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The impact of post-traumatic stress on the reproductive system of female military personnel, participants in the 44-day Karabakh War in Azerbaijan

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Abstract

The study analyzed hormonal profiles in women exposed to various types of psychoemotional stress during the 44-day Karabakh War. Women who had direct contact with the wounded and were exposed to intense military stress experienced a significant decrease in anti-Müllerian hormone (AMH) levels, reflecting depletion of ovarian reserve. While gonadotropin and steroid hormone levels showed variability and partial recovery, the AMH decrease was irreversible and determined a persistent loss of reproductive function. Women with less intense stress retained higher ovarian reserve and fertility potential. The results highlight the key importance of AMH as a marker of ovarian reserve and the need for early diagnosis and prevention of reproductive disorders in women exposed to prolonged psychoemotional stress.

Keywords: anti-Müllerian hormone, ovarian reserve, psychoemotional stress, Karabakh War

For many centuries women's social roles were primarily associated with housekeeping, child-rearing, and ensuring family well-being. However, in the modern era, these perceptions have undergone significant changes. The 21st century is characterized by the strengthening of gender equality principles, the expansion of women's professional opportunities, and their active involvement in virtually all spheres of public, economic, and political life [1].

Despite the progress achieved, a number of professional fields remain potentially unsafe for women's health. One of the most challenging and stressful fields is military service, associated with high physical and psycho-emotional stress. It has been established that intense physical activity, irregular work and rest schedules,

exposure to combat stressors, and adverse environmental factors can lead to disruptions in hormonal homeostasis and reduced reproductive function in female military personnel [2]. The hypothalamic-pituitary-ovarian axis is particularly affected, manifesting as changes in ovarian reserve, ovulatory disorders, and menstrual cycle abnormalities.

In Azerbaijan, as in many other countries, there is a steady increase in the number of women serving in the armed forces. Women successfully realize their potential in various military specialties, from providing highly qualified medical care to participating in operational and strategic management. These activities require not only a high level of professional competence but also significant physical endurance, stress resistance, and the ability to function effectively under time and resource constraints and constant uncertainty [3].

Military conflicts are one of the most powerful triggers for the development of post-traumatic stress disorder (PTSD). According to international studies, PTSD in women is associated with impaired ovarian reserve, decreased anti-Müllerian hormone (AMH) levels,

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an increased frequency of anovulatory cycles, the risk of miscarriage, and menstrual irregularities [4]. Chronic activation of the body's stress-releasing systems leads to an imbalance in neuroendocrine regulation, including suppression of the gonadotropic function of the pituitary gland

During the 44-day Karabakh War, women in the active combat zone were exposed to multiple stress factors: life-threatening conditions, the need to provide medical care to the wounded, participation in their evacuation, working under limited resources, chronic fatigue, and emotional exhaustion. The combination of these factors could lead to dysregulation of the hypothalamic-pituitary-ovarian axis, decreased ovarian reserve, and the development of functional disorders of the reproductive system [5, 6].

Female medical personnel working in hospitals located in close proximity to combat zones proved to be a particularly vulnerable group. The combination of high-intensity work, intermittent sleep, constant contact with seriously wounded patients, and psychological pressure increased their risk of developing burnout, PTSD, and associated reproductive health problems.

The aim of this study was to examine the impact of severe psychoemotional stress experienced during the 44-day Karabakh War on reproductive hormonal parameters in female military personnel.

Materials and Methods: The study was conducted at the clinical hospitals of the Ministry of Defense of the Republic of Azerbaijan and was a cross-sectional, controlled, comparative study aimed at assessing the reproductive function of women exposed to intense psychoemotional stress during the 44-day Karabakh War. The study included 136 women aged 19 to 48 who met the eligibility criteria.

To analyze the impact of varying levels of stress exposure, all participants were divided into three groups based on the nature of their service activities during the war: Group I (n = 67) — female military personnel working in hospitals where the wounded were admitted from the front lines. This group was considered the most susceptible to severe psychoemotional and physical stress; average age was 41.55 ± 4.08 years.

Group II (n = 41) included female military personnel who performed administrative and organizational functions outside of direct contact with the wounded; average age was 39.24 ± 5.28 years.

The control group (n = 28) included civilian women who had no military service and were not exposed to combat factors; average age was 38.07 ± 5.55 years.

Study inclusion criteria:

- women of reproductive age 19–48 years;
- no hormone therapy within the past 3 months;
- no diagnosed endocrine diseases (hyperprolactinemia, hypothyroidism, Cushing's syndrome, etc.);
- regular or irregular menstruation without signs of menopause.

Exclusion criteria for the study:

- pregnancy or lactation;
- oncological diseases;
- pelvic surgery;
- refusal to participate in the study.

All participants underwent hormonal profile testing using enzyme-linked immunosorbent assay (ELISA), including estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and AMH. Venous blood was collected in the morning (8:00–10:00 AM) on an empty stomach, following an overnight fast of 8–12 hours. To minimize physiological hormonal fluctuations, analyses were performed on days 2–4 of the menstrual cycle in women with regular menstruation.

Statistical data processing was performed using SPSS Statistics version 26.0. Due to the non-normal distribution of the parameters, non-parametric analysis methods were used. Descriptive data are presented as median (Me) and interquartile range [Q1; Q3]. Comparisons of quantitative parameters between groups were performed using the Mann–Whitney U test. Differences were considered statistically significant at $p < 0.05$. Correlation analysis was performed using Spearman's rank correlation coefficient (ρ).

To enhance reliability, intergroup comparisons were evaluated: p_1 – between Group I and the control group, p_2 – between Group II and the control group, and p_{1-2} – between Groups I and II.

Results and discussion. This study analyzed hormonal profile indicators in women exposed to various types of psychoemotional stress during the Karabakh War. Below is a table showing the hormonal profile levels in women in the three study groups (Fig. 1).

As can be seen from the presented graph, the level of estradiol in female military personnel working in hospitals (109.36 ± 75.71 pg/ml) was slightly lower compared to the indicators of participants working in the office — 128.68 ± 114.56 pg/ml and representatives of the control group — 123.20 ± 103.31 pg/ml, ($p > 0.1$). Despite the fact that the identified differences did not reach statistical significance, the obtained data are of some scientific interest. According to Schliep et al. (2018), long-term exposure to stress factors can lead to disruption of steroidogenesis, including a decrease in estradiol synthesis, which is associated with the suppression of the functional activity of granulosa cells and a change in the pulsed secretion of gonadotropin-releasing hormone [7]. Our study results are consistent with these mechanisms, allowing us to consider stress as a potential factor influencing ovarian function in women exposed to harsh military conditions, although the magnitude of this effect did not reach statistical significance.

LH and FSH levels did not differ significantly across all three groups. However, it

should be noted that FSH levels in both study groups — 11.77 ± 17.90 and 9.72 ± 19.88 — were significantly elevated compared to the control group (5.22 ± 2.68 , $p > 0.1$), reflecting a compensatory response of the hypothalamic-pituitary axis to decreased ovarian reserve and the decline of folliculogenesis. Furthermore, the high variability of these levels indicates individual differences in the hypothalamic-pituitary-ovarian axis' response to stress.

According to a number of studies, acute stress can initially cause an increase in LH and FSH, which is likely due to the stimulating effect of corticotropin-releasing hormone, whereas at later stages, stress can reduce their levels by suppressing its secretion [8]. This effect is realized through the influence of steroid hormones, including sex hormones, on the differentiation of pituitary gonadotropic cells, indirectly through catecholamines [9]. The absence of significant differences in our study is likely due to both the heterogeneity of the included participants and the fact that some of them were exposed to combined types of stress.

The AMH level deserves special attention, as it is the most informative marker of the functional state of the ovarian reserve. According to the results of our study, in women of the 1st group (military medical personnel

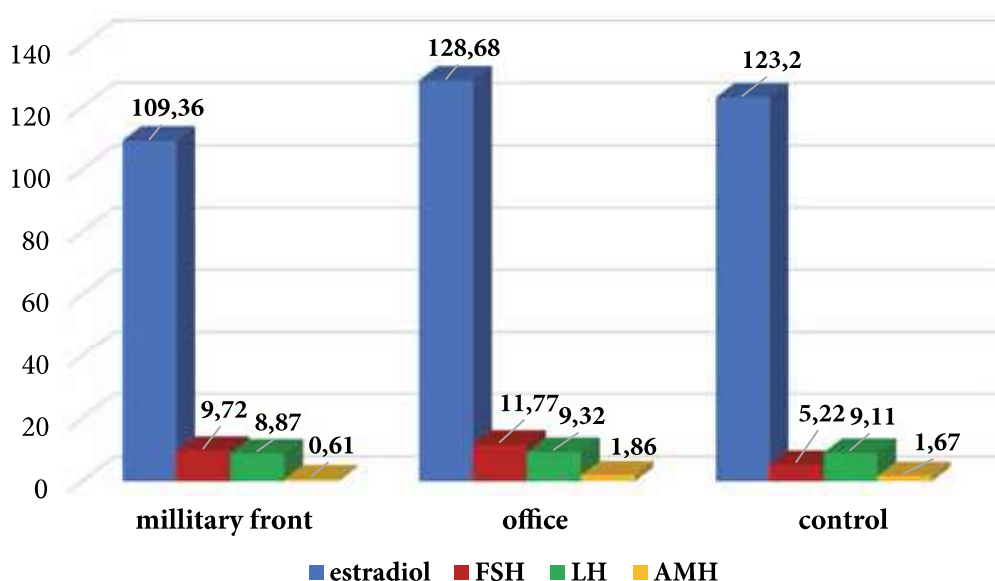


Fig. 1. Hormonal profile levels in women in the three study groups

directly working with the wounded), the average AMH level was 0.61 ± 0.55 ng/ml, and the median value was 0.442 ng/ml. These values were significantly lower than in women of the 2nd and 3rd groups ($p < 0.05$). This difference indicates a pronounced influence of chronic psychoemotional and physical stress, leading to a decrease in ovarian reserve in women of this category. Military conditions, a difficult work regime, a high degree of responsibility and persistent traumatic situations can disrupt the neuroendocrine balance and reduce the functional activity of the hypothalamic-pituitary-ovarian axis. As a result, the depletion of the follicular apparatus is accelerated, which is reflected in a decrease in AMH production [10,11]. Moreover, mental stress also increases the risk of premature ovarian failure, functional hypothalamic amenorrhea and polycystic ovary syndrome [12,13].

The average AMH level in female military personnel in Group 2, who had not been in contact with the wounded but served in combat conditions, was 1.86 ± 1.58 ng/ml, with a median of 1.47 ng/ml. This result is significantly higher than in Group 1, indicating preserved reproductive potential. Despite a certain degree of stress, its intensity and duration were lower than in Group 1, preserving ovarian reserve and, consequently, AMH levels.

In women in Group 3 (apparently healthy civilians who served outside of combat conditions), the average AMH level was 1.67 ± 1.12 ng/ml, with a median of 1.50 ng/ml. These values are statistically comparable to the results in Group 2, indicating stable ovarian reserve. Thus, the follicular potential of women in a relatively calm psychological environment remains within the physiological norm.

A comparative analysis of AMH levels revealed a statistically significant difference between the groups ($p < 0.05$), with the lowest levels recorded in women in Group 1. This confirms that chronic stress has a negative impact on the reproductive system. Low AMH levels (< 1 ng/ml) indicate a significant reduction in ovarian reserve and may reflect accelerated depletion of the follicular apparatus, while levels of 1–2 ng/ml indicate moderate reserve, and values above 2 ng/ml reflect

relatively high ovarian potential. Thus, the study results demonstrate a clear relationship between ovarian reserve and the intensity and duration of stress.

The years since the war have shown that the acute psychoemotional stress experienced by the participants during the 44-day Karabakh War has transformed into a persistent chronic stress condition.

This factor, according to accumulated data, can have a long-term negative impact on the reproductive system, manifesting itself in HPTA axis dysfunction, decreased ovarian reserve, and steroidogenesis dysfunction. A study found that a significant proportion of female military personnel directly exposed to death, severe injury, and critical situations were unable to achieve reproductive function in subsequent years, despite the lack of contraception. 80.6% of them did not use contraception for five years without becoming pregnant. These data were obtained from a survey conducted using a special gynecological chart developed by us. Several participants were diagnosed with various forms of reproductive pathology: five women had a history of miscarriage, and two had undergone surgical treatment for an ectopic pregnancy.

These data are consistent with the results of several studies showing that chronic stress is a significant risk factor for implantation failure, early reproductive failure, and tubular transport dysfunction [12].

These findings highlight the fundamental importance of AMH as a key marker for ovarian reserve and, consequently, a woman's potential reproductive function. Unlike gonadotropin or steroid hormone levels, which can be altered by stress and partially restored when hypothalamic regulation returns to normal, AMH levels reflect the quantitative state of the follicular pool and the ovary's capacity for folliculogenesis. Although the hypothalamic structures responsible for regulating reproductive function appear to have partially restored their activity after a period of acute psychoemotional stress, the decrease in AMH levels was irreversible.

A decrease in AMH levels indicates depletion of primary and preantral follicles, and this loss, according to numerous studies, is not

compensated for by physiological mechanisms and cannot be restored [14]. It was the significant reduction in ovarian reserve, rather than central neuroendocrine disorders, that was the primary factor determining the persistent loss of fertility in a significant proportion of women exposed to prolonged military stress [15].

These results highlight the need for further study of the impact of military and occupational stress on women's reproductive function, particularly in those categories exposed to prolonged psychological trauma. Comprehensive monitoring, timely diagnosis of decreased ovarian reserve, and the development of stress-modifying programs may be important for the prevention of reproductive disorders in this population.

Conclusions

1. The study found that women exposed to various types of psychoemotional stress during the 44-day Karabakh War exhibited

differences in hormonal profiles, reflecting the impact of stress factors on the reproductive system.

2. Estradiol levels were lower in military personnel working directly with the wounded compared to office workers and the control group, while LH and FSH levels did not show significant differences between the study groups.
3. AMH levels, the most informative marker of ovarian reserve, were significantly reduced in women in Group 1 (military medical personnel working with the wounded), indicating significant depletion of the follicular apparatus under the influence of chronic psychoemotional and physical stress.
4. Women in groups 2 and 3 had significantly higher AMH levels, indicating preserved ovarian reserve and reproductive potential under less intense or absent stress.

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Вплив посттравматичного стресу на репродуктивну систему жіночого військового персоналу, учасниць 44-денної Карабаської війни в Азербайджані

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Резюме

У дослідженні проаналізовано гормональний профіль жінок, які зазнали різних видів психоемоційного стресу під час 44-денної Карабаської війни. У жінок, які мали безпосередній контакт з пораненими і зазнали інтенсивного військового стресу, спостерігалось значне зниження рівня антимюллерівського гормону (АМГ), що свідчило про виснаження оваріального резерву. Хоча рівні гонадотропіну і стероїдних гормонів демонстрували мінливість і часткове відновлення, зниження АМГ було незворотним і визначало стійку втрату репродуктивної функції. Жінки, які зазнали менш інтенсивного стресу, зберегли вищий оваріальний резерв і потенціал фертильності. Результати підкреслюють ключове значення АМГ як маркера оваріального резерву та необхідність ранньої діагностики і профілактики репродуктивних розладів у жінок, які зазнали тривалого психоемоційного стресу.

Ключові слова: антимюллерівський гормон, оваріальний резерв, психоемоційний стрес, Карабаська війна.

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