TASHKENT MEDICAL ACADEMY

Journal of Educational and Scientific Medicine

Issue 5 | 2025

OAK.uz

Google Scholar

ISSN: 2181-3175

Journal of Education & Scientific Medicine
ISSN 2181-3175
Tashkent Medical Academy
Research Article
Open © Access

IMPACT OF STRESS ON FEMALE REPRODUCTIVE HEALTH: DISORDERS AND IMPLICATIONS

Ashurova Nigora Gafurovna
Bukhara State Medical Institute, Bukhara, Uzbekistan.
abdurazakova84@mail.ru
Tolibov Farrux Farhodovich
Bukhara state of medical institute named after ABU ALI IBN SINO, 2nd year Master's student
Bukhara, Uzbekistan

Abstract: The article examines contemporary aspects of stress-related diseases affecting the female reproductive system. It highlights that young women today experience the highest levels of stress, leading to conditions such as ovarian dysfunction, premenstrual tension syndrome, and benign mammary gland dysplasia. The mechanisms underlying these pathologies are discussed. Additionally, the article explores the effectiveness of long-term non-hormonal therapy using a standardized extract from Vitex agnus-castus (Ze440). It also considers the potential of a safe non-hormonal treatment for early menopausal symptoms based on Cimicifuga racemosa extract (Ze450), which aligns with treatment strategies for women experiencing menopausal disorders.

Keywords: stress-induced hyperprolactinemia, premenstrual tension syndrome, benign dysplasia of the mammary glands, standardized extract of fruits Vitex agnus castus Ze440, symptoms of menopausal disorders, early vasomotor symptoms, Cimicifuga racemosa Ze450 extract, safe therapy, medicine

Introduction :

Stress is a complex phenomenon that can have both beneficial and harmful effects on the human body. In some cases, it serves as a powerful motivator, inspiring personal growth, driving goal achievement, and encouraging problem-solving. During such moments, we experience an energy boost, work with greater efficiency, and ultimately achieve success. This type of stress, known as eustress, is considered positive.

However, stress often becomes a source of anxiety and negative emotions, forcing the body into an emergency state. In such cases, it can negatively impact health by disrupting sleep, increasing heart rate, altering breathing patterns, and raising blood pressure. This harmful form of stress, referred to as distress, can have serious consequences for both physical and mental well-being.

The causes of stress vary widely and depend on an individual's characteristics and responses. Stress reactions can be triggered by both external and internal factors.

External factors contributing to stress include everyday challenges such as traffic congestion, long lines in stores, and conflicts at work or within the family. Financial difficulties, such as job loss, lack of funds, or debt, also play a significant role. Additionally, social factors like low self-confidence, fear of judgment, and failures in social interactions can contribute to stress. Broader issues, such as political and economic instability, wars, natural disasters, pandemics, and financial crises, further exacerbate stress levels.

Internal factors, on the other hand, stem from an individual's personality traits and upbringing. These include negative thought patterns, such as over-focusing on problems, exaggerating the significance of events, or excessive worry about the future. Low self-esteem, fear of failure, and difficulty in asserting oneself can also contribute to stress. Perfectionism—characterized by an unrelenting pursuit of excellence, intolerance of

mistakes, and an inability to relax—can be another internal stressor. Additionally, dissatisfaction with life, whether due to a lack of personal goals, an unfulfilling job, or unhealthy relationships, can further amplify stress.

The way an individual perceives and responds to stress determines whether its effects will be positive or negative.

The Impact of Stress on the Female Reproductive System

Research indicates that women experience higher levels of stress compared to men. Over the past five years, 43% of women have reported increased stress levels, in contrast to 33% of men. This trend is further supported by a 10-point stress scale assessment, where women, on average, rate their stress level at 5.3, while men report a lower average of 4.6.

It is important to recognize that stress is not merely an abstract concept but a physiological response to external stimuli. It triggers a cascade of neuroendocrine changes that affect mental, physiological, and biochemical processes in the body. In response to stress, the body releases hormones such as cortisol, adrenaline, and norepinephrine, which prepare it to react in threatening situations. However, when stress becomes chronic, its impact can be detrimental, particularly to the female reproductive system.

Chronic stress can disrupt the hypothalamic-pituitary-ovarian axis (HPO axis)—a key regulatory system controlling the menstrual cycle. The HPO axis functions as follows: the hypothalamus, located in the brain, produces gonadotropin-releasing hormone (GnRH), which stimulates the pituitary gland to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These hormones then act on the ovaries, regulating egg maturation and the production of female sex hormones—estrogen and progesterone.

Chronic stress can disrupt this delicate system at multiple levels. Stress hormones, particularly cortisol, suppress GnRH secretion in the hypothalamus, leading to decreased production of LH and FSH. As a result, menstrual cycle irregularities, anovulation (lack of ovulation), infertility, and other reproductive health issues may occur.

In addition to hormonal disruption, stress also weakens the immune system, making the body more susceptible to infections and inflammation. Prolonged stress increases the risk of developing autoimmune disorders such as endometriosis, rheumatoid arthritis, and multiple sclerosis, all of which can negatively impact reproductive health.

Menstrual Cycle Disorders in Young Women – "Metropolis Syndrome"

Menstrual cycle irregularities are classified as ovarian dysfunction (E28) according to the International Classification of Diseases, 10th Revision (ICD-10). One of the contributing factors to ovarian dysfunction is sleep disturbances, which are particularly common among residents of large cities due to excessive light pollution and chronic stress exposure. As a result, sleep disorders are considered part of the so-called "metropolis syndrome."

For many women, the fast-paced urban lifestyle has a dual impact. On one hand, it offers comfort, cutting-edge technology, and opportunities for personal and career growth. On the other hand, it brings environmental challenges, poor dietary habits, sleep disruptions, circadian rhythm disturbances, and psychological changes such as stress, depression, and aggression, all of which negatively affect reproductive health. Studies show that menstrual irregularities occur 1.5 times less frequently in rural women compared to their urban counterparts. This may be attributed to "metropolis syndrome," where urban dwellers are more exposed to environmental stressors, leading to circadian rhythm disruptions and reduced melatonin production.

Melatonin is synthesized at night in a cyclical pattern regulated by the day-night cycle. Research has shown that Vitex agnus-castus (chaste tree) fruit extract enhances melatonin secretion in a dose-dependent manner, indicating its beneficial effects on sleep disturbances associated with menstrual cycle irregularities.

A double-blind, placebo-controlled study involving reproductive-aged women with premenstrual syndrome (PMS) symptoms demonstrated that taking 20 mg of standardized Vitex agnus-castus extract (Prefemin, Amaxa Ltd, UK) for three months led to a statistically significant reduction in PMS symptoms,

including menstrual cycle normalization. In contrast, a lower dose (8 mg) had only minor effects comparable to placebo, while a higher dose (30 mg) did not provide any additional significant benefits over the 20 mg dose.

Premenstrual Tension Syndrome – A Modern Women's Life Aspect

Premenstrual Tension Syndrome (classified as N94.3 in the International Classification of Diseases, 10th Revision - ICD-10) is defined as recurring physical, cognitive, behavioral, and mood changes occurring in the premenstrual phase. Approximately 90% of women report experiencing some symptoms associated with premenstrual tension syndrome, which negatively impact their daily functioning and are commonly referred to as premenstrual syndrome (PMS) [17].

The diagnostic criteria for premenstrual tension syndrome were established in 2000 by the American College of Obstetricians and Gynecologists (ACOG) [18]. According to these criteria, the presence of at least one physical (such as bloating, breast tenderness/swelling, swelling of the lower limbs, headaches) or psychological (such as irritability, mood swings, episodes of anger, depression, emotional instability, difficulties in personal or social life) symptom that appears five days before menstruation and resolves within four days after its onset, occurring in at least three consecutive cycles without the use of medication, indicates a diagnosis of premenstrual tension syndrome [18].

Benign Breast Dysplasia – A Leading Condition in Women's Reproductive Health

In 1981, the World Health Organization (WHO) introduced the term “breast dysplasia / fibrocystic disease”, defining it as a condition characterized by a wide range of proliferative and regressive changes in breast tissue, with an altered ratio of epithelial and connective tissue components . In the International Classification of Diseases, 10th Revision (ICD-10), this condition is classified as “benign breast dysplasia” (N60). The terms "benign breast dysplasia" and "fibrocystic disease" are synonymous, referring to a group of breast disorders caused by an imbalance between epithelial and connective tissue components, leading to localized or diffuse proliferative and regressive changes with varying clinical manifestations.

Since the breasts are part of the reproductive system, their diagnosis and treatment are closely linked to assessing and addressing changes in reproductive organs. Sex hormones play a crucial role in the development of breast conditions, making hormonal imbalance a key factor in the progression of these disorders. Identifying and treating benign breast diseases is an essential step in breast cancer prevention, as early intervention can help manage risks and maintain breast health.

Fetal Growth in an Adverse Intrauterine Environment and Fetal Programming

Experimental and clinical studies suggest that early-life stress can cause long-lasting changes in gene expression due to epigenetic modifications, leading to various metabolic and neurodevelopmental disorders. Research indicates that low birth weight is associated with an increased risk of metabolic syndrome and vascular diseases in adulthood, likely due to alterations in key hormonal pathways that regulate growth and development.

Stress is characterized as a disruption of homeostasis, and it is proposed that the fetus may respond to adverse intrauterine conditions by increasing placental CRH levels. As a result, abnormal trophoblast invasion, inadequate remodeling of spiral arteries, and high-resistance placental blood vessels can contribute to placental dysfunction, representing a state of compromised homeostasis. Such intrauterine stressors can lead to elevated placental CRH levels, increasing the risk of obstetric complications such as preeclampsia, intrauterine growth restriction (IUGR), and preterm birth.

Furthermore, excessive fetal cortisol levels can play a critical role in growth restriction and contribute to fetal programming, which links prenatal stress to long-term health outcomes. Elevated fetal cortisol may impair normal fetal growth and increase susceptibility to diseases in later life, including cardiovascular conditions and insulin resistance. The hypothalamic-pituitary-adrenal (HPA) axis, which regulates stress responses, is particularly vulnerable to programming during fetal development.

Impact of Prenatal Stress on HPA Axis Programming and Long-Term Health

Experimental studies in pregnant rats have demonstrated that exposure to various stressors, such as a low-protein diet and physical restraint, can lead to increased corticosteroid secretion later in life. Similarly, in humans, low birth weight—an indicator of prenatal stress—is linked to elevated plasma cortisol levels, dysregulated HPA axis function, and heightened cortisol responses to psychological stress. These physiological adaptations, triggered by adverse prenatal conditions, support fetal survival by restricting growth but may increase the risk of metabolic diseases if the postnatal environment is relatively stable.

The extent to which early environmental factors influence HPA axis programming depends on the timing and severity of intrauterine stress. A cross-sectional study involving 68 boys and 72 girls suggested that prenatal stressors not only contribute to low birth weight but also have long-term effects on stress responses, with male newborns displaying altered adrenocortical reactivity to stress and females exhibiting changes in baseline adrenocortical activity. This suggests that HPA axis programming may be gender-specific. Additionally, recent epidemiological data indicate that preterm birth is associated with reduced long-term survival and reproductive potential.

Hyperprolactinemia in Menopausal Women

Elevated prolactin levels under stress are not only common in younger women but also in those of menopausal age. The risk of developing breast cancer increases with age , despite the decline in estrogen levels in a woman's body. Prolactin can act as a catalyst for breast cancer development by inducing cell proliferation and inhibiting apoptosis.

Additionally, prolactin stimulates metabolic processes in breast tissues and, importantly, enhances the sensitivity of breast receptors to estradiol, leading to an increase in estrogen receptor density. As a result, hyperprolactinemia often causes excessive estrogenic influence on target organs, outweighing the effects of progesterone, which may contribute to hormonal imbalances and an increased risk of estrogen-dependent conditions.

The Role of Maternal Stress in Fetal Development

Both experimental and clinical studies have linked prenatal maternal stress—defined as stressful experiences during pregnancy—to adverse birth outcomes such as preterm birth and low birth weight, as well as an increased risk of long-term diseases in offspring. Elevated maternal glucocorticoid levels and maternal exposure to glucocorticoids have been associated with intrauterine growth restriction (IUGR), insulin resistance, and persistent dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in the child.

While maternal corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) do not cross the placenta, maternal glucocorticoids can, making them a primary factor in transmitting prenatal stress to the fetus. The enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) in the placenta serves as a protective barrier by converting active cortisol into its inactive form, cortisone. However, elevated maternal glucocorticoid levels or decreased 11β-HSD2 activity can increase fetal exposure to glucocorticoids, potentially disrupting normal development.

Research in both animals and humans suggests that various prenatal stressors—including maternal anxiety, relationship conflicts, and even large-scale events like natural disasters—can elevate the risk of metabolic and neurodevelopmental disorders in offspring. These may include insulin resistance, type 2 diabetes, cardiovascular disease, impaired cognitive function, behavioral disorders, autism, and schizophrenia. Additionally, maternal depression, anxiety, stress, and poor diet during pregnancy have been strongly linked to low birth weight, preterm birth, and insulin resistance in children.

Conclusion:

Women’s reproductive health is a complex and delicate system, highly responsive to various negative factors, including both acute and chronic stress. As a common aspect of modern life, stress can negatively impact health and quality of life, manifesting as ovarian dysfunction, premenstrual syndrome (PMS), and benign breast dysplasia.

To mitigate the effects of stress on reproductive health, the use of Prefemin (Amaxa Ltd, UK) is recommended. This standardized extract of Vitex agnus-castus (Ze440) demonstrates dose-dependent effectiveness, with optimal therapeutic benefits at a daily dose of 20 mg. Based on clinical trials, the European Medicines Agency has classified Ze440 (Prefemin, Amaxa Ltd, UK) under the status of "well-established medicinal use" for the comprehensive treatment of menstrual cycle disorders. Long-term use has shown that a once-daily tablet is well-tolerated, with minimal risk of side effects.

Menopause marks a significant transition in a woman's life, requiring an individualized medical approach to preserve physical, emotional, and overall quality of life. The management of early menopausal symptoms with the non-hormonal, effective, and safe medication Cimicifuga forte (Amaxa Ltd, UK) is recommended to alleviate vasomotor symptoms, prevent weight gain, and reduce insulin resistance.

References:

1. Anvarova Sh.A., Shukurov F.I., Tulametova Sh.A. Innovative methods for solving the problem of female infertility associated with endocrine disorders. Obstetrics, Gynecology and Reproduction. 2024;18(5):706-719. (In Russ.) https://doi.org/10.17749/2313-7347/ob.gyn.rep.2024.514(in Russian)

2. Chrousos, G.P. & P.W. Gold. 1992. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. JAMA267: 1244–1252.

3. Kalantaridou, S.N., E. Zoumakis, A. Makrigiannakis, et al.2010. Corticotropin-releasing hormone, stress and human reproduction: an update. J. Reprod. Immunol. 85: 33–38

4. Chrousos, G.P. & P.W. Gold. 1992. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. JAMA267: 1244–1252.

5. Tsvetkova E. The importance of melatonin in the regulation of metabolism, eating behavior, sleep, and the prospects for the use of melatonin drugs for obesity treatment. Obesity and metabolism. 2021;18(2):112–124. Available at: https://doi.org/10.14341/omet12279 (in Russian)

6. Shukurov F.I., Mamajanova D.M., Sattarova K.A., Yuldasheva N.Z. Estimation of the Efficiency of Belara Application in Adjuvant Therapy of Polycystic Ovarian Syndrome after Endosurgical Treatment//Éksperimentalnaya i Klinicheskaya Farmakologiya.2022. 85.,№8.-C.14-16. https://doi.org/10.30906/0869-2092-2022-85-8-14-16(in Russian)

7. Dongju S. Limbic response to stress linking life trauma and hypothalamus-pituitary-adrenal axis function. Psychoneuroendocrinology. 2019;99:38–46. doi: 10.1016/j.psyneuen.2018.08.023

8. Samara L. Stress-Induced Hyperprolactinemia: Pathophysiology and Clinical Approach. Obstet Gynecol Int. 2018;3:2018:9253083. doi: 10.1155/2018/9253083

9. Lynch CD, Sundaram R, Maisog JM, Sweeney AM, Buck Louis GM. Preconception stress increases the risk of infertility: results from a couple-based prospective cohort study--the LIFE study. Hum Reprod. 2014;29:1067-75.

10. Wesselink AK, Hatch EE, Rothman KJ, et al. Perceived stress and fecundability: a preconception cohort study of North American cou ples. Am J Epidemiol. 2018;187:2662-71.

11. Smith SM, Vale WW. The role of hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues Clin Neurosci. 2006;8:383-95.

12. Carrasco GA, Van de Kar LD. Neuroendocrine pharmacology of stress. Eur J Pharmacol. 2003;463:235-72.

13. Толибов, Ф. (2024). ИММУННАЯ СИСТЕМА: АНАТОМИЯ ЛИМФАТИЧЕСКОЙ СИСТЕМЫ И МЕХАНИЗМЫ ИММУННОГО ОТВЕТА. Журнал академических исследований нового Узбекистана, 1(2), 55-58.

14. Farxodivich, T. F. (2024). The Syndrome of External Secretory Function Insufficiency is a Common Complication of Chronic Pancreatitis.American Journal of Bioscience and Clinical Integrity 1 (10), 90-95

15. Farxodivich, T. F. (2024). Clinical Characteristics of Gastritis in Digestive Diseases. Research Journal of Trauma and Disability Studies, 3(3), 294-299.

16. Farxodivich, T. F. (2024). INFECTION OF COVID-19 ON COGNITIVE FUNCTIONS. SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES, 3(4), 325-330.

17. *Tolibov F.F.* - VIOLATION OF PLATELET AGGREGATION AND IMBALANCE OF HEMOSTASIS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS C//New Day in Medicine 6(68)2024 264-268 https://newdayworldmedicine.com/en/article/3758

18. *Tolibov F.F.*- CLINICAL AND MORPHOLOGICAL CORRELATIONS OF LIVER CIRRHOSIS.European Journal of Modern Medicine and Practice 4 (11), 515-520

19. TF Farhodivich.CHOLESTASIS IS A RISK FACTOR FOR THE DEVELOPMENT OF GALLSTONE DISEASE.Научный Фокус 2 (21), 317-321

20. *Tolibov F.F* IMPACT OF CORTICOSTEROID AND IMMUNOSUPPRESSIVE THERAPY ON THE COURSE OF CHRONIC HEPATITIS: RISKS AND PROSPECTS.Modern Science and Research 4 (2), 1123-1132

21. RK Shuhrat o'g'li, TF Farhodivich.DIABETIK NEVROPATIYA VA UNING ZAMONAVIY TERAPIYASI.JOURNAL OF INNOVATIONS IN SCIENTIFIC AND EDUCATIONAL RESEARCH 8 (1), 195-202

22. Dhabhar FS, Viswanathan K. Short-term stress experienced at the time of immunization induces a long-lasting increase in im munological memory. Am J Physiol Regul Integr Comp Physiol. 2005;289:R738-44.

23. Wingfield JC, Sapolsky RM. Reproduction and resistance to stress: when and how. J Neuroendocrinol. 2003;15:711-24.

24. Dilshodovna A. M. et al. THYROID DISORDERS AND PREGNANCY //Web of Medicine: Journal of Medicine, Practice and Nursing. – 2025. – Т. 3. – №. 4. – С. 295-303.

25. Nappi RE, Petraglia F, Genazzani AD, D'Ambrogio G, Zara C, Genazzani AR. Hypothalamic amenorrhea: evidence for a central derangement of hypothalamic-pituitary-adrenal cortex axis activity. Fertil Steril 1993;59:571-6. 10.

26. Fioroni L, Fava M, Genazzani AD, Facchinetti F, Genazzani AR. Life events impact in patients with secondary amenorrhea. J Psycho som Res. 1994;38:617-22. 11.

27. Facchinetti F, Matteo ML, Artini GP, Volpe A, Genazzani AR. An increased vulnerability to stress is associated with a poor outcome of in vitro fertilization-embryo transfer treatment. Fertil Steril. 1997;67:309-14. 12.

28. Whirledge S, Cidlowski JA. A role for glucocorticoids in stress-im paired reproduction: beyond the hypothalamus and pituitary. Endo crinology. 2013;154:4450-68.