

**MOLECULAR-GENETIC MECHANISMS OF CARCINOGENESIS IN BREAST
CANCER AMONG THE POPULATION OF THE SOUTHERN ARAL SEA REGION**

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Abstract. Southern Aral Sea region, including Khorezm province and adjacent territories, is characterized by unique ecological conditions due to the desiccation of the Aral Sea and climate changes. These factors significantly impact public health, leading to specific pathological changes at the cellular, tissue, and organ levels. This article examines the pathological changes in the lungs, hepatobiliary system, kidneys, and cardiovascular system, as well as their correlation with the ecological factors of the region. Additionally, the study highlights the role of environmental stressors in the development of these conditions and emphasizes the importance of early diagnosis and prevention within the region.

Keywords. Southern Aral Sea, Aral Sea, ecological factors, molecular-genetic mechanisms, carcinogenesis, breast cancer, population, genetic mutations, environmental stress, early diagnosis, disease prevention.

**МОЛЕКУЛЯРНО-ГЕНЕТИЧЕСКИЕ МЕХАНИЗМЫ КАНЦЕРОГЕНЕЗА ПРИ
РАКЕ МОЛОЧНОЙ ЖЕЛЕЗЫ У НАСЕЛЕНИЯ ЮЖНОГО ПРИАРАЛЬЯ**

***Аннотация.** Южное Приаралье включая Хорезмскую область и прилегающие территории, представляет собой регион с особыми экологическими условиями, обусловленными высыханием Аральского моря, изменением климата и антропогенной нагрузкой. Эти факторы оказывают значительное влияние на здоровье населения, вызывая развитие хронических и онкологических заболеваний. Одной из наиболее актуальных проблем является рост заболеваемости раком молочной железы среди женщин региона, что связано с воздействием токсических веществ, накапливающихся в окружающей среде.*

В данной статье рассматриваются патоморфологические изменения, возникающие в органах дыхательной, сердечно-сосудистой, гепатобилиарной системы и почек, а также молекулярно-генетические механизмы карциногенеза рака молочной железы. Особое внимание уделено влиянию экологических факторов на развитие этих патологий, что подтверждается данными патоморфологических и молекулярно-генетических исследований. Рассматриваются методы ранней диагностики и профилактики, направленные на снижение заболеваемости среди населения региона.

***Ключевые слова.** Южное Приаралье, Аральское море, экологические факторы, патоморфология, молекулярно-генетические механизмы, карциногенез, рак молочной железы, хронические заболевания, ранняя диагностика, профилактика.*

Introduction. The problem of the desiccation of the Aral Sea and its impact on public health remains one of the most pressing environmental issues in Central Asia. The Southern Aral Sea region, including the Khorezm region and adjacent territories, is the area most affected by this ecological catastrophe. The drying up of the sea has led to the formation of vast saline wastelands, from which the wind lifts toxic salt aerosols containing heavy metals, pesticides, and other harmful substances. Air, water, and soil pollution exert a complex negative impact on the human body, contributing to the development of various diseases, including oncological conditions. Of particular concern is the increasing incidence of breast cancer among women living in this region.

Studies indicate that chronic exposure to environmental toxins can contribute to mutations in genes that regulate the cell cycle and DNA repair, thereby increasing the risk of cancer development. In this regard, the study of pathomorphological changes in the human body exposed to the environmental factors of the Southern Aral Sea region presents significant scientific and practical interest.

Research Objective. The objective of this study is to analyze the pathomorphological changes occurring in the bodies of the population of the Southern Aral Sea region under the influence of environmental factors associated with the desiccation of the Aral Sea and the deterioration of the environment. Special attention is given to identifying diseases of the respiratory, cardiovascular, hepatobiliary, and urinary systems, as well as assessing molecular genetic changes that contribute to the development of chronic and degenerative diseases, including breast cancer.

Materials and Methods. To study the pathological changes occurring in the population of the Southern Aral Sea region, a comprehensive analysis and retrospective review of data collected from clinical-epidemiological observations, as well as pathomorphological and molecular genetic studies, were conducted. Particular attention was given to the impact of environmental factors such as toxic substances, heavy metals, and high levels of hypoxia on the health of the region's population. The study utilized biopsy samples of tissues and organs from residents of the Southern Aral Sea region suffering from various chronic diseases, including respiratory disorders, cardiovascular diseases, liver and kidney diseases, as well as oncological conditions. Tissue samples from the lungs, liver, kidneys, and heart were specifically selected for analysis, as these organs are the most vulnerable to pollutants prevalent in the region. Pathomorphological analysis involved various microscopy methods. Light microscopy was used to examine macroscopic tissue changes such as inflammatory processes, fibrosis, and dystrophic alterations, which serve as indicators of toxic exposure. Electron microscopy provided deeper insights into cellular and subcellular changes, including damage to cell membranes, mitochondria, and nuclear structure alterations caused by environmental stressors. Additionally, immunohistochemical studies were performed to identify specific biomarkers related to inflammation, apoptosis, and cell proliferation. These markers helped assess the extent of toxin exposure on cells and their potential transformation into tumor cells. Molecular genetic analysis was conducted using polymerase chain reaction (PCR) and DNA sequencing methods, allowing for the identification of genetic mutations associated with prevalent diseases, such as breast cancer, respiratory disorders, and cardiovascular diseases. The study also revealed genetic markers indicating increased susceptibility to certain diseases in the unique environmental conditions of the Southern Aral Sea region. Notably, mutations in oncogenesis-related genes were identified, confirming the link between environmental stress and cancer development in the region.

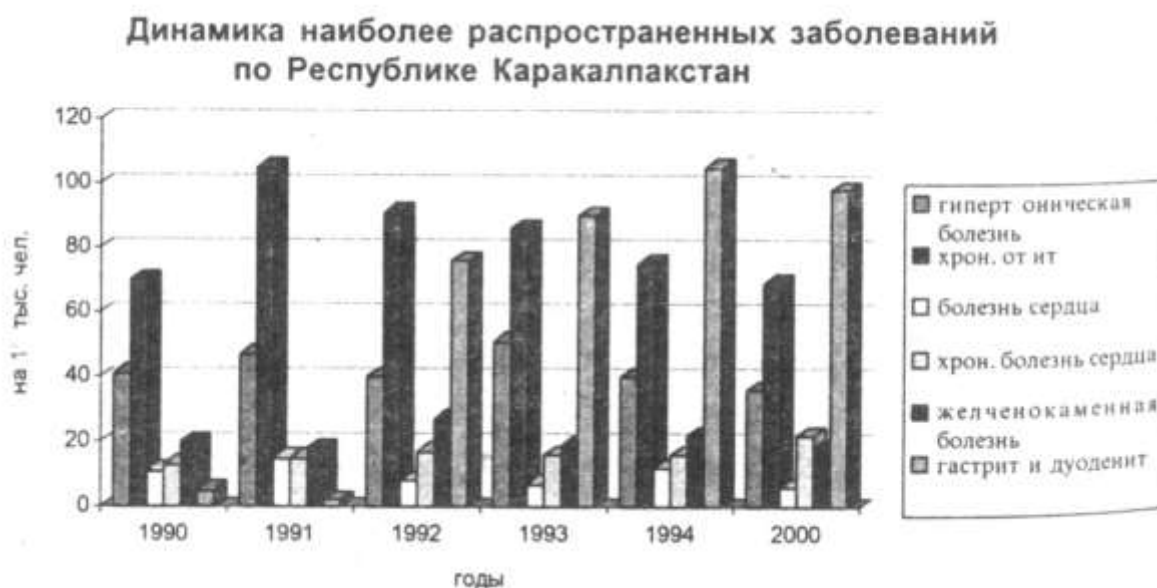
An essential part of the study was a six-month ecological monitoring period, during which data on soil, water, and air contamination by heavy metals and toxic substances were collected.

This helped establish a direct correlation between environmental pollution levels and disease prevalence among the local population. The concentration of substances such as lead, cadmium, mercury, and other toxic compounds significantly exceeded safe limits, confirming the direct relationship between environmental factors and public health deterioration. Statistical analysis of the data enabled the identification of correlations between pollution levels and disease incidence, providing valuable insights for developing effective preventive and therapeutic measures. As a control group, health data from populations in regions with more favorable environmental conditions were used, allowing for clear comparisons in disease prevalence and health outcomes. All materials and methods used in the study complied with ethical standards and were approved by the local ethics committee. The data collection and analysis process was carefully planned and executed in multiple stages to ensure high accuracy and reproducibility of results. Thus, the combination of pathomorphological, molecular genetic, and environmental research methods in this study provided a deeper understanding of the relationship between public health changes and environmental factors in the Southern Aral Sea region. Statistical data processing was carried out using SPSS software, a specialized tool for comprehensive data analysis. Correlation analysis methods were applied to identify links between environmental pollution levels and the incidence of various diseases.

Results and Discussion. The results of the study indicate a significant impact of environmental factors on the health of the population in the Southern Aral Sea region. This area, which has suffered the consequences of the ecological catastrophe caused by the desiccation of the Aral Sea, represents a unique zone with pronounced environmental stressors. Environmental changes, including air, water, and soil pollution, have severe health consequences for local residents, leading to the development of numerous diseases. Primarily, this concerns pathologies of the respiratory, cardiovascular, hepatobiliary, and urinary systems, as well as oncological diseases, including breast cancer. Respiratory diseases in the Southern Aral Sea region are characterized by a high prevalence of chronic bronchitis, emphysema, and chronic obstructive pulmonary disease (COPD). This is linked to prolonged exposure to pollutants, including dust, chemical emissions, and aerosols that are constantly present in the air. Regular inhalation of polluted air contributes to the development of chronic inflammatory processes in the lungs, as confirmed by pathomorphological changes such as fibrosis and emphysema in lung tissues.

A significant number of residents also suffer from asthma and other respiratory diseases, further highlighting the destructive impact of pollutants on the respiratory system.

Prolonged exposure to toxins such as heavy metals and pesticides negatively affects liver and kidney function. Liver tissue samples from local residents revealed changes characteristic of toxic hepatitis and fibrosis, including cell hyperplasia and increased fibrosis levels. These alterations can lead to liver cirrhosis with continued toxin exposure.



Additionally, signs of chronic kidney failure, such as interstitial fibrosis and tubular necrosis, were identified, confirming severe kidney dysfunction caused by water contamination with heavy metals and chemicals. Among cardiovascular diseases, hypertension and ischemic heart disease are particularly prevalent.

Pathomorphological studies of the cardiac muscle showed signs of hypertrophy and fibrosis, resulting from atherosclerotic changes triggered by air pollution and heightened stress levels. These changes have a direct impact on the progression of cardiovascular diseases, which, in combination with other pathologies, accelerate the overall deterioration of health. Equally alarming is the rising incidence of oncological diseases, particularly breast cancer among women in the region. Pathomorphological analysis of breast tumors revealed specific changes associated with environmental factors.

Mutations in the **BRCA1** and **BRCA2** genes, which play a key role in cell cycle regulation and DNA repair, were identified in tumor tissues. These genetic alterations increase the

predisposition to breast cancer, further exacerbated by exposure to toxins such as pesticides, heavy metals, and other chemical pollutants accumulated in the region's ecosystem.

Additionally, mutations in DNA repair genes, such as **p53**, were detected, confirming a high probability of breast cancer development under chronic exposure to environmental contaminants. The level of environmental pollution in the Southern Aral Sea region significantly exceeds permissible limits, directly impacting public health. Contamination of water with heavy metals such as lead and cadmium, as well as pesticides and other chemical substances that enter the body through water and food, has a devastating effect on various body systems, contributing to the development of cancer, respiratory diseases, liver and kidney disorders, and cardiovascular conditions. Comparisons with other regions show that disease prevalence in the Southern Aral Sea region is significantly higher. The incidence of breast cancer and other diseases in this area is two to three times greater than in other parts of the country, confirming that the environmental situation in the region has a direct effect on human health. Based on the study's findings, it is evident that comprehensive measures are needed to improve the region's environmental conditions and reduce air, water, and soil pollution levels. Disease prevention should become a priority in the region's healthcare system. Special attention should be given to early diagnosis, particularly for oncological, respiratory, and cardiovascular diseases, as well as raising public awareness about the risks associated with environmental pollutants. These measures will help improve the quality of life for the local population and reduce disease incidence in the region.

Conclusion. The results of the conducted study indicate a significant impact of environmental factors on the health of the population in the Southern Aral Sea region. This area,



which has experienced the consequences of an ecological disaster caused by the drying of the Aral Sea, represents a unique zone with pronounced environmental stressors.

Ecological changes, including air, water, and soil pollution, have serious health consequences for local residents, leading to the development of numerous diseases. Primarily, this concerns pathologies of the respiratory, cardiovascular, hepatobiliary, and urinary systems, as well as oncological diseases, including breast cancer. Clinical and epidemiological studies have revealed a high prevalence of various diseases among the population of the Southern Aral Sea region, confirming the negative impact of environmental factors on health.

Among the most common pathologies are chronic respiratory diseases (bronchial asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease), cardiovascular diseases (hypertension, ischemic heart disease, myocardial infarction, stroke), liver and biliary tract diseases (chronic hepatitis, liver cirrhosis, gallstone disease), kidney and urinary tract diseases (chronic pyelonephritis, urolithiasis, chronic renal failure), and oncological diseases (breast cancer, lung cancer, stomach cancer, colorectal cancer). Molecular genetic analysis has identified several significant changes in genes associated with the development of breast cancer in women living in the Southern Aral Sea region. A substantial proportion of breast cancer patients were found to have mutations in the BRCA1 and BRCA2 genes, which play a key role in DNA repair and genome stability maintenance.

The presence of mutations in these genes significantly increases the risk of developing breast cancer. Additionally, tumor cells exhibited mutations in the TP53 gene, one of the primary regulators of the cell cycle and apoptosis. Mutations in this gene can lead to disrupted control over cell growth and division, further contributing to tumor development. Breast cancer patients also demonstrated altered gene expression related to the metabolism of xenobiotics, including toxins entering the body from the environment. These changes may lead to impaired detoxification processes and facilitate the accumulation of harmful substances in the body. The identified molecular genetic alterations may be associated with exposure to environmental factors such as toxic air, water, and soil pollution. Further research is needed to explore in greater detail the mechanisms through which environmental factors influence breast cancer development at the molecular level.

The findings of this study are of significant importance for public health in the Southern Aral Sea region.

The obtained data highlight the necessity of developing and implementing comprehensive programs aimed at improving the environmental situation in the region, as well as preventing and early diagnosing diseases associated with environmental exposure.

Special attention should be given to environmental monitoring and control, reducing harmful factor exposure on the population, disease prevention and early diagnosis, and raising public awareness about the risks associated with environmental factors and the measures for disease prevention and health promotion. Implementing these measures will improve the environmental situation in the Southern Aral Sea region, reduce disease incidence, increase life expectancy, and significantly enhance the quality of life in the region.

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