alghamdi¹, Firoz Ahmed¹, Ammar Alfargh^{1,*}, Mohamed Afifi¹

1. Department of Biological Sciences, College of Science, University of Jeddah, Jeddah, Saudi Arabia

* amalfarga@uj.edu.sa

ABSTRACT

Background: COVID-19 pandemic has posed significant challenges to global healthcare systems, with emerging evidence suggesting a potential impact on endocrine function. This study aimed to investigate the impact of COVID-19 infection on some important body hormones.

Methods: Eighty three (83) individuals hospitalized with COVID-19 infection and 15 healthy one participated in this study to investigate the alterations in thyroid- stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), parathyroid hormone (PTH), prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH).

Results: The results indicated that, COVID 19 infection accompanied with a decrease in the levels of TSH, T3, ACTH in both diseased male and females, while the levels of estrogen and progesterone decreased in diseased females and testosterone levels decreased in diseased males as compared with non-diseased concomitant group. Inversely, the levels of PTH, PRL, LH and cortisol, increased in diseased male and female groups as compared with the concomitant non-diseased groups.

Conclusion: These findings suggest that COVID-19 has a substantial impact on hormonal balance, potentially necessitating clinical monitoring and management. Future research should explore the long-term endocrine effects of COVID-19.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, declared as global pandemic on March 11, 2020, by the World Health Organization (WHO) [1]. Following the initial report of COVID-19 in Wuhan, Hubei Province, China, in December 2019, the virus swiftly disseminated and pose a threat to health and economy across the globe [1].

SARS-CoV-2 spreads via virus-containing droplets from coughing, sneezing, and direct or indirect contact with infected individuals [2]. The SARS-CoV-2 virus enters host cells by attaching its spike protein to the ACE2 receptor situated on the surface of the host cell [3]. The viral genome spans approximately 30,000 nucleotides of plus-strand RNA, allowing for the direct synthesis of viral proteins using the host cellular machinery [1]. Study revealed several potential cis-acting RNA elements present in the SRAS-CoV-2 genome [4].

The genomic sequence of SARS-CoV-2 shares notable similarities with several coronaviruses, including high similarity with bat coronavirus RaTG13 [4, 5]. Additionally, SARS-CoV and MERS-CoV (Middle East Respiratory Coronavirus) also exhibit similarities with SARS-CoV-2 [4, 5]. SARS-CoV-2 primarily infect the lower respiratory systems and showed various clinical symptoms like asymptomatic, mild, moderate, and severe [6]. However, the most prevalent moderate clinical signs of COVID-19 include sneezing, coughing, fever, loss of smell and taste. Severe COVID-19 can lead to acute respiratory distress syndrome (ARDS), a critical complication marked by rapid onset of respiratory failure due to lung inflammation, potentially fatal if not promptly managed [7]. In the absence of specific antiviral treatments for COVID-19, supportive strategies aimed at enhancing overall health and respiratory function, including optimizing oxygenation, become imperative [8].

Understanding the factors influencing COVID-19 severity is crucial for managing patient outcomes and improving survival rates. Reports highlight the role of age in viral infection, with 87% of COVID-19 cases occurring in individuals aged 30 to 79 years, while only 2% to 3% were below the age of 19. The percentage of asymptomatic individuals testing positive for SARS-CoV-2 ranged from 5% to 80% [9]. Furthermore, hormones are pivotal in regulating metabolic processes, reproduction, stress response, and the immune system of the host, with variations observed between genders [10-12].

However, the clinical impact of factors such as age, gender, and hormones on SARS-CoV-2 infection remains inadequately studied, particularly in the Middle Eastern context. Hence, this study is dedicated to investigating the influence COVID-19 on some important hormone levels in Saudi Arabian patient in relation to age, gender.

METHODS

Ethical approval and informed consent

The study secured ethical approval from the Institutional Review Board (IRB) and Ethics Committee of Prince Mshari bin Saud Hospital. Additionally, the study procedures received approval from the University of Jeddah's Scientific and Medical Research Committee. Registration number: HAP-02-J-094, ensuring comprehensive adherence to ethical standards. Throughout this investigation, the principles outlined in the Declaration of Helsinki were strictly followed. Before participating in the study, all subjects provided written informed consent, emphasizing a commitment to ethical research practices.

Participant selection

Between January and February 2021, 83 individuals hospitalized with COVID-19 infection and 15 healthy one participated in the study. Criteria for inclusion involved patients with low to moderate disease severity, confirmed positive for COVID-19 either through nasopharyngeal swab testing or through real-time polymerase chain reaction (RT-PCR) testing. The selected participants exhibited common COVID-19 symptoms such as coughing, fever, sore throat, and shortness of breath, which were documented due to their high prevalence in confirmed cases. The study included individuals with confirmed COVID-19, as evidenced by a positive serum SARS-CoV-2 IgG antibody test post-symptom onset. Additionally, COVID-19 survivors who had undergone steroid treatment (oral, inhalation, topical, or intra-articular) were part of the study cohort. The age criteria for all participants ranged from a minimum of 20 years to 60 years or

older. Clinical and blood biochemical features of patients with COVID-19 were analyzed to exclude individuals with a known or suspected history of liver, heart, or kidney disease, diabetes, or pregnancy.

Furthermore, healthy, normal control subjects who met the study's criteria were chosen from a pool of physicians and coworkers, all of whom provided written informed consent before participating. Thus, this study comprised a diverse group, offering a significant cross-section of the population. Importantly, all COVID-19 participants were in excellent health before contracting the COVID-19 virus

Experimental design participants grouping

To systematically investigate the impact of COVID-19, participants were categorized into distinct groups. The first group served as a control and consisted of 15 healthy people of the same age as the others (4 males and 11 females). Group 2: 83 people with COVID-19 made up the patient group. Patients were further classified into two groups: Group A consisted of 28 male patients and Group B consisted of 55 female patients. Each group was divided into three subgroups according to age: the first included participants under 40 years old, the second included those between 40 and 59 years old, and the third consisted of those 60 years and older.

Blood samples collection and preparation

Hormone levels were measured by collecting blood samples from the participants who were granted permission for the procedure. Using aseptic venipuncture techniques, we extracted and collected 2 ml of blood from each participant into plain test tubes, allowing a clotting period of 10 minutes at room temperature. Subsequent centrifugation at 5000 x g for 5 minutes facilitated the separation of serum by the Universal 320 centrifuge by Hettich®. Following the isolation of the serum, for hormonal investigation

Investigation of serum hormones levels

Thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), parathyroid hormone (PTH), prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), progesterone (P3), cortisol, adrenocorticotrophic hormone (ACTH), and testosterone (TESTO). Were investigated using a commercial kit supplied by ROCHE® of catalogue numbers (606351, 602863, 556859, 611684, 608332, 610466, 526762, 563870, 589428, 556887, 630737, 589649). All measurements were done using Roche® Cobas 6000 c following the manufacturer-recommended procedures for each parameter.

Statistical analysis

All data were analyzed using a one-way analysis of variance (ANOVA) using SPSS statistical version 22 software package (SPSS, Inc, USA). by Duncan's test. Data were presented as mean $\pm$ SD and $P < 0.05$ was considered statistically significant.

RESULTS

COVID 19 infection accompanied with a decrease in the levels of TSH (figure 1 A), T3 (figure 1 B), ACTH (figure 3C) in both diseased male and females, while the levels of estrogen (figure 2 D) and progesterone (figure 2 A) deceased in diseased females and testosterone levels (figure 3D) decreased in diseased males as compared with non-diseased concomitant group. Inversely, the levels of PTH (figure 1D), PRL (figure 2A), LH (figure 2B) and cortisol (figure 3B), increased in diseased male and female groups as compared with the concomitant non-diseased groups.

Figures

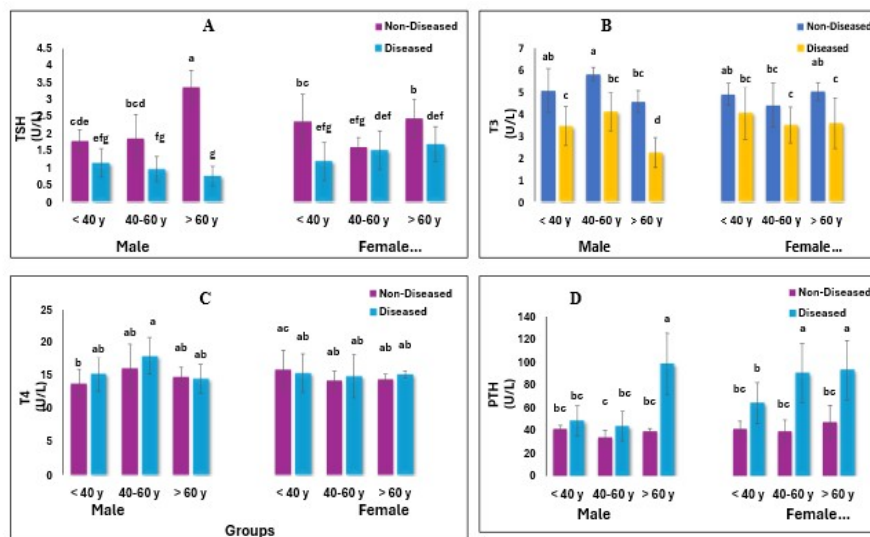


Figure 1: Effect of COVID-19 on TSH levels (A), T3 levels (B), T4 levels (C) and PTH (D) Columns carry different letters are statistically significant at $P \leq 0.05$.

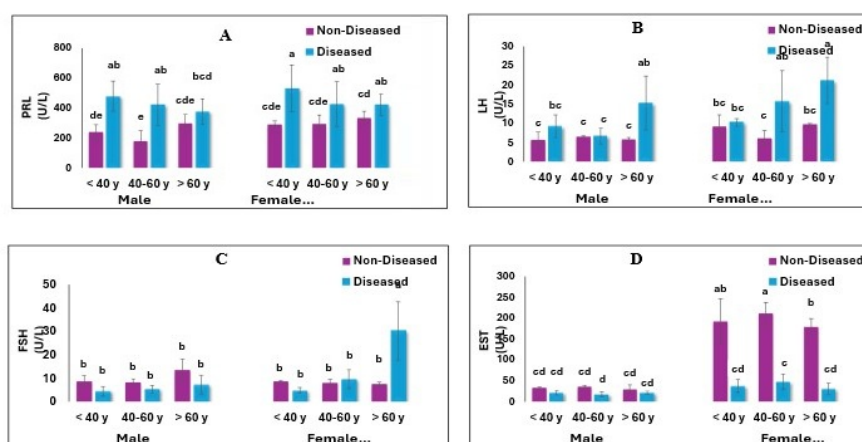


Figure 2: Effect of COVID-19 on PRL levels (A), LH levels (B), FSH levels (C) and EST (D) Columns carry different letters are statistically significant at $P \leq 0.05$.

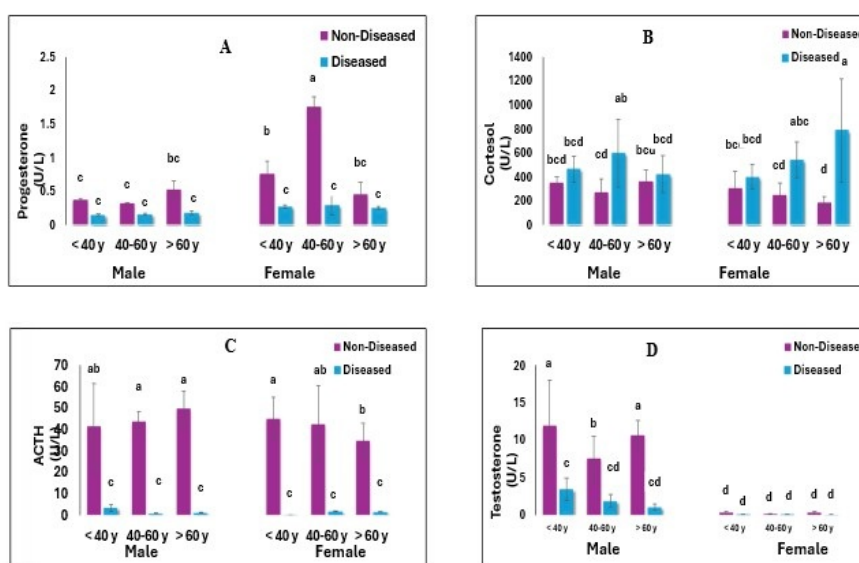


Figure 3: Effect of COVID-19 on progesterone levels (A), cortisol levels (B), ACTH levels (C) and Testosterone (D). Columns carry different letters are statistically significant at $P \leq 0.05$.

DISCUSSION

This work investigated the impact of COVID-19 on hormone parameters in individuals affected by the disease compared to those who were not. Moreover, we examined how COVID-19 severity is influenced by different hormone parameters, age and gender.

Hormonal parameters play a crucial role in evaluating the functionality of the endocrine system, regulating vital physiological processes such as metabolism, growth, reproduction, and stress and immune response. Key hormones including TSH, FT3, and FT4 are essential for thyroid function, while PTH maintains calcium and phosphorus balance. Hormones such as PRL, LH, and FSH are involved in reproductive processes, whereas cortisol and ACTH regulate stress response and metabolism. Testosterone, primarily synthesized in the testes, influences male reproductive functions and overall well-being. Estradiol and progesterone are crucial for female reproductive health and bone maintenance. These hormonal parameters are invaluable in diagnosing various endocrine disorders like hypothyroidism, hyperthyroidism, and Addison's disease, as well as monitoring their treatment. While the normal range for hormonal parameters varies based on age, gender, and other factors, deviations from these ranges may indicate underlying endocrine disorders. Understanding the intricate interplay of these hormones and their alterations in response to COVID-19 infection is essential for comprehensive patient care and management strategies [13]

This study showed that COVID-19 infection is associated with a significant decrease in TSH concentration in all diseased individuals as compared with their concomitant non-diseased individuals (figure 1A). This decrease was more pronounced in males than in females. This finding is consistent with the results of a number of other studies. For example, Chen et al. demonstrated that 56% of COVID-19 patients had significantly lower TSH and total T3 levels compared to controls and non-COVID-19 pneumonia patients [14]. The severity of COVID-19 correlated with reduced TSH and total T3 levels. Post-recovery, no significant differences in thyroid hormone levels were observed between COVID-19 patients and controls. TSH level is inversely related to IL-6 level in COVID-19 patients [15]. The study also found that the decrease in TSH levels was associated with an increased risk of developing hypothyroidism. The decrease in TSH concentration is likely due to the increased production of IL-6 and other pro-inflammatory cytokines, which can suppress the hypothalamic-pituitary-thyroid (HPT) axis.

The decrease in TSH levels in COVID-19-infected patients may have a number of implications for clinical management. For example, it is important to be aware of the potential for hypothyroidism in COVID-19-infected patients, especially those who are experiencing symptoms such as fatigue, weight gain, and hair loss. Additionally, it may be necessary to monitor TSH levels in COVID-19-infected patients, especially those who are at risk for developing hypothyroidism. COVID-19 significantly decreased the triiodothyronine (T3) concentration in both male and female patients compared to non-diseased individuals of the same age group (Figure 1B). These findings are consistent with the results of other studies, which have shown that COVID-19 can lead to decreased T3 levels [14]. The decrease in T3 concentration in COVID-19 patients is likely due to the increased production of pro-inflammatory cytokines, which can suppress the thyroid gland. Pro-inflammatory cytokines are proteins released by immune cells in response to infection or injury. They can have a variety of effects on the body, including suppressing the thyroid gland. Our study indicates no significant difference in T4 concentration between diseased and non-diseased individuals across age groups and genders (Figure 1 C). This aligns with previous research, which found no significant T4 level changes in COVID-19 patients compared to healthy controls [14]. Other studies found that TSH levels tend to increase with age, while free T4 levels remain relatively constant over time [17] (Duntas & Jonklaas, 2021). The relationship between TSH and free T4 is complex and nonlinear, and it differs by age and sex [15]. COVID-19 individuals had higher PTH concentration than corresponding non-diseased individuals (Figure 1 D). Overall, COVID-19 appears to significantly impact PTH concentration across various age groups and genders. Our study suggest that COVID-19 individuals had higher PRL and cortisol concentration than corresponding non-diseased individuals of different ages and genders (Figure 2 A) and support previous finding [18]. Our study suggests that individuals with COVID-19 exhibit significantly higher LH, concentrations compared to corresponding non-diseased individuals, particularly among males over 60 years old and females over 40 years old (Figure 2 B), while FSH increased significantly only in females over 60 years old (figure 2 C). Men with COVID-19 often show decreased testosterone with a compensatory rise in LH [19, 20], For women, FSH and/or LH elevations and transient ovarian dysfunction after infection – especially in older or peri/post-menopausal women supported by study of Gullo et al., [21] and Voros et al., [22]. COVID 19 has impact on both female and male

sex hormones, this study proved that the concentrations of EST (figure, 2 D) and progesterone (figure 3.A) significantly decreased in diseased female as compared with the non-diseased, while in males the testosterone decrease significantly in diseased individuals as compared with non-diseased (figure 3.D). Regarding testosterone levels the results of this study go at the same line with that of Salonia et al., [23] and Salciccia et al., [24] who report that testosterone lowered markedly in patients with COVID-19, with levels falling further with disease severity. Mohammed et al., [25] and MacArthur et al., [26] report lower estradiol/ progesterone or associations between low female hormones and worse COVID-19. Consistent with previous reports, we found significantly higher serum cortisol in COVID-19 patients compared with matched non-diseased controls (figure 3.B); pooled analyses and several cohort studies report similar cortisol elevations in acute SARS-CoV-2 infection [27]. Regarding ACTH, it decreased in diseased male and female groups as compared with the concomitant non-diseased groups figure 3 C), The adrenal gland and pituitary may express ACE2, making them potential targets for SARS-CoV-2. COVID-19 can cause a temporary inflammation of the pituitary (or other central regulation changes), leading to reversible central adrenal insufficiency [28]

This study demonstrates that COVID-19 infection significantly disrupts endocrine function, leading to marked hormonal imbalances across thyroid, adrenal, and reproductive axes. The observed decreases in TSH, T3, ACTH, estrogen, progesterone, and testosterone, alongside increases in PTH, PRL, LH, and cortisol, highlight a broad endocrine impact affecting both males and females. These findings emphasize the need for routine hormonal evaluation in COVID-19 patients, not only during acute illness but also in recovery. Long-term follow-up is crucial to determine whether these endocrine alterations persist, resolve, or contribute to post-COVID complications.

CONFLICT OF INTEREST

The authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Mohamed Afifi, conceptualized the study, carried out formal analysis, wrote the original draft, and supervised the research. Saleh N. Alghamdi, Firoz Ahmed, conceptualized the study and performed the biochemical assays. Ammar Alfargh revised and published the paper. All authors have reviewed and approved the final version of the manuscript.

ACKNOWLEDGMENT

We extend our gratitude to the Department of Biological Sciences at the University of Jeddah and Prince Mshari bin Saud Hospital for providing us with the facilities to conduct this research.

REFERENCES

1. Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chinese Medical Journal (English)*, (2020); 133(9): 1015-1024.
2. Lee EC, Wada NI, Grabowski MK, Gurley ES, Lessler J. The engines of SARS-CoV-2 spread. *Science*, (2020); 370(6515): 406-407.
3. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*, (2020); 181(2): 271-280.e8.
4. Ahmed F, Sharma M, Al-Ghamdi A, Al-Yami SM, Al-Shehri A, et al. A comprehensive analysis of cis-acting RNA elements in the SARS-CoV-2 genome by a bioinformatics approach. *Frontiers in Genetics*, (2020); 11: 1385.
5. Uddin M, Mustafa F, Rizvi TA, Loney T, Suwaidi HA, et al. SARS-CoV-2/COVID-19: viral genomics, epidemiology, vaccines, and therapeutic interventions. *Viruses*, (2020); 12(5).
6. Singh SJ, Barradell AC, Greening NJ, Bolton CE, Jenkins G, et al. Respiratory sequelae of COVID-19: pulmonary and extrapulmonary origins, and approaches to clinical care and rehabilitation. *Lancet Respiratory Medicine*, (2023); 11(8): 709-725.
7. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. *International Journal of Antimicrobial Agents*, (2020); 55(5): 105954.
8. Wang T, Du Z, Zhu F, Cao Z, An Y, et al. Comorbidities and multi-organ injuries in the treatment of COVID-19. *The Lancet*, (2020); 395(10228): e52.
9. Akin L, Gözel MG. Understanding dynamics of pandemics. *Turkish Journal of Medical Sciences*, (2020); 50(SI-1): 515-519.
10. Çabuk SA, Cevher AZ, Küçükardalı Y. Thyroid function during and after COVID-19 infection: a review. *touchREVIEWS in Endocrinology*, (2022); 18(1): 58-62.
11. De Vito P, Incerpi S, Pedersen JZ, Luly P, Davis FB, et al. Thyroid hormones as modulators of immune activities at the cellular level. *Thyroid*, (2011); 21(8): 879-890.

12. Ruggeri RM, Campennì A, Siracusa M, Frazzetto G, Gullo D. Subacute thyroiditis in a patient infected with SARS-CoV-2: an endocrine complication linked to the COVID-19 pandemic. *Hormones (Athens)*, (2021); 20(1): 219-221.
13. Szczepiński Ł, Okruszko MA, Szablowski M. Long-term effects of COVID-19 on the endocrine system: a pilot case-control study. *Frontiers in Endocrinology (Lausanne)*, (2023); 14: 1192174.
14. Chen M, Zhou W, Xu W. Thyroid function analysis in 50 patients with COVID-19: a retrospective study. *Thyroid*, (2021); 31(1): 8-11.
15. Lania A, Sandri MT, Cellini M, Mirani M, Lavezzi E, et al. Thyrotoxicosis in patients with COVID-19: the THYRCOV study. *European Journal of Endocrinology*, (2020); 183(4): 381-387.
16. Hadlow NC, Rothacker KM, Wardrop R, Brown SJ, Lim EM, et al. The relationship between TSH and free T4 in a large population is complex and nonlinear and differs by age and sex. *Journal of Clinical Endocrinology and Metabolism*, (2013); 98(7): 2936-2943.
17. Walsh JP. Thyroid function across the lifespan: do age-related changes matter? *Endocrinology and Metabolism (Seoul)*, (2022); 37(2): 208-219.
18. Al-Kuraishy HM, Al-Gareeb AI, Qusti S, Al-Maiah TJ, Cruz-Martins N, et al. The crucial role of prolactin-lactogenic hormone in COVID-19. *Molecular and Cellular Biochemistry*, (2022); 477(5): 1381-1392.
19. Cai Z, Zhong J, Jiang Y, Zhang J. Associations between COVID-19 infection and sex steroid hormones. *Frontiers in Endocrinology*, (2022); 13: 940675.
20. Wang S, Zhang A, Pan Y, Li X, Jiang W, et al. Association between COVID-19 and male fertility: systematic review and meta-analysis of observational studies. *World Journal of Men's Health*, (2023); 41(2): 311-329.
21. Gullo G, Lopez A, Loreto C, Rizzo F, Gullo A, et al. COVID-19 and female fertility: an observational prospective multicenter cohort study: upholding reproductive rights in emergency circumstances. *Diagnostics (Basel)*, (2024); 14(19): 2118.
22. Voros C, Mavrogianni D, Minaoglou A, Kaltsas G, Vassiliadi DA, et al. Unveiling the impact of COVID-19 on ovarian function and premature ovarian insufficiency: a systematic review. *Biomedicines*, (2025); 13: 407.
23. Salonia A, Pontillo M, Capogrosso P, Rastrelli G, Dell'Oglio P, et al. Severely low testosterone in males with COVID-19: a case-control study. *Andrology*, (2021); 9(4): 1043-1052.
24. Salciccia S, Moriconi M, Asero V, De Berardinis E, Busetto GM, et al. Systematic review and meta-analysis of serum total testosterone and luteinizing hormone variations across hospitalized COVID-19 patients. *Scientific Reports*, (2024); 14: 2786.
25. Mohammed GF, Saad HM. Severe COVID-19 has low testosterone, oestrogen levels, and impaired sexuality. *Sexologies*, (2022); 31(4): 477-486.
26. MacArthur T, Goswami J, Ramachandran D, Klein DA, Toth TL, et al. Estradiol and dihydrotestosterone levels in COVID-19 patients. *Mayo Clinic Proceedings*, (2023); 98(4): 559-568.
27. Amiri-Dashatan N, Koushki M, Parsamanesh N, Chiti H. Serum cortisol concentration and COVID-19 severity: a systematic review and meta-analysis. *Journal of Investigative Medicine*, (2022); 70(3): 766-772.
28. Porntharukchareon T, Dechates B, Sirisreetreerux S, Chantarangsu S, Phowthongkum P, et al. The existence of adrenal insufficiency in patients with COVID-19 pneumonia. *Frontiers in Endocrinology*, (2024); 15: 1337652.



This work is licensed under a Creative Commons Attribution- NonCommercial 4.0 International License. To read the copy of this license please visit: <https://creativecommons.org/licenses/by-nc/4.0/>