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Original article

SOME PATHOPHYSIOLOGICAL AND PSYCHOLOGICAL CHARACTERISTICS AND QUALITY OF LIFE IN ADOLESCENT GIRLS WITH ACNE VULGARIS IN MODERN CONDITIONS

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Acne vulgaris is a common disease, especially in adolescent girls, that develops due to increased anxiety.

The aim of the study was to establish the characteristics of the sympathoadrenal, vagoinsular and hypothalamic-pituitary-adrenal systems, anxiety and quality of life in adolescent girls with acne vulgaris in modern conditions.

Methods. 63 adolescent girls with acne vulgaris who consulted a dermatologist and 35 healthy individuals were examined in 2013; similar groups were formed in 2023 during martial law in the country: the study group—38 adolescent girls with manifestations of acne vulgaris who consulted a dermatologist and 32 healthy individuals (control group). To assess the severity of acne vulgaris, the Investigator's Global Assessment scale was used; to assess anxiety, the Spielberger scale, and to assess quality of life, the Dermatology Life Quality Index (DLQI) and the O.S. Chaban Quality of Life Scale (CQLS) were used. In sick and healthy adolescent girls, the excretion of adrenaline and noradrenaline in daily urine, the concentration of insulin, cortisol, testosterone, free testosterone, androstenedione, estradiol, and progesterone in the blood were determined by the enzyme-linked immunosorbent assay method. Study results were statistically processed using standard computer software using the paired Student's t-test with the calculation of the arithmetic mean (M) and the standard error of the arithmetic mean (m) or the Wilcoxon signed-rank test, depending on the normality of the distribution of differences. The normality of data distribution was checked using the Shapiro-Wilk test at a significance level of 0.01. When using all statistical methods, except for the Shapiro-Wilk test, the significance level was taken to be 0.05; the difference between the data was considered significant at $p < 0.05$. To determine structural relationships, correlation analysis was used, determining pair correlation coefficients—r.

Results. A statistically significant increase in the level of situational anxiety in healthy adolescent girls in modern conditions was established, which has increased even more in recent years.

Discussion. Patients with acne vulgaris are characterized by increased levels of stress hormones, androgens, and progesterone. In conditions of martial law, patients with acne vulgaris have higher anxiety and levels of stress hormones, as well as a reduced quality of life. In adolescent girls with acne vulgaris, under martial law conditions, anxiety is increased, quality of life is reduced, activity of sympatho-adrenal, vagoinsular and glucocorticoid function of adrenal glands is increased, which corresponds to the stage of anxiety of stress reaction, there is dysfunction of sex hormones, and quality of life is reduced.

Conclusions. The data obtained emphasize the multifactorial nature of acne pathogenesis, where the interaction of androgenic, stress, metabolic, and sex hormones forms a complex pathophysiological background of the disease.

Keywords: acne vulgaris, anxiety, quality of life, hormones

Introduction

One of the pressing challenges in modern dermatology is the increasing prevalence of skin disorders, particularly acne vulgaris. This condition is characterized by lesions of the sebaceous glands and hair follicles, which functioning is influenced by numerous endogenous and exogenous factors [1].

The high incidence of acne vulgaris among adolescent girls and women of reproductive age, the persistence of cosmetic defects, tendency toward recurrence, chronic course, resistance to treatment, and associated disturbances in psycho-emotional well-being and social adaptation—as well as the development of dysmorphophobia—all underscore the relevance of this issue [2].

These factors necessitate further investigation into the mechanisms of acne development and the identification of new pathogenic pathways in order to optimize treatment strategies for this patients cohort.

According to the literature, the prevalence of acne vulgaris in girls under the age of 18 reaches approximately 90%, decreasing to around 10% in patients by the age of 45 [3, 4, 5, 6].

The onset of acne vulgaris typically coincides with menarche, between the ages of 12 and 14, peaking at 14–18 years. Regression usually follows, although in nearly 20% of girls, resolution is delayed [2], and clinically significant forms are observed in approximately 15% [7].

Aesthetic changes in the skin of adolescent girls with acne vulgaris can negatively affect self-esteem and self-perception within peer groups, leading to heightened anxiety and neuroticism. This may contribute to the development of depressive disorders and a more severe course of the disease, further compounding the condition [8].

Common triggers of acne vulgaris in females include urbanization, increased mental activity, psycho-emotional stress, uncontrolled use of medications, unqualified cosmetic interventions, and irrational aesthetic procedures. However, identifying a definitive cause remains particularly challenging [9].

The pathophysiology of acne vulgaris is complex and multifactorial, involving numerous body systems and potential transformations among them. It also encompasses a wide array of interdependent histochemical and systemic dysfunctions that may influence the hormonal balance of adolescent girls, particularly androgen production, and are mediated through various biological mechanisms [7, 9].

Frequent flare-ups after brief remissions, a tendency toward recurrence, and the prolonged nature of acne contribute to the exhaustion of the body's adaptive resources, provoke psychological disturbances, and impair quality of life [10, 11].

Given the high prevalence and increasing incidence of acne vulgaris among adolescents, along with psycho-vegetative disturbances, cosmetic consequences, and its profound impact on quality of life, further investigation into this condition is both justified and necessary.

The aim of this study was to determine the specific features of the sympatho-adrenal, vagal-insular, and hypothalamic-pituitary-adrenal systems, as well as anxiety levels and quality of life in adolescent girls with acne vulgaris in current conditions.

Materials and Methods

The study was approved by the PSMU Ethics and Bioethics Committee on December 20, 2012, protocol number 108, and was conducted in accordance with the principles of the World Medical Association's Declaration of Helsinki, “Ethical Principles for Medical Research Involving Human Subjects” (2000). All patients and their parents gave their written informed consent for the collection and processing of clinical material.

This study was based on the clinical observation of adolescent girls who sought dermatological care for acne vulgaris. In 2013, the study group consisted of 63 girls, and the control group comprised 35 healthy individuals. Similar groups were formed in 2023, during martial law in Ukraine: the study group included 38 adolescent girls with clinical signs of acne vulgaris, while the control group comprised 32 healthy peers. All participants were aged between 16 and 18 years.

The study was approved by the local ethics committee of the participating healthcare institutions.

Inclusion criteria for all groups:

- Age between 16 and 18 years;
- Signed informed consent from both the participants and their parents;
- Presence of acne vulgaris (study group);
- Absence of dermatological diseases (control group).

Exclusion criteria:

- Presence of other dermatological conditions;
- Presence of severe comorbidities or psychiatric disorders.

To objectively evaluate clinical manifestations and dynamic changes in acne severity, the Investigator's Global Assessment (IGA) scale was applied [12]. Participants also completed three validated questionnaires:

1. Spielberger State-Trait Anxiety Inventory (to assess personal and situational anxiety);
2. Dermatology Life Quality Index (DLQI) [13];
3. O.S. Chaban's Clinical Quality of Life Scale (CQLS) [14].

To assess nervous system and endocrine function, the following parameters were measured: 24-hour urinary excretion of adrenaline and noradrenaline, and serum concentrations of insulin, cortisol, testosterone, free testosterone, androstenedione, estradiol, and progesterone, using enzyme-linked immunosorbent assay (ELISA).

Statistical analysis of the data was conducted using standard software. Depending on the distribution of the data, either the paired Student's t-test (for normally distributed data, with arithmetic mean (M) and standard error (m)) or the Wilcoxon signed-rank test was used. Normality was assessed using the Shapiro–Wilk test with a significance level of 0.01. For all other statistical methods, a significance level of 0.05 was adopted, and differences were considered statistically significant at $p < 0.05$. To determine structural relationships, correlation analysis was conducted using Pearson's correlation coefficient (r).

Results and discussion

Analysis of the data obtained from adolescent girls with acne vulgaris demonstrated that, over a 10-year period, there was no statistically significant increase in disease severity scores as assessed by the Investigator's Global Assessment (IGA) scale (Table 1) (Fig. 1, 2).

Table 1

Levels of personal and situational anxiety, and quality of life in patients with acne vulgaris (M±m

Indicator	**2013**		**2023**	
	Healthy		**Healthy**	
GA score (points)		2.27±0.08		2.35±0.09
Trait anxiety score (points)	41.3±1.4	46.4±1.7*	41.7±1.5	45.7±1.6
State anxiety score (points)	39.4±1.1	43.7±1.5*	43.5±1.6●	47.9±1.2●
LQI (Dermatology Life Quality Index), points		10.3±0.3		10.6±0.3
CQLS (Clinical Quality of Life Scale), points	70.5±2.7	59.6±2.0*	67.2±2.2	52.1±2.2*●

Notes:

$p < 0.05$ — statistically significant difference between patients with acne vulgaris and healthy individuals within the same year

$p < 0.05$ — statistically significant difference compared to the corresponding patient group in 2013

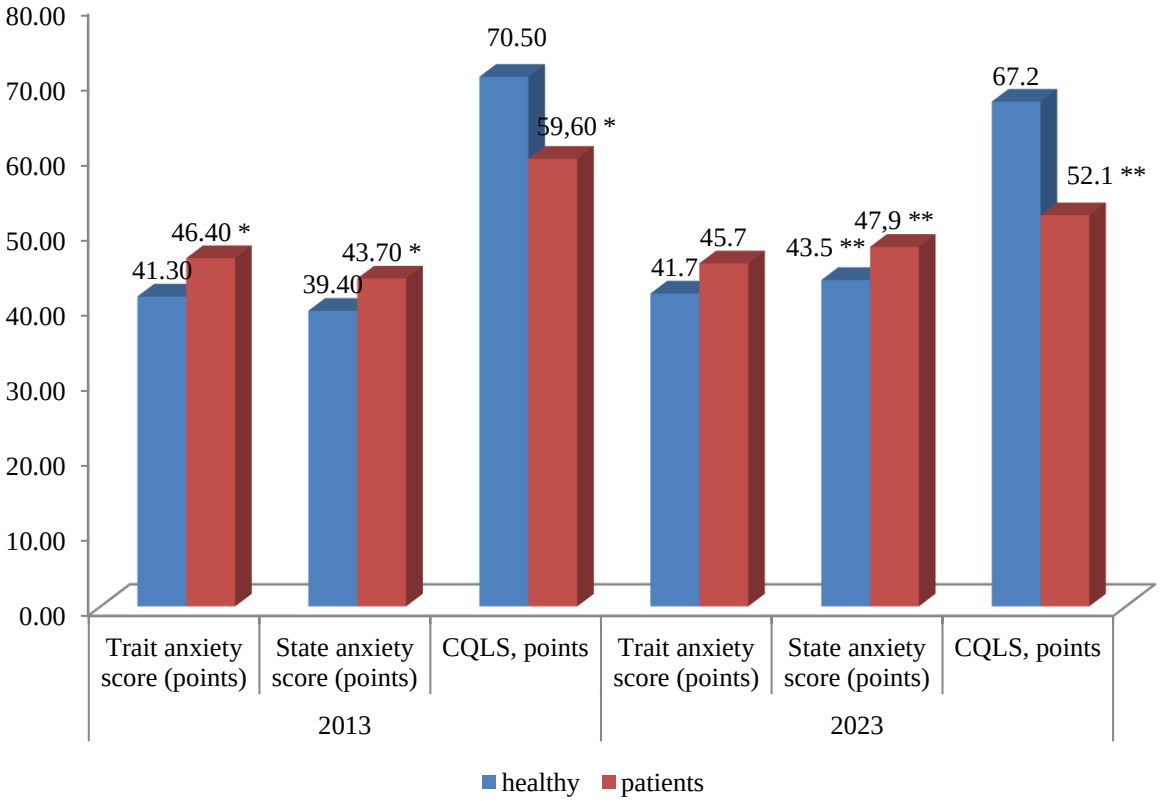

Figure 1. Dynamics of anxiety indicators in patients with acne vulgaris*

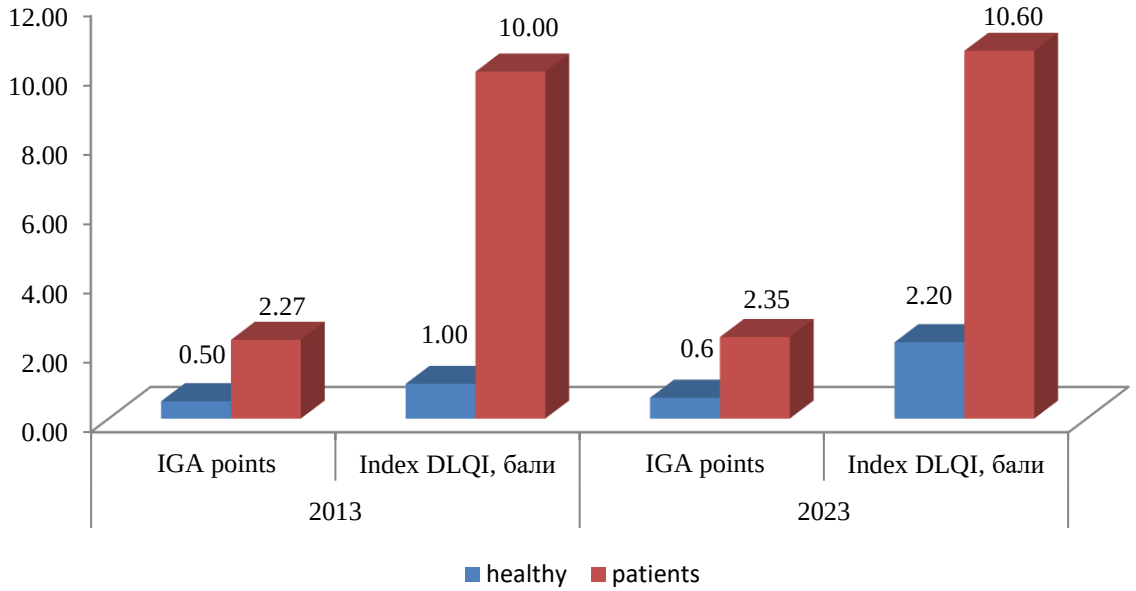

Figure 2. Quality of life in patients with acne vulgaris*

**Note to Figures 1, 2*: - significant difference ($p < 0.05$) between the corresponding indicators of patients with acne vulgaris compared to healthy subjects of the corresponding year of the study; ** - significant difference ($p < 0.05$) between the corresponding indicators of healthy subjects and patients in 2013 and 2023

As presented in table 1, stress and anxiety—as measured by the Spielberger State-Trait Anxiety Inventory influenced the course of acne vulgaris in adolescent girls. In 2013, patients demonstrated a significantly higher trait anxiety score compared to healthy peers. However, in 2023, no statistically significant difference was observed between the patient and control groups in this parameter. The trait anxiety level in healthy individuals remained comparable to that in 2013, while in patients it was slightly elevated relative to the control group.

Somewhat different trends were noted for state anxiety. In 2013, the mean state anxiety score in healthy girls was at the upper limit of the normal range, while in patients it significantly exceeded that of the control group. These findings suggest that living in modern conditions may contribute to increased anxiety in this population. Data collected in 2023, during the martial law period, revealed a statistically significant increase in state anxiety in both healthy and affected girls compared to data which was collected in 2013, underscoring the influence of current socio-political stressors on adolescent mental health.

Quality of life was also assessed in girls with acne vulgaris (Table 1). The DLQI scores in both 2013 and 2023 indicated moderate impairment, with no significant differences between the years. However, the CQLS scores were significantly lower in patients compared to healthy individuals in both years. Moreover, a further decline in CQLS scores in 2023 compared to 2013 was observed, highlighting the cumulative negative impact of acne and contemporary stressors on quality of life.

To explore the pathophysiological underpinnings of acne vulgaris in adolescent girls, we evaluated the interaction between the sympatho-adrenal, vagal-insular, and hypothalamic-pituitary-adrenal (HPA) systems. These systems are key components of the body's adaptive responses to extreme stimuli and involved in trophic regulation of tissues exposed to stress.

Compared to healthy individuals, patients exhibited elevated levels of adrenaline and noradrenaline excretion in 24-hour urine samples (Table 2), (Fig. 3, 4). Because catecholamine excretion reflects the activity of the sympatho-adrenal system, these findings indicate its heightened functional activity in patients. Furthermore, as shown in Table 2, the adrenaline/noradrenaline ratio was reduced in patients. This reduction was due to a disproportionately greater increase in noradrenaline excretion relative to adrenaline, indicating a predominance of the neural (adrenergic) response over the hormonal one. Given that the study involved patients during the acute stage of acne vulgaris, these findings suggest that sympatho-adrenal activity exceeded normal physiological limits.

Table 2

Hormone levels and their ratios in patients with acne vulgaris (M ± m)

Parameter	**2013p.**		**2023p.**	
	Healthy	**Patients**	**Healthy**	**Patients**
Adrenaline (nmol/day)	35.4±0.85	38.9±1.2	37.2±1.0	40.8±1.1*
Noradrenaline (nmol/day)	75.8±2.6	92.6±2.8*	85.4±3.1●	104.6±3.3*●
Cortisol (nmol/L)	265.6±8.6	369.8±11.2*	273.8±10.0	391.7±11.9*●
Insulin (μIU/mL)	6.4±0.15	7.7±0.18*	6.5±0.10	7.9±0.2*
Adrenaline / Noradrenaline ratio	0.47	0.42	0.44	0.39
Cortisol / Insulin ratio	41.5	48.0	42.1	49.6
Noradrenaline / Insulin ratio	11.8	12.0	13.1	13.2
Testosterone (nmol/L)	1.10±0.07	1.26±0.08	1.14±0.07	1.36±0.09
Free testosterone (pg/mL)	4.7±0.4	6.5±0.5*	5.3±0.5	8.4±0.7*●
Androstenedione (ng /mL)	1.7±0.15	2.9±0.26*	1.8±0.14	3.9±0.27*●
Estradiol (pg/mL)	152.6±7.8	163.4±7.0	161.7±6.8	174.1±8.3
Progesterone (nmol/L)	1.45±0.12	1.95±0.14*	1.56±0.17	2.28±0.16*

Notes: $p < 0.05$ — significant difference between patients and healthy individuals within the same year; ● $p < 0.05$ — significant difference between corresponding values in 2013 and 2023

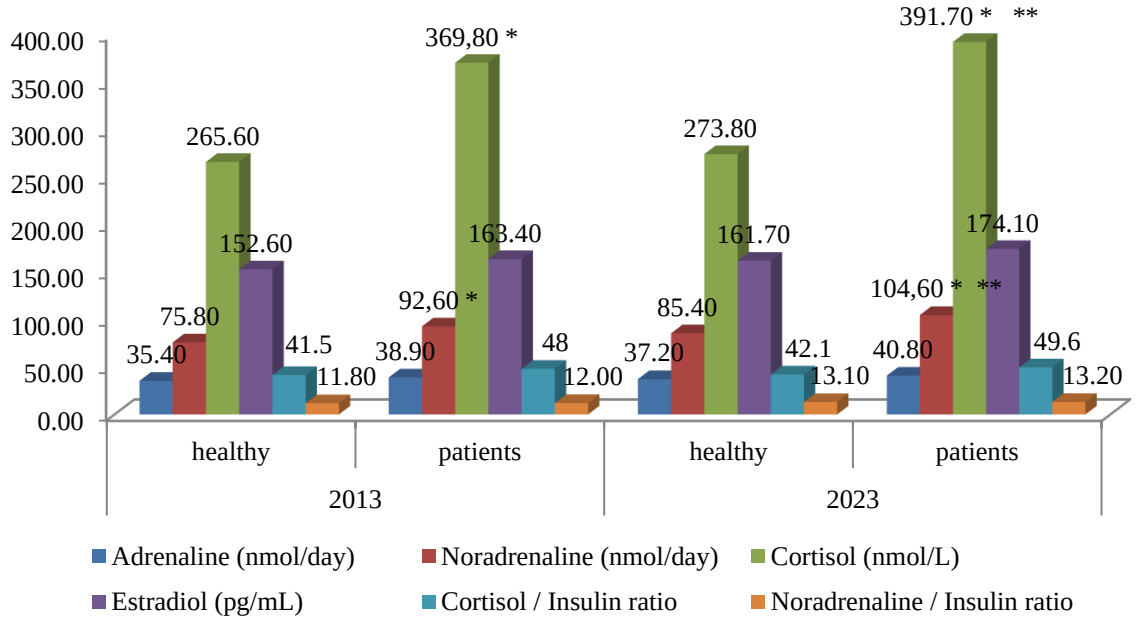

Figure 3. Level of sympathoadrenal system indicators in patients with acne vulgaris*

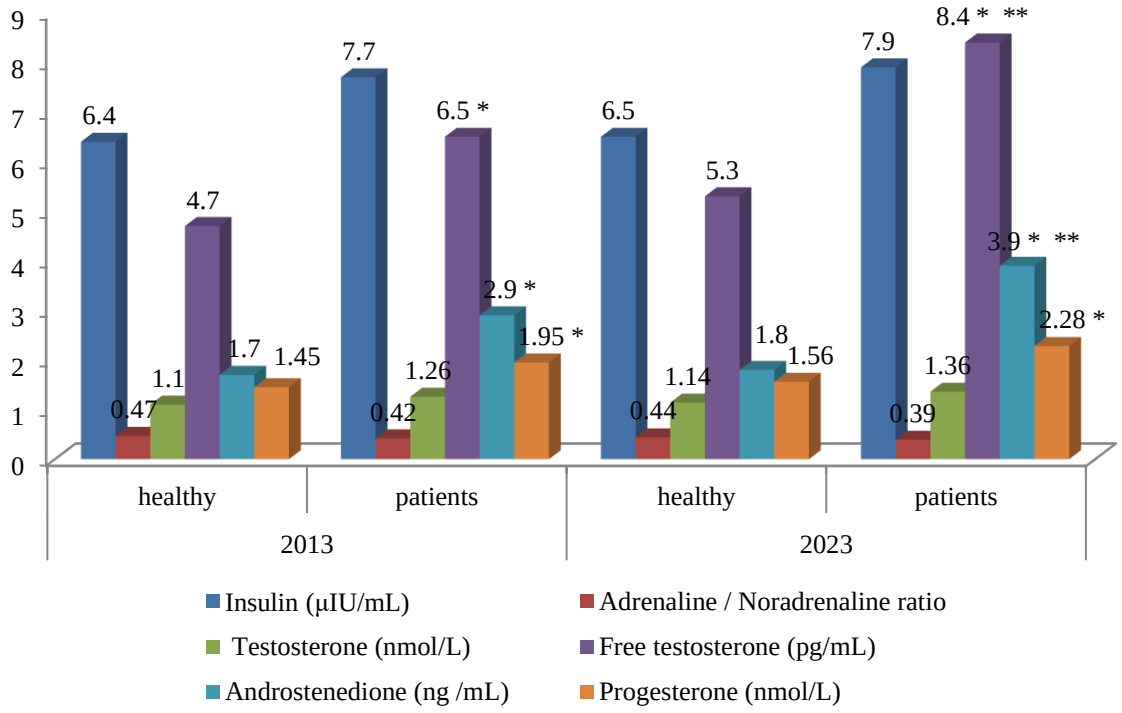

Figure 4. Level of indicators of the vagoinsular and hypothalamic-pituitary-adrenal systems in patients with acne vulgaris*

Notes to Figures 3, 4: * - significant difference ($p < 0.05$) between the corresponding indicators of patients with acne vulgaris compared to healthy subjects of the corresponding year of the study; ** - significant difference ($p < 0.05$) between the corresponding indicators of healthy subjects and patients in 2013 and 2023

Cortisol levels in patients were significantly higher than those in healthy individuals. A similar trend was observed for insulin levels. However, the cortisol-to-insulin ratio, considered one of the most objective indicators of stressor impact and compensatory activity, did not differ significantly between patients and controls.

Evaluation of autonomic nervous system function revealed a synergistic increase in both sympathetic and parasympathetic activity. Nonetheless, the ratio of urinary noradrenaline excretion to blood insulin concentration,

along with the noradrenaline/insulin ratio-which reflects the adequacy of autonomic response-suggests that sympathetic tone and reactivity predominated, indicating autonomic imbalance in patients.

Quantitative analysis of the sympatho-adrenal, vagal-insular, and adrenal glucocorticoid systems demonstrated a unidirectional increase in activity in the patient group. Although the nearly unchanged cortisol/insulin ratio implies an appropriate compensatory response to stress-induced tissue damage, the presence of sympatho-adrenal insufficiency and autonomic dysfunction indicates that the overall response was not fully adequate. Thus, it should be considered a stress response consistent with the alarm stage, triggered by a stimulus of extraordinary intensity.

Patients also exhibited a slight increase in total testosterone and a statistically significant elevation in free testosterone levels compared to healthy peers in both 2013 and 2023, reaffirming the role of this hormone in acne vulgaris pathogenesis. Elevated androstenedione and progesterone levels were also observed, while estradiol levels were similar between patients and controls.

In healthy girls, a comparison of hormone levels between 2013 and 2023 (Table 2) revealed a statistically significant increase only in noradrenaline levels in 2023; other hormones showed no significant differences. In contrast, patients examined in 2023 during martial law exhibited significantly higher levels of noradrenaline, cortisol, free testosterone, and androstenedione than in 2013.

Correlation analysis revealed a moderate positive association between acne severity (IGA score) and free testosterone ($r = +0.55$) and androstenedione ($r = +0.52$), along with weak correlations with noradrenaline ($r = +0.35$), cortisol ($r = +0.41$), insulin ($r = +0.32$), and progesterone ($r = +0.36$). These findings support the impact of hormonal imbalances on acne severity and confirm the multifactorial nature of its pathogenesis.

Associations were also identified between hormone levels and both trait and state anxiety. In patients, state anxiety was weakly but positively correlated with adrenaline ($r = +0.43$), noradrenaline ($r = +0.48$), and cortisol ($r = +0.37$). Similarly, trait anxiety showed weak positive correlations with adrenaline ($r = +0.39$), noradrenaline ($r = +0.46$), and cortisol ($r = +0.43$). Since trait anxiety develops early in life and remains relatively stable, these results suggest that elevated trait anxiety may form a background for hormonal dysregulation, thereby contributing to the development of acne vulgaris.

Published literature highlights the adverse impact of war on the mental health of young people and the need for targeted interventions to address the resulting disorders [15]. The psychological condition of patients—particularly increased anxiety and depression—is known to influence the onset and progression of acne vulgaris [8].

Our findings confirm elevated anxiety levels in healthy adolescent girls, consistent with observations reported by other researchers over the past decade [16]. Under current conditions, even higher levels of anxiety and stress-related hormone concentrations were recorded. These changes undoubtedly affect the psychological state of patients with acne vulgaris, as evidenced by our data on increased state anxiety and elevated stress hormone levels.

We observed that the functional activity of the sympatho-adrenal system in patients exceeded normal physiological limits, consistent with the alarm stage of the stress response. The intensity of the stimulus, therefore, may be considered extraordinary. These results suggest that the activation of the neural component of the sympatho-adrenal system—typically a critical element of adaptive physiological defense—no longer plays a sanogenetic (protective) role, but instead contributes pathogenetically, thereby becoming an important factor in the pathogenesis of acne vulgaris.

An increase in the concentration of androstenedione in the blood serum of patients with vulgar acne by 1 ng/ml (from 2.9±0. 26 to 3.9±0.27 ng/ml) and progesterone by 0.33 nmol/l (from 1.95±0.14 to 2.28±0.16 nmol/l), with almost identical levels of estradiol in patients and healthy individuals. This indicates the presence of sex hormone dysfunction in this cohort of patients, which is consistent with the data of other authors [1] and may be the background for the development of reproductive system disorders.

A statistically significant increase was found in 2023 during martial law in norepinephrine by 12 nmol/L (from 92.6±0.28 to 104.6±3.3 nmol/L), cortisol by 117.9 nmol/L (from 273.8±11.2 to 391.7±11.9 nmol/L), free testosterone by 1.9 pg/mL (from 6.5±0.5 to 8.4±0.7 pg/mL), and androstenedione by 1 ng/mL (from 2.9±0. 26 to 3.9±0.27 ng/mL), which can lead to a deterioration in hormonal status and, subsequently, reproductive function. Elevated insulin levels (from 7.7±0.18 to 7.9±0.2 μMO/ml) in patients with vulgar acne indicate probable insulin resistance in these

patients, which was also noted in the review [17]. Worsened situational anxiety and hormonal changes undoubtedly affected the quality of life of patients with acne vulgaris.

The results obtained require scientific research to correct the pathogenetic changes we have identified in the current conditions of both healthy individuals and patients with acne vulgaris.

We also identified elevated androstenedione and progesterone levels in the serum of patients, while estradiol levels remained comparable to those in healthy individuals. These findings indicate sex hormone dysfunction in this patient cohort, consistent with data from other studies [1], and may serve as a background for reproductive system disorders.

Significantly higher levels of noradrenaline, cortisol, free testosterone, and androstenedione were observed in 2023 (during the period of martial law) compared to 2013. This may reflect worsening endocrine dysregulation and potential impairment of reproductive function. Elevated insulin levels in patients suggest a likelihood of insulin resistance, as previously noted in the literature [17].

Increased state anxiety, hormonal imbalances, and autonomic dysregulation undoubtedly contributed to the reduced quality of life observed in patients with acne.

Altogether, these findings emphasize the urgent need for further scientific research focused on correcting the identified pathophysiological changes in both healthy individuals and patients with acne vulgaris under contemporary conditions.

Conclusions

The data obtained emphasize the multifactorial nature of acne pathogenesis, where the interaction of androgenic, stress, metabolic, and sex hormones forms a complex pathophysiological background of the disease. This indicates the advisability of a comprehensive approach to diagnosis and therapy, which should take into account the individual hormonal characteristics of patients to improve the effectiveness of treatment and prevent recurrence.

This study aimed to systematically evaluate the relationship between circulating hormone levels and the severity of vulgar acne. This approach not only deepens our understanding of the endocrine and neuroendocrine mechanisms underlying acne, but also provides a scientific basis for integrating hormonal assessment into routine clinical practice and developing targeted, individualized treatment methods.

1. In healthy adolescent girls in modern conditions, there is a statistically significant increase in situational anxiety by 4.1 points (from 39.4±1.1 to 43.5±1.6 points), an increase in norepinephrine levels by 9.6 nmol/day (from 75.8 ±2 6 to 85.4 ±3.1 nmol/day) and a slight decrease in quality of life (from 1.0±0.2 to 2.2±0.2 points).

2. It was found that under martial law conditions, adolescent girls with vulgar acne showed a statistically significant increase in situational anxiety by 4.2 points (from 43.7±1.5 to 47.9±1.2 points), a higher level of norepinephrine by 12 nmol/L (from 92.6±0.28 to 104.6±3.3 nmol/L), cortisol by 117.9 nmol/L (from 273.8±11.2 to 391.7±11.9 nmol/L), free testosterone by 117.9 nmol/L (from 273.8±11.2 to 391.7±11.9 nmol/L), androstendione by 1 ng/ml (from 2.9±0.26 to 3.9±0.27 ng/ml), and there is a further slight decrease in quality of life from 10.3±0.3 to 10.6±0.3 points.

3. In adolescent girls with vulgar acne, there is increased anxiety, reduced quality of life, increased activity of the sympathoadrenal, vagus-insular, and glucocorticoid functions of the adrenal glands, which correspond to the stage of anxiety stress reaction, and dysfunction of sex hormones.

4. The results of the study demonstrated significant associations between the hormonal profile and the severity of acne vulgaris. A moderate positive correlation was found between the levels of free testosterone (r+0.55) and androstenedione (r+0.52) and the severity of clinical manifestations of the disease, confirming the key role of androgens in the pathogenesis of acne. Additionally, weak correlations with levels of norepinephrine (r+0.35), cortisol (r+0.41), insulin (r+0.32), and progesterone (r+0.36) indicate the influence of neuroendocrine and metabolic factors on the course of the disease.

Further research should be aimed at developing correction of the identified pathogenetic changes in adolescent girls with acne.

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