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Studying the impact of COVID-19 on the progression of metabolic, neuroendocrine disorders and some immunological changes in women with acne

Acne is a multifactorial chronic inflammatory disease with primary damage to the pilosebaceous unit and the polymorphic clinical manifestations associated with overproduction of sebaceous glands, pathological desquamation of the sebaceous epithelium of the sebum follicles, activation of saprophytic, conditionally pathogenic microorganisms, and psychoemotional disorders. This is undoubtedly one of the most common dermatoses in clinical practice, accounting for 20–25 % of dermatology consultations. Today, especially in wartime, acne vulgaris remains a socially important problem in approximately half of patients with psychoemotional disorders, mainly of a depressive and anxiety associated nature with a sharp decrease in the quality of life of patients.

Objective – to study a pathogenic role of certain neuroendocrine, metabolic and immunological disorders as well their consequences in the development of acne in women who had COVID-19.

Materials and methods. 134 women with acne, aged 18 to 45 years old, were examined. The levels of cortisol and prolactin, C-reactive protein (C-RP), total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides (TG), concentration of cytokines, atherogenic index (AI), index HOMA (insulin resistance index) and anxiety were determined.

Results and discussion. Most of the examined patients with acne have shown varying degrees of changes in some neuroendocrine and metabolic indices. The total cholesterol level in patients with acne was higher by 27.78 % ($p < 0.001$), and in patients with acne associated with COVID-19 by 45.37 % ($p < 0.001$), compared with the control group. The HDL level was lower by 27.91 and 39.53 % ($p < 0.001$), respectively, compared with the control group, LDL was higher by 34.35 and 58.78 % ($p < 0.001$), respectively, and the TG level was twice as high ($p < 0.001$), as the control group level in both groups of women with acne. At the same time, an increase in the atherogenic index by 28.09 % ($p < 0.01$) and 37.02 % ($p < 0.001$) respectively, was also observed compared with the control group level, but without significant changes between the levels of both groups of women with acne. An increased level of pro-inflammatory cytokines, have been observed in patients of both groups, with insufficient synthesis of anti-inflammatory interleukins in all examined women with acne, at that, more significant abnormalities in the examined immune indices have been observed in patients who have had COVID-19.

Conclusions. High level of anxiety, the changes in cytokine profile, neuroendocrine and metabolic indices (C-RP, TC, HDL, LDL, TG, AI), have been observed in women with acne. At that, more significant abnormalities in the examined indices have been found in patients who have had COVID-19 that substantiates the necessity to develop new comprehensive methods of treatment, taking into account the impact of neuroendocrine and metabolic disorders and immunological changes associated with COVID-19.

Keywords

Acne, COVID-19, anxiety, metabolic, neuroendocrine disorders, immunological changes.

The global trend in COVID-19 is that the virus permanently turns into a seasonal disease, such as the flu. Every year, people will face the problem of the coronavirus, which will continue to mutate.

The known and studied nature of COVID-19 mutations currently does not indicate that the virus has become more aggressive for the human body. More and more often, COVID-19 proceeds as an acute

respiratory viral infection and evades an immune response, i.e. it affects a weakened immune system faster [10, 19]. According to the Ministry of Health of Ukraine, during the 2023/2024 epidemic season, more than 4.5 million Ukrainians suffered from acute respiratory viral infection, influenza and COVID-19. Concurrently, a new problem arises related to the consequences of this disease. Post-COVID-19 syndrome has been widely recognized both among social support groups and in the scientific and medical community. This condition is poorly understood, but it affects in various forms many patients who had COVID-19, regardless of the severity of the disease [6]. Post-COVID-19 syndrome is defined by the manifestation of clinical signs and symptoms that occur during or after COVID-19, persist for more than three months, and are not explained by an alternative diagnosis [14]. The most common symptoms include fatigue, impaired concentration, memory problems, sleep disorder, anxiety and depression [23]. The biological mechanisms underlying the long COVID remain unknown. The infection causes damage to cells and tissues in the human body, and often the metabolic disorders (for example, insulin resistance, increased lipid metabolism) [16], hyperglycaemia, hormonal imbalance, immune imbalance, etc. [29]. However, the consequences of COVID-19 and post-COVID-19 syndrome also affect the exacerbation and course of chronic skin diseases (acne, psoriasis, atopic dermatitis, eczema, etc.) [7, 12].

Acne is a multifactorial chronic inflammatory disease with primary damage to the pilosebaceous unit and the polymorphic clinical manifestations (comedones, papules, pustules, nodules, cysts, etc.) associated with overproduction of sebaceous glands, pathological desquamation of the sebaceous epithelium of the sebum follicles, activation of saprophytic, conditionally pathogenic microorganisms, and psychoemotional disorders [2, 17]. This is undoubtedly one of the most common dermatoses in clinical practice, accounting for 20–25 % of dermatology consultations. More than 80 % of acne sufferers are between the ages of 12 and 24. In developed countries, dermatosis affects 50–85 % of adolescents, of which 2/3 of cases are mild to moderate. Over the past decades, the incidence of acne in people over the age of 25 has increased, with women being affected more commonly. Today, especially in wartime, acne vulgaris remains a socially important problem in approximately half of patients with psychoemotional disorders, mainly of a depressive and anxiety associated nature with a sharp decrease in the quality of life of patients [2, 25].

According to a number of studies [15, 28], changes in the hormonal status, manifested by hyperandrogenism of various origin, are also con-

sidered the main factors in the development of acne. Hyperandrogenism is often considered as one of the components of the metabolic syndrome [1]. Hyperandrogenism can develop as a result of hyperprolactinemia, under the influence of which pathological changes occur in blood plasma in the form of induced production of squalene (precursor of sebaceous glands cholesterol) and increased dehydroepiandrosterone [7, 8, 17]. Since prolactin affects, directly or indirectly, all tissues of macroorganism, even an insignificant increase in its level in blood plasma can cause hyperandrogenism. During depression, prolactin is produced uncontrollably, which can have irreversible consequences. It has been found that prolactin has a negative effect not only on the secretion of gonadotropins with disruption of their circadian rhythm, but also on the level of other hormones of the reproductive system. At the same time, progesterone production increases and the estrogen-progesterone balance is disturbed, as well as metabolic changes appear associated with hypercortisolemia, vitamin D deficiency and hyperandrogenemia [2, 15].

Recently, the development of metabolic syndrome (MS) has played a significant role in the manifestation of acne exacerbation. The common pathogenetic links between MS and skin diseases are chronic inflammation, oxidative stress, imbalance between reactive oxygen species and antioxidants and presence of toll-like receptors that immediately respond to antigens and cause the production of immunoregulatory cytokines [1, 18]. Activation and/or damage to the endothelium leads to the development of immune and connective tissue responses, and immunosuppression leads to infections [5]. The basis for the formation of MS is insulin resistance (IR), which triggers false symptoms and leads, among other things, to the development of skin diseases or the aggravation of their course [13]. Since insulin receptors are expressed in epidermal keratinocytes, hyperinsulinemia can lead to increased proliferation of acro-infundibular keratinocytes in the duct of the sebaceous glands and failure of terminal differentiation of corneocytes, thereby causing follicular hyperkeratosis. Insulin also stimulates androgen synthesis, which leads to sebum overproduction and correlates with acne severity [1, 2, 7]. The insulin-like growth factor (IGF-1) is able to stimulate 5 α -reductase, enhance androgen receptor signal transduction and androgen synthesis by the adrenal glands and gonads, proliferation and lipogenesis in sebocytes [8, 24].

The markers of MS, along with the level of HbA1c, glycated albumin and insulin resistance (IR), include the level of triglycerides (TG), levels of high-density lipoproteins (HDL), low-density

lipoproteins (LDL) and very-low-density lipoproteins (VLDL); total cholesterol (TC), atherogenic index (AI) and the level of C-reactive protein (C-RP) [4], which is considered one of the most well-characterized and well-standardized [11], the increase of which was also found by a number of researchers in patients with acne [20, 21, 26].

One of the factors in acne progression is patient anxiety [25], which results in increased secretion of corticotropin, which stimulates the adrenal cortex and increases production of glucocorticoids and adrenal androgens. An increase in androgens leads to overproduction of sebum, which is a growth medium for *Propionibacterium acnes*. This is facilitated by stimulation of sebum secretion due to the increase in adrenaline production. An increase in glucocorticoids causes a shift in the immune response towards type 2 T helper cells with a decrease in the activity of macrophages and phagocytosis dysfunction. As a result, the immune response is weakened and uncontrolled reproduction of bacteria begins with colonization of the ducts of sebaceous glands with a simultaneous increase in the concentration of free fatty acids [2, 17, 27]. The anti-inflammatory cytokines, produced by macrophages, ensure the coordinated interaction of immune cells in the inflammatory process. The macrophages stimulate neutrophils, fibroblasts and endothelial cells and present antigens to T helper cells, which, together with mast cells, promote the production of anti-inflammatory interleukins [7, 9].

Thus, the development of acne occurs as a result of a comprehensive influence of external and internal causes, among which the disorders of endocrine system with excessive androgen production and estrogen deficiency, associated with genetic predisposition to the disease, play a significant role. A decreased immunological reactivity of the body, nidus of infection in the body or skin, epidermal barrier damage, sebum overproduction (seborrhea), decreased nonspecific skin and human body resistance, carbohydrate and lipid metabolism disorders, psychovegetative and hormone imbalance, etc. are the factors triggering and promoting acne. However, only isolated reports can be found in the literature sources showing a potential role of anxiety disorders and COVID-19 consequences in development or course of MS in the pathogenesis of acne. Furthermore, the data provided are often contradictory and not sufficiently substantiated. This determines the relevance of further study with a view to optimize treatment and preventive measures of exacerbation of the skin disease.

Objective — to study a pathogenic role of certain neuroendocrine, metabolic and immunological disorders as well their consequences in the development of acne in women who had COVID-19.

Materials and methods

A total of 134 women with acne, aged 18 to 45 years old, were examined. The control group consisted of 37 healthy female donors of similar age. A comprehensive examination of patients was carried out after obtaining written consent, in accordance with the principles of the Declaration of Helsinki on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine from and relevant laws of Ukraine, in a randomized manner with preliminary stratification for acne. All patients signed consent for examination and research (protocol No. 1 from January the 20th 2015, discussed and approved by the Committee on ethics of scientific research, experimental development and scientific works of Danylo Halytsky Lviv National Medical University.

The study did not include patients with acne who had any acute or chronic inflammation, polycystic ovary syndrome and anemia, as well as patients who had received treatment according to the protocol 1 month before the study (in case of systemic therapy) or 2 weeks before the study (in case of local therapy). All the patients examined were in Ukraine during the study, taking into account the impact of wartime on the course of the disease.

All patients with acne were divided into 2 groups for the study: Group 1 — women with acne, and Group 2 — patients with acne who had had COVID-19 3–12 months before the examination. The study included women with acne who have had a mild or moderate course of COVID-19 according to the criteria defined by order No. 1 722 of the Ministry of Health of Ukraine dated March 28, 2020.

The levels of cortisol and prolactin, C-RP, TC, HDL, LDL and TG in blood serum were determined in a laboratory in all patients using an analyzer and test system Cobas 6000, Roche Diagnostics (Switzerland). The prolactin level was tested on the 3rd to 5th day of a menstrual cycle. The C-RP was determined by the latex turbidimetry method twice with an interval of 2 weeks, and the average of two values was considered the result of the study. The atherogenic index, characterizing the ratio of atherogenic fractions of lipoproteins to non-atherogenic ones, was determined by the formula: $AI = (\text{total cholesterol } TC - HDL) / HDL$.

In order to assess insulin resistance, HOMA-IR (homeostatic model assessment for insulin resistance) was calculated by the formula: $HOMA = (\text{fasting glucose (mmol/L)} \times \text{fasting insulin (mU/L)}) / 22.5$. Blood sugar and insulin levels were determined in a laboratory following standard procedure. The value > 2.7 indicated insulin resistance [1]. The concentration of cytokines (IL-1 β , IL-4, IL-8, IL-10) in blood serum was determined by the enzyme-linked immunosorbent assay sandwich

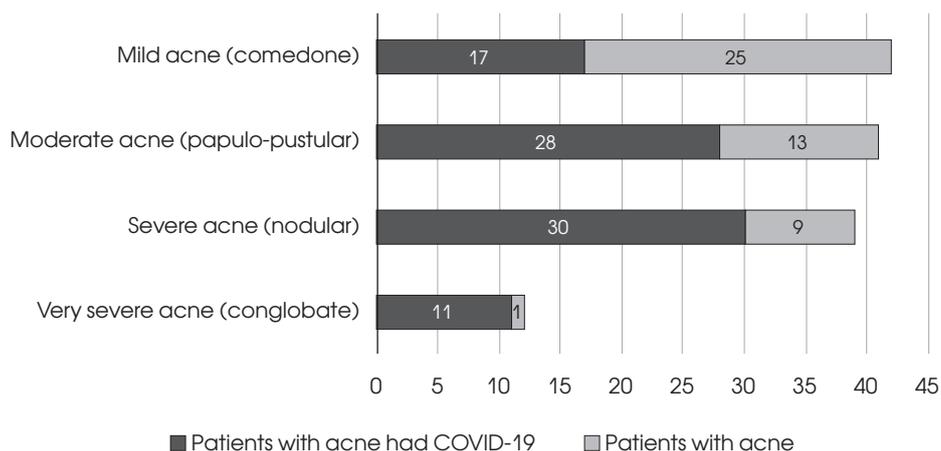


Fig. 1. Division of examined patients by degrees of severity of acne

method using standard BioSource International kits and the Bio-plex Pro Human Cytokine test systems (Austria) [18].

In order to assess anxiety in patients with acne, the State-Trait Anxiety Inventory developed by Spielberger–Khanin was used.

The methods of a systems approach and analysis, structural and logical analysis, and calculation of average and relative values were used in the paper. The quantitative indicators were checked for normal distribution showed by the Gaussian distribution. The average values are presented as the arithmetic mean with a standard squared deviation ($M \pm SD$). The obtained research data were processed by methods of variation statistics using Fisher’s (f) and Student’s criteria (t). The difference in mean values was considered significant at $p < 0.05$. The statistical processing of the research results was carried out on a personal computer using R-Studio programs [3].

Results and discussion

Based on clinical findings, 42 (31.3 ± 4.0) % patients were diagnosed with mild acne, 41 (30.6 ± 4.0) % – moderate acne, 39 (29.1 ± 3.9) % – severe acne and 12 (9.0 ± 2.5) % – extremely severe acne. It should be noted that 86 ($64.2 \pm 4,1$) % women with acne who had COVID-19 and only 48 ($35.8 \pm 4,1$) % persons with no prior history of COVID-19 were examined. The division of women with acne by degrees of severity of acne is shown in Fig. 1.

When measuring the levels of state and trait anxiety, high levels of anxiety were observed in all examined women with acne according to the table of interpretation of the results of Spielberger–Khanin test. At that, the levels of trait anxiety in women with acne were higher, compared with those of the state anxiety. The index of trait anxiety in women with acne was by 18.91 % higher ($p > 0.05$), compared with the index of state anxiety, and in

women with acne who had COVID-19 – by 14.68 % ($p > 0.05$), compared with the index of state anxiety. However, significant differences ($p < 0.05$) in both indices of anxiety were observed in women depending on COVID-19 in past medical history, namely in women with acne who had COVID-19 the index of trait anxiety was higher by 39.26 % and the index of state anxiety was higher by 44.39 % compared with the group of women who had acne (Fig. 2).

The significant changes in all examined indices (serum cortisol and prolactin and HOMA index) that depended on COVID-19 in past medical history and meaningfully differed from the values of the control group were detected in women with acne (Table 1).

It should be noted that cortisol level increased by 19.98 % ($p < 0.01$) was observed in women with acne and cortisol level decreased by 17.36 % ($p < 0.01$) was observed in patients with acne with

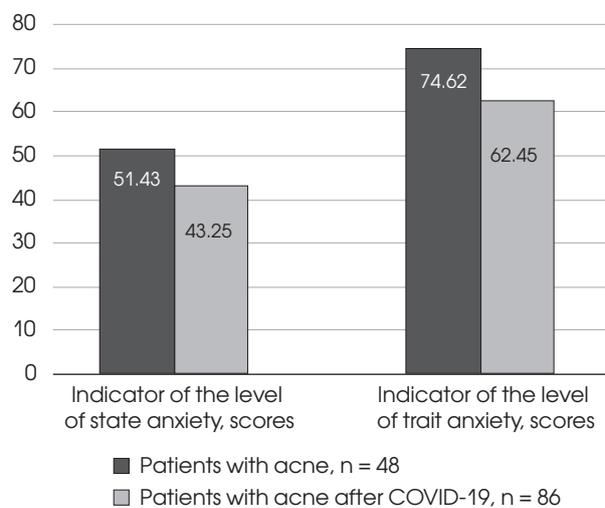


Fig. 2. Indicators of the level of state and trait anxiety in women with acne and women with acne after COVID-19

Table 1. Level of cortisol, prolactin, C-reactive protein in blood serum and HOMA index in women with acne and women with acne after COVID-19

Indices	Serum cortisol, nmol/L	Serum prolactin, mIU/L	HOMA index	C-reactive protein, mg/L
Women with acne, n ₁ = 48	546.5 ± 16.72*	341.3 ± 7.92	2.73 ± 0.40	6.9 ± 0.94*
Women with acne after COVID 19, n ₂ = 86	376.8 ± 18.33* p ₁₋₂ < 0.001	419.2 ± 6.88*** p ₁₋₂ < 0.001	3.79 ± 0.54* p ₁₋₂ > 0.05	8.7 ± 0.62*** p ₁₋₂ > 0.05
Indices of control group, n = 37	455.8 ± 25.54	315.4 ± 19.34	2.44 ± 0.52	4.6 ± 0.22

Note. Degree of significance of difference in indices in relation to the control group: *p < 0.05; **p < 0.01; ***p < 0.001; p₁₋₂ — significance of difference in indices in patients with acne and patients with acne after COVID-19.

Table 2. Level of metabolic indices of the blood serum of patients with acne and women with acne after COVID-19

Indices	Total cholesterol, mmol/L	High-density lipoproteins, mmol/L	Low-density lipoproteins, mmol/L	Triglycerides, mmol/L	Atherogenic index
Women with acne, n ₁ = 48	5.52 ± 0.17***	1.24 ± 0.09**	3.52 ± 0.19***	2.29 ± 0.09***	3.01 ± 0.06**
Women with acne after COVID-19, n ₂ = 86	6.28 ± 0.24*** p ₁₋₂ < 0.05	1.04 ± 0.14** p ₁₋₂ > 0.05	4.16 ± 0.22*** p ₁₋₂ ≤ 0.05	2.62 ± 0.14*** p ₁₋₂ > 0.05	3.22 ± 0.12*** p ₁₋₂ > 0.05
Indices of control group, n = 37	4.32 ± 0.15	1.72 ± 0.12	2.62 ± 0.10	1.07 ± 0.04	2.35 ± 0.24

Note. Degree of significance of difference in indices in relation to the control group: *p < 0.05; **p < 0.01; ***p < 0.001; p₁₋₂ — significance of difference in indices in patients with acne and patients with acne after COVID-19.

prior history of COVID-19, compared with the index of the patients from the control group. When measuring the level of prolactin in serum, it was found that its level was increased by 8.21 % in women with acne compared with the index of the patients from the control group (p > 0.05) and increased by 32.91 % (p < 0.001) in patients with acne with prior history of COVID-19. When determining the level of C-reactive protein in serum of patients with acne of Group 1, an increase by 1.5 times was observed compared to the indicator of the control group (p < 0.05), and an almost twofold increase of this indicator was observed in patients with acne of Group 2 (p < 0.001), with no significant difference between both groups of patients with acne. It should be noted that the highest C-RP values were observed in patients with papulopustular acne and amounted to 7.3 ± 0.54 and 9.1 ± 0.48 (p < 0.001), respectively, compared to the control group.

When calculating HOMA index in patients with acne, the changes in the index were also revealed compared with the indices of the patients from the control group: increase by 11.89 % (p > 0.05) in patients with acne and increase by 52.87 % (p < 0.05) in patients with acne with prior history of COVID-19. Besides, an increase of HOMA index was observed along with a body weight gain and lack of sleep in patients with acne associated with COVID-19, which was further confirmed by the indices of anxiety, particularly of a trait one.

When analysing the metabolic indices of the blood serum of patients with acne, a deviation in lipid metabolism indices was observed compared to the indicators of the control group. The results of biochemical studies have shown various blood lipid disorders in the examined acne patients. Lipid imbalance has been detected in 38 (79.16 %), i.e. the majority of patients with acne, and in 82 (95.35 %) patients with acne who have had COVID-19. Moderate changes in the form of hypercholesterolemia, hypertriglyceridemia, an increase in the high-density HDL-C and LDL-C and an increase in the AI have been observed (Table 2).

The total cholesterol level in patients with acne was higher by 27.78 % (p < 0.001), and in patients with acne associated with COVID-19 by 45.37 % (p < 0.001), compared with the control group. The HDL level was lower by 27.91 and 39.53 % (p < 0.001), respectively compared with the control group, LDL was higher by 34.35 and 58.78 % (p < 0.001) respectively, and the TG level was twice as high (p < 0.001) as the control group level in both groups of women with acne. At the same time, an increase in the atherogenic index by 28.09 % (p < 0.01) and 37.02 % (p < 0.001) respectively, was also observed compared with the control group level, but without significant changes between the levels of both groups of women with acne.

To assess the cytokine profile in women with acne, we have determined pro-inflammatory (IL-1β,

IL-8) and anti-inflammatory (IL-4, IL-10) interleukins in blood serum. The significant changes ($p > 0.05$) in pro-inflammatory cytokine values have been observed in all examined women with acne, namely, an almost twofold increase in the level of IL-1 (β) in women with acne with no prior history of COVID-19, and increase by 2.86 times in women who have had COVID-19, and IL-8 respectively, by 2.96 and 1.54 times ($p > 0.05$) and anti-inflammatory interleukins, namely: IL-4, respectively: an increase by only 1.9 times and 1.57; IL-10 by 1.88 and 1.59.

These data indicate an insufficient immune response (synthesis of an insufficient amount of anti-inflammatory interleukins, especially in patients with acne who have had COVID-19 associated with state and trait anxiety).

Today, especially amid the chronic stress [25], neuroendocrine [2, 17] and metabolic disorders [11, 13] play a significant role in the manifestation of exacerbation and course of acne. The common pathogenetic links between metabolic changes and skin diseases are chronic inflammation, oxidative stress, imbalance between reactive oxygen species and antioxidants and presence of toll-like receptors that immediately respond to antigens and cause the production of immunoregulatory cytokines. In our paper, we have determined some neuroendocrine and metabolic indices separately in women with acne and women with acne with prior history of COVID-19. We have found that most of the examined patients with acne showed varying degrees of changes in some neuroendocrine and metabolic indices, which coincides with the data of other researchers. However, we have found significant changes in serum cortisol level (increase in women with acne and decrease in women with acne with prior history of COVID-19, increase in serum prolactin and HOMA index with more significant deviations in women with acne with prior history of COVID-19 compared to women with acne with no prior history of COVID-19), which will be important for prescribing pathogenetically feasible treatment. Besides, it has been found that total cholesterol level in all patients with acne was significantly higher ($p < 0.001$), but in patients with acne associated with COVID-19, this level was higher by 45.37 % ($p < 0.001$), compared with the control group, and by 13.7 % ($p < 0.05$), compared with the levels in the group of women with acne who

had not COVID-19. The HDL level was lower by 27.91 and 39.53 % ($p < 0.001$), respectively, compared with the control group, LDL was higher by 34.35 and 58.78 % ($p < 0.001$) respectively, and the TG level was twice as high ($p < 0.001$) as the control group level in both groups of women with acne. At the same time, an increase in the atherogenic index by 28.09 % ($p < 0.01$) and 37.02 % ($p < 0.001$), respectively, was also observed compared with the control group level, but without significant changes between the levels of both groups of women with acne. In our opinion, COVID-19 is considered as a trigger in initiating the development of metabolic and neuroendocrine changes in women with acne.

There are many reports in the literary sources about the impact of stress and anxiety on the course of acne [2, 25]. We have studied the level of trait and state anxiety in women with acne and in women with acne who had COVID-19 in our work in a differentiated manner. An increase in anxiety levels was noted, characterized by higher trait anxiety scores, especially in the group of women with acne who had recovered from COVID-19, which will require a more detailed examination of such patients in order to improve the identified conditions.

The significant changes in cytokine profile indices, in particular, an increased level of pro-inflammatory cytokines (IL-1 β and IL-8) with insufficient synthesis of anti-inflammatory interleukins (IL-4 and IL-10) have been observed in all examined women with acne, which is confirmed by other authors [18, 20]. At that, more significant abnormalities in the examined immune indices have been observed in patients with prior history of COVID-19. A strong and moderate correlational relationship (from + 0.6 to 0.9) between the nature of changes in the above-mentioned indices and COVID-19 in the medical history has been detected in the course of our study.

Conclusions

High level of anxiety, the changes in cytokine profile, neuroendocrine and metabolic indices (C-RP, TC, HDL, LDL, TG, AI), have been observed in women with acne. At that, more significant abnormalities in the examined indices have been found in patients who have had COVID-19 that substantiates the necessity to develop new comprehensive methods of treatment, taking into account the impact of neuroendocrine and metabolic disorders and immunological changes associated with COVID-19.

There is no conflict of interests.

Participation of the authors: concept and design of the study – O.O. Syzon, M.O. Dashko; collection of material, processing of material – O.O. Syzon, M.O. Dashko, I.S. Diskovsky; writing of the text, statistical processing of data, editing – O.O. Syzon, M.O. Dashko.

References

1. Болотна ЛА, Саріан ОІ, Ємченко ЯО. Інсулінорезистентність та хронічні запальні дерматози. Український журнал дерматології, венерології, косметології. 2024;1(92):61-68. doi: 10.30978/UJDVK2024-1-61.
2. Запольський МЕ, Лебедюк ММ, Ніточко ОІ, Тимофєєва ІМ. Аналіз факторів, що ускладнюють клінічний перебіг вугрової хвороби. 2023;3(92):19-24. doi: 10.30978/UJDVK2023-3-19.
3. Лапач СН, Чубенко АВ, Бабич ПН. Основные принципы применения статистических методов в клинических испытаниях. К.:Морион; 2002. 160 с.
4. Соколова ЛК, Пушкарьов ВМ, Тронько МД. Предіабет і метаболічний синдром. Характеристика і маркери. Ендокринологія. 2021;26(2):179-187. doi: 10.31793/1680-1466.2021.26-2.179.
5. Bernales Salinas A. Acne vulgaris: role of the immune system. *Int J Dermatol*. 2021;60:1076-1081. doi: 10.1111/ijd.15415.
6. Carod-Artal FJ. Post-COVID-19 syndrome: epidemiology, diagnostic criteria and pathogenic mechanisms involved. *Rev Neurol*. 2021;72(11):384-396. doi: 10.33588/rn.7211.2021230.
7. Cheng YF, Zhao H, Li J, et al. Factors aggravating acne vulgaris during the COVID-19 pandemic in China: a web-based cross-sectional survey. *Eur Rev Med Pharmacol Sci*. 2022 Oct;26(19):7305-7312. doi: 10.26355/eurrev_202210_29925.
8. Clayton RW, Göbel K, Niessen CM, et al. Homeostasis of the sebaceous gland and mechanisms of acne pathogenesis. *Brit J Dermatol*. 2019;181:677-690. doi: 10.1111/bjd.17981.
9. Conforti C, Giuffrida R, Fadda S, et al. Topical dermatocosmetics and acne vulgaris. *Dermatol Ther*. 2021;34(1):e14436. doi: 10.1111/dth.14436.
10. Daye M, Temiz SA, Işık B, et al. Evaluation of the effect of COVID-19 pandemic on dermatological diseases with dermatological quality life index. *Dermatol Ther*. 2020;33(6):e14368. doi: 10.1111/dth.14368.
11. Devaraj S, Singh U, Jialal I. Human C-reactive protein and the metabolic syndrome. *Curr Opin Lipidol*. 2009;20(3):182-189. doi: 10.1097/MOL.0b013e32832ac03e.
12. Gelfand JM, Armstrong AW, Bell S, et al. National Psoriasis Foundation COVID-19 Task Force guidance for management of psoriatic disease during the pandemic: Version 2-Advances in psoriatic disease management, COVID-19 vaccines, and COVID-19 treatments. *J Am Acad Dermatol*. 2021;84(5):1254-1268. doi: 10.1016/j.jaad.2020.12.058.
13. Gonzalez-Saldivar G, Rodriguez-Gutierrez R, Ocampo-Candiani G, et al. Skin manifestations of insulin resistance: from a biochemical stance to a clinical diagnosis and management. *Dermatol Ther (Heidelb)*. 2017;7:37-51. doi: 10.1007/s13555-016-0160-3.
14. Hallek M, Adorjan K, Behrends U, et al. Post-COVID Syndrome. *Dtsch Arztebl Int*. 2023;27;120(4):48-55. doi: 10.3238/arztebl.m2022.0409.
15. Hazarika N. Acne vulgaris: new evidence in pathogenesis and future modalities of treatment. *J Dermatol Treat*. 2021;32(12):277-285. doi: 10.1080/09546634.2019.1654075.
16. Kadhem Al-Hakeim H, Tahseen Al-Rubaye H, Abdulsahib S, Jubran, et al. Increased insulin resistance due to long COVID is associated with depressive symptoms and partly predicted by the inflammatory response during acute infection. *Braz J Psychiatry*. 2023;45(3):205-215. doi: 10.47626/1516-4446-2022-3002.
17. Layton AM, Ravenscroft J. Adolescent acne vulgaris: current and emerging treatments. *Lancet Child Adolesc Heal*. 2023;7:136-144. doi: 10.1016/S2352-4642(22)00314-5.
18. Liu Y, Sun Q, Xu H, et al. Serum level changes of inflammatory cytokines in patients with moderate to severe acne vulgaris treated with dual-wavelength laser. *Chinese Journal of Plastic and Reconstructive Surgery*. 2023;5(2):47-52. doi: 10.1016/j.cjprs.2023.05.001.
19. Masood S, Tabassum S, Naveed S, Jalil P. COVID-19 Pandemic & Skin Care Guidelines for Health Care Professionals. *Pak J Med Sci*. 2020;36(COVID 19-S4):115-117. doi: 10.12669/pjms.36.COVID19-S4.2748.
20. Mohammed R.HE, Mohammed GF, Abd-el-Hamid AS, Eyada M.MK. Correlation of IL-8 and C-reactive protein serum levels with the severity of inflammatory acne vulgaris: a comparative study. *ARC J Dermatol*. 2016;1:10-15. doi: 10.20431/2456-0022.0101002.
21. Namazi MR, Parhizkar AR, Jowkar F. Serum levels of hyper-sensitive-C-reactive protein in moderate and severe acne. *Indian Dermatol Online J*. 2015;6(4):253-257. doi: 10.4103/2229-5178.160256.
22. Palamar B, Palamar S, Miyer T, et al. Studying anxiety as a predictor in students to predict the development of burnout. *Wiad Lek*. 2023;76(5pt1):1054-1061. doi: 10.36740/WLek202305125.
23. Pierce JD, Shen Q, Cintron SA, Hiebert JB. Post-COVID-19 Syndrome. *Nurs Res*. 2022;71(2):164-174. doi: 10.1097/NNR.0000000000000565.
24. Sadowska-Przytocka A, Gruszczyńska M, Ostalowska A, et al. Insulin resistance in the course of acne – literature review. *Postepy Dermatol Alergol*. 2022;39(2):231-238. doi: 10.5114/ada.2021.107101.
25. Samuels DV, Rosenthal R, Lin R, et al. Acne vulgaris and risk of depression and anxiety: A meta-analytic review. *J Am Acad Dermatol*. 2020;83:532-541. doi: 10.1016/j.jaad.2020.02.040.
26. Taweel EI, Aziz AS, Rehab M, et al. Type I and type II acute-phase proteins in acne vulgaris. *Journal of the Egyptian Women's Dermatologic Society*. 2019;16(1):31-36. |doi: 10.4103/JEWD.JEWD_3_19.
27. Tobiasz A, Nowicka D, Szeptietowski JC. Acne vulgaris – novel treatment options and factors affecting therapy adherence: a narrative review. *J Clin Med*. 2022;19;11(24):7535. doi: 10.3390/jcm11247535.
28. Vasam M, Korutla S, Bohara RA. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. *Biochem Biophys Rep*. 2023;36:101578. doi: 10.1016/j.bbrep.2023.101578.
29. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infect Dis (Lond)*. 2021;53(10):737-754. doi: 10.1080/23744235.2021.1924397.

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Вивчення впливу наслідків COVID-19 на прогресування метаболічних, нейроендокринних розладів та деяких імунологічних порушень у жінок з акне

Акне — багатофакторне хронічне запальне захворювання, що характеризується первинним ураженням сально-волосяних фолікулів, поліморфними клінічними проявами на тлі гіперпродукції сальних залоз, патологічною десквамацією епітелію себофолікулів, активацією сапрофітних, умовно-патогенних мікроорганізмів та психоемоційними розладами. Це один з найпоширеніших дерматозів у клінічній практиці, на який припадає 20–25 % консультацій. Сьогодні, особливо під час воєнного стану, акне залишається соціально важливою проблемою приблизно у половині пацієнтів із формуванням психоемоційних розладів переважно депресивного та тривожного характеру, що супроводжуються різким зниженням якості їхнього життя.

Мета роботи — визначити патогенетичну роль деяких нейроендокринних, метаболічних, імунологічних порушень, а також їхніх наслідків у розвитку і перебігу акне у жінок після перенесеного COVID-19.

Матеріали та методи. Під нашим спостереженням перебувало 134 жінок, хворих на акне, віком від 18 до 45 років. Усім хворим проводили лабораторне дослідження вмісту кортизолу та пролактину, С-реактивного білка (С-РБ), загального холестерину (ЗХ), ліпопротеїнів високої щільності (ЛПВЩ), ліпопротеїнів низької щільності (ЛПНЩ), тригліцеридів (ТГ) у сироватці, визначали тривожність, індекс атерогенності (ІА), індекс НОМА (індекс інсулінорезистентності), концентрацію цитокінів у сироватці крові.

Результати та обговорення. В обстежених виявлено зміни деяких нейроендокринних та метаболічних показників різного ступеня виразності. Так, у пацієток з акне рівень загального холестерину був вищим на 27,78 % ($p < 0,001$), а з акне після COVID-19 — на 45,37 % ($p < 0,001$) порівняно з показником у групі контролю. Вміст ЛПВЩ був нижчим відповідно на 27,91 та 39,53 % ($p < 0,001$) порівняно з таким у групі контролю, ЛПНЩ — вище відповідно на 34,35 та 58,78 % ($p < 0,001$), а у жінок обох груп ТГ вдвічі ($p < 0,001$) перевищував показник у групі контролю. При цьому також відмічено підвищення коефіцієнта атерогенності — відповідно на 28,09 % ($p < 0,01$) та 37,02 % ($p < 0,001$) порівняно з показником у групі контролю, проте без вірогідних змін між показниками у жінок обох груп. Виявлено вірогідні значні зміни показників цитокінового профілю, особливо підвищення рівня прозапальних цитокінів у хворих обох груп із недостатнім синтезом протизапальних інтерлейкінів у всіх обстежених з акне, причому значніші відхилення досліджуваних імунних показників спостерігали у тих, хто перехворів на COVID-19.

Висновки. Високі показники рівня тривожності, зміни цитокінового профілю, нейроендокринних та метаболічних показників (СРБ, ЗХ, ЛПВЩ, ЛПНЩ, ТГ, ІА) спостерігали у всіх обстежених з акне, причому значніші відхилення показників були у пацієток, які перехворіли на COVID-19, що обґрунтовує необхідність пошуку нових комплексних методів лікування з огляду на вплив нейроендокринних, метаболічних та імунологічних змін, асоційованих із перенесеним COVID-19.

Ключові слова: акне, COVID-19, тривожність, метаболічні, нейроендокринні розлади, імунологічні порушення.

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