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Causes of Morbidity and Mortality from Breast Cancer

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ABSTRACT
This article is directed to disclosure of influence of possible risk factors of developing of a breast cancer with application of the systematic review and meta-analysis. The data specifying that the high incidence and breast cancer mortality at women are caused by age and racial features are presented in article; reliable risk factors of development of a breast cancer are analyzed; potential factors, influence and which predictive value is discussed are revealed. Materials of article open a complex of the factors promoting decrease in risk of incidence and breast cancer mortality, pay attention to preliminary systematic diagnostics at women, indicating the reasons of wide circulation of a breast cancer.

Keywords: breast cancer, risk factors, reasons, incidence, mortality.

INTRODUCTION

The breast cancer (BC) takes the leading positions among malignant tumors and in the last decade strongly wins first place in structure of oncological incidence and mortality of women in Russia and also is a serious problem of public health care around the world. According to the GLOBOCAN-2008, BC database meets most often and makes 22,9% of total of malignant oncological diseases. Mortality from BC is also in the lead, being 13,7% of total of lethal outcomes of malignant oncological diseases [1]. The peak of incidence of BC in Russia is the share of age group of 55-64 years. Average age of patients with for the first time in life the diagnosed BC in 2012 was 61 years. For the last decade the standardized indicator of incidence of BC has grown by 100 000 population with 38,89 to 46,17, at average annual speed.

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In structure of mortality of women from malignancies the largest specific weight also has BC, being 17,1%. From 2002 to 2012 the standardized mortality indicator from BC on 100 000 population has decreased a little (with 17,2 to 15,94), keeping the leading positions. Average annual rate of a gain of mortality at the same time was-0,67%. Average age of the patients who have died of BC in 2012 was 65,3 years of a gain of 1,8%.

According to GLOBOCAN-2008, in the countries of Europe indicators of occurrence and mortality from BC are higher, than from other forms of malignant new growths, making 28% and 17% of total of malignant diseases, according to [1].

The standardized indicator of incidence of BC in the USA is the highest among other malignant diseases. In 2009 he has made 123,1 cases on 100 000 population. The standardized mortality indicator from BC in the USA is in the second place after the standardized indicator of mortality from cancer of a lung and makes 22,2 cases on 100 000 population.

The reasons of wide circulation of BC are various and connected with existence of various risk factors.

Division of risk factors into two big groups is standard: reliable and potential factors.

Reliable risk factors are called factors of external and internal environment which influence on risk of development of BC is proved. The female, age, the menstrual status, hormonal factors, family and own oncological anamnesis, the ionizing radiation, alcohol, genetic factors concern them.

Potential risk factors of development of BC are factors of external and internal environment, influence and which predictive value is discussed. The excess body weight and obesity (especially in the post-menopausal period), a hypothyroidism, liver diseases, a hypertension, diabetes, medical abortions, insolation belong to this group of risk factors during vigorous physical activity. The role of many of these factors is finally not studied and is actively discussed in scientific literature.

MATERIALS AND METHODS

The statistical materials of the EMBASE, MEDLINE and GLOBOCAN-2008 databases connected with the breast cancer and the reasons causing his emergence and also the results of researches published in references are the cornerstone of the analysis. Have been used given to the state statistical reporting which are the basis for development and assessment of results of nation-wide anticarcinogenic programs that are also applied in the comparative analysis of indicators of the oncological help, in various populations at the international level and among regions of Russia, in scientific developments.

RESULTS

Age Differences

In most European countries, breast cancer incidence rates among women aged over 50 years are about 2 per 1000 per year. Morbidity keeps growing, especially among women aged 50 to 64 years. Also, this disease is the single common cause of death among women aged 40 to 50 years. In opinion of British scientists, age is believed to be one of the leading

risk factors for breast cancer. At the same time, in some countries incidence rates are getting lower during post-menopausal period.

The age when the disease starts, and death from breast cancer significantly depend on geographical characteristics of women's habitual residence. These characteristics differ in the west and east of Eurasia. Environmental factors significantly affect morbidity and mortality, even more than genetics. However, in general, the incidence rate varies about 2 per 1000 among women over 50, about 15 women are at high risk of breast cancer [2]. At the same time, the number of female patients over 65 has increased from 14.5% to 21.3% for the past 30 years. So, different researchers' data demonstrate that in future more women of this age will be vulnerable to breast cancer [3].

A share of young women in the total group of patients can be 5-10%. For example, there were only 107 patients younger than 35 years among 1398 women followed-up for 99 months [4]. During the long-term follow-up period, additional factors affecting morbidity and mortality have been found in younger women comparing to older women. In the proportional hazard model, which included clinical treatment-related variables, and pathological features of the disease, age under 35 years remained the most significant prognostic factor for recurrence, distant recurrence, and overall mortality [4]. Anthropometric parameters (height and weight) affect morbidity and mortality as well. For instance, the 6-18 year follow-up on women aged 30 to 69 years (about 570,000 patients) has shown that tall women at any age groups were at high risk both of morbidity and mortality from breast cancer. Overweight is considered to be a risk factor for morbidity only during postmenopausal period, and for mortality - at all age groups [4]).

Effect of Overweight

Epidemiological data indicate a positive relationship between the body anthropometric parameters (height and weight), and breast cancer in postmenopausal women. However, as the scientists clarify, most researches did not have a sufficient number of observations to study the relationship between mortality from breast cancer and a wide range of anthropometric parameters in postmenopausal women. Prospective clinical study to determine the relationship between body mass index (BMI) and mortality from breast cancer was initiated in the US population in 1982. In 14 years, 2852 cases of malignant breast cancer were revealed among 424,168 postmenopausal women with no cancer history. The study determined that the mortality from breast cancer significantly increases with increasing BMI (OR = 3.08; 95% CI = 2.09 - 4.51 for BMI ≥ 40,0 as compared to a BMI of 18.5 - 20,49). Approximately 30-50% of deaths from breast cancer are confirmed to be in postmenopausal obese women. The mortality from breast cancer also increased with increasing weight. It means, overweight in postmenopausal women is believed to be an important predictor of malignant breast cancer. The obtained results highlight the importance of maintaining a healthy weight throughout a person's life [5].

According to some authors, obesity is believed to be a risk factor for breast cancer, and affects survival of women diagnosed with this disease. However, currently no study has revealed cause-effect relationships regarding the fact that post-diagnosis weight loss improves survival.

In many literary sources, obesity is specified as associated not only with an increased risk of breast cancer, but also with an adverse prognosis with the disease in history. However, the authors hereof point out that there is no sufficient data in the literature on obesity impact on the treatment effectiveness. That's why the scientists have analyzed connection of obesity with the results of treatment with tamoxifen of women with hormone-dependent breast cancer. The group consisted of 3385 women enrolled in the National surgical adjuvant breast and bowel cancer project. The randomized, placebo-controlled clinical trial included the study of risk of breast cancer recurrence, contralateral tumors, new primary cancer, and mortality in this group of patients. These values were evaluated in relation to the BMI using statistical modeling with the adjustment of other prognostic factors [6]. The mean follow-up was about 166 months. As a result, it was revealed that the risk of breast cancer recurrence was the same for women with obesity (BMI> 30.0 kg / m2), and for women with normal body weight (BMI <25.0; OR = 0.98, 95% CI = 0.80 - 1.18). The risk of breast cancer was higher in obese women than in underweight women or in those with normal body weight (OR = 1.58, 95% CI = 1.10 - 2.25) as the risk of other primary malignant tumors (OR = 1.62, 95% CI = 1.16 - 2.24). The risk of death associated with breast cancer was also higher in obese women than in those with normal body weight (OR = 1.31, 95% CI = 1.12 - 1.54), as well as a higher risk of death due to causes not related to breast cancer (OR = 1.49, 95% CI = 1.15 - 1.92). At the same time, tamoxifen reduced the risk of recurrence and death from breast cancer, regardless of BMI. Thus, it is concluded that obesity does not affect the efficacy of treatment with tamoxifen for women with metastases in the axillary lymph nodes from the hormone-dependent breast cancer. However, since obesity is associated with an increased risk of cancer of the other breast or primary cancer, and overall mortality, the researchers have concluded that overweight may have an adverse prognosis for women with breast cancer history [7].

Effect of Physical Activity

Revealing modifiable risk factors that reduce the risk of disease recurrence and improve survival in patients with breast cancer history is considered to be an urgent problem of modern science. The purpose of this study was to examine the effect of physical activity on reducing mortality from breast cancer at an early stage of the disease and after treatment. The sample consisted of 1970 women. The prospective study was conducted to examine behavioral risk factors and their impact on health, which were associated with the work, living conditions and rest. Age-adjusted results showed that higher levels of physical activity were associated with a reduced risk of recurrence and mortality from breast cancer ($p = 0.05$ and 0.07 respectively to the highest levels of physical activity comparing to the lowest). The obtained data suggest that regular physical activity can be useful for patients with breast cancer in terms of reducing the overall mortality [8].

Some scientists state that women over the age of 55 often suffer from breast cancer, which in 77% of cases are fatal. It is also should be considered that postmenopausal women have other age-related health problems, which may affect the treatment prognosis and tactics. The purpose of the study was to examine the burden of comorbidity in patients with breast cancer and to evaluate the disease connection with age, treatment, and early mortality. Thus, 1800 patients were grouped into 3 age categories: 55 to 64 years, 65 to 74 years and

older than 75 years of age. As a result, 73% (in 1312 cases) breast cancer was diagnosed at stage I and II, 10% (188) - stage III and IV, and 17% (300) - unspecified stage. Thus it was revealed that patients in the older age groups were treated under the protocols significantly less ($p < 0,001$), and women aged 70 years and older have significantly less chances to get dissection of axillary lymph nodes defined by regression analysis ($p < 0,001$). Diabetes, renal failure, stroke, liver diseases, history of malignancy other than breast cancer, and smoking were considered to be significant factors of early mortality in the statistical model, which also included the age and breast cancer stages. 263 patients (15%) died during the 30-month follow-up period. However, breast cancer was the main cause of death in 135 cases (51.3%), cardiovascular diseases - in 45 (17.1%) and other types of cancer - in 22 (8.4%). The authors of the study concluded that the decision on patients' treatment is based not only on breast cancer but also on other age-related diseases. Thus, comorbidity in older patients may limit treatment options, and increase the risk of death from causes other than breast cancer. It should be noted that despite high rates of diagnosed breast cancer at the age above 70, the less aggressive treatment strategy was proved to be effective at this age. It has been revealed that axillary lymph nodes require special attention in patients in their eighth and ninth decade of life [9].

Effect of Comorbidities

The researchers conducted the systematic review and meta-analysis to compare the overall survival of cancer patients with diabetes mellitus and without it (Barone, 2008). Diabetes was associated with a high incidence of death (OR = 1.41; 95% CI = 1.28 - 1.55) compared to patients with normal blood sugar levels regardless of the type of cancer (OR = 1.61; 95% CI = 1.46 - 1.78) [10].

This analysis was conducted to determine the impact of comorbid conditions on appearance and mortality from breast cancer at an early stage. Women participated in the randomized study (total 2542 patients) were questioned regarding wide spectrum of their diseases (cardiovascular, diabetes, gall bladder, gastrointestinal tract, arthritis, and osteoporosis), and disorders (high blood pressure, high cholesterol level). The participants in the study have been observed for 7.3 years on the average (range 0.8 - 15.0). The regression analysis was used for assessment. In general, 406 new cases of breast cancer and 242 cases of death were determined. The patients with diabetes mellitus have more than a twofold increase in the risk of breast cancer (OR = 2.1, 95% CI = 1.3 - 3.4) and mortality (OR = 2.5, 95% CI 1.4 – 4.4). Statistically questionable, the large number of comorbidities increased risk of breast cancer. However, compared to patients with no concomitant diseases, the patients with 3 or more co-morbidities have OR = 2.1, 95% CI = 1.3 - 3.3 for mortality. Finally, diabetes is associated with an adverse prognosis for breast cancer. Considering that 85% of deaths have been caused by breast cancer, these findings suggest that multiple comorbidities may reduce the chance of survival and increase the risk of breast cancer [10].

Effect of Depression

In some papers, the authors note that breast cancer patients' depression impact on mortality is still unclear. In this field, in [8] a retrospective study was conducted with subjects with affective and anxiety disorders enrolled into groups. The authors found that a

significantly higher risk of mortality was observed in breast cancer patients suffering from depression [11].

The scientists have examined the depression effect on treatment and survival of older women with breast cancer. To achieve this study purpose, the researchers conducted the retrospective analysis of medical records. 24,696 women aged 67 to 90 years diagnosed with breast cancer between 1993 and 1996 were examined. Total 1841 women of 24,696 (7.5%) were diagnosed with depression within 2 years before breast cancer diagnosis. However, no difference was detected in relation to tumor size or disease stage at diagnosis for women with or without depression. The women with depression were proved to be treated less (59.7% vs. 66.2%, $p < 0.0001$), and this difference did not depend on age, ethnicity, and comorbidity. Besides, women with depression are at a higher risk of death (HR = 1.42; 95% CI = 1.13 - 1.79). Thus, it was concluded that women with depression are at a higher risk of early treatment cessation, and an adverse prognosis regarding survival after breast cancer diagnosis [12].

Effect of External Factors

In the US, a group of scientists set a goal to reveal negative effects of sunlight on the death rate from breast, ovarian, colon, and prostate cancer. The researchers analyzed the death certificates in 24 US states from 1984 to 1995. Multiple regression was used as a model that included age, gender, race, socioeconomic status, physical activity, as well as exposure to sunlight, not only in the residence area, but also in the subjects' professional activity. Thus, the research results demonstrated that the sun's rays cause breast cancer (odds ratio (OR) was 0.82 at 95% confidence interval (CI) - from 0.70 to 0.97) [13].

Epidemiological and laboratory data indicate that vitamin D may play a certain role in reducing the risk of breast cancer. The researchers evaluated the link between the total average sunlight reaching the ground, and mortality from breast cancer. The risk of breast cancer in large areas of the US was inversely proportional to the local sunlight intensity ($r = -0.80$, $p = 0.0001$). The ecological character of the research pointed to the probable indirect connection with dietary and socio-economic factors of the disease [14].

There are data showing that electric and magnetic components of the electromagnetic fields (EMF) may cause cancer. Recent experimental studies confirmed the conclusion that exposure to low-frequency EMF reduces melatonin production, thereby increasing the sensitivity of hormone-dependent cancers, such as breast cancer. Data was collected between 1985 and 1989, the analysis confirmed that women working under increased EMF conditions die more often from breast cancer compared to the control group (OR = 1.38;. 95% CI = 1.04 - 1.82) [15].

Geographic Variation

Relationship of cancer subtypes with menopause, mitotic index, nuclear pleomorphism, and women's survival after diagnosis was determined. Basal breast cancer was confirmed to be common among African-American premenopausal women (39%) as compared to African-American postmenopausal women (14%), and other than African-American women (16%) of all age groups ($p < 0.001$), while prevalence of other breast cancer

subtypes is not varied depending on race or menopause. Additionally, basal tumors had significantly more mutations (44% vs. 15%, p <0,001), a higher mitotic index (OR = 11.0; 95% CI = 5.6 - 21.7), evident nuclear pleomorphism (OR = 9.7, 95% CI = 5.3 - 18.0). The conclusion was made that basal breast cancer was may indicate an adverse prognosis for young African-American women [16].

In the literature, there is certain information regarding the survival of African women with breast cancer compared to European women. The study (Eley, 1994) enrolled 1130 women (612 518 African and European descent) living in Atlanta, New Orleans, and Oakland, aged 20 to 79 years, diagnosed with primary invasive breast cancer. Information on the disease stage, indicated treatment, comorbidities, and demographic factors was obtained from anamnesis, hospital records, and test results. Race and age were found to be leading risk factors for mortality from breast cancer. Thus, racial differences made approximately 75% survival for patients [17].

In 2006, the American Cancer Society assessed causes of morbidity and death from breast cancer. As reported, the incidence of breast cancer increased dramatically among women of different races from 1980 to 1987 (the period of increased mammography screening rates), and then, from 1987 to 2002, continued to grow, but slower. The breast cancer incidence was increased among the African-American women over 50, women of other races under 50 years, but decreased among the African-American women under 50 years. Thus, about 70% of women aged 40 years and older passed annual mammograms, and incidence rates varied by race and ethnicity [18].

Breast cancer is believed to be the most common cancer among American women in different ethnic groups. However, despite currently the impact of women's psychosocial characteristics on morbidity and mortality from breast cancer is being thoroughly studied, there is not enough information in the literature about women of different ethnic groups with the confirmed disease in different socio-economic conditions. In [19] the qualitative research was conducted with survived diagnozed women. Total survived 102 women were interviewed, 24 were African-American, 34 - Asian, 26 - Hispanic, and 18 - Caucasian. The scientists set the goal to reveal important ethnic differences for choozing the treatment type. For example, the Asians and Hispanics were more likely to receive a mastectomy, but the African-American were less likely to receive adjuvant therapy, including radiation or chemotherapy. Among the survived women, most usually had a satisfactory quality of life. The women mostly specified general health state disorders, capacity for work, cancer recurrence or metastasis, and psycho-social problems associated with worry about their children's future, the family illness-related burden, change in body appearance, and libido among their concerns about the changed future life quality. Other problems include poor awareness among patients about breast cancer, and about health care issues such as insurance and the cost of medical services. In addition, women indicated the following problems during treatment: a language barrier with the medical personnel, cultural factors related to their thoughts of disease, their gender roles and family responsibilities (eg, self-sacrifice). These women reported that their spiritual beliefs were critical in overcoming stress. This study extended knowledge of psychosocial problems of breast cancer among women of different ethnic groups, as well as specific cultural influences (eg, food) and socio-

environmental factors on survival, morbidity, and mortality in this group of patients. In general, women of various ethnic minorities were characterized by high morbidity and mortality from breast cancer, and a later diagnosis of this disease [20].

Hereditation

A factor of heredity should be considered as one of the causes of morbidity and mortality from breast cancer, as the authors of the paper (Ford, 1995), show. In certain families combined breast and ovarian cancer, caused by mutations in certain genes, is recorded. The scientists confirmed that the share of cancer cases in the general population, associated with the BRCA1 gene mutation, is about 5.3% in the under 40 year age group, 2.2% in those aged 40 to 49 years, and 1.1% aged 50 to 70 years [21].

Some authors showed the need for hormone replacement therapy in menopausal women with an increased risk of breast cancer. Random sampling was 41,837 women aged 55 to 69 years in Iowa. The rates of morbidity (n = 1085) and overall mortality (n = 2035) in 8 years of follow-up were calculated using the data of the State Health Registry of Iowa and the National Death Index. The scientists reported that 12.2% of women with breast cancer had a burdened family history. It was revealed that women with a burdened family history of breast cancer, who passed hormone replacement therapy, had a lower overall death risk than women not using hormone replacement therapy (OR = 0.67, CI = 0.51 - 0.89). The findings suggest that hormone replacement therapy in women at high risk for breast cancer may be associated with a significant reduction in overall mortality [21].

Breast cancer is the most common cause of death among women worldwide. At the same time, many of the risk factors are associated with estrogen. The risk increases in case of early menarche, late menopause, overweight in postmenopausal women, certain gene mutations, as well as oral contraceptives or alcohol. Giving birth, breastfeeding, and physical activity reduce the risk [22].

Raloxifene hydrochloride is a selective estrogen receptor modulator that has an antiestrogenic effect on the breast and endometrial tissues. In this regard, the researchers set out to determine whether women on raloxifene had the lower the risk of invasive breast cancer. The study enrolled women with osteoporosis to take raloxifene or placebo for 40 months from 1994 to 1998 in 25 countries. This work resulted in 30 breast cancer cases confirmed in 5,129 women who took raloxifene, versus 27 of 2,576 women who took placebo (OR = 0.24; 95% CI = 0.13 - 0.44; $p < 0.001$). Raloxifene was proved to reduce the risk of estrogen receptor-positive breast cancer by 90% (OR = 0.10; 95% CI = 0.04 - 0.24), but not estrogen receptor-negative breast cancer (OR 0.88; 95% CI = 0.26 - 3.0). However, raloxifene increased risk of venous thromboembolism (OR = 3.1; 95% CI = 1.5 - 6.2) but does not increase risk of endometrial cancer (OR = 0.8; 95% CI = 0.2 - 2.7). Thus, the risk of invasive breast cancer in postmenopausal women with osteoporosis was reduced by 76% within 3 years of treatment with raloxifene [23].

The scientists also noted that breast adenocarcinoma is the most common cancer and the second leading cause of death in the United States. About 43,500 women died from breast cancer in 1998. The researchers also say that estrogen plays an important role in breast cancer

pathogenesis. For example, women with high serum estradiol had the highest risk of this disease.

Tamoxifen citrate, which inhibits estrogen in breast tissues, improves survival in women with estrogen receptor-positive breast cancer. The scientists reported that tamoxifen reduced risk of breast cancer by about 50% in women at high risk of the disease because of age (over 60 years), or combination of other risk factors. However, in addition to an increased risk of thromboembolic diseases, tamoxifen increased risk of endometrial cancer [24].

This article presents the latest international descriptive epidemiological data on invasive breast cancer in women, including morbidity, mortality, and survival, as well as information on mammography. Incidence rates were significantly higher in developed countries than in less developed countries (71.7/100,000 and 29.3/100,000, respectively), while the corresponding mortality rates were 17.1/100,000 and 11.8/100,000. The five-year assessment of the relative survival ranged from 12% in some parts of Africa and up to 90% in the US, Australia, and Canada. Improved survival of breast cancer patients in more developed regions of the world during recent decades was associated with mammography screening for population and regular use of adjuvant therapy [25].

Mutations in BRCA1 and BRCA2 genes are known to be in most family cases of breast and ovarian cancer, and often associated with early-onset breast cancer. Mutations in BRCA1 and BRCA2 genes were studied in blood samples of young patients with breast cancer in the UK. Mutations were detected in 15 (5.9%) of 254 (100%) of women with breast cancer diagnosed at the age under 36 years (9 or 3.5% with BRCA1 mutation and 6 or 2.4% - BRCA2) and 15 (4.1%) of 363 (100%) of women diagnosed at the age from 36 to 45 (7 or 1.9% with BRCA1 mutation and 8 or 2.2% - BRCA2). 11% (6 of 55) of patients with first degree relatives with ovarian or breast cancer under 60 years were carriers of mutant genes, compared to 45% (5 of 11) of patients with 2 or more first and second degree relatives. The scientists suggested that carriers of BRCA1 and BRCA2 mutations were 3.1% and 3.0% of breast cancer patients under 50 years, 0.49% and 0.84% of patients with breast cancer above 50 years, and 0.11% and 0.12% of women in the general population. It was concluded that BRCA1 and BRCA2 gene mutations had approximately equal contribution to early-onset breast cancer in the UK and made a certain share of familial risk of this disease [26].

A significant increase in the incidence of breast cancer, benign breast disease, benign skin tumors, and congenital malformations was observed among children of parents with a breast cancer history. The biological mechanism of association between breast cancer and skin tumors can be understood with a deeper genetic study to learn more about the etiology of breast cancer [27].

DISCUSSIONS

The main purpose of this study was to conduct a meta-analysis including recent studies on the issue. Adjusted individual hazard indications in the studies were randomized. 43 women diagnosed with breast cancer between 1963 and 2005 were included into the meta-analysis. The sample in different studies ranged from 100 to 424,168 (on average 1,192). The meta-analysis showed unfavorable survival rates in obese women. However, the survival

rate varied slightly depending on the body mass index evaluation method or severity of fat deposits at the waist and hips. At the same time, significant differences were confirmed in menopause or post-menopause women diagnosed before or after 1995, and depending on chemotherapy or its absence. The authors have concluded that currently it seems unreasonable to classify obesity as an additional burden for women diagnosed with breast cancer. That is why the conclusion is made that further researches should focus upon assessment of other possible risk factors for morbidity and mortality from breast cancer, such as diabetes mellitus or chemotherapy type (drug dose), as well as the change in body weight.

Many scientists believe that excess body weight is associated with an adverse outcome in postmenopausal women with breast cancer. To study this theory, 1360 Australian women with breast cancer aged under 60 have been examined. Obesity is defined by a body mass index ≥30 kg/m^2. It was confirmed that obesity increased with age ($p < 0.001$), and was often associated with increased breast cancer recurrence ($p = 0.02$), mortality in this group of women ($p = 0.06$), larger tumors ($p = 0.002$), and axillary lymph nodes lesions ($p = 0.003$), but not with hormone receptor sensitivity ($p \geq 0,6$) or the reduced first cycle dose of adjuvant chemotherapy ($p = 0.1$). So, obesity was associated with an adverse prognosis for premenopausal and postmenopausal women [28].

A group of the scientists studied the cause-effect relationship between physical activity, diet, obesity, and survival rate after diagnosis with breast cancer. A prospective study was conducted with 1490 women treated at an early stage of the disease between 1991 and 2000. Univariate analysis showed reduced mortality that was hardly associated with consuming more fruits and vegetables, increased physical activity, and normal body mass index. In multivariate Cox model, the combined use of five or more daily servings of fruits and vegetables was associated with a significant indicator of survival (HR = 0.56; 95% CI = 0.31 - 0.98). Approximately 50% reduction in risk associated with a healthy lifestyle was observed in women suffering from obesity or not, despite the fact that fewer obese women were physically active (16% vs. 30%). As a result, a significant protective effect of a healthy lifestyle was revealed necessitating an additional study of the combined effect of diet and physical activity on survival of women with breast cancer.

The authors of the paper (Patterson R.E., 2010) noted that diabetes is strongly associated with mortality from all causes in 6 of 7 studies. A significantly higher mortality risk (OR = 1.49; 95% CI = 1.35 - 1.65) was observed in patients with breast cancer and diabetes, compared to the comparison group without diabetes. Three of the four studies showed that diabetes was associated with a more severe breast cancer stage. Diabetes was also associated with changed treatment of breast cancer and increased toxicity of chemotherapy. Further researches are required to study pathophysiological interactions between diabetes and breast cancer [29].

The analysis of the literature shows big differences in the survival, morbidity, and mortality from breast cancer in women in different countries and regions. Many complex factors underlie these changes, including the population structure (eg, age, race, and ethnicity), lifestyle, environment, socio-economic status, prevalence of risk factors, mammography, disease stage at diagnosis, and access to high-quality care. The scientists point out that further researches are required to understand the causes of breast cancer

morbidity and mortality differences worldwide. The study of this issue would contribute to development of adapted strategies to reduce morbidity in general, and development of care standards for different groups of the population, and reduce the burden of breast cancer.

CONCLUSION

A literary analysis of the issue has demonstrated that age and racial characteristics are considered to be main causes of high morbidity and mortality from breast cancer in women. However, among relevant factors, the scientists also highlight geographic variability, environmental factors (solar radiation, electric and magnetic components of electromagnetic fields), anthropometric parameters (tall and fat), comorbid conditions (several diseases, depression and diabetes), race, breast cancer type, oral contraceptives, hormonal menopause therapy, alcohol consumption, inherited cancer risks. Besides, factors reducing breast cancer risks are highlighted as well, such as birth-giving and breastfeeding, physical activity, various vegetables and fruits, annual mammography. The analysis of the literature has revealed a complex of factors increasing and decreasing risks of morbidity and mortality from breast cancer. The analysis of statistical data and literature has allowed to reveal a complex of reliable and potential risk factors of development of a breast cancer; the factors reducing probability of developing of a breast cancer are analysed.

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