DOI 10.29254/2523-4110-2024-2-173/addition-9-12
UDC 618.19-006(477.53)

Novykov K. R., Lytvynenko L. P., Fylenko B. M., Roiko N. V., Prylutskyi O. K., Proskurnia S. A.

BREAST CANCER IN THE POLTAVA REGION: CLINICAL AND MORPHOLOGICAL ASPECTS

Poltava State Medical University (Poltava, Ukraine)

Анотація: *Метою дослідження було аналіз клініко-епідеміологічних та деяких патоморфологічних аспектів раку молочної залози на основі ретроспективного аналізу післяопераційного матеріалу. Проведено аналіз 238 протоколів патогістологічних висновків та мікроскопічне дослідження післяопераційного матеріалу раку молочної залози. Під час проведення дослідження визначали вік хворих, ступінь диференціювання, гістологічний варіант пухлини та їх взаємозв'язок.*

Встановлено, що між ступенем диференціювання раку та віком пацієнток не має кореляційного зв'язку. Було визначено, що розмір пухлини на момент її виявлення має прямий кореляційний зв'язок зі ступенем її диференціювання. При гістологічному дослідженні було виявлено, що всі карциноми, незалежно від ступеня диференціювання, характеризувались проростанням у стінки кровоносних та лімфатичних судин. ВДР не давав метастази, ПДР метастазував у 52,4% випадків, а НДР – у 59% випадків. Різні гістологічні типи РМЗ демонструють гетерогенні клініко-патологічні характеристики. Встановлено, що розмір пухлини, проростання у лімфатичні та кровоносні судини та метастазування має кореляційний зв'язок зі ступенем диференціювання.

Ключові слова: *диференціювання, метастазування, гістологічний тип, прогноз.*

Abstract. *The aim of the study was to analyse the clinical and epidemiological and some pathomorphological aspects of breast cancer based on a retrospective analysis of postoperative material. We analysed 238 protocols of pathological reports and microscopic examination of postoperative breast cancer material. During the study, the age of patients, the degree of differentiation, the histological variant of the tumour and their relationship were determined.*

It was found that there was no correlation between the degree of cancer differentiation and the age of the patients. It was determined that the size of the tumour at the time of its detection has a direct correlation with the degree of its differentiation. The histological examination revealed that all carcinomas, regardless of the degree of differentiation, were characterised by invasion of the walls of blood and lymphatic vessels. Highly differentiated cancer did not metastasise, moderately differentiated cancer metastasised in 52.4% of cases, and low-grade cancer metastasised in 59% of cases. Different histological types of breast cancer demonstrate heterogeneous clinical and pathological characteristics. It was found that the size of the tumour, invasion of lymphatic and blood vessels, and metastasis are correlated with the degree of differentiation.

Key words: *differentiation, metastasis, histological type, prognosis.*

Connection of the publication with planned research works.

The scientific research was carried out within the complex interdepartmental research topic of Poltava State Medical University "Regularities of morphogenesis of organs, tissues and vascular and nervous formations in norm, pathology and under the influence of external factors", state registration number 0118U004457.

Introduction.

Every year, the health care system around the world faces an increase in morbidity and mortality from malignant neoplasms. Breast cancer (BC) is the most common oncological disease in women, accounting for 30% of all malignant neoplasms [1] and remains the main cause of cancer-related mortality in women [2, 3].

The reasons for the development of breast cancer can be numerous endogenous (genetic) and exogenous (environmental) factors. Improper lifestyle, environmental factors, and socio-psychological factors are associated with its occurrence [4]. Genetic and environmental factors lead to the accumulation of mutations in certain genes of germ or somatic cells, which determine the malignancy of a tumor with unlimited uncontrolled autonomous growth. The risk of breast cancer increases with age, but certain non-genetic factors can cause wide variations in the time of onset of the disease in terms of age. Approximately 10% of women with breast cancer have a hereditary predisposition [1, 5, 6, 7, 8].

In Ukraine, every fourth case of breast cancer is diagnosed at late stages [9], therefore new studies of clinical, morphological and epidemiological aspects are always actual from both a theoretical and a practical point of view.

The aim of the study.

To study clinical-epidemiological and some pathomorphological aspects of breast cancer based on a retrospective analysis of postoperative material.

Object and research methods.

The material was taken from the Poltava Regional Pathological Anatomical Bureau (PRPAB) for the year 2023. An analysis of the protocols of pathohistological conclusions and a microscopic examination of the postoperative material delivered from the Poltava Regional Clinical Oncology Dispensary (PRCOD) was carried out. During the study, the age of the patients, the degree of differentiation, the histological variant of the tumor and their relationship were determined.

In 2023, 238 women with breast cancer were operated on in PRCOD, whose postoperative material was delivered to PRPAB. The average age of the patients was 65.1±10.45 years. The material was fixed in a 10% formalin solution. Paraffin blocks were made from tumor pieces taken from different areas, followed by the production of histological preparations stained with hematoxylin and eosin. The pathogistological conclusion

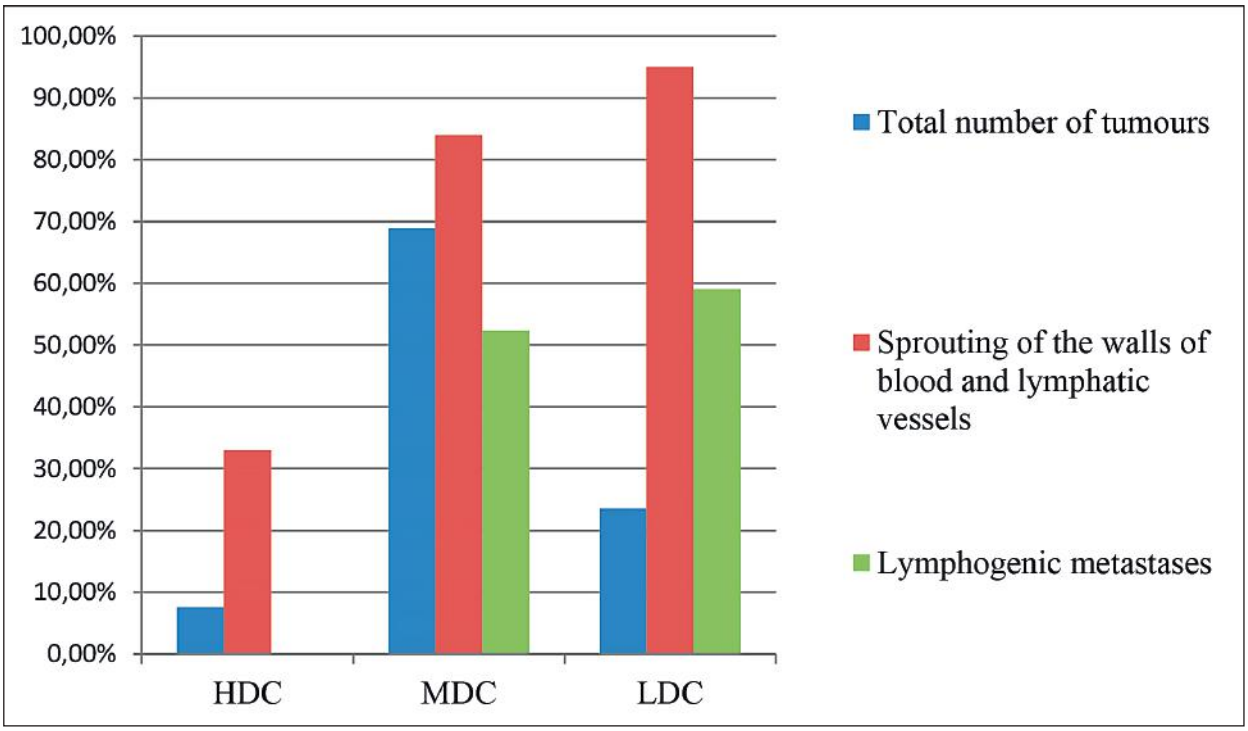

Figure 1 – Characteristics of invasive growth and metastasis of breast cancer.

was formulated taking into account the classification of breast cancer of the World Health Organization [10].

Research results and their discussion.

According to the degree of differentiation, the studied material was divided into three groups: highly differentiated (HDC) (n=18, 7.56%), moderately differentiated (MDC) (n=164, 68.91%) and low differentiated (LDC) (n=56, 23.53%) carcinomas. It was established that there is no correlation between the degree of cancer differentiation and the age of the patients.

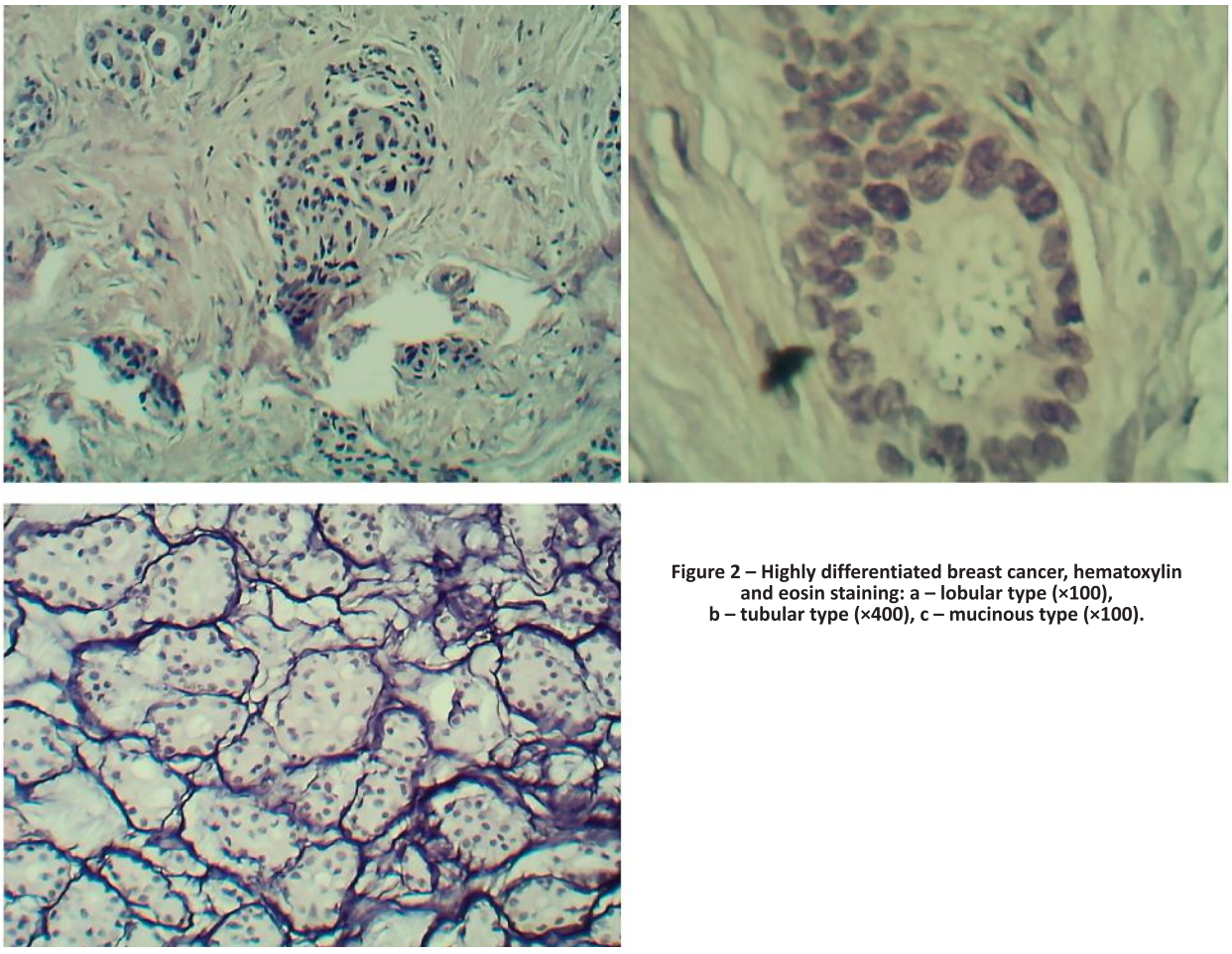

Figure 2 – Highly differentiated breast cancer, hematoxylin and eosin staining: a – lobular type (×100), b – tubular type (×400), c – mucinous type (×100).

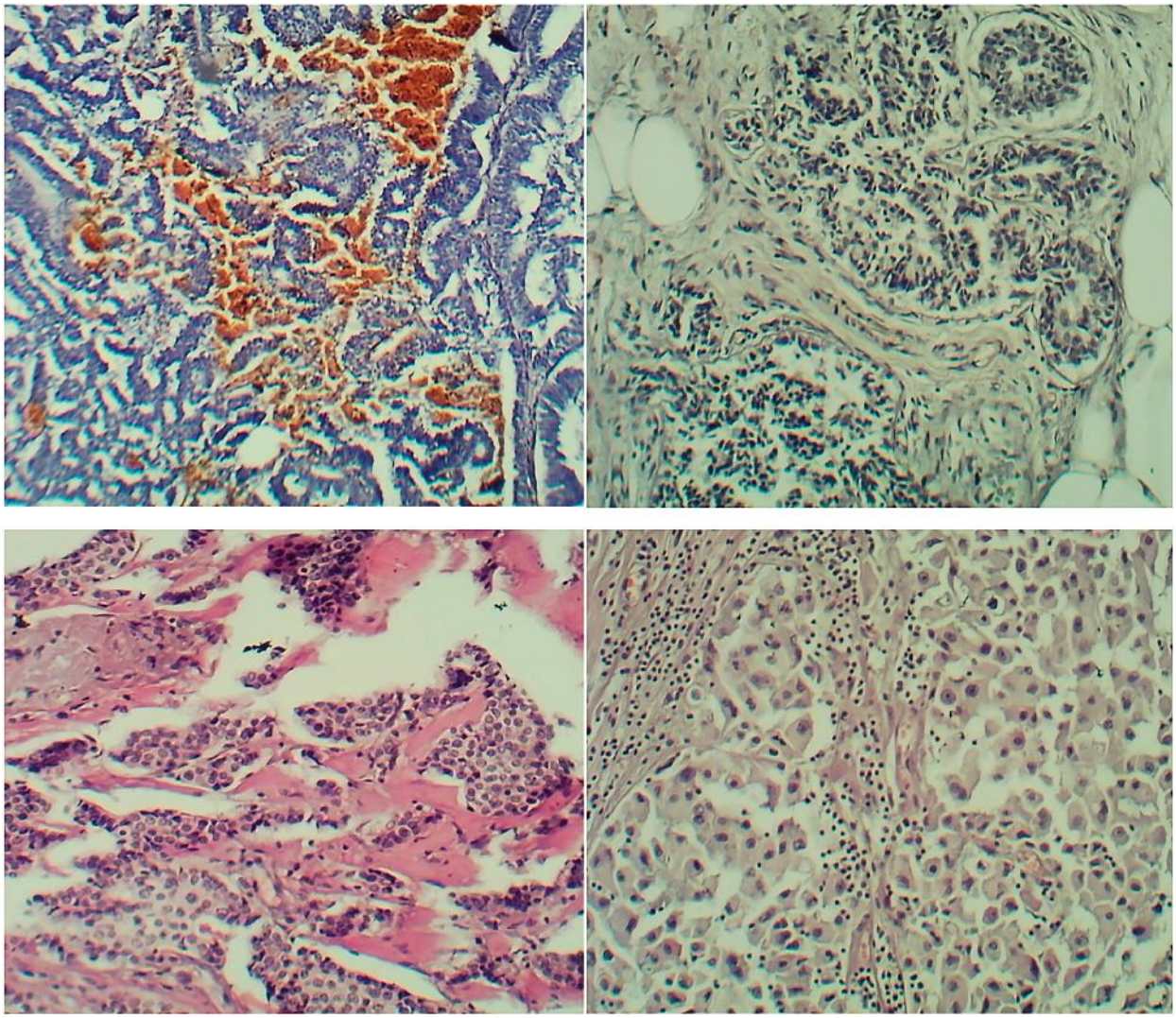

Figure 3 – Moderately differentiated breast cancer, hematoxylin and eosin staining: a – micropapillary type (×100), b – multicentric type (×100), c – lobular type (×100), d – mixed type (×400).

The average size of the tumor (T) in the largest diameter in HDC was 2.33±1.28 cm, in MDC – 2.65±1.44 cm, and in LDC – 3.27±1.36 cm. It was determined that the size of the tumor at the time of its detection has a direct correlation with the degree of its differentiation.

As is known, the size of the tumor (T) is one of the classic indicators of the stage of cancer of the TNM system, which is currently considered an outdated concept in connection with the development of molecular oncomorphology. However, according to individual reports [11], the prognostic significance of stage T does not lose its relevance. It was found that in patients with T4Nx or TxN3 tumors, T4 tumors have a worse prognosis than N3 tumors regardless of other prognostic factors. It is assumed that the presence of a large number of pluripotent (stem) cancer cells can allow small tumors to give distant metastases [12]. However, the degree of malignancy of cancer stem cells is determined by two factors: the ability to migrate and proliferate. Small tumors with multiple lesions of the lymph nodes have a higher migratory capacity than proliferative. Larger tumors with widespread involvement of lymph nodes, as a rule, have the ability to both migrate and proliferate. Therefore, as follows from the above, the size of the tumor remains an important prognostic factor [11].

The prognosis of breast cancer is closely related to metastasis, a complex process that results in secondary distant tumors. Metastasis of breast cancer is ensured by a complex of mechanisms (cellular, ability to invade, evasion of immune surveillance, microenvironment regulation, etc.), some of which depend on the degree of differentiation [13].

During histological examination, it was found that all carcinomas, regardless of the degree of their differentiation, were characterized by germination into the walls of blood and lymphatic vessels: HDC cancer – in 33% of cases, MDC – in 84% of cases, LDC – in 95% of tumors. However, HDC did not metastasize, MDC metastasized in 52.4% of cases, and LDC – in 59% of cases **(fig. 1)**. This indicates that the degree of differentiation is an important prognostic factor that indicates the ability of breast cancer to metastasize.

Highly differentiated (G1) breast cancer was represented by lobular (44.4%), papillary (16.7%), tubular (16.7%), multicentric (11.1%) and mucinous (11.1%) types **(fig. 2)**.

Moderately differentiated breast cancer (G2) was characterized by five histological types: nonspecific (51.2%), lobular (26.2%), multicentric (2.4%), micropapillary (1.8%), and mixed (18.4%) **(fig. 3)**. All cases of low

differentiated (G3) breast cancer were represented by a nonspecific type. The size of the tumors did not depend on its histological type.

The highest frequency was MDC, the histological types of which were characterized by the germination into the walls of lymphatic and blood vessels with different frequency: non-specific type – in 89.3% of cases, lobular – in 72.1%, mixed – in 90%, micropapillary – in 66.7% and multicentric – in 100% of cases. Metastasis was also observed with different frequency: non-specific type – in 51.2% of cases, lobular – in 46.5%, mixed – in 66.7%, micropapillary – in 66.7% and multicentric – in 50% of cases. That is, there is no significant difference in the frequency of metastasis in different tumor types.

It is obvious that breast cancer is a heterogeneous disease with a significant number of phenotypic features. Establishing an accurate diagnosis is necessary to optimize the prognosis and prescribe appropriate treatment for patients. Our study confirms the well-known facts that verification of the degree of differentiation and histological type of the tumor will provide an opportunity to predict prognostic features or treatment options [14]. For example, chemotherapy is used in the preoperative period for LDC, which is usually not performed in HDC. However, for MDC, which is represented by a heterogeneous phenotype, prognosis and treatment remain a particularly difficult issue [15].

The conducted study showed that there are significant differences in the clinical and pathological characteristics of breast cancer, including the size of the tumor, the frequency of metastasis, depending on the degree of differentiation of the tumor and its types. Although there is no obvious difference in the frequency of MDC metastasis, which is confirmed by some studies. However, full-fledged treatment of breast cancer should comprehensively combine all characteristics of the tumor for a better prognosis and increase the survival of patients, as there are studies that discussed the clinical effectiveness of treatment depending on histological types [16].

Conclusions.

Therefore, different histological types of breast cancer show heterogeneous clinical and pathological characteristics. It was established that the degree of differentiation of breast cancer does not depend on the age of patients. However, the size of the tumor at its detection, germination in lymphatic and blood vessels and metastasis has a correlation with the degree of differentiation of breast cancer. Moderately differentiated breast cancer is a heterogeneous group by histological types of tumors. This group of tumors needs additional research methods to determine the course of treatment and prognosis.

References

1. Karim AM, Kwon JE, Ali T, Jang J, Ullah I, Lee YG, et al. Triple-negative breast cancer: epidemiology, molecular mechanisms, and modern vaccine-based treatment strategies. Biochemical Pharmacology. 2023;212:115545. DOI: 10.1016/j.bcp.2023.115545.
2. Nolan E, Lindeman GJ, Visvader JE. Deciphering breast cancer: from biology to the clinic. Cell. 2023;186(8):1708-1728. DOI: https://doi.org/10. 1016/j.cell.2023.01.040.
3. Starchenko II, Korobchanska AB, Fylenko BM, Roiko NV, Cherniak VV. The relationship of breast cancer, biomineralization disorders and bone metastases: a bibliographical analysis. Problemy ekologiyi ta medytsyny. 2023;27(3-4):41-45. DOI: 10.31718/mep.2023.27.3-4.08.
4. Obeagu EI, Obeagu GU. Breast cancer: A review of risk factors and diagnosis. Medicine. 2024;103(3):e36905. DOI: 10.1097/MD.00000000000 36905.
5. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes & diseases. 2018;5(2):77-106. DOI: 10.1016/j.gendis.2018.05.001.
6. Chornobay AV, Chornobay MA, Myasoyedov SD, Sorokin BV. Polimorfizm geniv, yak odyn z genetychnykh faktoriv ryzyku vynyknennya zloyakisnykh novoutvoren. Visnyk problem biologiyi i medytsyny. 2018;1(143):46-51. DOI: 10.29254/2077-4214-2018-1-2-143-46-51. [In Ukrainian]
7. Kravchenko OV, Bashtan OP, Chornobai AV, Mukovoz OE, Hahal OV. Clinical case: synchronous malignancy: left breast and ovarian cancer associated with hereditary BRCA1: 5382 INS C – mutation. Visnyk problem biologiyi i medytsyny. 2023;2(169):244-251. DOI: 10.29254/2077-4214-2023-2-169-244-251.
8. Babenko VI, Sydorenko MI, Fylenko BM, Royko NV, Novoseltseva TV. Morfologichnyi analiz poyednanogo raku molochnoyi zalozy ta raku yayechnyka. Aktualni problemy suchasnoyi medytsyny: Visnyk Ukrayinskoyi medychnoyi stomatologichnoyi akademiyi. 2019;3(67):113-116. DOI: 10.31718/2077-1096.19.3.113. [in Ukrainian].
9. Vovk OYa, Khorosh MV, Golovanova IA. Modyfikovani faktory, shcho pov'yazani z rakom molochnoyi zalozy. Ukrayina. Zdorov'ya natsiyi. 2023;3(73):20-26. DOI: 10.32782/2077-6594/2023.3/03.
10. Muller K, Jorns JM, Tozbikian G. What's new in breast pathology 2022: WHO 5th edition and biomarker updates. J Pathol Transl Med. 2022;56(3):170-171. DOI: 10.4132/jptm.2022.04.25.
11. Liu Y, He M, Zuo W-J, Hao S, Wang Z-H, Shao Z-M. Tumor Size Still Impacts Prognosis in Breast Cancer With Extensive Nodal Involvement. Frontiers in Oncology. 2021;11:585613. DOI: 10.3389/fonc.2021.585613.
12. Chen W, Qin Y, Wang D, Zhou L, Liu Y, Chen S, et al. CCL20 triggered by chemotherapy hinders the therapeutic efficacy of breast cancer. PLoS Biol. 2018;16:e2005869. DOI: 10.1371/journal.pbio.2005869.
13. Park M, Kim D, Ko S, Kim A, Mo K, Yoon H. Breast Cancer Metastasis: Mechanisms and Therapeutic Implications. International Journal of Molecular Sciences. 2022;23(12):6806. DOI: 10.3390/ijms23126806.
14. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30:1194-220. DOI: 10.1093/ annonc/mdz173.
15. Jayanthi VSPKSA, Das AB, Saxena U. Grade-specific diagnostic and prognostic biomarkers in breast cancer. Genomics. 2020;112(1):388-396. DOI: 10.1016/j.ygeno.2019.03.001.
16. Han Y, Wang J, Xu B. Clinicopathological characteristics and prognosis of breast cancer with special histological types: A surveillance, epidemiology, and end results database analysis. The Breast. 2020;54:114-120. DOI: 10.1016/j.breast.2020.09.006.