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ROLE OF THE SKIN MICROBIOME IN CHILDREN WITH ATOPIC DERMATITIS AND ITS IMPLICATIONS FOR TARGETED THERAPY

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Atopic dermatitis in children is a chronic, relapsing inflammatory skin disease frequently associated with alterations of the skin microbiome, which may influence disease severity and treatment outcomes. The aim of this study was to characterize the skin microbial colonization in children with Atopic dermatitis and assess its clinical significance. A total of 128 children with chronic recurrent Atopic dermatitis were examined using bacteriological and mycological analysis of skin lesions. Staphylococcal colonization was identified in 88 % of patients, predominantly Staphylococcus aureus, either as a single pathogen or in association with fungi and other bacteria. Isolated staphylococcal colonization was more common in younger children, whereas mixed microbial infections predominated in older age groups and were associated with more severe disease and reduced responsiveness to conventional therapy. These findings highlight the important role of skin microbiome dysbiosis in the pathogenesis of Atopic dermatitis and support the implementation of personalized therapeutic approaches based on microbial profiling.

Key words: atopic dermatitis, skin microbiome, microbial colonization, fungal colonization.

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РОЛЬ МІКРОБІОМУ ШКІРИ У ДІТЕЙ З АТОПІЧНИМ ДЕРМАТИТОМ НА ШЛЯХУ ВІД ДИСБІОЗУ ДО ТАРГЕТНОЇ ТЕРАПІЇ

Атопічний дерматит у дітей характеризується хронічним рецидивуючим перебігом та часто супроводжується порушенням шкірного мікробіому, що може впливати на тяжкість захворювання та ефективність лікування. Метою дослідження було охарактеризувати особливості мікробної колонізації шкіри у дітей з Атопічним дерматом та оцінити її клінічне значення. Обстежено 128 дітей із хронічним та безперервно-рецидивуючим перебігом Атопічного дерматиту шляхом бактеріологічного та мікологічного дослідження уражених ділянок шкіри. Встановлено, що у 88 % пацієнтів виявлялася стафілококова колонізація шкіри, переважно Staphylococcus aureus, як в ізольованому вигляді, так і в асоціації з грибковою або іншою бактеріальною флорою. У дітей раннього віку частіше спостерігалася ізольована стафілококова колонізація, тоді як у старших дітей переважали мікст-інфекції, що асоціювалися з тяжчим перебігом захворювання та резистентністю до традиційної терапії. Отримані результати підтверджують важливу роль порушень шкірного мікробіому у патогенезі Атопічний дерматит та обґрунтовують доцільність персоналізованих терапевтичних підходів із урахуванням мікробного профілю пацієнта.

Ключові слова: атопічний дерматит, мікробіоценоз шкіри, мікробна колонізація, грибкова колонізація.

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Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting approximately 20 % of children and 10 % of adults worldwide. The disease significantly impairs patients' quality of life due to its recurrent course, persistent pruritus, and visible skin lesions. This condition is frequently associated with other atopic diseases, such as asthma and allergic rhinitis, further complicating its management. Clinically, AD is characterized by xerosis (dry skin), intense itching, and eczematous lesions. Its pathogenesis involves a complex interplay of genetic predisposition, skin barrier dysfunction, and environmental allergens, leading to immune dysregulation and inflammation.

AD typically begins in early childhood, often presenting with lesions on the cheeks and scalp and progressing to crusted erosions. It is associated with other atopic conditions, including asthma and allergies, as well as complications such as skin infections. Visible symptoms, social stigma, and discomfort significantly affect patients' quality of life and mental health [4].

Recent data indicate that in children with a chronic, continuously relapsing course of AD and resistance to conventional therapy, staphylococcal skin colonization was observed in 83.6 % of cases, either as a monoinfection or as part of mixed infections (Staphylococcus + fungi and Staphylococcus + other bacterial flora).

According to recent data from the Ministry of Health of Ukraine, allergic dermatoses account for 20 % of the overall structure of allergic diseases registered in Ukraine and 50–66.4 % of allergic pathology in children, being predominantly represented by atopic dermatitis (AD).

The unfavorable upward trend in the prevalence of this group of diseases is driven by a number of factors. Among external factors, particular importance is attributed to environmental pollution, especially in industrialized regions, as well as continuous exposure in daily life and occupational settings to a wide range of chemical agents (household chemicals, cosmetic products, construction materials, metals, and synthetic materials used in clothing and footwear). The increasing incidence of allergic dermatoses is also associated with the widespread use of various medications, including vitamins, dietary supplements, preserved foods, and fast food products. According to epidemiological studies, the rise in allergic dermatoses may also be linked to the growing number of individuals engaged in so-called "allergenic" occupations (e.g., construction workers, chemists, and food industry workers) [2].

The microbiota plays a fundamental role in the development, maturation, and regulation of the host immune system. In turn, the immune system has largely evolved to maintain symbiotic relationships between the host and these highly diverse and dynamic microbial communities. Under optimal conditions, this interplay between the immune system and the microbiota enables the induction of protective responses against pathogens while preserving regulatory pathways involved in tolerance to harmless antigens.

However, in high-income countries, excessive antibiotic use, dietary changes, and the loss of constitutive partners such as helminths may have contributed to the selection of a microbiota with reduced resilience and diversity, impairing the establishment of balanced immune responses [1, 12, 15].

As the outermost barrier of the body, the skin serves as the first line of defense against external pathogens and environmental exposures. At the same time, it harbors a complex and diverse microbiome composed of bacteria, fungi, viruses, and microeukaryotes, collectively referred to as the skin microbiome. Most of these microorganisms are commensals [3, 10]. The skin provides a protective niche that supports microbial survival by facilitating both competition and cooperation, while supplying essential nutrients [4].

The skin microbiome plays a crucial role in host defense against pathogenic microorganisms, a function known as colonization resistance [3, 13]. This is achieved through the direct inhibition or modulation of pathogen virulence via the secretion of antimicrobial peptides (AMPs) and other bioactive molecules. In addition, certain microbial species stimulate keratinocytes, thereby signaling the host to initiate an immune response. The balance of interactions among microbial communities, as well as between microbes and the host, is essential for maintaining skin health.

Beyond its role in disease pathogenesis, emerging evidence suggests that the skin–microbiome axis also plays a critical role in maintaining skin homeostasis throughout life. Age-related alterations in microbial composition may contribute to local inflammation, oxidative stress, and activation of matrix metalloproteinases (MMPs), thereby accelerating the degradation of extracellular matrix components such as collagen and elastin and promoting wrinkle formation. These findings highlight the broader significance of microbial regulation in preserving skin health.

However, this complex host–microbiome balance is delicate, and its disruption may lead to dysbiosis and contribute to the development of skin diseases.

Local vascular disturbances in affected skin areas lead to increased vascular permeability, edema, intensification of inflammatory processes, enhanced oxidative stress, the development of metabolic disturbances, and toxic changes. A direct correlation has been observed between the severity of cutaneous manifestations and functional disturbances of the nervous system [8]. In these patients, comorbid conditions often include endocrine dysfunction, metabolic disorders, and gastrointestinal pathology [6, 10].

AD represents a significant medical and social concern, the importance of which is underscored by the increasing prevalence of this condition across all age groups and a tendency toward more severe disease courses [4, 11]. In the future, an increase in the frequency of chronic forms with a continuously relapsing course and resistance to conventional therapy is anticipated. One of the factors contributing to the severity of AD is the aggressive colonization of the skin by bacterial, fungal, and viral flora.

The purpose of the study was to characterize the skin microbiome in children with atopic dermatitis and to investigate its potential role in disease pathogenesis and targeted therapeutic approaches.

Materials and methods. The study was conducted by the staff of the Department of Skin and Venereal Diseases at Poltava State Medical University and was carried out at the Center of Dermatology and Venereology of the Sklifosovsky Regional Clinical Hospital. The study was conducted from January 2025 to November 2025.

A total of 86 patients with Atopic dermatitis and 42 patients with chronic eczema in the exacerbation stage were examined. The study included 128 children (52.3 % girls and 47.7 % boys) aged 1–15 years. According to age, the participants were divided into four groups: Group I (1–3 years) – 33 children (25.8 %); Group II (3–7 years) – 21 children (16.4 %); Group III (7–12 years) – 36 children (28.1 %); and Group IV (12–15 years) – 38 children (29.7 %).

The diagnosis of patients with Atopic dermatitis and with chronic eczema was performed in accordance with the medical and technological documents for the standardization of medical care in atopic dermatitis, approved by Order No. 670 of the Ministry of Health of Ukraine dated July 4, 2016.

The study included patients who met the following criteria: clinically confirmed diagnosis of atopic dermatitis and chronic eczema, established by a dermatologist according to the unified clinical protocol for providing medical care; age from 1 year to 15 years; presence of clinical manifestations of the disease (erythema, papules, vesicles, lichenification, itching); presence of exacerbation of the disease at the time of inclusion in the study; signed informed consent to participate from parents; absence of systemic antihistamine or immunosuppressive therapy during a specified period before the start of the study (if necessary, 7–14 days).

Patients were excluded from the study if the following factors were present: presence of other dermatological diseases that may affect the clinical picture (psoriasis, skin mycoses, infectious dermatoses); use of systemic glucocorticosteroids, immunosuppressants or biological therapy during a period that may affect the results of the study; presence of acute infectious diseases at the time of examination; refusal to participate in the study or withdrawal of informed consent.

The study included patients of all ages and both sexes, with a predominance of girls. The main aim of the study was to characterize the skin microbiome in children with atopic dermatitis and chronic eczema and to investigate their potential role in the pathogenesis of the disease and the possibilities of targeted therapy.

In addition, the lack of a separate control group is due to the practical realities of the design of an observational study, which aimed to characterize the skin microbiome in children with atopic dermatitis and chronic eczema and to investigate its role in the pathogenesis of the disease and the possibilities of targeted therapy.

To assess the skin microbiota, bacteriological analysis was performed using inoculation onto culture media, including Mueller–Hinton agar, a selective medium for the isolation of *Neisseria gonorrhoeae* (HIMedia Laboratories Pvt. Ltd., Mumbai, India), and Sabouraud agar (SANIMED-M Ltd., Kharkiv, Ukraine), followed by bacterioscopic examination for culture identification.

Samples were obtained by skin scraping, followed by washing with sterile distilled water along the perimeter of the most recent lesions. The washings were inoculated onto Sabouraud agar and meat-peptone agar in two Petri dishes. The cultivation period was at least 7 days, and up to 12 days for the detection of dermatophytes, at a temperature of 27–30ºC. Fungal identification was performed using microscopic methods. Bacteria were isolated and identified using standard bacteriological and bacterioscopic techniques.

The study was conducted in accordance with the applicable laws of Ukraine regulating clinical research, the Code of Ethics of the Physician of Ukraine, the Code of Ethics of the Scientist of Ukraine, and the Declaration of Helsinki of the World Medical Association, "Ethical Principles for Medical Research Involving Human Subjects." The study protocol was approved by the Commission on Ethics and Biomedical Ethics of Poltava State Medical University (Approval No. 234, January 23, 2025).

Results of the study. The results of microbial and fungal skin colonization were analyzed in children with AD characterized by a chronic, continuously relapsing course; in most cases, the effect of previously administered therapy was insufficient

Prior to enrollment in the study, children with atopic dermatitis and chronic eczema received standard therapy in accordance with current international guidelines (American Academy of Dermatology, European guidelines ETFAD/EADV) and the national clinical protocol of the Ministry of Health of Ukraine for the management of atopic dermatitis. Basic therapy included regular use of emollients (2–4 times daily), topical corticosteroids of varying potency depending on disease severity and lesion localization, as well as topical calcineurin inhibitors as steroid-sparing agents. In cases of secondary infection, topical antiseptics were administered, and antibacterial or antifungal agents were used when clinically indicated. The duration of prior treatment ranged from several weeks to several months and was determined by the severity and clinical course of the disease prior to study inclusion.

All children underwent cultural, mycological, and bacteriological examination of the skin. During the study, six groups of patients were identified based on the composition of microbial colonization.

Staphylococcal colonization of the skin was the most frequently detected, observed in 82.6 % of cases. Among patients with confirmed staphylococcal colonization, the following distribution was identified: *Staphylococcus aureus* in 55 % of cases, *Staphylococcus epidermidis* in 39.7 %, and a combined presence of *S. aureus* and *S. epidermidis* in 5.3 % of patients.

Clinical features observed in children with AD included: a tendency toward poor responsiveness to conventional antiallergic therapy; a predominantly moderate disease course (68.7 %), with localized forms of involvement; a chronic, persistently relapsing disease course.

Isolated staphylococcal skin colonization in children aged 1–3 years was observed significantly more frequently ($p<0.01$) than in other age groups. In this age group, AD predominantly presented in a localized form, mainly affecting the face, particularly the cheeks, and was characterized by fine lamellar scaling, microvesicles, excoriations, and crust formation.

In older children, the lesions were more frequently localized in the flexural areas, particularly the antecubital fossae and large skin folds. In children aged 3–12 years, the disease was characterized by papular eruptions with a tendency to coalesce and form lichenified plaques, accompanied by numerous excoriations. In children older than 12 years, an adolescent form of the disease was observed, with involvement of the elbow and knee flexures, as well as the neck, and marked lichenification within the affected areas.

In the second group of patients, the proportion of children older than 7 years was significantly higher ($p<0.01$) compared to younger age groups. The disease severity was predominantly severe (61.4 %), characterized by widespread involvement, with lesions localized on the face, neck, flexural surfaces of the extremities, and large skin folds; nail plate involvement was observed in 15.6 % of patients.

In Groups 3 and 4, similar to the two previous groups, a continuously relapsing course was observed, along with a high level of resistance to conventional antiallergic therapy. Patients in Group 5 exhibited a widespread form of the disease, often with a severe course, and reported exacerbation of skin symptoms following the consumption of yeast-containing foods. Isolated fungal skin colonization was more frequently observed in school-aged children: in 34.3 % of children aged 7–12 years and in 41.7 % of those aged 12–15 years.

The results of the mycological analysis showed that, in children from this group, the following were isolated: yeast fungi in 47.8 % of cases, dermatophytes in 29.8 %, molds in 12.4 %, and associations of multiple fungal groups in 10 % of cases.

Thus, the obtained results demonstrated that in children with a chronic, continuously relapsing course of AD and resistance to conventional therapy, staphylococcal skin colonization was observed in 82 % of cases, occurring both as isolated colonization and as mixed infections involving combinations of staphylococci with fungal flora or other bacterial pathogens. This high level of colonization indicates a significant role of bacterial microbiota in the pathogenesis of chronic AD, particularly in cases characterized by persistent and relapsing disease.

Isolated staphylococcal skin colonization was more frequently detected in younger children (under 3 years of age) and was associated with a moderate disease course. In these patients, AD predominantly presented as localized forms, with involvement of specific skin areas such as the cheeks, antecubital fossae, or scalp. The findings suggest that even low levels of staphylococcal colonization may exacerbate skin inflammation, increase sensitivity to allergens, and reduce the effectiveness of standard anti-inflammatory and antiallergic therapies.

In school-aged children, mixed infections were more commonly observed, with staphylococci coexisting with fungal colonization and, in some cases, other bacterial flora. The combination of bacterial and fungal colonization significantly aggravated the severity of AD, manifested by an increased extent of skin involvement, intense pruritus, frequent exacerbations, and difficulties in achieving disease control with conventional therapeutic approaches. In such cases, the inflammatory process was often accompanied by eczematous eruptions, crusted lesions, lichenification, and secondary infections, substantially impairing patients' quality of life and increasing psychological distress.

Discussion. The mechanisms by which staphylococcal colonization exacerbates the severity of AD are associated with disruption of the skin barrier, activation of local immune responses, and the secretion of bacterial toxins [9]. In particular, *Staphylococcus aureus* is capable of producing superantigens that activate T-cell–mediated immune responses and increase the levels of proinflammatory cytokines in the skin, including IL-4, IL-13, and TNF-α. This leads to intensified pruritus, epidermal damage, and the development of chronic inflammation. Fungal colonization, in turn, induces additional immune activation through interleukin-mediated pathways and complement activation, further exacerbating the imbalance between inflammatory and regulatory processes in the skin.

The presence of staphylococcal infection in children with chronic AD is also closely associated with resistance to conventional therapy, including topical corticosteroids, calcineurin inhibitors, and antihistamines. This may be explained by reduced drug penetration in colonized skin areas, increased expression of inflammatory mediators, and alterations in the skin microbiome that sustain chronic inflammation. Such conditions complicate symptom control and often necessitate the use of systemic antibiotics, antifungal agents, or biologic therapies, highlighting the importance of precise microbiological evaluation prior to selecting an optimal therapeutic strategy.

For the effective selection of further treatment strategies in children with continuously relapsing Atopic dermatitis and resistance to standard antiallergic therapy, comprehensive bacteriological and mycological examination of the skin is required [14]. This approach enables identification of the types and quantities of colonizing microorganisms, determination of their sensitivity to antibiotics and antifungal agents, and the development of individualized therapeutic strategies. For example, in patients with predominant staphylococcal colonization, the use of topical antiseptic agents is appropriate, whereas in cases of mixed infections, a combination of antibacterial and antifungal therapies is recommended.

To effectively select further treatment strategies for children with persistently recurring atopic dermatitis and resistance to standard antiallergic therapy, a comprehensive bacteriological and mycological examination of the skin is necessary [7]. This approach allows not only to identify the types and quantitative composition of colonizing microorganisms, but also to assess their potential pathogenic role in maintaining chronic inflammation and disrupting the skin barrier function. In addition, determining antimicrobial and antifungal drug susceptibility profiles provides a rational basis for targeted therapy and helps reduce the risk of treatment failure and antimicrobial resistance [3,5].

Importantly, increasing evidence suggests that microbial dysbiosis in atopic dermatitis is not simply a secondary phenomenon, but an active factor in disease exacerbation through mechanisms such as superantigen production, biofilm formation, and modulation of host immune responses. In particular, colonization with Staphylococcus aureus is associated with increased disease severity, enhanced Th2-mediated immune responses, and compromised epidermal barrier integrity. Fungal and mixed microbial colonization may further amplify inflammatory pathways, leading to a more persistent and treatment-resistant clinical course.

Thus, microbiological skin profiling should be considered an integral component of personalized treatment strategies for atopic dermatitis in children. In clinical practice, patients with predominantly staphylococcal colonization may benefit from the use of topical antiseptics and targeted antibacterial interventions, whereas cases with mixed bacterial-fungal colonization require combined antimicrobial and antifungal therapy. Such an individualized approach may increase treatment efficacy, reduce relapse rates, and contribute to better long-term disease control.

Furthermore, analysis of the skin microbiota allows for prediction of disease course, assessment of the risk of exacerbations, and individualization of preventive measures [2]. For instance, children with recurrent relapses associated with staphylococcal colonization may require regular microbiota monitoring, optimization of hygiene practices, and the use of probiotic or prebiotic agents aimed at restoring the balance of the skin microbiome and reducing the frequency of exacerbations.

Conclusion

The obtained data indicate that microbial skin colonization is a key factor influencing the severity of atopic dermatitis in children. Isolated staphylococcal colonization predominates in early childhood, whereas more complex mixed infections are characteristic of older children. Identification of the presence and nature of microbial colonization enables improvement of treatment efficacy, reduction of therapeutic resistance, and enhancement of disease prognosis.

Based on these findings, the following clinical approaches may be recommended:

1. Regular bacteriological and mycological assessment of children with chronic and relapsing AD.
2. Individualization of therapy based on the type of colonizing microorganism and its antimicrobial susceptibility profile.
3. Combination of anti-inflammatory therapy with antimicrobial agents in cases of mixed infections.
4. Implementation of preventive strategies aimed at maintaining a balanced skin microbiome, including appropriate skin care and the use of probiotics.
5. Monitoring and modification of environmental factors that may influence skin colonization, such as hygiene, diet, and exposure to chemical irritants.

Based on the obtained results, contemporary management of AD in children should take into account the state of the skin microbiome, its interaction with the immune system, and its potential role in the development of resistance to standard therapy. These findings support the integration of microbiological monitoring into clinical practice as a key step toward optimizing treatment strategies and improving patients' quality of life. Future research priorities include the continued development of disease-modifying therapies that can potentially alter the long-term course of AD, as well as investigating recurrence rates upon the cessation of current treatments. These emerging trends and research priorities underscore the ongoing commitment to further optimize AD management and improve the long-term outcomes of patients.

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Conflict of interest. The authors have no conflicts of interest to declare.

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IMPACT OF ARMED CONFLICT IN UKRAINE ON MALE REPRODUCTIVE FUNCTION DURING MARTIAL LAW

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Given that debates persist within the scientific community regarding the magnitude of the impact of stressors on infertility, this study aimed to evaluate the influence of psycho-emotional state under conditions of military aggression on male reproductive function parameters. A retrospective analysis of semen parameters and psycho-emotional status was conducted in 895 clinically healthy men aged 21–42 years over the 2016–2025 period. Anxiety and depression were evaluated using the GAD-7 and PHQ-9 scales, respectively. Semen analysis was performed in strict accordance with WHO recommendations. Beginning in 2022, a statistically significant increase in anxiety levels and the emergence of mild depressive symptoms were observed among the evaluated men. Concurrently, a marked decline was noted in sperm concentration, motility, and the percentage of morphologically normal forms, alongside an accumulation of abnormal and immotile spermatozoa. Over the 2023–2025 period, key semen parameters deviated beyond the acceptable reference intervals. Prolonged psycho-emotional stress under war conditions is strongly associated with the deterioration of semen quality and reduced male fertility. These findings underscore the critical need for further investigation and the development of targeted interventions aimed at preserving male reproductive health.

Key words: stress, fertility, reproduction, endocrine disorders, demographic situation.

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ВПЛИВ ВІЙСЬКОВОЇ АГРЕСІЇ В УКРАЇНІ НА СТАН ЧОЛОВІЧОЇ РЕПРОДУКТИВНОЇ ФУНКЦІЇ ВПРОДОВЖ ВОЄННОГО СТАНУ

Враховуючи, що у науковій спільноті досі ведуться дискусії щодо того, наскільки сильним є вплив стресових факторів на безпліддя, метою роботи стала оцінка впливу психоемоційного стану в умовах військової агресії на показники чоловічої репродуктивної функції. Для цього проведено ретроспективний аналіз показників спермограми та психоемоційного стану у 895 клінічно здорових чоловіків віком 21–42 років за період 2016–2025 рр. Оцінку тривожності та депресії здійснювали за шкалами GAD-7 та PHQ-9. Аналіз еякуляту проводили відповідно до рекомендацій ВООЗ. Встановлено, що з 2022 року у чоловіків спостерігається достовірне підвищення рівня тривожності та поява ознак легкої депресії. Паралельно відзначено зниження концентрації сперматозоїдів, їх рухливості та частки морфологічно нормальних форм, а також зростання кількості патологічних і нерухомих сперматозоїдів. У 2023–2025 рр. показники спермограми виходили за межі референтних значень. Таким чином, тривалий психоемоційний стрес в умовах війни асоційований із погіршенням показників спермограми та зниженням фертильності чоловіків. Отримані результати вказують на необхідність подальших досліджень і розробки заходів щодо збереження чоловічого репродуктивного здоров’я.

Ключові слова: стрес, фертильність, репродукція, ендокринні порушення, демографічна ситуація.

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In European countries, as well as in Ukraine, male infertility accounts for 50% of cases where couples fail to conceive [1, 2, 6]. The impact on male reproductive function is driven by numerous factors, including hormonal, environmental, infectious, and genetic variables, as well as lifestyle choices and exposure to toxic substances [2, 11]. Each of these can significantly impair sperm quality, hormonal profiles, and the overall function of the reproductive system. Among these factors, stress occupies a prominent place and is an increasingly pressing issue in the modern world [3–5].

Under martial law in Ukraine, the burden on the mental and physical health of the population has escalated dramatically, particularly among men involved in combat operations or living under high-stress conditions [1].

It is hypothesized that sustained, rising stress levels can induce hormonal imbalances that disrupt reproductive function, particularly affecting hormonal shifts and semen quality parameters [3, 7, 10]. Investigating these changes is highly important, as it provides a deeper understanding of how extreme circumstances affect reproductive health, a vital factor in preserving the country's demographic potential [1].