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SOCIAL ASPECTS OF EARLY PREVENTION OF BREAST CANCER

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Annotation. As a result of the conducted study, it was found that the majority of female patients do not know how to perform breast self-examination and are unaware of its rules. At the same time, they either fear or are not aware of the existence of specialists such as oncologists or mammologists. Moreover, most respondents - 55.3% reported having breast-related problems. Most women have some understanding of breast cancer, and the majority of respondents indicated that they received information from mass media. 53.5% of those surveyed believe that public information literacy contributes to the early detection of breast cancer. This indicates that the information provided in medical institutions, aimed at the early detection of breast oncological diseases, is insufficient and requires improvement. 76.6% of respondents know who a mammologist is and what diseases they treat. The majority of female patients underwent mammographic screening – 68.7%. However, it should be noted that prevention and informational support remain at an insufficient level, as confirmed by the obtained results. For instance, 55.3% of respondents reported that they received information about mammographic screening from mass media.

Key words: breast cancer, pregnancy-associated breast cancer (PABC), breast cancer during, pregnancy, risk factors, reproductive factors, epidemiology, early diagnosis, metastasis,

Introduction. Breast cancer (BC) diagnosed during pregnancy is referred to in international terminology as Carcinoma mamma, Pregnancy-associated breast cancer (PABC) or breast cancer associated with pregnancy. PABC is diagnosed during an existing pregnancy, during lactation, or within the first year after delivery [1]. PABC occurs in approximately 1 in 3,000 to 1 in 10,000 pregnant women [2].

Among all malignancies diagnosed during pregnancy, breast cancer ranks second in frequency after cervical cancer. One in ten women will develop breast cancer during their lifetime, with a mortality rate accounting for half of the incidence. About 12% of breast cancers are diagnosed between ages 20-34 [3], 25% by age 45, although the predominant age range for diagnosis is 32–38 years. In 7.3% of women under 45, breast cancer is detected during pregnancy or lactation. The average age of pregnant women diagnosed with breast cancer ranges from 33 to 36 years; 14% are under 35 years, 11% under 40 years, and 7.3–10% are 40–45 years old. According to the «Key Performance Indicators of the Obstetric and Gynecological Service in 2012,» in the Russian Federation, breast cancer was diagnosed at a late stage (III–IV) in 36.5% of women in 2008, 36.1% in 2009, 35.8% in 2010, 35.2% in 2011, and 34.7% in 2012 among those registered with a first-time diagnosis [4]. The number of women who died from breast cancer in Russia was 23,008 in 2011 (29.9 per 100,000 female population) and 22,170 in 2012 (28.8 per 100,000). The number of women newly diagnosed with breast cancer was 55,184 in 2011 and 56,154 in 2012.

Methods. The proportion of breast cancers detected during preventive examinations was only 27.1% in 2011 and 28% in 2012. The number of women living with a breast cancer diagnosis for five years or more was 56% in 2008, 56.7% in 2009, 57% in 2010, 57.6% in 2011, and 57.9% in 2012. Among newly registered patients, 9.6% died within one year of diagnosis in 2008, 9.5% in 2009, 8.7% in 2010, 8.7% in 2011, and 8.3% in 2012. According to the “natural history” of breast cancer growth, the actual doubling time of the primary tumor is approximately 90–110 days. Depending on the tumor cell doubling rate, tumors are classified as:

- Rapidly growing tumors with a doubling time of less than 30 days (20% of cases);
- Moderately growing tumors with a doubling time of 90–100 days (60%);

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- Slowly growing tumors with a doubling time greater than 110 days (20%).

Results and Discussion. The potential growth rate averages 6.6–15.3 days (range 0.8–109 days). The “natural history” of tumor growth begins from the “first” cell to 40 volume doublings (10^{13} cells, ~ 1 kg tumor mass), after which the organism dies.

Approximately three-quarters of the tumor’s life occurs in the preclinical stage, which, given current diagnostic capabilities, requires preclinical detection of breast cancer when the tumor contains fewer than 10^9 cells and measures less than 1 cm^3 in volume. When diagnosing breast cancer (BC), it is necessary to consider risk factors associated with diseases of the breast and other organs. For example, proliferative forms of fibrocystic breast disease and benign breast tumors significantly increase the risk of BC [5]. Breast trauma and untreated lactational mastitis also raise the risk. Genital risk factors for BC are known as well [6].

Endometrial and ovarian cancers double the likelihood of developing BC.

Hyperestrogenic states are a proven factor of significantly increased BC risk. Natural menopause before age 45 reduces the risk of BC by half compared to women menstruating after age 54. The lowest incidence of tumors is observed with induced menopause before age 35 [7]. Major known risk factors for BC include:

- Mutations in the BRCA1 and BRCA2 genes;
- Age over 35, especially over 65;
- High breast tissue density in postmenopause;
- Proliferative forms of benign breast dysplasia (atypical hyperplasia, intraductal papilloma);
- High bone mineral density in postmenopause;
- Neuroendocrine disorders and other conditions, including stress accompanied by moderate hyperprolactinemia;
- Induced abortion;
- Obesity, particularly in postmenopause;
- Late first pregnancy (after age 30);
- Lack of breastfeeding or short-term breastfeeding (less than 1 month);
- Early menarche (before age 12);
- Menopause after 55;
- Endocrine anovulatory infertility;
- Nulliparity;
- Menstrual cycle disorders (progesterone deficiency);
- Gynecological diseases (uterine fibroids, endometriosis, endometrial hyperplasia);
- Oncological pathologies (endometrial, ovarian, colorectal cancer);
- Inflammatory breast diseases (mastitis);
- Excessive alcohol consumption.

The role of prolactin in the etiopathogenesis of BC is noteworthy. Lactation is known to protect the breast from oncogenesis. Studies by O.I. Kit et al. (2013) compared sex hormone and prolactin levels in tumor tissue of women of different ages and menstrual statuses with BC [8]. A general trend of hyperprolactinemia, absolute or relative hyperestrogenism, hypoandrogenism, and progesterone deficiency was observed, against varying levels of sex hormone-binding globulin depending on age. It is suggested that a temporary increase in prolactin and estrone, along with decreased progesterone and testosterone, is a pathognomonic factor for BC development, independent of age.

Women with BC are categorized into four clinical-endocrinological forms:

- Adrenal (age 50–59);
- Ovarian (age 36–49);
- Thyroid (age under 35);
- Involutional (age over 60).

Timely diagnosis and correction of endocrine disorders are an integral part of BC prevention.

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BRCA1 and BRCA2 gene mutations, found in 30–70% of women with hereditary BC, result in receptor-negative tumors in 90% of cases. HER-2/neu overexpression is less common than in sporadic BC, and the prognosis is less favorable. Prophylactic bilateral mastectomy reduces BC risk by 90% or more, while bilateral oophorectomy reduces it by 50–70%. Environmental and lifestyle factors also influence BC risk: radiation, geographic factors, diet, and alcohol consumption. BC risks are closely related to a woman's reproductive function. The role of pregnancy in BC risk and outcomes remains debated. Some data suggest pregnancy makes normal breast cells less susceptible to potential oncogenic transformation. Pregnancy induces long-lasting changes in gene expression linked to reduced BC risk, with research focusing on precursor cells.

Protective effects of pregnancy against BC include:

- Full-term pregnancy reduces the time breast tissue predominantly consists of type 1 and 2 lobules, which are most vulnerable to carcinogens.
- Breastfeeding maximizes type 4 lobules, which have the lowest carcinogenic potential.
- Pregnancy and lactation reduce the number of menstrual cycles and ovulations.

Delayed full-term pregnancy after age 20 increases premenopausal BC risk by 5% per year and postmenopausal risk by 3% per year. Each subsequent pregnancy reduces BC risk by 10%.

Other data indicate that pregnancy may increase short-term BC risk by stimulating growth of cells already undergoing early malignant changes (more common in older reproductive-age women). However, early pregnancy (before age 20) provides long-term protection through differentiation of normal mammary stem epithelial cells that might otherwise undergo neoplastic transformation. Pregnancy can promote survival and carcinogenesis of cells in which ErbB2 is activated, leading to early lesions and tumor growth, with associated Wnt1 superexpression.

Certain reproductive factors are confirmed BC risk factors:

- Nulliparity;
- Late full-term pregnancy;
- Spontaneous abortion in the second trimester;
- Preterm birth before 32 weeks;
- Induced abortion.

Each induced abortion increases the risk of future preterm births, while preterm birth before 32 weeks doubles BC risk. Second-trimester spontaneous abortion, preterm birth before 32 weeks, and induced abortion increase BC risk because type 1 and 2 lobules (vulnerable to cancer) do not transform into resistant type 4 lobules. Induced abortion increases BC risk more than spontaneous abortion, with the highest risk 10–14 years after the first induced abortion. High parity (five or more births) increases BC-specific mortality and overall mortality in both premenopause and postmenopause. Natural History and Comprehensive Prevention of Breast Cancer.

According to the «natural history» of tumor growth, the actual growth rate of breast cancer (BC) is 22.9 times lower than it could be, considering the proliferative activity. This phenomenon is explained by the loss of 95.5% of tumor cells due to necrosis, metastasis, or transition of cells into the non-proliferative G0 phase.

Corresponding Member of the Russian Academy of Sciences, Professor Lev Andreevich Ashrafyan, at the XV All-Russian Scientific Forum «Mother and Child» (September 2014, Moscow), in his report «Metastasis of Breast Cancer as Part of Early Carcinogenesis,» emphasized that the main paradigm of therapy for malignant processes involves not only treatment of the primary tumor but also the prevention and management of metastatic disease. This requires interventions aimed at suppressing inflammation, demethylation, and inhibition of angiogenesis. To achieve this, medications and therapies should target:

- Suppression of inflammation;
- Inhibition of angiogenesis;
- Stimulation of apoptosis;

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- Control of tumor stem cell differentiation;
- Demethylation of tumor suppressor genes.

Conclusion. Thus, comprehensive prevention of BC in women before and after pregnancy, as well as the prevention of recurrence and metastasis, requires a multidisciplinary team approach. Obstetricians and gynecologists should conduct regular preventive examinations, implement screening programs, and identify women at high or very high risk of BC. Coordination with endocrinologists, oncologists, psychologists, dietitians, and other specialists is essential.

The chemoprotective properties of certain unique medications appear promising for successful and effective BC prevention.

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