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THE MAIN CAUSES OF FIBROADENOMA DEVELOPMENT IN YOUNG
GIRLS UNDER THE CONDITIONS OF UZBEKISTAN

Yusupbekov Abrorbek Ahmedjanovich

Almuradova Dilbar Muradovna

Ikromova Guli Ne'matovna

¹Prof. MD, Deputy Director, Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology, Tashkent, Uzbekistan, ORCID:0000-0002-7747-0989

²PhD, Associate professor of Department of Oncology, oncohematology and radiation oncology. Tashkent State Medical University, Tashkent, Uzbekistan.

dilbardoc@mail.ru ORCID:

³2nd Year master's student, Department of Oncology, Oncogematology and Radiation Oncology Tashkent State Medical University, Tashkent, Uzbekistan.

guliikromova0720@gmail.com ORCID:0009-0005-988-2713

Abstract: Fibroadenoma represents the most common benign breast tumor affecting young women. In recent decades, breast disorders, particularly non-malignant tumors, have increasingly influenced women's health worldwide. Among these conditions, fibroadenoma predominates, especially in adolescents and young adults. Reports from different studies indicate that fibroadenomas account for approximately 50–70% of all benign breast lesions. Although the highest prevalence is observed between the ages of 15 and 25, the tumor may occur from childhood through the menopausal period. The high frequency of fibroadenoma in young women highlights its importance, as it has implications for reproductive health, emotional well-being, and future maternal potential. According to the World Health Organization (WHO) and the American Cancer Society (ACS), the incidence is estimated at 1.5–2% among females younger than 20, increasing to 8–10% by the age of 25. Epidemiological data from Uzbekistan demonstrate that nearly 7–9% of women aged 18–25 are diagnosed with fibroadenoma. These findings underline the clinical and public health significance of this condition.

Keywords: fibroadenoma, young women, breast tumors, hormonal imbalance, endemic goiter, estrogen/progesterone ratio, prolactin, iodine deficiency, reproductive health.

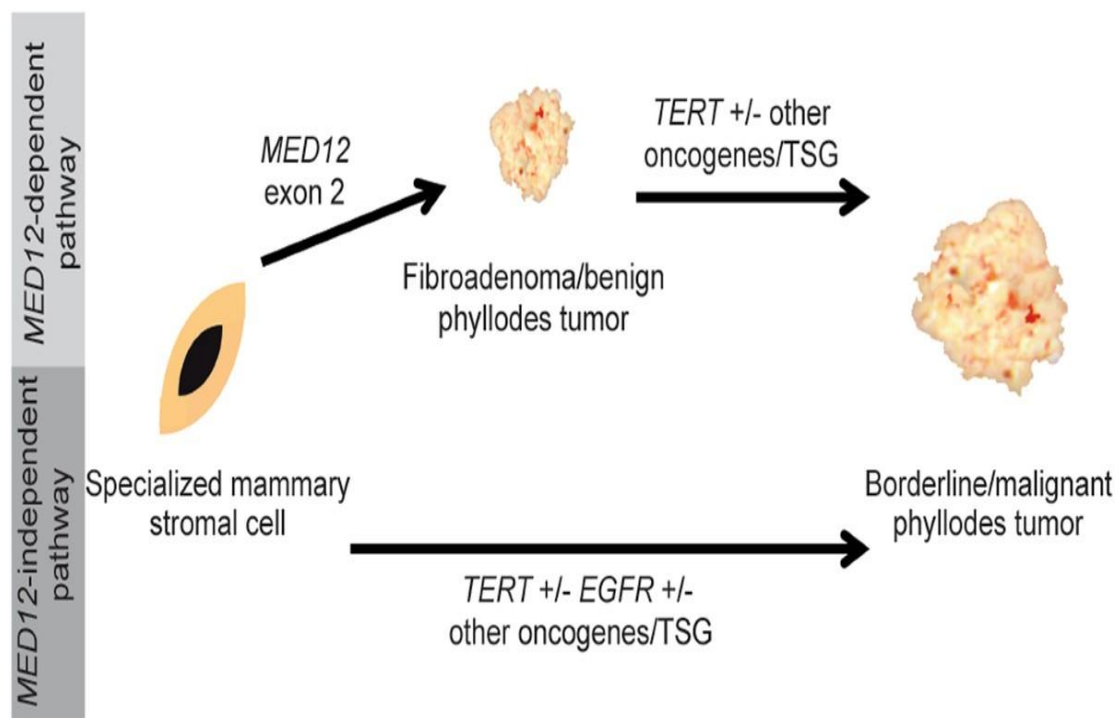
INTRODUCTION

Fibroadenoma is recognized as the most prevalent benign breast tumor in young women, typically diagnosed between the ages of 15 and 25, and accounts for up to 70% of all benign breast neoplasms [2]. Its development is influenced by endocrine changes during puberty, reproductive system immaturity, hereditary predisposition, and various environmental exposures. In Uzbekistan, the rising incidence of fibroadenoma among young women has emerged as a significant medical and social concern [12]. Both observational and clinical investigations conducted locally have shown that the condition is strongly linked to disturbances in estrogen–progesterone balance, thyroid dysfunction (particularly endemic



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goiter), increased prolactin secretion, psychosocial stress, and dietary factors. Epidemiological evidence suggests that fibroadenoma occurs in 7–13% of women of reproductive age (13–45 years) [1,2]. The onset frequently coincides with puberty, a period marked by rapid hormonal fluctuations involving estrogen, progesterone, and prolactin. Major contributors identified include hormonal dysregulation (hyperprolactinemia, estrogen/progesterone imbalance) [1,4,6], reproductive characteristics (early menarche, delayed or absent pregnancy) [2,8], and genetic susceptibility [5]. Additional influences such as ecological factors (iodine deficiency, pesticide exposure, and other xenobiotics) and endocrine disorders (notably endemic goiter and other thyroid conditions) [7,12,13] further increase the risk. Stressful life events and poor dietary habits also play a role [3,5]. While fibroadenoma is benign, certain cases show rapid enlargement or potential malignant transformation, underscoring the importance of careful clinical monitoring. Environmental exposures, particularly iodine deficiency and pesticide contact, have also been identified as aggravating risk factors. This study provides a systematic overview of the leading causes and risk factors of fibroadenoma in young women and highlights its strong association with endemic goiter. Clinical significance of fibroadenoma. Although fibroadenoma is considered a non-malignant breast tumor, early detection and continuous follow-up remain essential. Rapidly growing lesions may cause cosmetic breast asymmetry, pain, and psychological distress, contributing to increased anxiety in affected women [14]. In rare cases, malignant transformation can occur either within the fibroadenoma itself or in surrounding breast tissue (Figure 1).



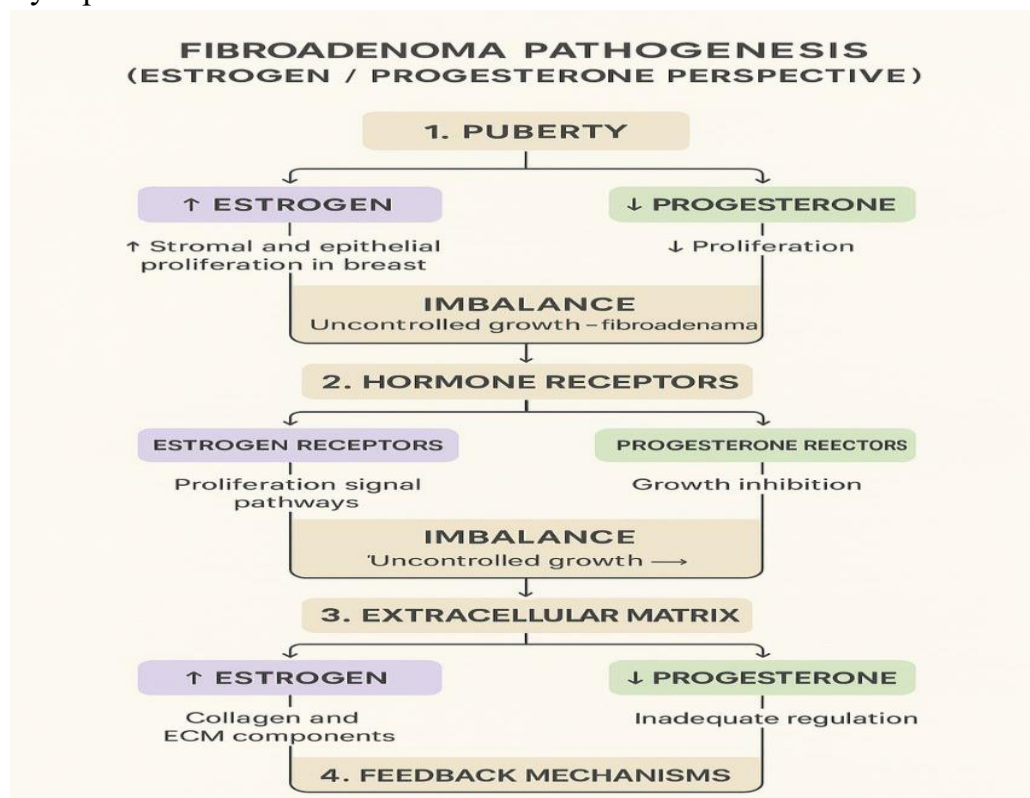
1-Picture. Malignant changes in fibroadenoma tissue

According to published data, the likelihood of malignant transformation in fibroadenoma ranges between 0.002% and 0.125% [13]. Although the probability is

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minimal, the condition warrants detailed investigation due to its impact on the psychological well-being and future reproductive health of young women.

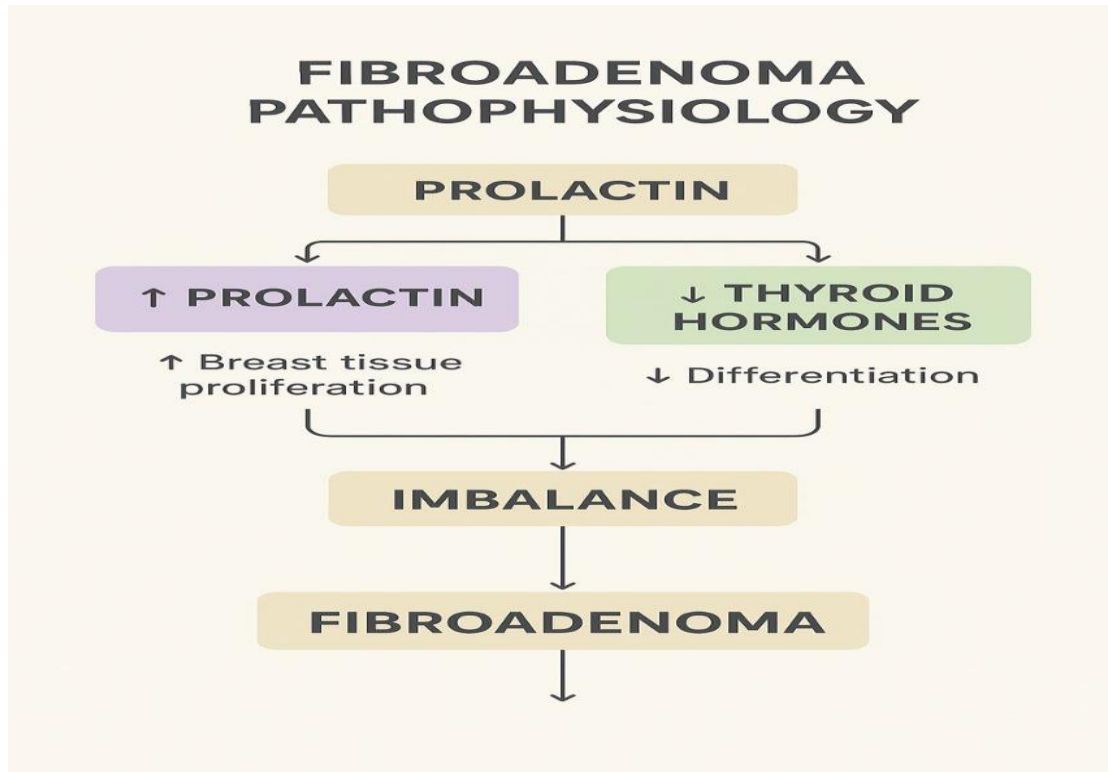
Pathogenesis and hormonal factors. Hormonal imbalance is considered one of the leading mechanisms in fibroadenoma development. Alterations in estrogen and progesterone levels play a particularly significant role. During puberty, heightened estrogen secretion stimulates proliferation of stromal and epithelial cells in the breast; when this growth becomes dysregulated, fibroadenomas may form. Normally, progesterone counteracts excessive proliferation, but insufficient levels of this hormone can facilitate tumor development. The hormone-dependent nature of fibroadenoma is illustrated schematically in Figure 2. Elevated prolactin concentrations, along with thyroid hormone disturbances (TSH, T3, T4), also substantially contribute to the disease process (Figure 3). Furthermore, several studies suggest that insulin resistance and endocrine changes associated with metabolic syndrome may represent additional risk factors.



2-Picture. Hormone-dependent pathogenesis of fibroadenoma

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Elevated prolactin levels and disturbances in thyroid hormones (TSH, T3, T4) also contribute significantly to fibroadenoma pathogenesis (Figure 3).



3-Picture. Contribution of disturbances in thyroid and prolactin hormones in fibroadenoma pathogenesis

Some studies additionally suggest that insulin resistance and metabolic syndrome-related hormonal imbalances may serve as additional risk factors.

Genetic and hereditary factors. A strong hereditary component has been confirmed by multiple studies. Women with a first-degree relative (mother, sister, or aunt) affected by fibroadenoma have nearly twice the risk of developing the condition themselves. Genetic variations, including mutations in ESR1 (the estrogen receptor gene), BRCA1/2, and other polymorphisms, may alter the breast tissue's responsiveness to hormones, thereby predisposing individuals to fibroadenoma. Recognizing this genetic contribution is important for shaping preventive strategies and designing personalized therapeutic approaches.

Environmental and lifestyle factors. In recent years, environmental exposures and lifestyle habits have been increasingly recognized as contributors to fibroadenoma development in young women. Endocrine-disrupting chemicals found in plastics, pesticides, cosmetics, and certain food additives may mimic estrogen or interfere with its metabolism. Unhealthy dietary practices, frequent intake of calorie-dense and fatty foods, sedentary behavior, chronic psychological stress, and irregular sleep patterns further accelerate fibroadenoma progression..

Scientific problem and research relevance.

The high prevalence of fibroadenoma among young women, along with its multifactorial links to hormonal, genetic, and environmental influences, as well as the difficulties in accurate diagnosis, highlight the urgent need for further scientific

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investigation. A deeper understanding of its etiology, risk determinants, and preventive strategies is crucial to safeguarding the health of the younger generation and ensuring future reproductive potential.

Objective.

This study aims to thoroughly examine the underlying causes of fibroadenoma in young women, identify key hormonal and hereditary contributors, assess the role of environmental and lifestyle factors, determine high-risk groups, and propose effective screening methods together with practical clinical recommendations.

MATERIALS AND METHODS

This research was designed as an observational–analytical study with both cross-sectional and prospective components. It was carried out during 2024–2025 at the Department of Mammology, Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology, Tashkent City Branch. A total of 420 young women aged 15–25 years were enrolled.

The investigation was implemented in two sequential phases:

1. Identification of potential risk factors through epidemiological observation and structured questionnaires.
2. Evaluation of biological mechanisms associated with fibroadenoma using clinical, laboratory, and instrumental approaches.

Study groups. Participants were divided into two cohorts:

Main group (n=210): patients diagnosed with fibroadenoma.

Control group (n=210): healthy females without fibroadenoma.

Clinical assessment. All participants underwent examination by an oncologist and gynecologist. Data collected included family history (maternal or sibling breast disease), age at menarche, menstrual cycle characteristics, reproductive history, contraceptive use, chronic endocrine disorders, and lifestyle factors such as stress, sleep, and nutrition.

Instrumental methods. Breast ultrasound was performed to determine the size, number, and localization of lesions. Histopathological examination of surgical specimens was conducted to confirm fibroadenoma.

Laboratory methods. Hormonal testing (FSH, LH, estradiol, progesterone, prolactin, TSH) was performed using ELISA. Additional biochemical analyses included insulin, glucose, and lipid profile (cholesterol and triglycerides).

Psychological and sociological evaluation. Questionnaires covered lifestyle, nutrition, physical activity, and environmental exposures. Psychological status was assessed using the Beck Depression Inventory (BDI) and Hamilton Anxiety Scale (HAM-A) following diagnosis.

Statistical analysis. Data analysis was performed with SPSS version 26.0. Descriptive statistics were expressed as mean $\pm$ standard deviation (SD). Comparisons between groups used Student's t-test and chi-square test. Logistic regression analysis was applied to determine significant risk factors. Statistical significance was accepted at $p < 0.05$.



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Ethical considerations. Approval was obtained from the Ethics Committee of Tashkent State Medical University (No. 24/2025). Written informed consent was secured from all participants; for minors, parental consent was additionally obtained.

Limitations. The study was restricted to Uzbekistan, which may limit the generalizability of the findings to other populations. Women above 25 years of age were not included, therefore characteristics of fibroadenoma in older groups were not addressed..

RESULTS

Clinical ResResu. Out of 420 participants, 210 young women diagnosed with fibroadenoma were included in the main study group, with a mean age of 20.4 ± 2.7 years. Analysis revealed that 68% (143 cases) had hormonal imbalances (elevated estrogen, decreased progesterone, increased prolactin), 22% (46 cases) demonstrated hereditary predisposition (maternal or sibling history of fibroadenoma), and 10% (21 cases) showed links to environmental or lifestyle influences, including stress, sleep deprivation, and frequent fast-food consumption. The average tumor size was 2.3 ± 0.8 cm, with 78% (164 cases) measuring less than 2 cm and 22% (46 cases) exceeding 2 cm. Fibroadenomas were unilateral in 61.4% (n=129) and bilateral in 38.6% (n=81), while multiple tumors were observed in 24.2%, typically associated with endocrine dysfunction. Pain, often related to the menstrual cycle, was reported in 37.1% of patients. In contrast, no tumors were detected in the control group, though 8.6% displayed features of mastopathy.

Hormonal Findings.

No		Main group	Control group	
1	Follicle-Stimulating Hormone	$9,8 \pm 3,2$ IU/L	$6,2 \pm 2,1$ IU/L	$p<0,01$ $r=0,14$
2	Estradiol	$45,6 \pm 12,3$ pg/mL	$72,1 \pm 15,8$ pg/mL	$p<0,001$ $r=0,22$
3	Progesterone	$8,1 \pm 2,9$ ng/mL	$12,4 \pm 3,6$ ng/mL	$p<0,01$ $r=0,14$
4	Prolactin	$26,7 \pm 5,3$ ng/mL	$18,2 \pm 4,6$ ng/mL	$p<0,001$ $r=0,23$

These findings demonstrate estrogen deficiency with concurrent hyperprolactinemia, which likely disturbs the estrogen–progesterone balance and drives fibroepithelial proliferation. Elevated prolactin nearly doubled the risk of fibroadenoma (OR=1.9; 95% CI: 1.2–3.1), while thyroid hormone abnormalities (increased TSH) raised the risk by 1.4-fold.

Lifestyle and Environmental FacFacto Survey data showed that 42.9% (90 cases) of patients lived under chronic stress compared with 18.6% (39 cases) of controls ($p=1.2 \times 10^{-7}$, $r=0.26$). Poor dietary habits were reported by 37.6% (79 cases) versus 20% (42 cases) of



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controls ($p=0.0001$, $r=0.19$), while 28.1% (59 cases) experienced chronic sleep deprivation compared with 15% (32 cases) of controls ($p=0.0021$, $r=0.15$). Residence in polluted areas doubled the risk of fibroadenoma (OR=2.14; 95% CI: 1.4–3.2). Nearly one-quarter of affected girls presented with multiple fibroadenomas, highlighting the need for continuous ultrasound surveillance. A unique feature of this work is that, for the first time in Uzbekistan, the causes of fibroadenoma in young women were analyzed on a large scale using a comprehensive hormonal, genetic, and environmental approach. Findings indicate that fibroadenoma is primarily driven by hormonal imbalance, particularly estrogen deficiency and elevated prolactin, while genetic polymorphisms (ESR1, BRCA1) increase susceptibility. Stress, poor diet, and adverse ecological factors further accelerate disease progression. Regular screening, hormonal evaluation, and targeted preventive strategies are therefore recommended.

Conclusion. This large-scale investigation confirms that fibroadenoma in young women results from the interaction of multiple risk factors. The leading causes identified were hormonal imbalance (68%), hereditary predisposition (22%), and lifestyle/environmental influences (10%). Estrogen and progesterone deficiencies were central to pathogenesis, with prolactin and thyroid dysfunction further increasing susceptibility.

Key Findings:

1. Epidemiological profile. Fibroadenoma was present in half of all participants, most frequently between 20–25 years of age. One-third of patients had bilateral or multiple tumors.

2. Hormonal imbalance. Low estradiol and progesterone combined with elevated prolactin were key drivers of fibroadenoma, promoting abnormal stromal and epithelial growth.

3. Lifestyle and environmental risks. Stress, inadequate sleep, poor nutrition, and residence in ecologically unfavorable areas significantly increased fibroadenoma occurrence, often doubling the risk.

4. Scientific and practical contribution. This is the first comprehensive study in Uzbekistan to investigate fibroadenoma in young women, integrating clinical, hormonal, genetic, and environmental perspectives. The results provide an evidence base for preventive measures, early diagnosis, and clinical monitoring.

Here results demonstrate that patients with fibroadenoma showed estrogen deficiency and increased prolactin levels. This condition may disrupt the estrogen/progesterone balance and stimulate fibroepithelial proliferation in the breast.

Lifestyle and Environmental Factors. According to the questionnaire results: 42.9% (90 cases) of girls with fibroadenoma reported living under constant stress (compared to 18.6% [39 cases] in the control group; $p=1.2\times 10^{-7}$, $r=0.26$). 37.6% (79 cases) had a dietary habit of consuming high-calorie foods rich in fats and sugars (compared to 20% [42 cases] in the control group; $p=0.0001$, $r=0.19$). 28.1% (59 cases) reported chronic sleep deprivation (<6 hours per night) (compared to 15% [32 cases] in the control group; $p=0.0021$, $r=0.15$).

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Girls living in environmentally polluted areas were found to have a two fold higher risk of developing fibroadenoma (OR=2.14; 95% CI: 1.4–3.2). Our data further showed that about 24% of girls with fibroadenoma had multiple tumors. This highlights the need for continuous ultrasound monitoring in such cases.

A distinctive feature of our study is that, for the first time in Uzbekistan, the causes of fibroadenoma in young girls were investigated on a large scale with a comprehensive hormonal and environmental analysis. The findings indicate that fibroadenoma in young girls is most often associated with hormonal imbalance and elevated prolactin. Genetic polymorphisms, particularly ESR1 and BRCA1, may increase susceptibility to the disease. Stress, poor nutrition, and adverse environmental conditions are factors that accelerate fibroadenoma development. Such girls require regular screening, hormonal monitoring, and the development of preventive measures.

CONCLUSION

The results of this large-scale study demonstrate that multiple interacting factors contribute to the development of fibroadenoma in young girls. The main causes are: Hormonal imbalance (68%), Hereditary predisposition (22%), Lifestyle factors (10%)

An increase in estrogen and progesterone deficiency represent the key pathogenic mechanism of fibroadenoma. Prolactin and thyroid hormones also contribute to the increased risk. As preventive measures, it is recommended to maintain a healthy lifestyle, reduce stress, and undergo regular breast examinations by a mammologist.

Main Findings:

1. Epidemiological characteristics of fibroadenoma. Among 420 young girls, fibroadenoma was identified in half of the participants, indicating that this pathology is also common in adolescence and early reproductive age. The incidence was highest between 20–25 years. In nearly one-third of patients, fibroadenoma presented as bilateral or multiple tumors, reflecting its distinctive clinical presentation.

2. Hormonal imbalance. Girls with fibroadenoma had low estradiol levels and progesterone deficiency, while prolactin levels were significantly elevated. This hormonal imbalance promotes epithelial and stromal proliferation in the breast, leading to fibroadenoma formation.

3. Lifestyle and psychosocial factors. Stress, sleep deprivation, poor dietary habits, and residence in environmentally unfavorable areas emerged as important additional contributors to fibroadenoma development. Statistical analysis showed that these factors doubled the likelihood of tumor occurrence.

4. Scientific and practical novelty. For the first time in Uzbekistan, the causes of fibroadenoma in young girls were comprehensively investigated using clinical, hormonal, and environmental analysis. This integrated approach provided a deeper understanding of fibroadenoma etiology.



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