PEDIATRICS

PSYCHOEMOTIONAL STATE AND HORMONAL STATUS OF ADOLESCENT GIRLS IN THE POST-COVID PERIOD

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RESUME

Introduction. *Post-COVID syndrome (PCS) in children and adolescents represents a relevant medical and social problem. Adolescent girls may be particularly vulnerable to the development of psychoemotional and endocrine disorders associated with PCS due to hormonal changes during the pubertal period.*

The aims. *To assess the psychoemotional status and hormonal profile in adolescent girls depending on the presence of post-COVID syndrome symptoms, and to establish correlations between psychoemotional indicators and hormone concentrations of the hypothalamic-pituitary-thyroid-adrenal axis in the post-COVID period.*

Materials and methods. *A total of 126 girls aged 11–16 years were examined: 44 with PCS symptoms (main group); 40 without PCS symptoms (comparison group); and 42 conditionally healthy girls (control). The main group was divided into subgroups depending on the time period after COVID-19: 3–5 (n = 11), 6–9 (n = 12), 11–12 (n = 10), and 13–24 months (n = 11). Psychoemotional status was assessed using the SAN (Well-being, Activity, Mood) scale, BDI-1A, and A.M. Prikhozhan's Manifest Anxiety Scale. Concentrations of TSH, free T4, and cortisol were determined by enzyme-linked immunosorbent assay.*

Results. *Girls with PCS symptoms showed more pronounced forms of depressive symptomatology, increased anxiety, and reduced activity and well-being. Elevated levels of TSH and cortisol were observed compared to control groups. The differences persisted throughout the entire post-COVID period with maximum severity at 6–12 months after COVID-19. Correlations were established between the severity of depressive symptoms and TSH concentration (p = 0.002), and between anxiety and cortisol (p = 0.001) in respondents throughout the post-COVID period.*

Conclusion. *The established correlations between psychometric indicators and hormone concentrations indicate the involvement of neuroendocrine mechanisms in the pathogenesis of psychoemotional manifestations of PCS. The results substantiate the need for comprehensive examination of adolescent girls with PCS symptoms for timely diagnosis and correction of disorders.*

Keywords: *COVID-19, Post-COVID syndrome, adolescent girls, psychoemotional status, anxiety, depression, cortisol, TSH, hormonal status, pubertal period*

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ПСИХОЭМОЦИОНАЛЬНОЕ СОСТОЯНИЕ И ГОРМОНАЛЬНЫЙ СТАТУС У ДЕВОЧЕК-ПОДРОСТКОВ В ПОСТКОВИДНОМ ПЕРИОДЕ

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РЕЗЮМЕ

Введение. *Постковидный синдром (ПКС) у детей и подростков представляет актуальную медико-социальную проблему. Девочки-подростки могут быть особенно уязвимы к развитию психоэмоциональных и эндокринных нарушений на фоне ПКС в связи с гормональными перестройками пубертатного периода.*

Цель. *Оценить психоэмоциональное состояние и гормональный статус у девочек-подростков в зависимости от наличия симптомов постковидного синдрома, а также установить взаимосвязь между показателями психоэмоционального состояния и концентрацией гормонов гипофизарно-тиреоидно-надпочечниковой системы в постковидном периоде.*

Материалы и методы. *Обследовано 126 девочек 11–16 лет: 44 с симптомами ПКС (основная группа); 40 без симптомов ПКС (группа сравнения); и 42 условно здоровые девочки (контроль). Основная группа разделена на подгруппы в зависимости от временного периода после COVID-19: 3–5 (n = 11), 6–9 (n = 12), 11–12 (n = 10) и 13–24 месяцев (n = 11). Психоэмоциональное состояние оценивалось с использованием методик САН, BDI-1A и шкалы явной тревожности А.М. Прихожан. Определялись концентрации ТТГ, Т4 св. и кортизола методом иммуноферментного анализа.*

Результаты. *У девочек с симптомами ПКС выявлены более выраженные формы депрессивной симптоматики, повышенная тревожность, сниженная активность и самочувствие. Отмечается повышенный уровень ТТГ и кортизола по сравнению с контрольными группами. Различия сохранялись на протяжении всего постковидного периода с максимальной выраженностью в период 6–12 месяцев после COVID-19. Установлена взаимосвязь между выраженностью депрессивных симптомов и концентрацией ТТГ (p = 0,002), тревожностью и кортизолом (p = 0,001) у респондентов на протяжении всего постковидного периода.*

Заключение. *Установленные корреляции между психометрическими показателями и концентрацией гормонов свидетельствуют о вовлечении нейроэндокринных механизмов в патогенез психоэмоциональных проявлений ПКС. Результаты обосновывают необходимость комплексного обследования девочек-подростков с симптомами ПКС для своевременной диагностики и коррекции нарушений.*

Ключевые слова: *COVID-19, постковидный синдром, девочки-подростки, психоэмоциональное состояние, тревожность, депрессия, кортизол, ТТГ, гормональный статус, пубертатный период*

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INTRODUCTION

The COVID-19 pandemic, caused by a novel coronavirus infection, has significantly impacted the health of people of all ages, including children and adolescents. Clinical experience has shown that the effects of this infection go beyond the acute phase of the disease, and can lead to long-term symptoms, known as "post-COVID syndrome" or "Long COVID-19" [1-3]. According to the World Health Organization, post-COVID syndrome (PCS) in children and adolescents is defined as the presence of persistent or new symptoms that develop 3 months or more after the initial infection with SARS-CoV-2, lasting for at least 2 months and not explained by other diagnoses [4]. Clinical manifestations of this syndrome in children and adolescents include a wide range of symptoms, such as fatigue, sleep disorders, cognitive dysfunction, headaches, anosmia, and psychoemotional disorders [5, 6]. These symptoms may persist for months or even years after COVID-19 infection, making it challenging to resume normal life activities [7, 8].

Modern research indicates a high prevalence of psychosocial and emotional disorders in children and adolescents with PCS [9, 10]. It has been demonstrated that this group of patients experiences increased anxiety, depression, cognitive dysfunction, and behavioral disorders [11, 12]. However, the pathogenic mechanisms underlying these conditions remain poorly understood. Nevertheless, there is speculation about a link between these disorders and the effect of the virus on the central nervous system, as well as dysfunction of the hypothalamic-pituitary-adrenal axis [13, 14]. Oxidative stress is believed to play a significant role in the pathogenesis of PCS, as studies have shown changes in the lipid peroxidation-antioxidant defense system among children and adolescents who have experienced COVID-19 [15, 16]. These alterations may contribute to the development of endocrinological disorders and psychoemotional dysfunction.

Growing evidence suggests that COVID-19 may affect endocrine function, in particular the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-adrenal axes [17, 18]. Reports of subacute thyroiditis and thyroid dysfunction in the post-COVID period in adult patients have been published [19, 20]. Studies of children who have recovered from COVID-19 have also revealed thyroid dysfunction, which can impact growth, development, and metabolic processes in childhood and adolescence [21]. Puberty is a time of significant changes in the endocrine system that can influence the course and severity of the post-COVID syndrome in adolescents. It is of particular interest to study the functional state of the hypothalamic-pituitary-thyroid-adrenal axis in adolescent girls, as this axis plays a crucial role in regulating metabolic processes, stress responses, and the psychoemotional state. Additionally, adolescent girls may be more susceptible to the development of psychoemotional disorders in the post-COVID period compared to boys of a similar age. This could be attributed to both hormonal factors associated with puberty, such as fluctuations in estrogen and progesterone levels that affect neurotransmitter systems, as well as socio-psychological factors such as increased emotional reactivity, coping strategies, and social expectations [2].

Investigating the link between the psychoemotional state and the hypothalamic-pituitary-thyroid-adrenal axis in adolescent girls during the post-COVID period is important for several reasons. Firstly, adolescence represents a critical phase for the development of women's reproductive health, and any disturbances in the endocrine system may have long-term consequences for health. Secondly, hormonal changes are closely associated with the psychoemotional state of adolescents, which may exacerbate the symptoms of post-COVID syndrome. Thirdly, understanding the pathogenic mechanisms underlying the development of disorders in this age group is essential for developing effective strategies for their identification, management, and treatment.

Despite the increasing attention to the issue of post-COVID syndrome in children and adolescents, research into the condition of the thyroid and adrenal glands in this age group remains limited [17, 21]. Virtually no studies have been conducted to assess the psychoemotional state and the functioning of the hypothalamic-pituitary-thyroid-adrenal axis in adolescent girls in the post-COVID period.

Therefore, investigating the psychoemotional state and functioning of the hypothalamic-pituitary-thyroid-adrenal axis in adolescent girls in the post-COVID period presents a significant scientific and practical challenge. The findings from such studies could contribute to a better understanding of the pathogenetic mechanisms underlying the development of PCS in adolescents and could help to optimize medical and psychological treatment for this patient population.

THE AIM OF THE STUDY

To assess the psychoemotional state and hormonal status in adolescent girls based on the presence of post-COVID syndrome symptoms, and to establish correlations between psychoemotional state parameters and hormone concentrations of the hypothalamic-pituitary-thyroid-adrenal axis in the post-COVID period.

MATERIALS AND METHODS

Study design

From November 2021 to May 2025, 126 girls aged 11 to 16 years (mean age 14.84 ± 1.81 years) underwent examination at the clinic of the Scientific Centre for Family Health and Human Reproduction Problems.

At the initial stage of the study, data on the health status of all participants was collected (sex, age, body mass index, COVID-19 PCR test results, details of the acute COVID-19 phase, post-COVID symptoms, and family

history of COVID-19). The presence of post-acute COVID-19 symptoms was determined in accordance with clinical guidelines from the World Health Organization for defining a clinical case of post-COVID-19 condition in children and adolescents (dated February 16, 2023) [4]. To include a participant in the main group with post-COVID symptoms (PCS), they must have experienced one or more of the following: 1) symptoms that developed during or following a COVID-19 infection; 2) symptoms that have persisted for at least two months; 3) symptoms that could not be explained by alternative diagnoses; 4) symptoms that significantly impacted daily activities, such as academic performance, physical activity, and social interactions.

Symptoms of PCS were identified through clinical interviews. The research team, consisting of a pediatrician and psychologist, jointly decided to identify respondents with PCS and include them in the study based on a combination of clinical data, psychological test results, and laboratory parameters.

The comparative group consisted of adolescent girls who experienced COVID-19 within a similar timeframe, but who did not report any symptoms or have clinical manifestations of PCS during a structured interview and psychological assessment.

Based on the data collected, all participants were categorized into three groups:

1. The main group – participants with identified symptoms of PCS (n = 44), consisting of adolescent girls who had COVID-19 between 3 and 24 months before the study and currently experienced health complaints.
2. The comparative group – participants without symptoms of PCS (n = 40), consisting of adolescent girls who had COVID-19 between 3 and 24 months before the study but did not currently experience any health issues.
3. The control group (n = 42), consisting of generally healthy adolescent girls with no history of SARS-CoV-2 infection.

The main group was then divided into four subgroups based on the time since COVID-19 infection:

Subgroup 1.1 (n = 11): 3–5 months after COVID-19 infection.

Subgroup 1.2 (n = 12): 6–9 months after COVID-19 infection.

Subgroup 1.3 (n = 10): 11–12 months after COVID-19 infection.

Subgroup 1.4 (n = 11): 13–24 months after COVID-19 infection.

The second phase assessed the psychoemotional state and hormonal status of adolescent girls in each subgroup.

Eligibility criteria

Inclusion criteria for the study: (1) age 11–16 years (all respondents); (2) a history of laboratory-confirmed mild to moderate COVID-19 (3–24 months before the study) (in the main and comparative groups); (3) presence of symptoms of the post-COVID syndrome (in the main group); (4) absence of symptoms of the post-COVID syndrome (in the comparative group); (5) absence of a positive PCR test for SARS-CoV-2 infection and/or possible COVID-19 symptoms in the medical history (in the control group).

Exclusion criteria for the study: (1) failure to meet the inclusion criteria; (2) the presence of a pituitary microadenoma, hypothalamic dysfunction, obesity, arterial hypertension, or hypogonadism; (3) current or recent (within the past 6 months) use of hormonal medications (thyroid hormone, glucocorticoid hormone); (4) a history of thyroid dysfunction; (5) refusal by the adolescent or their legal representative to participate in the study.

Research methods

Data on the health status of all participants were collected, their psychoemotional state (including well-being, activity, mood, anxiety, and severity of depressive symptoms) was assessed, and serum levels of thyroid-stimulating hormone, free thyroxine, and cortisol were measured.

Clinical history. The following health data were analyzed: sex, age, body mass index (BMI), presence/absence of a positive PCR test for SARS-CoV-2, characteristics of the acute phase of COVID-19, and family history of COVID-19.

The symptoms of PCS were identified through a clinical interview, which included a structured questionnaire for the adolescent girl and her parent/guardian regarding the presence and severity of the following symptoms: fatigue, rapid fatigability; cognitive impairment (memory loss, decreased concentration); sleep disturbances; headaches; mood lability, anxiety; anosmia/dysgeusia; dyspeptic manifestations, and other complaints. To objectify the symptoms, validated psychological methods (WAM, BDI-1A, and the Children's Form of Manifest Anxiety Scale) were used, as well as clinical and laboratory examination data.

The severity of the acute phase of COVID-19 was retrospectively assessed among participants in the main study group in accordance with the Interim Guidelines for the Prevention, Diagnosis, and Treatment of the Novel Coronavirus Infection COVID-19 (Version 17, dated December 14, 2022) [22]. According to these guidelines, mild cases were characterized by symptoms of a respiratory infection, including a low-grade fever (less than 38°C), no shortness of breath, and no evidence of lung damage. In some cases, the only noticeable symptom was loss of smell or taste. Moderate cases were associated with severe fever (a prolonged temperature above 38°C for more than 5 days), shortness of breath, reduced SpO_2, and lung abnormalities typical of viral infection based on computed tomography scans. Treatment for these patients was typically on an outpatient basis [23].

Psychological diagnostics. The following methods were employed to assess the psychoemotional state of adolescent girls: the Beck Depression Inventory (BDI-1A) adapted by N.V. Tarabrina; the "Well-Being. Activity. Mood" (WAM) questionnaire, developed by V.A. Doskin et al.; and the Children's Form of Manifest Anxiety Scale, developed by A.M. Prikhozhan.

Using the Beck Depression Inventory (BDI-1A), developed by A. Beck in 1978 and adapted by N.V. Tarabrina in 2001 [24], the presence of depressive symptoms among adolescent girls was assessed. The scale consists of 13 sets of statements that correspond to various groups of depressive symptoms. Each statement on the scale can be rated from 0 to 3 points, depending on the severity of the symptoms. The overall score ranges from 0 to 9, indicating the absence of depressive symptoms, while scores between 10 and 15 indicate mild depression (or subdepression), scores between 16 and 19 indicate moderate depression, and scores above 20 indicate severe depression.

The "Well-being. Activity. Mood" (WAM) questionnaire, developed in 1973 by V.A. Doskin, N.A. Lavrentieva, V.B. Sharai, and M.P. Miroshnikov [25], consists of 30 pairs of opposing characteristics that the respondent uses to evaluate their state. The respondent marks the number that corresponds to the strength of the particular state. When processing the results, the points obtained are recalculated according to the rule: all positive states always receive high points, and negative states receive low points. The scale is set so that values decrease or increase from 7 to 1 or from 1 to 7, depending on the position of the opposing characteristics in the table. Based on the points obtained, the well-being, activity, and mood levels of the respondent were determined. A score of less than 3.5 points indicates a low level, 3.6-5.5 a moderate level, and over 5.6 a high level of well-being, activity and mood.

To identify anxiety as a relatively stable personality trait among adolescent girls, the Children's Form of Manifest Anxiety Scale was employed [26]. The scale, developed by A.M. Prikhozhan, is based on the adult and child versions of the Taylor Manifest Anxiety Scale (J. Taylor, 1951, 1953; A. Castenada, B.R. McCandless, D.S. Palermo, 1956) and contains 65 items. Analysis of respondents' responses allows for the calculation of "raw" anxiety scores. These "raw" scores are then converted into scale scores (stens) by comparing a subject's data with normative parameters from a group of adolescents of similar age and sex. Based on these resulting scale scores, the severity level of the respondent's anxiety can be determined. Specifically, 1–2 stens indicate a low level of anxiety; 3–6 stens a normal level of anxiety; 7–8 stens for slightly elevated anxiety; 9 stens for high anxiety; and 10 stens for very high anxiety.

Laboratory research methods. Venous blood samples were collected between 8:00 a.m. and 9:00 a.m., on an empty stomach, following generally accepted guidelines. The collection occurred on days 5–9 of the menstrual cycle or during amenorrhea prior to treatment. The blood was then centrifuged at 3,000 RPM for 10 minutes, and the resulting serum was separated and stored in a -80°C freezer until testing. The samples were thawed only once prior to use.

All adolescent girls underwent a hormonal profile assessment. The serum concentrations of thyroid-stimulating hormone (TSH, μIU/ml), free thyroxine (free T4, pmol/l), and cortisol (nmol/l) were measured using enzyme-linked immunosorbent assay (ELISA) with Alkor–Bio test systems (Russia) and the Cobos ELL (USA) enzyme-linked immunosorbent assay system.

Ethical approval

The study was conducted in accordance with the principles outlined in the World Medical Association's Declaration of Helsinki (1964, revised in 2013), and was approved by the Biomedical Ethics Committee of the Scientific Centre for Family Health and Human Reproduction Problems (protocol No. 7, dated October 2, 2020). Parents (or legal representatives) of participants and adolescent girls were informed about the aims, nature, and diagnostic procedures of the study and provided voluntary, informed consent to participate in the research.

Statistical analysis

Sample size calculation principles: no pre-calculated sample size used.

Methods of statistical data analysis: statistical analysis was performed using Statistica 8.0 (StatSoft, Inc., USA). Prior to conducting statistical analysis, the distribution of each variable was assessed using the Shapiro – Wilk test. Quantitative data were described using the arithmetic mean and standard deviation, presented in the format M ± σ. characteristics were presented as absolute counts and event frequencies (percentage of occurrences), and comparisons were made using the Pearson's χ^2 test. Comparisons between independent groups were conducted using the Student's *t*-test. The relationship between variables was assessed using Spearman's correlation coefficient (r), with correlations classified as weak (r = 0.10–0.39), moderate (r = 0.40–0.69), or strong (r = 0.70–1.00). A significance level of $p \leq 0.05$ was used for all statistical tests.

THE RESULTS OF THE STUDY

Analysis of clinical and anamnestic data revealed that the age characteristics of the study participants were comparable across all study groups (Table 1). The mean age of the participants was 14.84 ± 1.81 years, and there were no statistically significant differences in age between the groups ($p = 0.672$). Similarly, analysis of body mass index did not reveal any statistically significant differences between the groups ($p > 0.05$).

A retrospective analysis of the clinical manifestations and severity of COVID-19 during the acute phase of the disease revealed that the majority of participants in the study group (55 %) and in the comparative group (53 %) experienced a moderate course of the disease. A history of a mild COVID-19 infection was observed in 45 % of girls in the study group and 47 % of girls in the comparative group ($p > 0.05$).

Therefore, the study groups were similar in terms of age, body mass index, and the severity of the acute phase of COVID-19.

According to the clinical and anamnestic data obtained, out of the 84 participants who had COVID-19,

40 adolescent girls did not report any health complaints and formed a comparative group without symptoms of post-COVID syndrome (PCS), while 44 participants, who were included in the main group, reported complaints that, according to the clinical guidelines of the World Health Organization for defining a clinical case of post-COVID condition in children and adolescents (dated February 16, 2023), can be classified as manifestations of PCS [4]. The range of post-COVID symptoms among adolescent girls was diverse. Specifically, symptoms of asthenia (weakness, fatigue, rapid fatigability, and decreased resistance to physical activity) were reported by 38 girls (87 %). Cognitive impairment (difficulty concentrating, problems with memory, mental performance and other cognitive issues) was reported by 37 participants (83 %). Mood lability (excitability, tearfulness), irritability, anxiety, or fears (concern for one's health, fear of being alone, or feeling like someone is watching) was reported in 33 participants (76 %), as well as sleep disturbances (difficulties falling asleep, frequent awakenings). Long-term olfactory and gustatory disturbances were reported by 22 individuals (49 %), while dyspeptic symptoms (decreased appetite, abdominal pain, nausea, and in some cases, vomiting) were reported by 14 participants (31 %), and other complaints related to past disease were reported by 5 adolescent girls (12 %). It was observed that the identified symptoms of PCS had a negative impact on the daily activities of the respondents, manifesting themselves through changes in diet, levels of physical and mental activity, behavior, academic performance, and social adjustment.

In addition, subgroups were identified from the main study group based on the duration of PCS symptoms since COVID-19 infection. Specifically, 12 individuals (27 %) reported PCS symptoms between 3–5 months after the disease, 13 individuals (30 %) reported PCS symptoms between 6–9 months after the disease, 8 respondents (18 %) reported PCS symptoms between 11–12 months after the disease, and 11 respondents (25 %) reported PCS symptoms between 13–24 months after COVID-19 diagnosis.

Let us now turn to an analysis of the data collected through the survey. The psychoemotional state parameters for adolescent girls in the post-COVID period are presented in Table 2.

When comparing the parameters of the psychoemotional state between groups of individuals who had experienced COVID-19 and conditionally healthy individuals, the following patterns were observed.

According to the WAM method, the rate of low well-being among patients with PCS symptoms was 27 %, which significantly differed from the prevalence of this parameter among groups without PCS (10 %, $p_{5\text{-}6} = 0.015$) and among conditionally healthy individuals (10 %, $p_{5\text{-}7} = 0.014$). The rate of low activity among respondents with PCS symptoms was recorded in 41 % of cases, which was statistically significantly higher than groups without PCS (20 %, $p_{5\text{-}6} = 0.013$) and among the control group (19 %, $p_{5\text{-}7} = 0.007$). A low emotional state level was observed in 7 % of respondents with PCS symptoms, 3 % of adolescent girls without PCS, and 5 % of conditionally healthy individuals. No statistically significant differences were found between these groups ($p > 0.05$). This may indicate a negative impact of past infection on well-being, including strength, perception of health status, and fatigue, as well as activity, such as mobility and functional tempo, primarily among participants with post-COVID symptoms.

According to the Children's Form of Manifest Anxiety Scale, developed by A.M. Prikhozhan, the frequency of elevated, high, and very high anxiety levels among adolescents with PCS symptoms was 20 %, 5 %, and 16 %, respectively, compared to only elevated (15 %) and high (2 %) anxiety levels among those without PCS symptoms. In the control group, anxiety parameters did not exceed normal values.

TABLE 1

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF ADOLESCENT GIRLS IN THE STUDY GROUPS

Parameter	Study groups						
	With PCS symptoms					Without PCS ($n = 40$)	Control ($n = 42$)
	3-5 months ($n = 12$)	6-9 months ($n = 13$)	11-12 months ($n = 8$)	13-24 months ($n = 11$)	Total ($n = 44$)		
	1	2	3	4	5	6	7
Age, M ± σ	14.8 ± 1.4	14.5 ± 1.7	14.4 ± 1.7	14.2 ± 1.9	14.5 ± 1.6	14.8 ± 1.5	14.2 ± 1.6
BMI (kg/m^2), M ± σ	18.9 ± 1.0	19.8 ± 1.6	19.6 ± 1.0	18.9 ± 1.1	19.3 ± 1.3	19.2 ± 1.1	19.8 ± 1.8
	Severity of COVID-19						
Mild, % (n)	42 ($n = 5$)	54 ($n = 7$)	25 ($n = 2$)	55 ($n = 6$)	45 ($n = 20$)	47 ($n = 19$)	–
Moderate, % (n)	58 ($n = 7$)	46 ($n = 6$)	75 ($n = 6$)	45 ($n = 5$)	55 ($n = 24$)	53 ($n = 21$)	–

Note. PCS – post-COVID syndrome; BMI – body mass index.

TABLE 2

DISTRIBUTION OF ADOLESCENT GIRLS BY LEVEL OF PSYCHOEMOTIONAL STATE IN THE POST-COVID PERIOD (%)

Parameter	Study groups						
	With PCS symptoms					Without PCS (n = 40)	Control (n = 42)
	3-5 months (n = 12)	6-9 months (n = 13)	11-12 months (n = 8)	13-24 months (n = 11)	Total (n = 44)		
	1	2	3	4	5	6	7
Well-being level							
High	17	15	50	27	25	32	40
Moderate	50	46	38	55	48	58	50
Low	33	39	12	18	27	10	10
Reliability of differences	p_{1-2} = 0.790; p_{1-3} = 0.939; p_{1-4} = 0.693; p_{1-6} = 0.141; p_{1-7} = 0.580; p_{2-3} = 0.745; p_{2-4} = 0.864; p_{2-6} = 0.217; p_{2-7} = 0.744; p_{3-4} = 0.664; p_{3-6} = 0.170; p_{3-7} = 0.591; p_{4-6} = 0.350; p_{4-7} = 0.876; **p_{56} = 0.015; p_{57} = 0.014;** p_{6-7} = 0.403						
Activity level							
High	17	8	50	18	20	15	14
Moderate	50	31	25	46	39	65	67
Low	33	61	25	36	41	20	19
Reliability of differences	p_{1-2} = 0.623; p_{1-3} = 0.511; p_{1-4} = 0.908; p_{1-6} = 0.289; p_{1-7} = 0.078; p_{2-3} = 0.252; p_{2-4} = 0.674; p_{2-6} = 0.738; p_{2-7} = 0.260; p_{3-4} = 0.360; p_{3-6} = 0.056; **p_{37} = 0.016;** p_{4-6} = 0.345; p_{4-7} = 0.096; **p_{56} = 0.013; p_{57} = 0.007;** p_{6-7} = 0.197						
Mood level							
High	50	23	50	36	39	42	62
Moderate	42	69	50	55	54	55	33
Low	8	8	–	9	7	3	5
Reliability of differences	p_{1-2} = 0.551; p_{1-3} = 0.908; p_{1-4} = 0.778; p_{1-6} = 0.600; p_{1-7} = 0.786; p_{2-3} = 0.413; p_{2-4} = 0.810; p_{2-6} = 0.812; p_{2-7} = 0.706; p_{3-4} = 0.689; p_{3-6} = 0.524; p_{3-7} = 0.718; p_{4-6} = 0.927; p_{4-7} = 0.933; p_{5-6} = 0.395; p_{5-7} = 0.626; p_{6-7} = 0.784						
Anxiety level							
Low	17	23	–	9	14	8	43
Normal	50	47	38	46	45	75	57
Elevated	25	15	12	27	20	15	–
High	8	–	–	9	5	2	–
Very high	–	15	50	9	16	–	–
Reliability of differences	p_{1-2} = 0.595; p_{1-3} = 0.355; p_{1-4} = 0.850; p_{1-6} = 0.309; **p_{17} = 0.015**; p_{2-3} = 0.768; p_{2-4} = 0.732; p_{2-6} = 0.086; **p_{27} = 0.002**; p_{3-4} = 0.482; **p_{36} = 0.041**; **p_{37} < 0.001**; p_{4-6} = 0.221; **p_{4-7} = 0.009**; **p_{5-6} = 0.006**; **p_{5-7} < 0.001**; p_{6-7} = 0.118						
Severity of depressive symptoms							
Absence	67	39	74	64	59	72	100
Mild	–	8	–	9	5	15	–
Moderate	8	15	13	9	11	5	–
Pronounced	8	23	–	9	11	8	–
Severe	17	15	13	9	14	–	–
Reliability of differences	p_{1-2} = 0.742; p_{1-3} = 0.474; p_{1-4} = 0.285; **p_{1-6} = 0.015**; **p_{1-7} < 0.001**; p_{2-3} = 0.424; p_{2-4} = 0.274; **p_{2-6} = 0.002**; **p_{2-7} < 0.001**; p_{3-4} = 0.898; p_{3-6} = 0.109; **p_{3-7} = 0.013**; p_{4-6} = 0.082; **p_{4-7} = 0.009**; **p_{5-6} = 0.006**; **p_{5-7} = 0.011**; **p_{6-7} < 0.001**						

Note. PCS – post-COVID syndrome; p – significance level for differences between study groups, as determined by Pearson's χ^2 test; here and in Tables 3 and 4, statistically significant values are highlighted in bold.

These differences were statistically significant when comparing the group with PCS symptoms with the group without PCS symptoms ($p_{5-6} = 0.006$) and with the control group ($p_{5-7} < 0.001$).

According to the Beck Depression Inventory (BDI-1A), a small number of participants in the group with PCS symptoms showed mild depressive symptoms (5 %), moderate depressive symptoms (11 %), and severe depressive symptoms (14 %). In the group without PCS, these figures were 15 %, 5 %, 8 %, respectively. No depressive symptoms were found in the control group. The severity of depressive symptoms among adolescent girls with PCS symptoms remains significantly higher than in the group without PCS symptoms ($p_{5-6} = 0.006$) and in conditionally healthy individuals ($p_{5-7} < 0.011$). The difference is statistically significant.

Differences were observed between the group of participants without PCS symptoms and those who were conditionally healthy, with regard to the severity of depressive symptoms only ($p_{6-7} < 0.001$).

Analysis of the dynamics of the psychoemotional state among subgroups of respondents with PCS symptoms has revealed the following patterns.

In the period between 3 and 5 months after the disease, the respondents with PCS symptoms exhibited the following parameters of psychoemotional state: a low level of well-being was observed in 33 % of respondents; low activity levels were recorded in 33 % of respondents; and a low level of mood was registered in 8 % of respondents. Anxiety levels were less pronounced during this period, with elevated levels noted in 25 % and high levels in 8 % of respondents. Statistically significant differences were observed compared to a group of conditionally healthy controls ($p_{1-7} = 0.015$). Depressive symptoms were more pronounced during this time, with moderate and severe symptoms occurring in 8 % and severe symptoms in 17 %, respectively. Significant differences were found compared to the group without PCS symptoms ($p_{1-6} = 0.015$) and conditionally healthy individuals ($p_{1-7} < 0.001$).

By 6–9 months after COVID-19 infection, respondents with PCS symptoms experienced a shift in their psychoemotional profiles. Low levels of well-being were noted in 39 % of respondents. An increase in low activity levels was observed in 61 % of cases. Low mood levels were reported by 8 % of respondents, while a moderate increase in anxiety levels was noted, with elevated levels being reported in 15 % and very high levels being reported by 15 %. Statistically significant differences were identified when compared to a group of conditionally healthy individuals ($p_{2-7} = 0.002$). Depressive symptoms were distributed as follows: mild in 8 %, moderate in 15 %, pronounced in 23 %, and severe in 15 % of respondents. Statistically significant differences persisted when compared to the group without PCS symptoms ($p_{2-6} = 0.002$) and conditionally healthy individuals ($p_{2-7} < 0.001$).

In the period between 11 and 12 months after COVID-19, respondents who had experienced PCS syndrome reported the following changes in their psychoemotional state. A low level of well-being was found in 12 % of the respondents, indicating an improvement trend. A low activity level decreased in 25 % of cases, and significant differences were found compared to a group of conditionally healthy individuals ($p_{3-7} = 0.016$). The level of anxiety continued to increase, with elevated levels reported by 12 % and very high levels by 50 % of respondents. These differences were statistically significant compared to both conditionally healthy individuals ($p_{3-7} < 0.001$) and those without PCS symptoms ($p_{3-6} = 0.041$). Moderate and severe depressive symptoms were reported in 13 % of respondents each, with significant differences compared to the group of conditionally healthy individuals remaining ($p_{3-7} = 0.013$).

In the period between 13 and 24 months after COVID-19, respondents with PCS symptoms showed a partial stabilization of their psychoemotional state parameters. A low level of well-being was observed in 18 % of adolescent girls, while a low level of activity was recorded in 36 % of cases, indicating a slight increase compared to the previous period. Low mood levels were registered in 9 % of respondents with PCS symptoms. Elevated, high, and very high levels of anxiety persisted in 27 %, 9 %, and 9 %, respectively. Statistically significant differences were found between the group with PCS and the group of conditionally healthy individuals ($p_{4-7} = 0.009$). Depressive symptoms exhibited an even distribution, with mild, moderate, pronounced, and severe degrees being reported in 9 % each. Significant differences remained between the individuals with PCS and those without any health issues ($p_{4-7} = 0.009$).

An analysis of the psychoemotional state of adolescent girls who experienced PCS symptoms revealed persistent disturbances throughout the post-COVID period. The severity of depressive symptoms among adolescent girls with PCS was significantly higher than in respondents without PCS or conditionally healthy individuals, and persisted at a statistically significant level throughout the post-COVID period.

Despite the overall downward pattern in poor health outcomes, differences were observed between the non-PCS and control groups throughout the post-COVID period. Similarly, activity parameters showed similar trends, with the most significant impairments occurring between 6 and 9 months after COVID-19.

Therefore, in adolescent girls with PCS symptoms, a deterioration in their psychoemotional state has been observed, mainly during the first 12 months after the disease, which has manifested itself in an increase in the frequency of a low well-being level, decreased activity levels, increased anxiety levels, as well as an increase in depressive symptoms when compared to the control group consisting of individuals without PCS symptoms and conditionally healthy individuals.

Analysis of hormonal status parameters revealed statistically significant differences between the study groups (Table 3). The hypothalamic-pituitary-thyroid axis parameters (TSH and free T4) in adolescent girls remained within reference values regardless of PCS symptoms

or the time since the onset of the disease. However, cortisol levels in adolescent girls with PCS symptoms were on average higher than the reference range (average for the group: 592.00 ± 322.72 nM/l; with a maximum value of 1438.00 nM/l).

When comparing the hormonal status parameters between groups of individuals who had COVID-19 and those who were conditionally healthy, the following patterns emerged. The level of thyroid stimulating hormone (TSH) in the group with PCS symptoms was 2.45 ± 1.32 μIU/ml, significantly different from that in the group without PCS symptoms (1.98 ± 0.75 μIU/ml; $p_{5-6} = 0.008$, $t = 2.012$) and compared to conditionally healthy individuals (1.69 ± 0.62 μIU/ml; $p_{5-7} < 0.003$, $t = 3.407$). The level of free thyroxine (free T4) in the group with PCS symptoms was 14.56 ± 2.68 pM/l and also showed statistically significant differences compared to the group of conditionally healthy individuals ($p_{5-7} = 0.038$, $t = 1.314$). The most significant differences were observed in the level of cortisol concentrations. In the group with PCS symptoms, the parameter reached 592.00 ± 322.72 nM/l, significantly exceeding the values in the comparative groups (454.63 ± 132.44 nM/l; $p_{5-6} < 0.012$, $t = 2.506$) and in conditionally healthy individuals (446.50 ± 110.70 nM/l; $p_{5-7} < 0.001$, $t = 2.770$). At the same time, in 9 adolescent

TABLE 3

INDICATORS OF HORMONAL STATUS OF ADOLESCENT GIRLS IN THE POST-COVID PERIOD (M ± σ)

Study groups			TSH r.r. 0.23 – 3.40 μIU/ml	Free T4 r.r. 10.00 – 23.20 pM/l	Cortisol r.r. 142.00 – 558.00 nM/l
With PCS symptoms	**3-5 months, *n* = 12**	1	2.47 ± 1.45	13.68 ± 2.76	470.67 ± 170.41
	6-9 months, *n* = 13	2	2.90 ± 1.42	14.91 ± 2.76	521.92 ± 308.26
	11-12 months, *n* = 8	3	1.99 ± 1.28	14.40 ± 2.24	876.25 ± 461.39
	13-24 months, *n* = 11	4	2.25 ± 1.04	15.23 ± 2.89	600.45 ± 253.13
	Total, *n* = 44	5	2.45 ± 1.32	14.56 ± 2.68	592.00 ± 322.72
Without PCS, *n* = 40		6	1.98 ± 0.75	14.65 ± 2.28	454.63 ± 132.44
Control, *n* = 42		7	1.69 ± 0.62	13.92 ± 1.72	446.50 ± 110.70
Reliability of differences			$p_{1-2} = 0.837$;	$p_{1-2} = 0.465$;	$p_{1-2} = 0.221$;
			$p_{1-3} = 0.608$;	$p_{1-3} = 0.640$;	**$p_{1-3} < 0.012$;**
			$p_{1-4} = 0.287$;	$p_{1-4} = 0.624$;	$p_{1-4} = 0.172$;
			$p_{1-6} = 0.005$;	$p_{1-6} = 0.572$;	$p_{1-6} = 0.252$;
			$p_{1-7} < 0.011$;	$p_{1-7} = 0.069$;	$p_{1-7} = 0.063$;
			$p_{2-3} = 0.751$;	$p_{2-3} = 0.765$;	**$p_{2-3} = 0.017$;**
			$p_{2-4} = 0.413$;	$p_{2-4} = 0.254$;	$p_{2-4} = 0.853$;
			$p_{2-6} = 0.014$;	$p_{2-6} = 0.525$;	**$p_{2-6} = 0.005$;**
			$p_{2-7} = 0.002$;	$p_{2-7} = 0.724$;	**$p_{2-7} = 0.011$;**
			$p_{3-4} = 0.668$;	$p_{3-4} = 0.307$;	**$p_{3-4} = 0.007$;**
			$p_{3-6} = 0.091$;	$p_{3-6} = 0.902$;	**$p_{3-6} < 0.013$;**
			$p_{3-7} = 0.015$;	$p_{3-7} = 0.330$;	**$p_{3-7} < 0.002$;**
			$p_{4-6} = 0.215$;	$p_{4-6} = 0.208$;	**$p_{4-6} = 0.003$;**
			$p_{4-7} = 0.051$;	**$p_{4-7} = 0.009$;**	**$p_{4-7} < 0.001$;**
			$p_{5-6} = 0.008$;	$p_{5-6} = 0.607$;	**$p_{5-6} < 0.012$;**
			$p_{5-7} < 0.003$;	**$p_{5-7} = 0.038$;**	**$p_{5-7} < 0.001$;**
			$p_{6-7} = 0.800$	$p_{6-7} = 0.074$	$p_{6-7} = 0.449$

Note. PCS – post-COVID syndrome; TSH – thyroid stimulating hormone; free T4 – free thyroxine; r.r. – reference ranges; *p* – significance level for differences between study groups, as determined by Student's *t*-test.

girls (21 %) with PCS symptoms, the serum TSH level exceeded 3.4 μU/ml, with an average value of 4.5 ± 0.8 μU/ml and a maximum value of 6.0 μU/ml, corresponding to subclinical hypothyroidism (elevated TSH level with normal free T4 levels).

Analysis of the dynamics of hormonal parameters in subgroups of respondents with PCS symptoms has revealed the following patterns.

In the period between 3 and 5 months after COVID-19, hormonal parameters remained within the reference ranges: average TSH levels were 2.47 ± 1.45 μIU/ml, free T4 was 13.68 ± 2.76 pM/l, and cortisol was 470.67 ± 170.41 nM/l. However, statistically significant differences compared to groups without PCS symptoms and conditionally healthy individuals were only observed in TSH levels ($p_{1-6} = 0.005$, $t = 1.588$; $p_{1-7} < 0.011$, $t = 2.761$; respectively).

In the period between 6 and 9 months after COVID-19, respondents with PCS symptoms showed a change in their hormonal profile. The TSH level in the blood serum increased to 2.90 ± 1.42 μIU/ml, while free T4 increased to 14.91 ± 2.76 pM/l and cortisol reached 521.92 ± 308.26 nM/l. Significant differences were observed between the groups without PCS symptoms and conditionally healthy individuals in TSH concentrations ($p_{2-6} = 0.014$, $t = 3.032$; $p_{2-7} < 0.002$, $t = 4.379$, respectively) and cortisol levels ($p_{2-6} = 0.005$, $t = 1.115$; $p_{2-7} < 0.011$, $t = 1.350$, respectively).

In the period between 11 and 12 months after COVID-19, respondents with PCS symptoms demonstrated the most significant deviations in their hormonal profiles compared to pre-pandemic levels. Specifically, TSH levels decreased to 1.99 ± 1.28 μIU/ml, while free T4 levels increased to 14.40 ± 2.24 pM/l. Cortisol levels increased sharply to 876.25 ± 461.39 nM/l, indicating statistically significant differences in TSH levels and cortisol levels compared to those in conditionally healthy individuals ($p_{3-7} = 0.015$, $t = 1.011$; $p_{3-7} < 0.002$, $t = 5.468$, respectively). Moreover, among adolescent girls, cortisol levels were statistically significantly higher during this period compared to other subgroups and those without PCS symptoms ($p_{1-3} < 0.012$, $t = -2.803$; $p_{2-3} = 0.017$, $t = -2.119$; $p_{3-4} = 0.007$, $t = 1.676$; $p_{3-6} = 0.013$, $t = 5.007$, respectively).

In the period between 13 and 24 months after COVID-19, respondents with PCS symptoms demonstrated a partial normalization of hormonal profile parameters. Specifically, TSH levels were 2.25 ± 1.04 μIU/ml, free T4 levels were 15.23 ± 2.89 pM/l, and cortisol levels were 600.45 ± 253.13 nM/l. Significant differences with respect to the parameters of conditionally healthy individuals were still observed in terms of TSH and cortisol concentrations in the blood ($p_{4-7} = 0.051$, $t = 2.253$; $p_{4-7} < 0.001$, $t = 3.036$, respectively). Additionally, among adolescent girls, only cortisol levels were statistically significantly higher compared to those of respondents without PCS symptoms ($p_{4-6} < 0.003$, $t = 2.605$).

The hormonal status parameters in adolescent girls without PCS symptoms were slightly higher than in the group of conditionally healthy individuals. However, no significant differences were observed between the two groups ($p > 0.05$).

Statistically significant correlations were observed between psychoemotional state and hypothalamic-pituitary-thyroid-adrenal axis parameters during the post-COVID period (Table 4). It is worth noting that correlation analysis did not reveal any statistically significant relationships between parameters of psychoemotional state and free T4 levels, either in the overall group of girls with PCS or in subgroups based on the time since COVID-19 infection (all $p > 0.05$).

In summary, a strong direct correlation was observed between the severity of depressive symptoms as measured by the Beck scale and TSH levels (r = 0.897, $p = 0.002$), as well as between anxiety levels as assessed by the A.M. Prikhozhan questionnaire and cortisol levels (r = 0.991, $p = 0.001$). A negative correlation was found between parameters of well-being as measured by the WAM method and TSH levels, with higher TSH levels associated with decreased well-being levels (r = -0.798, $p = 0.006$), decreased activity levels (r = -0.898, $p = 0.002$) and decreased mood levels (r = -0.521, $p = 0.015$). Analysis of changes in psychological well-being over time showed the strongest correlations in the period between 6 and 9 months after COVID-19 infection, with increases in TSH associated with worsening well-being, decreased mood, and increased severity of depressive symptoms (r = -0.837, $p = 0.002$; r = -0.305, $p = 0.028$; r = 0.899, $p = 0.002$, respectively). In the 3–5 and 13–24-month periods after COVID-19 infection, there were strong correlations observed between increases in TSH levels and decreases in activity (r = -0.798, $p = 0.006$). Increases in morning cortisol levels were also correlated with increases in anxiety throughout the post-COVID period, with the strongest correlations occurring in the period between 11 and 12 months after infection (r = 0.832, $p < 0.002$). It should be noted that the correlation between anxiety and cortisol levels is a well-known physiological phenomenon that reflects the activation of the hypothalamic-pituitary-adrenal axis during times of stress. However, in the context of the post-COVID syndrome, this correlation takes on particular significance, as elevated cortisol and anxiety levels persist for up to 24 months after infection, potentially indicating dysregulation of stress-response mechanisms in the body in the post-COVID period.

The established correlations between the psychoemotional state and the hormonal status confirm that post-COVID disturbances affect multiple regulatory systems in the body and manifest through interconnected mechanisms. The identified relationships between psychoemotional state parameters (anxiety, depression, and subjective well-being) and concentrations of hormones from the pituitary, thyroid, and adrenal glands indicate the involvement of neuroendocrine regulation in the pathogenesis of the psychoemotional manifestations of PCS in adolescent girls.

DISCUSSION

Most available data on the health status of individuals in the post-COVID period focus on outcomes among previously hospitalized children and adolescents, and do not include patients with a milder course of the infection [8]. Furthermore, the samples often consist of the results of phone interviews with parents or guardians based on pre-designed questionnaires [14]. Our study took into consideration the self-reported complaints of adolescent girls as well as their health data and laboratory and instrumental test results. This enabled us to identify autonomic and psychoemotional disorders associated with PCS in 44 adolescent girls, which caused significant distress in daily life and persisted over a prolonged period after COVID-19 infection. Additionally, there was no correlation between mild to moderate COVID-19 clinical course and the development of PCS symptoms.

The results obtained demonstrate the complex impact of SARS-CoV-2 on the psychoemotional and endocrine systems of adolescent girls in the post-COVID period. The identified psychoemotional disorders in these girls are consistent with international studies showing a high incidence of depressive and anxiety disorders in the post-COVID period. A detailed analysis of their psychoemotional state revealed a predominance of high levels of situational and personal anxiety, as well as lower levels of well-being (strength, self-perception of health, and fatigue) and emotional state [13]. In the study conducted by K.V. Zhmerenetsky et al., children aged 15–17 who had COVID-19 showed lower levels of well-being (strength, self-perception of health, and fatigue) and emotional state (4.1 ± 1.28 and 4.4 ± 1.08 points) compared to those who had not been infected (5.016 ± 1.23 vs. 5.3 ± 1.09) [27].

It should be noted that adolescence is a period characterized by increased susceptibility to stress, owing to active neural development, hormonal changes, and the establishment of psychosocial identity. Furthermore, adolescent girls are more likely to experience psychoemotional difficulties compared to boys, possibly due

TABLE 4

RESULTS OF CORRELATION ANALYSIS OF PSYCHOEMOTIONAL STATE INDICATORS WITH THYROID-STIMULATING HORMONE AND CORTISOL CONCENTRATIONS OF ADOLESCENT GIRLS IN THE POST-COVID PERIOD (SPEARMAN'S CORRELATION COEFFICIENT)

Study groups		Hormone WB	Psychoemotional state parameters				
			WB	Act.	M	Anx.	D
With PCS symptoms	3-5 months (*n* = 12)	TSH	**-0.698 *p* < 0.011**	**-0.897 *p* < 0.002**	-0.343 *p* = 0.275	0.129 *p* = 0.688	**0.695 *p* < 0.013**
		Cortisol	-0.063 *p* = 0.846	0.088 *p* = 0.787	-0.056 *p* = 0.863	**0.688 *p* < 0.011**	0.077 *p* = 0.811
	6-9 months (*n* = 13)	TSH	**-0.837 *p* < 0.002**	**-0.697 *p* < 0.013**	**-0.305 *p* = 0.028**	-0.364 *p* = 0.221	**0.899 *p* < 0.002**
		Cortisol	0.371 *p* = 0.212	0.371 *p* = 0.212	0.069 *p* = 0.823	**0.689 *p* < 0.013**	-0.377 *p* = 0.204
	11-12 months (*n* = 8)	TSH	**-0.676 *p* < 0.014**	**-0.676 *p* < 0.011**	-0.635 *p* = 0.091	-0.013 *p* = 0.976	**0.694 *p* < 0.011**
		Cortisol	-0.122 *p* = 0.774	-0.293 *p* = 0.482	0.120 *p* = 0.778	**0.832 *p* < 0.002**	0.168 *p* = 0.691
	13-24 months (*n* = 11)	TSH	**-0.695 *p* < 0.012**	**-0.798 *p* < 0.006**	-0.534 *p* = 0.090	0.274 *p* = 0.415	**0.698 *p* < 0.013**
		Cortisol	-0.256 *p* = 0.448	-0.246 *p* = 0.466	-0.059 *p* = 0.862	**0.695 *p* < 0.014**	0.219 *p* = 0.518
	Total (*n* = 44)	TSH	**-0.798 *p* < 0.006**	**-0.898 *p* < 0.002**	**-0.521 *p* < 0.015**	-0.035 *p* = 0.821	**0.897 *p* < 0.002**
		Cortisol	0.058 *p* = 0.708	0.038 *p* = 0.808	0.061 *p* = 0.693	**0.991 *p* < 0.001**	-0.043 *p* = 0.780

Note. PCS – post-COVID syndrome; TSH – thyroid stimulating hormone; WB – well-being; Act. – activity; M – mood; Anx. – anxiety; D – symptoms of depression.

to hormonal imbalances, heightened emotional reactivity, and variations in coping mechanisms.

The findings of thyroid function abnormalities in the form of elevated TSH levels with normal free T4 concentrations may be attributed to both the direct cytopathic effect of the virus on the thyroid gland and the indirect effect through the hypothalamic-pituitary axis [28]. Our results are supported by the research conducted by Lazareva et al. [21]. The authors found that in the post-COVID period, TSH secretion levels in children aged 5–17 were doubled (mean 4.9 ± 0.38; max = 7.78 μU/ml) compared to the reference group of healthy children (mean 1.56 ± 0.08 μU/ml) while free T4 remained within reference ranges.

The mechanism of thyroid dysfunction in COVID-19 may be due to several factors. Firstly, direct damage to thyrocytes, as the thyroid gland expresses ACE2 receptors, which serve as the entry point for SARS-CoV-2 [20]. Secondly, a systemic inflammatory response, with an increase in pro-inflammatory cytokines (IL-6, TNF-α, and IL-1β), can disrupt the synthesis and secretion of thyroid hormones [29]. Thirdly, a stress-induced increase in cortisol levels can inhibit the function of the hypothalamic-pituitary-thyroid axis [30].

Elevated cortisol levels in adolescent girls with PCS may reflect a chronic activation of the hypothalamic-pituitary-adrenal axis. This could be due to both direct effects of the virus on adrenal glands and prolonged psychoemotional stress associated with PCS symptoms. Hypercortisolism, in turn, may exacerbate thyroid dysfunction and contribute to the development of psychoemotional disorders.

The established correlations between psychoemotional state and hormonal parameters support the concept of a close interplay between the endocrine and nervous systems. Increased levels of thyroid hormones are linked to the emergence of depressive symptoms, while hypercortisolism contributes to the development of anxiety disorders.

The temporal dynamics of the identified disorders indicate peak severity in the period between 6 and 12 months after COVID-19, followed by a trend towards improvement. However, even up to 13–24 months after the disease, the parameters have not returned to control group levels, indicating the persistent nature of long-term post-COVID-19 complications.

CONCLUSION

Post-COVID syndrome in adolescent girls is characterized by dysfunctions of the psychoemotional state and endocrine system. These changes include thyroid dysfunction (subclinical hypothyroidism) and adrenal dysfunction (hypercortisolism), as well as the development of depressive and anxious symptoms. The correlations between the psychoemotional state and hormonal parameters support the concept of an interaction between the endocrine and nervous systems. Therefore, we recommend actively screening adolescent girls for post-COVID syndrome symptoms three months after infection. If any complaints are reported, a comprehensive clinical, psychological, and hormonal examination is warranted. A multidisciplinary approach involving a pediatrician, psychologist, and endocrinologist is recommended for rehabilitation. It is important to pay particular attention to girls during the 6–12-month period after COVID-19, as psychoemotional and hormonal disturbances reach their peak at this time.

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Conflicts of interest

The authors declare no conflicts of interest.

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