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HORMONAL REGULATION IN POST-COVID COMPLICATIONS: EFFECTS ON THE ADRENAL GLANDS, THYROID, AND METABOLISM

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Abstract

The aim of the study was to identify specific features of hormonal regulation in patients during the post-COVID period, with a focus on adrenal function, thyroid activity, and metabolism. The study included 62 patients (34 women and 28 men) aged 22 to 64 years, who underwent treatment and rehabilitation for 3–6 months after COVID-19. Patients were divided into two groups: without steroid therapy (n=32) and with steroid therapy (n=30). Hormonal profile parameters (cortisol, TSH, free T4, HbA1c, HOMA-IR), carbohydrate and lipid metabolism, as well as instrumental findings were assessed. In patients without steroid therapy, subclinical hypothyroidism, insulin resistance, dyslipidemia, and reduced cortisol levels were more frequently observed. In patients receiving steroid therapy, a more pronounced recovery of the hormonal profile and stabilization of metabolism were noted; however, the risk of secondary adrenal insufficiency persisted. Post-COVID syndrome is accompanied by significant endocrine disorders, requiring comprehensive monitoring and individualized rehabilitation programs.

Keywords

COVID-19, endocrine complications, adrenal glands, thyroid gland, metabolism, thyroid-stimulating hormone, insulin resistance, dyslipidemia; rehabilitation, graded physical activity.

Introduction. The COVID-19 pandemic has revealed a wide spectrum of systemic complications, among which endocrine dysregulation occupies a special place. Viral infection and subsequent post-COVID conditions affect the hypothalamic–pituitary–adrenal axis, thyroid function, and metabolic processes, making the study of these changes highly relevant to clinical practice [1,2,3].

Several national studies have demonstrated disturbances in carbohydrate metabolism, instability of glucose and HbA1c levels, as well as signs of insulin resistance in patients after COVID-19 [4]. In addition, thyroid dysfunction has been reported, including the development of post-COVID thyroiditis and autoimmune disorders [1,5]. An important area of research remains the role of graded physical activity and rehabilitation measures, which contribute to the stabilization of metabolic processes and improvement of respiratory and endocrine function [1,7,10].

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International studies confirm the systemic impact of COVID- 19 on the endocrine system. Panesar et al. (2024) demonstrated an association between infection and thyroid dysfunction [7], while Wei et al. (2023) described adrenal impairment in post- COVID patients [11]. Koch (2024) emphasized hormonal imbalances and complex immune disturbances in long COVID [9]. Metabolic disorders, including the development of post- COVID metabolic syndrome, were comprehensively analyzed by Wang et al. (2023) [14].

Particular attention has been given to the coexistence of COVID- 19 and diabetes. Bornstein et al. (2020) proposed practical recommendations for the management of diabetic patients during the pandemic [13], while Pal and Banerjee (2020) highlighted new links between COVID- 19 and endocrine diseases [12]. Esmaeilzadeh et al. (2022) provided a systematic review of metabolic and hormonal complications of COVID- 19 [8].

Thus, accumulated national and international evidence underscores the high clinical significance of post- COVID endocrine disorders. Their investigation not only helps to elucidate mechanisms of hormonal dysregulation but also contributes to the development of effective rehabilitation strategies aimed at restoring adrenal, thyroid, and metabolic balance.

Objective. To determine the specific features of hormonal regulation in post-COVID complications, with emphasis on the functional state of the adrenal glands, thyroid gland, and metabolic processes, as well as to identify the clinical and pathophysiological mechanisms underlying these disturbances in order to develop effective rehabilitation strategies.

Materials and Methods. This study was designed to provide a comprehensive assessment of hormonal regulation in patients who had recovered from COVID-19. The cohort included men and women aged 18 to 65 years who underwent inpatient treatment and outpatient rehabilitation for 3–6 months following infection. Inclusion criteria were a confirmed COVID-19 diagnosis by PCR, the presence of clinical manifestations of post-COVID syndrome, and informed consent to participate. Exclusion criteria included severe comorbidities that prevented full examination.

Endocrine evaluation comprised measurement of morning serum cortisol (08:00–09:00), thyroid-stimulating hormone (TSH), and free thyroxine (fT4) using enzyme immunoassay. Carbohydrate metabolism was assessed by fasting glucose, glycated hemoglobin (HbA1c), and insulin levels, followed by calculation of the HOMA-IR index to evaluate insulin resistance. Lipid profile analysis included total cholesterol, LDL, HDL, and triglycerides.

Instrumental methods involved thyroid ultrasound to detect structural changes and signs of thyroiditis, as well as computed tomography or magnetic resonance imaging of the adrenal glands when clinically indicated. All examinations were performed using certified equipment meeting international standards, with mandatory calibration of instruments.

Statistical analysis was conducted using SPSS Statistics 26.0. Variational statistical methods were applied, with mean values (M) and standard errors (m) calculated. Differences between groups were assessed using Student's t-test for independent samples and the χ^2 test for categorical data. Statistical significance was set at $p<0.05$.

Thus, the methodological framework ensured a comprehensive evaluation of endocrine function in post-COVID patients, allowing identification of specific features of hormonal regulation and metabolic disturbances depending on disease severity and concomitant therapy.

Results. The study included 62 patients who had recovered from COVID-19, comprising 34 women and 28 men aged 22 to 64 years. All participants were in the post-COVID period lasting from three to six months after recovery, which allowed assessment of both early and more delayed consequences of the infection. Patients were divided into two groups: Group 1 (n=32) consisted of individuals who had not received steroid therapy, while Group 2 (n=30) included those who had been administered glucocorticoids during the acute phase of the disease.

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In Group 1, post-COVID syndrome manifestations were more frequent, including instability of carbohydrate metabolism, episodes of hyperglycemia and hypoglycemia, elevated thyroid-stimulating hormone (TSH) levels, as well as complaints of pronounced asthenia and reduced work capacity. This group demonstrated a higher incidence of subclinical hypothyroidism, insulin resistance, and dyslipidemia, indicating insufficient compensation of endocrine functions without pharmacological support.

In Group 2, where patients had received steroid therapy, a more pronounced recovery of the hormonal profile was observed. Cortisol levels in most patients remained within the physiological range, HbA1c values showed a tendency to decrease, and thyroid function was more stable. However, some patients exhibited signs of secondary adrenal insufficiency, necessitating additional monitoring and dynamic follow-up.

Table 1.

Hormonal profile indicators in post-COVID patients

Parameter	Group 1 (no steroids, n=32)	Group 2 (with steroids, n=30)	Reference range
Cortisol (µg/dL)	9.8 ± 2.1	14.2 ± 2.5	6–18
TSH (mIU/L)	4.8 ± 1.2	2.9 ± 0.9	0.4–4
Free T4 (pmol/L)	10.5 ± 2.3	14.1 ± 2.7	10–22
HbA1c (%)	6.8 ± 0.7	5.9 ± 0.5	
HOMA-IR	3.1 ± 0.9	2.2 ± 0.6	

Analysis of the hormonal profile (Table 1) revealed that in patients without steroid therapy, serum cortisol levels were reduced (9.8 µg/dL), indicating possible exhaustion of the hypothalamic–pituitary–adrenal axis. In the steroid-treated group, values were higher (14.2 µg/dL), closer to the physiological range. TSH levels in Group 1 averaged 4.8 mIU/L, suggesting a tendency toward subclinical hypothyroidism, whereas in Group 2 they were closer to normal (2.9 mIU/L). Free T4 in patients without steroids was at the lower limit of normal (10.5 pmol/L), while in the steroid group values were higher (14.1 pmol/L), indicating better preservation of thyroid function.

HbA1c in Group 1 was 6.8%, corresponding to prediabetes, whereas in Group 2 it was lower (5.9%), closer to normal values. The HOMA-IR index was elevated in patients without steroids (3.1), while in the steroid group it remained within acceptable limits (2.2).

Table 2.

Metabolic parameters in post-COVID patients

Parameter	Group 1 (no steroids, n=32)	Group 2 (with steroids, n=30)	Reference range
Fasting glucose (mmol/L)	6.1 ± 0.8	5.3 ± 0.6	3.9–5.5
Total cholesterol (mmol/L)	5.9 ± 1.1	5.1 ± 0.9	
Triglycerides (mmol/L)	2.1 ± 0.6	1.6 ± 0.4	
LDL cholesterol (mmol/L)	3.7 ± 0.8	3.0 ± 0.7	
HDL cholesterol (mmol/L)	1.0 ± 0.2	1.3 ± 0.3	

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Analysis of metabolic indicators demonstrated that patients without steroid therapy continued to exhibit features of metabolic syndrome. Fasting glucose levels were elevated (6.1 mmol/L), exceeding the normal range, whereas in the steroid group values were closer to normal (5.3 mmol/L). Total cholesterol in Group 1 was 5.9 mmol/L, above reference values, compared to 5.1 mmol/L in Group 2. Triglycerides were increased in patients without steroids (2.1 mmol/L), while in the steroid group they were closer to normal (1.6 mmol/L). LDL cholesterol in Group 1 reached 3.7 mmol/L, indicating increased risk of atherosclerosis, whereas in Group 2 it was lower (3.0 mmol/L). HDL cholesterol was reduced in patients without steroids (1.0 mmol/L), while in the steroid group it was higher (1.3 mmol/L), reflecting a more favorable lipid profile.

Thus, the results indicate that patients without steroid therapy more frequently exhibited signs of hormonal and metabolic dysregulation, including hypothyroidism, insulin resistance, and dyslipidemia. In contrast, patients who had received steroid therapy showed values closer to normal ranges, suggesting more effective compensation of endocrine and metabolic disturbances. Nevertheless, the risk of complications associated with prolonged glucocorticoid exposure persisted, underscoring the need for individualized rehabilitation strategies and comprehensive endocrinological monitoring.

Discussion. The results of this study confirm that post-COVID syndrome is accompanied by significant disturbances in hormonal regulation and metabolic processes. Patients who did not receive steroid therapy more frequently exhibited dysfunction of the thyroid gland, adrenal glands, and carbohydrate metabolism. Elevated TSH levels combined with reduced free T4 values indicate the development of subclinical hypothyroidism, consistent with national reports describing post-COVID thyroiditis and autoimmune dysfunction [1,3,6].

Reduced cortisol levels in Group 1 suggest possible exhaustion of the hypothalamic–pituitary–adrenal axis. Similar findings have been reported in international studies, which describe secondary adrenal insufficiency in some post-COVID patients [11]. This condition may be related both to direct viral tissue damage and to the impact of cytokine storm, leading to dysregulation of the body's stress response.

Carbohydrate metabolism disturbances in patients without steroid therapy (elevated HbA1c and HOMA-IR) indicate the development of insulin resistance and prediabetes. These findings align with studies demonstrating the association of COVID-19 with metabolic syndrome and exacerbation of diabetes mellitus [14]. Notably, in Group 2, HbA1c and HOMA-IR values were closer to normal, suggesting more effective compensation of carbohydrate metabolism when steroid therapy was combined with rehabilitation.

Analysis of the lipid profile revealed persistent dyslipidemia in patients without steroid therapy—elevated total cholesterol, triglycerides, and LDL cholesterol, with reduced HDL cholesterol. These changes increase the risk of cardiovascular complications and require comprehensive corrective measures. In contrast, patients in Group 2 demonstrated a more favorable lipid profile, which may be associated with reduced systemic inflammation and a more stable hormonal background.

Overall, the findings highlight differences in the nature of endocrine disturbances depending on therapy. Patients without steroid support more often exhibited instability of metabolic processes and hormonal balance, whereas those treated with steroids showed more pronounced recovery of endocrine function. However, the risk of complications related to prolonged glucocorticoid exposure persisted, including secondary adrenal insufficiency and lipid metabolism disorders.

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These data emphasize the need for individualized rehabilitation programs and comprehensive endocrinological monitoring in the post-COVID period. Both the baseline condition of the patient and the specifics of prior therapy must be considered. The optimal approach combines regular monitoring of the hormonal profile, correction of metabolic disturbances, and the use of graded physical activity, which contributes to stabilization of gas exchange processes and improvement of overall functional status [4,8].

Conclusion. This study demonstrated that post-COVID syndrome is accompanied by pronounced disturbances in hormonal regulation and metabolic processes, affecting the adrenal glands, thyroid gland, and carbohydrate metabolism. Patients who did not receive steroid therapy more frequently exhibited signs of subclinical hypothyroidism, insulin resistance, dyslipidemia, and reduced cortisol levels, suggesting possible exhaustion of the hypothalamic–pituitary–adrenal axis. These findings highlight the instability of the endocrine system and the need for comprehensive monitoring.

In patients who received steroid therapy, a more pronounced recovery of the hormonal profile was observed: cortisol levels and thyroid function parameters were more often within normal ranges, while carbohydrate and lipid metabolism appeared more stable. However, some patients remained at risk of secondary adrenal insufficiency and lipid metabolism disturbances, necessitating careful follow-up and individualized rehabilitation programs.

The results confirm that endocrine complications represent an important component of post-COVID syndrome. Their management requires a comprehensive approach, including regular endocrinological monitoring, hormonal profile assessment, correction of metabolic disturbances, and the use of graded physical activity as part of rehabilitation. Individualization of patient management strategies, taking into account the severity of the infection and the nature of prior therapy, is of particular importance.

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