



# **ANALYSIS OF THE ROLE OF THE BRCA1 AND BRCA 2 GENES AS A PREDICTOR OF BREAST CANCER. PREVALENCE OF BREAST CANCER IN THE REPUBLIC OF UZBEKISTAN.**

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<b>Article history:</b>	<b>Abstract:</b>
<b>Received:</b> December 11 <sup>th</sup> 2022 <b>Accepted:</b> January 11 <sup>th</sup> 2023 <b>Published:</b> February 17 <sup>th</sup> 2023	According to the World Health Organization, breast cancer is the most common type of cancer, with over 2.2 million cases reported in 2020. One in twelve women will develop breast cancer in their lifetime, which is the leading cause of cancer death in women. In 2020, about 685,000 women died from this disease. In the structure of malignant neoplasms for 2020, the leading position in our Republic is occupied by breast cancer, while the incidence rate is 11.2 per 100,000 population.

**Keywords:** Breast cancer, risk factors, BRCA1 and BRCA2, incidence of rural and urban population, Uzbekistan.

## **OBJECTIVE .**

To study the features of the spread of breast cancer in the territory of the Republic, among the urban and rural population.

The study of factors that play a starting role in the occurrence of breast cancer.

Study of the prevalence of BRCA1 and BRCA2 genes and their polymorphic variants in patients with breast cancer.

Measures to prevent the risk of developing breast cancer based on the presence of predictor genes.

## **MATERIALS AND METHODS:**

The incidence of breast cancer in the republic was studied for the period from 2015 to 2019. Information about first-time cases was compiled on the basis of data from the cancer registry of the Republican Cancer Research Center of the Republic of Uzbekistan. On the numerical composition of the population of the republic and regions, data were used from the official website of the State Committee of the Republic of Uzbekistan. The calculation of intensive and standardized indicators was carried out according to the methodological recommendations of the Moscow Research Institute of Oncology. P.A. Herzen.

On the basis of intensive and standardized indicators, the incidence rates of breast cancer were determined. The latter were calculated on the average number of cases over 4 years (2015-2019). Standardized indicators were calculated in a direct way, while using the world standard for the age distribution of the population, which is recommended by the IARC and used in the monograph Cancer Incidence in Five

Continents. Statistical processing of the material was carried out using Excel 2010, Statistica 6.0. The assessment of the significance of differences was carried out according to the Student's criteria based on the t u p indicators. A p value <0.05 was considered statistically significant.

## **RESULTS:**

In the course of our study and calculation of standardized indicators, the prevalence of breast cancer in the Republic of Uzbekistan for 2015-2019 per 100,000 population is: 2015-4302, 2016-4018, 2017-3871, 2018-3918, 2019-4213 patients with ovarian cancer. At the same time, the proportion of patients who were registered in the institutions of Uzbekistan for 5 years or more from the moment the diagnosis of OC was established at the end of the reporting year in 2015-2019,% of neoplasms from the number of those registered was: 2015-45.3%, 2016-43%, 2017-42%, 2018-39.1% 2019-40.3%. It should also be noted that the mortality of patients from malignant neoplasms in the Republic for 2015 was 314 patients, 2016 - 412, 2017 - 416, 2018 - 463, 2019 - 371 patients with OC. Mortality of patients within a year from the moment of diagnosis of a malignant neoplasm (from among patients registered for the first time in the previous year) in Uzbekistan in 2015-0.2; 2016-0.5; 2017-0.5; 2018-0.6; 2019-0.5. Information on the treatment of ovarian cancer first registered in 2019 and subject to treatment included: 1) patients who completed specialized treatment 453, with 53.3% of those newly diagnosed; 2) patients who received radical treatment - 12.8%, palliative - 3.8%, high-tech - 1.8%. 3)



patients who received only drug therapy 20.8%, combined 61.0%.

We also studied the factors that play a triggering role in the occurrence of breast cancer. These include: early (before 12 years) menarche and / or late (after 55 years) menopause, late (after 30 years) first birth and nulliparous women, age over 50 years, a family history of breast cancer (especially in direct relatives in premenopause), BRCA-1 gene mutations; BRCA-2. It is important to note that in addition to trigger factors, there are also modifying factors such as: obesity, abortion, late first pregnancy, oral contraceptive use in patients with BRCA, long-term hormone replacement therapy, physical inactivity, smoking, alcohol abuse, chemical, physical and biological factors (ionizing radiation, trauma, chemical carcinogens).

We studied the BRCA genes (Breast Cancer gene), which include BRCA1 and BRCA2, the first of which is located in the long arm of chromosome 17 at position 21.31, and the second is located in the long arm of chromosome 13 at position 13.1. More than 2,000 variants of pathogenic mutations in the BRCA1 and BRCA2 genes are currently known. In addition, these genes are quite large - 24 and 27 exons, respectively. Therefore, a complete analysis of the BRCA1 and BRCA2 gene sequences is a laborious, costly, and time-consuming process.

However, some nationalities are characterized by a limited range of significant mutations (the so-called "founder effect"). Thus, in the population of Russian patients of Slavic origin, up to 90% of detected pathogenic BRCA1 variants are represented by only three mutations: 5382insC, 4153delA, 185delAG. This fact makes it possible to significantly speed up the genetic testing of patients with signs of hereditary breast cancer. These genes have many polymorphic variants, each of which is responsible for the manifestation of a particular mutation in target cells. For example: In cancer patients of the Slavic population, as well as the Ashkenazi ethnic group, pathogenic variants 185delAG, T181G, 4153delA, 5382insC in the BRCA-1 gene and 1528delAAAA, 1099SX C>G, 6174delT, 9318delAAAA in the BRCA-2 gene are most often detected. The population frequency of occurrence of these common mutations is quite low (no more than 1%). The detection of these mutations is usually associated with an increased risk of developing breast cancer. The BRCA-1 185delAG, 5382insC, and BRCA-2 6174delT variants are associated with an increased risk of breast cancer with long-term oral contraceptive use. The BRCA-1 variant 185delAG or 5382insC corresponds to more unfavorable histological malignancy of the tumor. The

BRCA-1 and BRCA-2 polymorphisms are not strictly specific for breast cancer. The pathological BRCA-2 genotype increases the risk of stomach, colon, endometrial, pancreas, bladder, biliary tract, and melanoma.

In connection with the above data, we have identified those cases when it is necessary to pass an analysis to detect BRCA1 and BRAC2 mutations:

- 1) Patients under 45 years of age with a diagnosis of breast cancer.
- 2) Patients under the age of 50 with breast cancer, if the family has at least one close blood relative with such a diagnosis.
- 3) Also in the event that a patient under 50 years of age with breast cancer has an unknown family history of cancer.
- 4) Patients with breast cancer under the age of 60 - if, according to the results of a histological examination, the tumor is triple-negative (there is no expression of ER, PR, HER2 markers).
- 5) All patients diagnosed with ovarian cancer and breast cancer.
- 6) If a man is diagnosed with breast cancer.
- 7) If prostate cancer is diagnosed (with a Gleason score > 7) if there is at least one relative with breast cancer aged less than 50 years or if there are at least two relatives with breast cancer, pancreatic cancer or prostate cancer.
- 8) If a relative has a BRCA1 or BRCA mutation

In our Republic, due to the increase in the number of patients with breast cancer, all females should take the following preventive measures, such as:

Monthly self-examination from the age of 18, clinical examination of the breast ultrasound or magnetic resonance imaging from 25 years of age + screening from 45-65 years of age, male carriers of a mutation in the BRCA1 / 2 genes are recommended to undergo an annual clinical examination of the mammary glands starting from the age of 35. From the age of 40, it is advisable to perform a screening examination of the prostate gland.

In our Republic, breast cancer is treated by the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSNPMTSOiR) and its branches in the regions.

On April 4, 2017, the President of the country signed the Decree "On measures to further develop the oncological service and improve oncological care for the population of the Republic of Uzbekistan for 2017-2021". According to this program, the reorganization of the RSNPMTSOiR and its branches in the regions, modernization and equipping with new modern equipment (including party mammographs) has begun.



Doctors undergo specialization and improvement in leading oncological centers in Russia, Europe, Korea, India and other countries. The "Soglom Avlod Uchun" Foundation conducts preventive examinations among women of different age categories with the involvement of doctors of various specialties, including mammologists. It should be noted with regret that at present in our country there are no funds that fully deal with cancer patients, as well as a large-scale volunteer movement.

Decree of the President of the Republic of Uzbekistan No. 5130 dated May 27, 2021

"ON THE FURTHER IMPROVEMENT OF THE SYSTEM OF PROVIDING HEMATOLOGICAL AND ONCOLOGICAL SERVICES TO THE POPULATION" prevention of cancer among the population with the help of a mobile mammograph and ultrasound machines in all branches, including in Tashkent, of the Republican Specialized Oncological and Radiological Scientific and Applied Medical Center is carried out in these areas for early detection of dangerous tumors.

October is recognized worldwide as Breast Cancer Awareness Month

## REFERENCES

1. National Breast Cancer Foundation, inc. [Genetic Testing for Breast Cancer](#).
2. National Breast Cancer Foundation, inc. [BRCA: The Breast Cancer Gene](#).
3. National Cancer Institute. [BRCA Mutations: Cancer Risk and Genetic Testing](#).
4. Mayo Clinic. [BRCA gene test for breast and ovarian cancer risk](#).
5. Jesse T. Casaubon; John-Paul Regan. [BRCA 1 and 2. Treasure Island \(FL\): StatPearls Publishing; 2019 Jan-](#)
6. Genetics Home Reference. [BRCA1 gene](#).
7. Genetics Home Reference. [BRCA2 gene](#).
8. Ielizaveta Gorodetska, Iryna Kozeretska, and Anna Dubrovska. [BRCA Genes: The Role in Genome Stability, Cancer Stemness and Therapy Resistance](#). J Cancer. 2019; 10(9): 2109–2127. Published online 2019 May 14. doi: 10.7150/jca.30410.
9. Official site of the RUSSCO program. Mutations in the BRCA1 and BRCA2 genes.
10. Federal State Budgetary Institution "National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov" of the Ministry of Health of the Russian Federation. Oncogenetics. mutations in the brca1, brca 2

and chek2 genes associated with breast and ovarian cancer.

11. Xuan Li and Wolf-Dietrich Heyer. Homologous recombination in DNA repair and DNA damage tolerance. Cell Res. author's manuscript; available in PMC 2011 May 4. Cell Res. 2008 Jan; 18(1): 99–113. doi: 10.1038/cr.2008.1.
12. L.N. Lyubchenko, E.I. Batenev. Medical genetic counseling and DNA diagnostics for hereditary predisposition to breast cancer and ovarian cancer. A guide for doctors. Federal State Budgetary Scientific Institution "Russian Cancer Research Center named after N.N. Blokhin.
13. Register of medicines of Russia. Tamoxifen.
14. Inês Godet and Daniele M. Gilkes. BRCA1 and BRCA2 mutations and treatment strategies for breast cancer. Integr Cancer Sci Ther. author's manuscript; available in PMC 2017 Jul 11. doi: 10.15761/ICST.1000228.