BIOCHEMICAL AND HORMONAL FACTORS IN THE DEVELOPMENT OF ALOPECIA IN WOMEN: DIAGNOSTIC SIGNIFICANCE FOR TRICHOLOGICAL PRACTICE

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Summary

The article is devoted to the study of biochemical and hormonal factors that may be associated with pathological hair loss, their diagnostic significance for trichological practice. Alopecia is not just a cosmetic defect, but a serious pathological process that may "hide" damage to other organs and systems. The aim of the study was to systematize current medical knowledge about the hormonal etiology of alopecia and to develop recommendations for trichologists on cooperation with doctors when endocrine disorders are suspected. To achieve this goal, we analyzed current scientific and methodological literature using theoretical methods of analysis, generalization, and synthesis. The main search was conducted in the Scopus, Google Scholar, LinkedIn, EuroPub, and ResearchBib databases. The main biochemical and hormonal changes in the female body that may be associated with alopecia were identified.

The most common causes of alopecia in women are non-scarring causes, such as telogen alopecia (or telogen effluvium) and female pattern hair loss (also known as androgenetic alopecia). Telogen alopecia is caused by a disruption in the hair growth cycle and is characterized by the loss of telogen hair. Androgenetic alopecia is characterized by the absence of complete baldness, but only a slow decrease in hair density on the head, mainly in the central (parietal) area, while maintaining hair growth in the frontal (forehead) area.

The life cycle of the hair follicle, a tiny self-renewing mini-organ with a complex structure characterized by periodic growth, plays a central role in the development of hair loss. Fundamentally, alopecia is characterized by an imbalance in the phases of the follicle's life cycle, namely the acceleration of the transition from anagen to telogen.

The life cycle of the hair follicle can be directly affected by deficiencies in certain nutrients (including vitamins and trace elements), changes in thyroid hormone levels, sex hormones and their ratio to each other, the presence of chronic inflammatory diseases associated with an increase in circulating inflammatory cytokines, harmful habits, acute or chronic stress with increased cortisol concentration, etc.

It is the presence of numerous factors affecting the hair growth cycle, significant gender differences in their impact, and several main types of alopecia in women with different pathogenesis that require a comprehensive approach to the additional examination of such women and the selection of individualized treatment for alopecia.

Key words: alopecia, hair loss, alopecia in women, trichology, female alopecia, biochemical factors of alopecia, hormonal factors of alopecia.

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1. Introduction

Alopecia, or pathological hair loss, is a disorder characterized by a disruption in normal hair production. It can develop in people of both sexes at different stages of life. Hair loss is not just a cosmetic complaint that significantly impairs quality of life and lowers self-esteem. It is a complex clinical problem because it can be associated with a wide range of factors, such as stress, nutrient deficiency, hormonal imbalance, and can be one of the first signs of disease in other organs and systems.

The causes of alopecia are divided into scarring and non-scarring, which statistically account for the majority of cases seeking trichological help. The main types of non-scarring alopecia in women are telogen effluvium (TE or telogen effluvium) and female pattern hair loss (FPHL or androgenetic alopecia). TE can be acute or chronic in nature. It is caused by a disruption in the hair growth cycle and is characterized by the loss of telogen hair *(Bilik L., Kokcam I., & Esen M., 2024).* FFA is non-scarring diffuse alopecia, characterized by thinning and thinning of hair mainly in the parietal (central) area while preserving the frontal (frontal) area of hair growth, while complete baldness is usually not observed, only a slow decrease in hair density on the head *(Vozianova S.V., Bolotna L.A., & Sarian O.I., 2022).*

Data on the incidence of alopecia among women varies significantly across different regions of the world and depends on the age of the respondents. According to statistics, the incidence of alopecia at the age of 30 is about 12-15%, while at the age of 60, this figure is already 30-40% *(Herskovitz I., & Tosti A., 2013; Vozianova S.V., Bolotna L.A., & Sarian O.I., 2022).*

The life cycle of the hair follicle, a tiny self-renewing mini-organ with a complex structure characterized by periodic growth, plays a central role in the development of hair loss. The life cycle of scalp follicles lasts several years and consists of the following main phases: anagen (active growth and remodeling of the hair), catagen (regression phase), telogen (rest and dormancy phase), and exogen (phase of immediate hair loss or shedding) (Fig. 1) *(Vozianova S.V., Bolotna L.A., & Sarian O.I., 2022).*

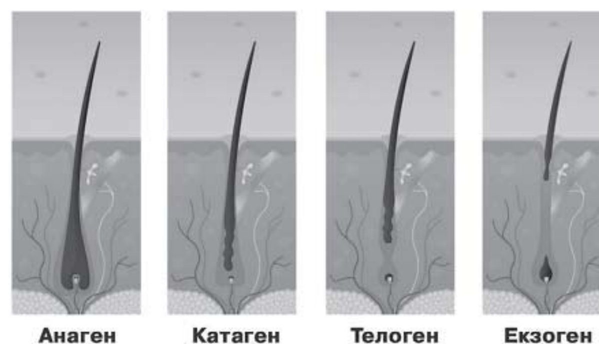

Fig. 1. Life cycle of a hair follicle (Vozianova Bolotna & Sarian, 2022)

Each hair follicle goes through 10 to 30 cycles during its lifetime. At the same time, due to the fact that individual hair follicles are in different phases of the cycle under normal healthy conditions, the density and total number of hairs remain relatively stable. It is believed that most people have about 100,000 hairs on their head at any given time, and losing 100-150 hairs per day is normal *(Natarelli N., Gahoonia N., & Sivamani R. K., 2023).*

The life cycle of a hair follicle can be directly affected by deficiencies in certain nutrients (vitamins and trace elements), hormonal imbalances, the presence of chronic diseases and their severity, harmful habits, stress, etc.

The aim of the study is to systematize current medical knowledge about the hormonal etiology of alopecia and to develop recommendations for trichologists on cooperation with doctors when endocrine disorders are suspected.

2. Research methods

To achieve this goal, we analyzed contemporary scientific and methodological literature using theoretical methods of analysis, generalization, synthesis, induction, and deduction. The main search was conducted in the Google Scholar, Scopus, PubMed, Web of Science, LinkedIn, and EuroPub databases. The main biochemical and hormonal indicators were established, changes in which are most often associated with pathological hair loss in women (alopecia).

3. Research results and their discussion

As mentioned earlier, the main organ whose dysfunction causes alopecia is the hair follicle and the disruption of its life cycle. More specifically, alopecia is fundamentally characterized by an imbalance between anagen and telogen: the acceleration of the transition from anagen to telogen leads to an increase in the number of hairs falling out, while factors that act in the opposite direction – increasing the transition from telogen to anagen – lead to hair growth and can be used in trichological practice for treatment. The fact is that the exogenous time does not change, so the reduction of the previous phases (primarily anagen) leads to a prolongation of the "pause" between the life cycles of the follicle until the beginning of the next anagen, During this time, the follicle does not produce hair and remains "empty," which initially leads to its reduction (miniaturization) with subsequent deletion *(Redler S., Messenger A.G., & Betz R.C., 2017).*

Inflammation is one of the factors contributing to the transition from anagen to telogen and, accordingly, to faster hair loss. As early as 1975, A. Lattanand and W.C. Johnson noted the presence of lymphocytes and histiocytes or significant perivascular infiltration of mast cells in tissues collected from patients with androgenetic alopecia *(Lattanand A., & Johnson W.C., 1975).* Subsequently, similar histological changes in various types of alopecia were described both in animal experiments and in human studies *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).* It should be noted that not only local inflammation of the scalp (as in atopic dermatitis or psoriasis) but also systemic inflammation plays a role in the development of alopecia. The latter, in turn, is characterized by an increase in circulating pro-inflammatory cytokines in the blood, such as interleukin-1α and 1β, tumor necrosis factor-α, C-reactive protein, etc. *(English R.S., 2018).*

Literature data and observational findings indicate that nutrients, including vitamins, minerals, and trace elements, have a significant impact on hair health and hair loss rate. For example, children with protein-energy malnutrition (kwashiorkor, marasmus, and marasmic-kwashiorkor conditions) experience changes in their skin and hair. Deficiencies in essential amino acids such as histidine, leucine, valine, and cysteine are very common in patients with various types of alopecia *(Gowda D., Premalatha V., & Imtiyaz D.B., 2017).* Correction of protein deficiency with dietary supplements containing marine proteins and glycosaminoglycans

significantly improves patients' self-esteem and quality of life and is associated with an increase in the number of terminal hairs, their diameter, and a decrease in hair loss compared to placebo *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).*

Deficiencies in omega-3 and omega-6 fatty acids may contribute to an increase in the proportion of hair follicles in the telogen phase and, as a result, alopecia. Arachidonic acid (omega-6 fatty acid) in mouse models has demonstrated the ability to stimulate the expression of growth factors such as fibroblast growth factor FGF-7 and FGF-10, which are involved in hair growth, and arachidonic acid supplements can prolong the anagen phase, promoting hair shaft elongation *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).*

Micronutrients, including vitamins, in physiological doses promote cell renewal of matrix cells in hair follicle bulbs, thereby regulating the normal follicle cycle. However, excessive uncontrolled consumption can negatively affect hair parameters, increasing hair loss *(Almohanna H.M. et al., 2018).*

Vitamin A can stimulate stem cells and induce anagen, but excessive use of vitamin A-rich supplements and excess levels of vitamin A in the blood serum can have a detrimental effect on hair parameters *(Almohanna H.M. et al., 2018).*

B vitamins, such as niacin (vitamin B3), biotin (vitamin B7), folic acid (vitamin B9), and cyanocobalamin (vitamin B12), are associated with hair loss, but alopecia is not the leading symptom of their deficiency, but rather an additional clinical finding. Moreover, the use of drugs or supplements containing these vitamins without first determining their deficiency may be associated with worsening hair condition and increased hair loss *(Almohanna H.M. et al., 2018; Natarelli N., Gahoonia N., & Sivamani R.K., 2023).*

Vitamin D is an important nutrient in the body with many different functions, but its role in hair loss is not fully understood and controversial. A review conducted by Gerkowicz A. et al. found significantly lower vitamin D levels in patients with female pattern hair loss and telogen alopecia than in the control group *(Gerkowicz A. et al., 2017).* Other authors, however, noted the opposite changes in their studies, and monotherapy with vitamin D supplements was not associated with a reduction in the manifestations of alopecia *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).*

There is a belief that vitamin E, due to its antioxidant activity and inhibition of lipid peroxidation, can increase hair growth, but there is no data on the benefits of taking supplements rich in this vitamin. Moreover, excess vitamin E increases the risk of bleeding and reduces the production of thyroid hormones, which in turn can contribute to hair loss.

The main minerals involved in regulating the hair growth cycle are iron, zinc, and selenium. Zinc is an important component of various metalloenzymes that regulate protein synthesis and cell division, so its deficiency is associated with hair loss (including various types of non-scarring alopecia) and brittle hair in patients. Importantly, alopecia associated with zinc deficiency is reversible, so it is necessary to assess serum zinc levels in patients with unexplained alopecia before prescribing zinc supplements *(Guo E.L., & Katta R., 2017).*

The mineral selenium participates in the protection against oxidative damage and morphogenesis of hair follicles. Despite the reduction in alopecia and repigmentation of hair when selenium supplements are used by patients with selenium deficiency, as with other minerals, there is no evidence of the benefits of these supplements in patients without selenium deficiency. Moreover, selenium toxicity, along with skin blisters, gastrointestinal symptoms, and memory problems, can cause generalized hair loss *(Guo E.L., & Katta R., 2017).*

Iron deficiency is the most common nutrient deficiency in the world and may contribute to the development of telogen alopecia. Free iron inside cells leads to damage to the cellular

apparatus through the formation of free radicals. That is why it is stored intracellularly in a complex with the protein ferritin, whose level in blood serum serves as a marker of the total level of iron storage in the body. The potential effect of iron on the hair growth cycle is related to its function as a cofactor for the enzyme ribonucleotide reductase, which regulates the rate of DNA synthesis *(Guo E.L., & Katta R., 2017).* Since hair follicle cells divide rapidly, they require constant use of this enzyme, and iron deficiency can limit its effectiveness. This, in turn, leads to a decrease in cell metabolism and regeneration and causes a decrease in hair growth. Most studies indicating a decrease in ferritin levels in patients with alopecia compared to a healthy control group *(Agarwal S. et al., 2019; Bilik L., Kokcam I., & Esen M., 2024; de Queiroz M., Vaske T.M., & Boza J.C., 2021; Al-Fawaeir S., & Al-Odat I., 2025)* are limited to a specific period in a woman's life (pregnancy, perimenopause, or menopause). This fact limits the transfer of the results obtained to the general population, since these periods of a woman's life can significantly affect the health of her hair. Given that studies involving men did not observe a significant difference in ferritin levels between the main and control groups, it is likely that its deficiency in women is more important for hair condition or causes other pathological changes in the body that directly lead to alopecia *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).*

Thyroid dysfunction (both hypo- and hyperthyroidism) can cause reversible diffuse hair loss and promote premature transition from anagen to telogen, potentially leading to telogen effluvium. In this case, alopecia is often the only sign of thyroid dysfunction *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023).* In an in vitro study analyzing the direct effect of T3 and T4 hormones on human hair follicles, their inhibitory effect on the apoptosis of hair matrix keratinocytes was found, and T4 additionally stimulated their proliferation *(van Beek N. et al., 2008).*

Hair loss is observed in approximately 33% of people with hypothyroidism and 50% of people with hyperthyroidism. In hypothyroidism, an increase in telogen can lead to increased dryness, brittleness, and stiffness of the hair, accompanied by a decrease in the proliferation of hair bulb cells, causing progressive hair thinning *(Hussein R.S., Atia T., & Bin Dayel S., 2023).* In 2015, Contreras-Jurado C. et al. showed in an experimental study that mice with a deficiency of thyroid hormone receptors had reduced stem cell activation and accumulation in the follicles. On the other hand, prolonged stimulation with thyroid hormones promotes the differentiation of progenitor cells, which subsequently leads to depletion. Thus, the authors concluded that both deficient and excessive levels of thyroid hormones can contribute to the transition from anagen to telogen and hair loss, and therefore thyroid-stimulating hormone and thyroxine levels should be determined as part of a standard examination for non-scarring alopecia *(Contreras-Jurado C. et al., 2015).*

Sex hormones and sex hormone derivatives formed in the body during their metabolism have a significant impact on hair growth and loss. One such derivative is dihydrotestosterone (DHT), an androgenic steroid hormone produced in target tissues from testosterone under the action of the enzyme 5-alpha-reductase type 2. Although androgens increase the size of hair follicles in androgen-dependent areas, they can lead to miniaturization of scalp follicles and contribute to androgenetic alopecia. After binding to androgen receptors in the hair follicle, DHT promotes a shortening of the anagen phase and a lengthening of the telogen phase, leading to increased apoptosis of hair cells and, thus, hair loss *(Bassino E., Gasparri F., & Munaron L., 2020).* Although men with genetically determined higher levels of 5-alpha-reductase and androgen receptor activity in hair follicles are more likely to suffer from male pattern androgenetic alopecia, and those with a deficiency of this enzyme are less likely to develop alopecia, the usefulness of determining DHT levels in blood serum during routine hair loss examinations is

a subject of debate. Thus, Urysiak-Czubatka I. et al., after analyzing DHT concentrations in the blood serum of women and men with androgenetic alopecia and healthy women and men without hair loss, found elevated DHT concentrations in the blood serum of both individuals with alopecia and the control group, with no statistically significant difference between the groups. In addition, the authors found no correlation between DHT concentrations and the progression of alopecia *(Urysiak-Czubatka I., Kmieć M.L., & Broniarczyk-Dyła G., 2014)*.

Numerous studies have been devoted to the influence of testosterone and estrogen on hair parameters, including the duration of the anagen phase. Observation of hair parameters during pregnancy, the postpartum period, and menopause in women has contributed to the formation of the opinion that estrogen has a protective effect against hair loss, since each of these stages in a woman's life is characterized by a significant difference in estrogen concentration. During pregnancy, which is characterized by high estrogen levels, hair growth and diameter increase, while hair loss decreases. However, it should be noted that this does not take into account changes in other factors associated with pregnancy, such as increased levels of human chorionic gonadotropin, progesterone, prolactin, growth factors, and cytokines, which may also contribute to these hair changes. Conversely, a decrease in estrogen and progesterone levels after childbirth is associated with postpartum telogen alopecia, while estrogen depletion during menopause is associated with a decrease in hair density and diameter, a reduction in the duration of the anagen phase, and the development of female pattern hair loss *(Grymowicz M. et al., 2020)*.

Absolute values of estrogen or testosterone cannot unequivocally indicate the risk of alopecia onset and progression, as their levels in the body are regulated not only by the gonads but also by other endocrine glands. Therefore, they may not differ significantly from the values of the control group. Moreover, sex hormones are not limited to testosterone and estrogen, but also include other substances: luteinizing and follicle-stimulating hormones, prolactin, progesterone, sex hormone-binding globulin, dehydroepiandrosterone sulfate, etc. Determining these substances and their ratios has greater diagnostic significance than the absolute values of testosterone and estrogen *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023; Ohn J. et al., 2022; Al-Fawaeir S., & Al-Odat I., 2025)*.

Cortisol is the main stress hormone that can affect the cyclical regulation of hair growth, promoting the transition from anagen to telogen. In addition, it reduces the synthesis of glycosaminoglycans and proteoglycans (such as versican and decorin), which are necessary for the normal functioning of hair follicles and the hair growth cycle. Versican protects cells from oxidative stress-induced apoptosis, and decorin promotes hair growth by acting as an anagen inducer. Thus, high cortisol levels lead to a decrease in synthesis and an increase in the breakdown of hair follicles, resulting in hair loss.

Stress with increased cortisol levels can often be the initiator of hair loss and then become its consequence. After all, hair loss itself causes stress or exacerbates existing stress, contributing to the formation of a "pathological circle" *(Natarelli N., Gahoonia N., & Sivamani R.K., 2023)*. However, modern methods of determining cortisol levels in blood, saliva, or hair have certain technical difficulties and are quite expensive. Moreover, they do not always indicate the current state of the patient (especially hair testing, which is more of an indicator of chronic stress) and have not shown a clear link to the development, severity, and type of alopecia in clinical practice.

Thus, many different factors contribute to the development and progression of pathological hair loss in women, requiring a comprehensive approach to examining such women. These examinations should not be limited to a direct examination by a trichologist, but should also include an examination of other organs and systems of the body. That is why close cooperation

between trichologists and dermatologists on the one hand and doctors of other specialties (primarily family doctors, endocrinologists, and gynecologists) on the other is the key to establishing the correct diagnosis and, accordingly, prescribing the correct and effective treatment in each specific case.

4. Conclusions

Thus, pathological hair loss (alopecia) in women is a multifactorial pathological condition, the development and progression of which involves various mechanisms, the combination and degree of manifestation of which differ in each individual woman.

Hair growth is mediated by a complex cycle consisting of anagen, catagen, telogen, and exogen, which is influenced by many factors, inducing the transition from anagen to telogen and vice versa, thereby causing the development and progression of alopecia in women. These factors include markers of inflammation, certain nutrients, including vitamins and minerals, thyroid hormones, cortisol, sex hormones, and others.

Numerous studies on the influence of various factors associated with hair loss cannot fully explain the mechanisms of alopecia. Moreover, there are quite a few contradictions related to the influence of a specific factor, because even establishing a close correlation between a certain indicator and the presence of alopecia is not always confirmed by attempts to correct this indicator with medication or dietary supplements.

It is the presence of numerous factors affecting the hair growth cycle, significant gender differences in their influence, and several main types of alopecia in women with different pathogenesis that require a comprehensive approach to the additional examination of such women and the selection of individualized treatment for alopecia.

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