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REVIEW

Epidemiological characteristics of and risk factors for breast cancer in the world

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Aim: Breast cancer is the most common cancer among women and one of the most important causes of death among them. This review aimed to investigate the incidence and mortality rates of breast cancer and to identify the risk factors for breast cancer in the world.

Materials and methods: A search was performed in PubMed, Web of Science, and Scopus databases without any time restrictions. The search keywords included the following terms: breast cancer, risk factors, incidence, and mortality and a combination of these terms. Studies published in English that referred to various aspects of breast cancer including epidemiology and risk factors were included in the study. Overall, 142 articles published in English were included in the study.

Results: Based on the published studies, the incidence rate of breast cancer varies greatly with race and ethnicity and is higher in developed countries. Results of this study show that mortality rate of breast cancer is higher in less developed regions. The findings of this study demonstrated that various risk factors including demographic, reproductive, hormonal, hereditary, breast related, and lifestyle contribute to the incidence of breast cancer.

Conclusion: The results of this study indicated that incidence and mortality rates of breast cancer is rising, so design and implementation of screening programs and the control of risk factors seem essential.

Keywords: breast cancer, risk factor, incidence, mortality, epidemiology

Introduction

Cancer is one of the main causes of mortality worldwide.[1,2] In 2008, 8 million deaths were recorded as a result of malignant diseases, and this figure is estimated to reach 11 million by 2030.[3] Breast cancer is the most common cancer among women and one of the most important causes of death among them.[4] Breast cancer is a multifactorial disease[5] and various factors contribute to its occurrence. Although the disease occurs all over the world, its incidence, mortality, and survival rates vary considerably among different parts of the world, which could be due to many factors such as population structure, lifestyle, genetic factors, and environment.[6] Changes in risk factors have led to an increase in the prevalence of breast cancer, which is increasing every day.[7] Although screening people can reduce the burden of breast cancer, side effects, over-diagnosis, and increased costs are the disadvantages of this method. Classification of women based on risk factors for breast cancer can be effective in improving risk-free methods and designing targeted breast cancer screening programs.[8]

Review articles are one of the main resources for program design and policy making and can provide a clear view of the various aspects of a phenomenon for researchers.[9]

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This review aimed to investigate the prevalence and mortality rate of breast cancer and also to identify the risk factors for breast cancer in the world by combining and summarizing the results of various population-based studies conducted in the world.

Materials and methods

Search method

Both authors performed searches in PubMed, Web of Science, and Scopus databases without any time restrictions. The search keywords included the following terms: breast cancer, risk factors, incidence, and mortality and a combination of these terms. A list of related articles was also searched, and studies published in English that referred to various aspects of breast cancer including epidemiology and risk factors were included in the study. Qualitative studies, studies related to therapeutic and diagnostic aspects, and studies with insufficient focus on the goals of this study were excluded from the present study. Studies were selected based on the review of the article title, abstract, and full text of the articles. In the initial search, 765 articles were obtained from three databases and 54 articles were obtained using manual search. After removing duplicates, the titles and abstracts of 625 articles were reviewed using EndNote software. After the initial screening, 207 articles were included in the study, of which 59 articles were excluded for scientific reasons (editorial: 3, insufficient data: 16, duplicate: 16, qualitative studies: 7, case reports: 4, full text not available: 13). Finally, 148 articles published in English were included in the study.

Results

Types of breast cancer

Based on various factors such as etiology, clinical presentation, molecular characteristics, and response to treatment, breast cancer was divided into different groups.[10] The estrogen receptor (ER), the progesterone receptor (PR), and the HER2 are the most commonly used classification of invasive breast cancer, which is used to provide therapeutic approaches and to predict clinical outcomes.[11] The incidence rate of different hormone receptor-positive breast cancer varies in different regions. Milne et al[12] found that ER-negative breast cancer was correlated with breast cancer risk in *BRCA1* mutation carriers. In a study among women 50 years of age and older, relative to non-Hispanic whites, women of certain ethnic group (African Americans, Native Americans, Filipinos, Chinese, Koreans, Vietnamese, Indians/Pakistanis, Mexicans, South/Central Americans, and Puerto Ricans living in the United States) 1.4- to 3.1-fold more likely to have estrogen receptor-negative/progesterone receptor-negative breast cancer.[13] Yip et al in a study in Malaysia showed that ethnicity and grade were significantly associated with ER positivity rates. They stated that between 1994 and 2008, every 5 years, the proportion of ER+ breast cancers increased by 2%.[14] The results of a study in Southeast Asia showed that Malay and Indian women were more likely to have unfavorable tumor characteristics such as hormonal negative, poorly differentiated tumors, high-grade tumors, and thus poorer survival after breast cancer.[15] In a study by Parise et al,[16] Asian Pacific Islanders had an increased risk of having the ER–/PR–/HER2+ subtype. Another study that was conducted by Yamashita et al[17] showed that ER-positive tumors significantly increased among Japanese women.

Incidence

Breast cancer is the second most common cancer in the world and the most common cancer among women.[4] Lifetime risk of developing breast cancer in every woman in the United States is 12.4% or one in eight women.[18] In 2012, 1.67 million new cases of breast cancer were identified worldwide, accounting for 25% of all cancers.[4] Although cancer exists anywhere in the world, its incidence rate is higher in developed countries, and the incidence rate of breast cancer varies greatly with race and ethnicity.[19] The incidence rate of breast cancer varies among different parts of the world,[20] varying from 27 per 100,000 in Middle Africa and East Asia to 92 per 100,000 in Northern America.[4] The incidence rate of breast cancer is estimated to reach 3.2 million by 2050.[6] With increasing population age in developed countries, the incidence rate of breast cancer among older people is increasing.[6] In 2017, approximately 252,710 new cases of invasive breast cancer and 6,341 cases of breast cancer in situ were diagnosed in the United States.[18] Nearly 24% of all breast cancer cases occur in the Asia-Pacific region, with the highest rates seen in China, Japan, and Indonesia.[21,22] In addition to Japan, the prevalence of breast cancer is increasing among Asian and American women, with Korea accounting for the highest prevalence of breast cancer in 1988–2006 and Southeast Asia in 1988–2013.[23] It was estimated that 277,054 new cases of breast cancer were diagnosed in East Asia in 2012. This figure was 107,545 in Southeast Asia and 223,899 in south-central Asia.[24] Due to better access to screening and

therapeutic programs, the survival rate of breast cancer is increasing, and the 5-year survival rate was 89% between 2005 and 2011.[25] The 1-year survival rate of breast cancer in European countries varies from 94.1% in Scotland to 97.1% in Italy.[26] Because of the delay in seeking diagnosis of and treatment for breast cancer among African women, survival rate is low among them.[27] The incidence (age-standardized rate per 100,000) of breast cancer in different regions of the world is as follows: more developed regions: 74.1, less developed regions: 31.3, Western Europe: 96.0, Northern America: 91.6, Northern Europe: 89.4, Australia/ New Zealand: 85.8, South-Central Asia: 28.2, and Eastern Asia: 27.0.[166]

Mortality

Breast cancer is the fifth leading cause of cancer death in 2012 worldwide, with a record of 324,000 deaths in 2012, and it was the most common cause of death in less developed countries. Also, with 197,000 deaths accounting for 15.4% of all deaths, breast cancer was the second cause of death in developed countries after lung cancer.[4] The mortality rate of breast cancer is estimated to increase by 2020 in many parts of Europe.[28] Although the prevalence of breast cancer is higher in developed countries, higher mortality rates are observed in less developed regions.[29] Furthermore, 89% of deaths from breast cancer in the United States in 2017 occurred in women aged 50 years or older.[18] Due to improved therapeutic and diagnostic methods and the promotion of breast cancer management in the high-income countries, a significant reduction in mortality rate of breast cancer is seen in these countries.[30] The age-standardized mortality rate (ASMR) of breast cancer in the world is 12.9 (31) and Africa has the highest ASMR around the world.[32] The mortality rate varies from six cases per 100,000 people in East Asia to 20 cases per 100,000 people in Western Africa.[4] The mortality-to-incidence rate ratio in North America is 0.16, which indicates a higher survival rate, and in Asia it is between 0.23 and 0.48.[31] Most Asian countries are low- to middle-income countries, and therefore, breast cancer is one of the main causes of mortality in these countries.[33] The mortality (age-standardized rate per 100,000) of breast cancer in different regions of the world is as follows: More developed regions: 14.9, less developed regions: 11.5, Western Europe: 16.2, Northern America: 14.8, Northern Europe: 16.4, Australia/ New Zealand: 14.5, South-Central Asia: 13.5, and Eastern Asia: 6.1.[166]

Risk factors

Table 1 shows factor related to breast cancer.

Demographic factors

Gender

Breast cancer is often a disease that is unique to women and is a rare malignancy in men, accounting for less than 1% of all cases of cancer.[34] Breast cancer occurs more often in older adult males who have had hormonal imbalance, exposure to radiation, and family history of breast cancer, and the most common risk factor for this disease among men is mutation of *BRCA2* gene.[34,35]

Age

After gender, age is the most important known risk factor for breast cancer.[36] The incidence rate of breast cancer increases significantly with age and reaches its peak in the age of menopause and then gradually decreases or remains constant.[31] In a case–control study, the age more than 50 years was associated with the incidence rate of breast cancer.[37] However, breast tumors in younger women appear in larger size, advanced stages, positive lymph nodes, and weaker survival.[38]

Blood group

The results of a review study showed that women with blood group A and Rhesus positive have a higher risk of developing breast cancer, while women with blood group AB and Rhesus negative have a lower risk of developing breast cancer.[39] Although these results were confirmed by a study in 2015,[40] many researchers found no relationship between the blood group and breast cancer.[41,42]

Reproductive factors

The correlation between reproductive factors and breast cancer is related to the effect of ovarian hormones that begin at the puberty age and continues during the monthly cycles, and these hormones are also affected by the number of pregnancies and ultimately decrease in menopause.[36]

Age of menarche

The findings of a case–control study indicated that younger age during menarche increases the risk of breast cancer by two times (OR, 2.83; 95% CI, 1.02–7.86).[36] This result has been confirmed by many other studies.[31,43–45] The result of a large population cohort study of 11,889 women in China

Table 1 Risk factors related to the breast cancer in the world

Risk factors		Protective	Predisposing	Controversial
Demographic	Female gender		✓	
	Age		✓	
	Blood group			✓
Reproductive	Age of menarche			✓
	Late age of menopause		✓	
	Full-term pregnancy	✓		
	Abortion			✓
	Ovulatory menstrual cycle	✓		
	Pregnancy characteristics	✓	✓	
Hormonal	Hormonal contraceptive methods		✓	
	Ovulation-stimulating drugs			✓
	Postmenopausal hormone therapy		✓	
Hereditary	Genetic factors		✓	
	Positive family history of breast cancer		✓	
Breast related	Lesser lactation duration	✓		
	More breast density			✓
	Benign breast disorders		✓	
Lifestyle	Obesity and overweight		✓	
	Alcohol consumption		✓	
	Smoking		✓	
	Coffee			✓
	Diet		✓	
	More physical activity	✓		
	Vitamin D	✓		
	Duration of sleep			✓
Others	Air pollution		✓	
	Night work		✓	
	Socioeconomic status		✓	
	Diabetes		✓	
	Radiation		✓	

showed that younger age during menarche is associated with an increased risk of breast cancer (95% CI, 1.1–3.4).[46] However, in other studies, younger age during menarche was not associated with an increased risk of breast cancer.[47,48] A study in Italy showed no relationship between breast cancer and duration of menstruation cycles.[49]

Age of menopause

The age of menopause over 50 years is associated with an increased risk of breast cancer.[31,44,50] The results of a case–control study also confirmed the association between older age in menopause and the incidence of breast cancer (OR, 2.43; 95% CI, 1.2–4.9).[36]

Full-term pregnancy

Among parous women, the risk of breast cancer decreases with increasing parity.[31,45,51] In a case–control study, older age during the first childbirth was the most important risk factor for breast cancer, with relative risk of more than six times (OR, 6.34; 95% CI, 2.04–27).[36] A study indicated that every childbirth reduces the risk of PR+ and ER+ cancers by up to 10% (RR per birth, 0.89; 95% CI, 0.84–0.94), and women who were older at their first childbirth had a 27% increased risk of developing breast cancer (RR, 1.27; 95% CI, 1.07–1.50).[52] The results of the studies showed that full-term pregnancy is considered as a protective factor.[50,51] The results of a study showed that breast cancer is more likely to occur in nulliparous women than women who have more than three children (OR, 1.98; 95% CI, 1.12–3.49).[53] However, in some studies, multiparity was associated with a reduced risk of developing breast cancer,[44,47] and based on the results of a case–control study, having more than five full-term pregnancies is associated with an increased risk of breast cancer.[37] In a study of African-American women, high parities were associated with an increased risk of developing breast cancer among people younger than 45 years (incidence rate ratio [IRR] for

four or more births, 2.4; 95% CI, 1.1–5.1) and a decreased risk among people older than 45 years (IRR, 0.5; 95% CI, 0.3–0.9).[54] In a prospective cohort study, nulliparity was associated with large tumors (>20 mm; RR, 1.89; 95% CI, 0.91–3.91), high Ki67 levels (RR, 1.95; 95% CI, 0.93–4.10), high cyclin D1 levels (RR, 2.15; 95% CI, 0.88–5.27), grade III (RR, 2.93; 95% CI, 1.29–6.64), and HER2-positive tumors (RR, 3.24; 95% CI, 1.02–10.25).[55]

In addition to full-term pregnancy, early maternal age reduces the risk of developing breast cancer by up to 23%.[44] There is a positive correlation between the age of more than 26 years during the first childbirth and lobular disease (OR, 1.35; 95% CI, 1.03–1.78).[56] Older age at first full-term pregnancy is associated with an increased risk of developing breast cancer.[31,37,44,47] In a case–control study, first full-term pregnancy in women aged 20 years or older is associated with 40%–50% increased risk of breast cancer.[45] Older age at the last childbirth is also associated with an increased risk of developing breast cancer (OR, 2.15; 95% CI, 1.52–3.08),[43] although no significant relationship was found between the breast cancer and the time of last childbirth in the another study.[54]

Abortion

The results of a study showed that higher incidence rate of abortion was associated with an increased risk of developing breast cancer (OR, 6.26; 95% CI, 4.16–9.41).[43] However, this finding was not confirmed in another study. The reanalysis of findings from 53 epidemiologic studies showed that self-induced or natural abortion does not increase the risk of developing breast cancer.[57]

Ovulatory menstrual cycle

The ovulatory menstrual cycle may have a protecting role against breast cancer (OR, 0.44; 95% CI, 0.23–0.81).[53]

Pregnancy characteristics

Pregnancy, especially the first pregnancy, plays an important role in the risk of developing breast cancer. The results of studies showed that the risk of breast cancer is almost doubled in women who give birth to their first child before the 33 weeks of gestation (OR, 2.1; 95% CI, 1.2–3.9).[58,59] In a study, the risk of developing breast cancer increased in multiple births (OR, 1.8; 95% CI, 1.1–3.0).[58] Moreover, the results of this study showed a relationship between placental abruption in the first pregnancy and an increased risk of developing breast cancer (OR, 1.8; 95% CI, 1.1–3.0).[58] The results of various studies indicated the protective role of preeclampsia in breast cancer,[58,60–62] which can be due to decreased levels of estrogen hormone and insulin-like growth factor 1 (IGF-1) and increased levels of IGF-1-binding protein, hCG, and AFP.[58] The result of a case–control study showed an inverse relationship between nausea and vomiting during pregnancy and the risk of developing breast cancer.[62]

Hormonal factors

Contraceptive methods

The role of contraceptive pills in the incident of breast cancer has been addressed in various studies.[63–65] Based on the results of a case–control study, the use of oral contraceptive pill is associated with an increased risk of developing breast cancer (OR, 9.50; 95% CI, 3.38–26.7).[43] This result was confirmed in other studies.[44,49,50] Meanwhile, according to the findings of a study by McDonald and coworkers,[65] which was conducted on 35- to 64-year-old women, current (RR, 1; 95% CI, 0.8–1.3) or previous use (RR, 0.9; 95% CI, 0.8–1) of contraceptive pills was not associated with an increased risk of developing breast cancer. Williams et al[56] showed a relationship between the current use of contraceptives and breast lobular tumors (OR, 1.86; 95% CI, 1.08–3.20). Researchers, regarding the association of medroxyprogesterone acetate with breast cancer, have stated that this correlation may be due to the diagnosis of mammary tumors or the growth of existing mammary tumors.[66] An increased risk of developing breast cancer diminishes 5–10 years after the discontinuation of hormonal contraceptives.[67]

Ovulation-stimulating drugs

The result of a case–control study showed that using ovulation-stimulating medications for more than 6 months increases the risk of developing breast cancer.[68] However, this finding was not confirmed in other studies.[69,70]

Postmenopausal hormone therapy

A reanalysis of 51 epidemiological studies showed that risk of developing breast cancer increases with the hormone replacement therapy (HRT) use (RR, 1.023; 95% CI, 1.011–1.036), and this risk decreases following the discontinuation of HRT use and diminishes after 5 years.[71] Results of a study that examined 1 million women found that the current use of HRT is associated with the increased mortality rate and risk of developing breast cancer (adjusted RR, 1.66; 95% CI, 1.58–1.75), and this risk is higher in those who use estrogen–progesterone combination methods than in those who use other HRT methods (RR, 2.00; 95% CI, 1.88–2.12).[72] These results are consistent with the results of a study that

stated that adding progesterone to HRT treatment significantly increases the risk of developing breast cancer (OR, 1.24; 95% CI, 1.07–1.45).[73] In a cohort study, the researchers emphasized that the selection of progesterone in HRT should be based on the risk of developing breast cancer. They reported that this risk is lower in estrogen–progesterone or estrogen–dydrogesterone methods than other methods.[74] The result of a case–control study showed that the use of HRT in postmenopausal women and in carriers of *BRCA1* mutations does not increase the risk of developing breast cancer.[72]

Hereditary factors

Genetic factors

Although several genetic factors contribute to the incidence of breast cancer, approximately 40% of hereditary breast cancer cases occur due to mutations in the *BRCA1* and *BRCA2* genes inherited through the dominant autosomal method.[75] The results of a study show that 55%–65% of carriers of *BRCA1* mutation and 45% of carriers of *BRCA2* mutation develop breast cancer by the age of 70 years.[76] Based on a prospective cohort study, the risk of cumulative breast cancer by the age 80 years was 72% in the carriers of *BRCA1* mutation (95% CI, 65%–79%), and this amount was 69% in the carriers of *BRCA2* mutation (95% CI, 61%–77%).[77] Changes in human interferon α-2b may be involved in the onset and progression of breast cancer in addition to other risk factors.[78] In a case–control study, matrix metalloproteinase (MMP-2 c-735-T) polymorphisms were associated with an increased risk of developing breast cancer. Furthermore, MMP-2c allele may also increase the risk of developing breast cancer at a younger age by 1.64-fold (OR, 1.64; 95% CI, 1.01–2.7).[79]

Family history of breast cancer

Family history of breast cancer is one of the major risk factors, which has been mentioned in various studies.[36,37,43,80–82] Researchers reported that women with a family history of breast cancer (two or more cases in women younger than 50 years or three or more cases at any age) who are negative in terms of *BRCA* mutations are approximately 11 times more likely to develop breast cancer.[83] The history of early-onset breast cancer in immediate relatives is a risk factor for the occurrence of breast cancer in *BRCA1* and *BRCA2* carriers.[84] Based on the result of a case–control study, the history of breast cancer is associated with a twofold increase in the risk of developing contralateral breast cancer (RR, 2.1; 95% CI, 1.4–3.0).[84] In a hospital-based cohort of 5,359 women, no relationship was found between the family history of breast cancer and the severity and mortality associated with the breast cancer (adjusted proportional OR, 1.00; 95% CI, 0.85–1.17). Accordingly, researchers stated that the clinical management of breast cancer among women with or without family history of breast cancer and knowledge of underlying mutations should not be different.[85] Having a family history of breast cancer may candidate individual for chemoprevention with tamoxifen or intensified breast screening with a magnetic resonance imaging.[83]

Breast-related factors

Lactation

Breast feeding is a protective factor against breast cancer, and many researchers have pointed to the role of lactation in breast cancer prevention.[31,86] Based on the results of various studies, the length of lactation is associated with breast cancer.[43,44,50,87] The protective effect of lactation increases with increasing duration of lactation.[44] The result of a case–control study showed that the combination of two protective factors (two or more childbirth and lactation for more than 13 months) could reduce the risk of developing breast cancer by up to 50%.[88] Furthermore, breastfeeding may be associated with improvements in prognosis and a decreased rate of recurrence (HR, 0.70; 95% CI, 0.53–0.93) and an increased rate of survival among breast cancer patients, although this effect is different in different ER states.[89] The protective effect of breast feeding on breast cancer risk has not been proven in other studies.[90,91]

Breast density

Breast density, which means the amount of total dense tissue in the breast,[87] has been described in numerous studies as an independent risk factor for breast cancer.[80,87] In an observational cohort study, there was no correlation between breast density and breast cancer in women with atypical hyperplasia.[92] Based on the results of a case–control study, breast density increased after initiating estrogen and progesterone administration, showing an increase of 3.4% in the risk of developing breast cancer with every 1% increase in the breast density.[93] Based on the results of a cohort study, breast density was associated with an increase in the risk of ER-positive (HR, 2.13; 95% CI, 1.89–2.40) and ER-negative invasive breast cancer (HR, 1.68; 95% CI, 1.34–2.11), and the rate of this increase decreased with the age.[94] Although the results of a prediction protocol showed a fivefold increase in the risk of developing breast cancer in high breast density patients,[95] the results of a cohort study showed no relationship between breast cancer and breast density.[81]

Benign breast disorders

Cancer is a multifactorial disease, and benign breast diseases are one of the most important risk factors for breast cancer.[5,49,96] The results of a cohort study indicated that benign breast diseases are associated with an increased risk of ER-positive and ER-negative invasive breast cancer, and the rate of this increase is different in different age.[94] However, in another study, atypical hyperplasia may only be seen in 5% of women with fibrocystic mastosis.[97] The results of a case–control study indicated that HRT and breast hyperplasia are associated with an increased risk of developing breast cancer in patients with benign breast disease (OR, 5.56; 95% CI, 2.05–15.06). The risk of breast cancer decreases in postmenopausal women with benign breast disease.[98] The researchers, after conducting another study, concluded that the association between benign breast disorders and breast cancer depends on the histological classification of the disease and family history of breast cancer.[99]

Lifestyle factors

Obesity and overweight

The correlation between obesity and breast cancer has been considered in several studies.[31,80,94,100,101] Obesity is correlated with breast cancer due to higher rates of conversion of androgenic precursors to estrogen through peripheral aromatization in adipose tissue. On the other hand, high levels of insulin and insulin-like factors in response to obesity can stimulate the growth of cancer cells.[102] According to a prospective observational study, among 74,177 women, 17% of ER+/PR+ postmenopausal breast cancer and 14% of postmenopausal breast cancer attributed to the weight gain of more than 5 kg from the age of 18 years.[103] Results of a study showed that prepregnancy obesity is an independent risk factor for long-term malignancies, such as ovarian and breast cancer (adjusted HR, 1.4; 95% CI, 1.1–1.9).[104] Body mass index (BMI) also plays a role in survival of patients and is an independent predictor of overall survival in patients with breast cancer.[105] Results of a study showed that postmenopausal women who were obese (BMI≥30 kg/m^2) at the time of breast cancer diagnosis had a lower disease-free survival (HR, 1.43; 95% CI, 1.11–1.86) and overall survival (HR, 1.56; 95% CI, 1.14–2.14) compared to nonobese women.[106] Researchers of a prospective cohort study reported that obesity mainly affects the elderly.[102] A cohort study also showed a positive correlation between breast cancer and the height.[107]

Alcohol consumption

In various studies, the role of alcohol carcinogens and its correlation with breast cancer has been addressed.[100,108] Results of a European Prospective Investigation into Cancer and Nutrition (EPIC) showed a relationship between alcohol consumption and the hormone receptor-positive and hormone receptor-negative breast tumors. The results of this study showed that time of alcohol consumption can affect the risk of developing breast cancer, and the risk of developing breast cancer is higher among those who consume alcohol before the first full-term pregnancy.[109] In a case–control study, after the old age in the first childbirth, alcohol consumption, with a 4.2-fold increase, was one of the main risk factors for breast cancer.[36] In a population-based case–control study, there was a correlation between alcohol consumption and ER+ invasive lobular carcinoma (OR, 1.25; 95% CI, 0.99–1.58) and ER+ invasive ductal carcinoma.[110] These results were also confirmed in another study.[111]

Smoking

Active smoking (HR, 1.16; 95% CI, 1.00–1.34), especially in postmenopausal women,[112] and prenatal smoking (HR, 1.18; 95% CI, 1.10–1.27 for every increase of 20 pack-years)[113] are associated with an increased risk of developing breast cancer. The result of a study showed that spouses' exposure to passive smoking is a risk factor for developing breast cancer, and in particular, this contributes to the increased risk of ER +/PR+ double-positive breast cancer (adjusted OR, 1.46; 95% CI, 1.05–2.03; P=0.027).[114] According to the results of a study, there is a consistent dose–response relationship between the number of years of smoking before the first childbirth (HR, 1.60; 95% CI, 1.42–1.80) and the risk of developing breast cancer in short-term and long-term smokers, as well as in those who smoke 10 or more cigarettes per day.[115]

Coffee

Overall, the data on coffee consumption and breast cancer risk are controversial. Although different studies did not support the role of coffee in breast cancer risk,[116,117] a case–control study revealed that increase in daily coffee consumption was correlated with significant decrease in ER-negative breast cancer among postmenopausal women.[118] In a study by JK et al,[119] authors found negative association between coffee intake and ER+/PR– breast tumors. Ganmaa et al conducted a cohort study and have not found the relationship between coffee and risk of developing breast cancer. However, they stated that there was a weak inverse association between coffee and postmenopausal breast cancer.[120] On the contrary, Yaghjyan et al[121] stated that drinking coffee is associated with an increased risk of developing breast cancer among people who have used hormone in the past.

Diet

The relationship between diet and nutrition and cancer has been the focus of many researchers and has been addressed in various studies. In a case–control study, there was a relationship between nonvegetarian diet and breast cancer.[36] The result of a case–control study showed that diet containing low polyunsaturated and saturated fatty acids in breast cancer is more important than overall fat intake.[122] The results of another study showed that the risk of developing breast cancer increases with the increase in total consumption of meat (HR, 1.20; 95% CI, 0.86–1.68) and nonprocessed meat (HR, 1.20; 95% CI, 0.86–1.68).[123] The results of a European prospective study on cancer and nutrition showed a significant association between saturated fat consumption and the risk of developing breast cancer (HR, 1.13; 95% CI, 1.00–1.27; *P* for trend, 0.038).[124] However, Harris et al[125] found that diet during adolescence could increase the incidence rate of breast cancer at premenopausal age. The result of a study showed that the distributions of Fe, Cu, and Zn concentrations were higher in malignant tissues than in benign tissues. The researchers pointed out that this may be the cause or outcome of breast cancer.[126]

Physical activity

The results of a prospective cohort study of 74,171 women aged 50–79 years showed that increased physical activity is associated with a reduction in the risk of developing breast cancer in postmenopausal women. In this study, more physical activity was associated with more benefits (RR, 0.86; 95% CI, 0.78–0.95).[127] Researchers in an observational study stated that physical activity after the diagnosis of breast cancer may reduce the risk of death as a result of the disease. They stated that the greatest benefit of exercise was seen among people who had 3–5 hours walking per week at an average speed.[128] Reducing mortality and morbidity of breast cancer in people who exercise have also been confirmed in other studies.[31,129,130]

Vitamin D

According to the results of a study, there is an inverse relationship between the serum 25 OH vitamin D and breast tumor size in patients with breast cancer. Moreover, this study showed an improvement in the outcomes of breast cancer with appropriate status of vitamin D.[131] The result of a case–control study showed that women with vitamin D deficiency have 27% increased risk of developing breast cancer compared to those with normal serum 25 OH vitamin D levels.[132] Researchers have confirmed this conclusion and stated that fourth quartile of 25 OH vitamin D level has three times the risk of developing breast cancer compared to the first quartile.[132] In a cohort study, serum levels above 25 OH vitamin D and regular use of vitamin D supplement were associated with a reduction in the incidence rate of breast cancer after menopause over a 5-year follow-up period.[133] Finally, Shekarriz-Foumani and Khodaie,[134] in a systematic review, found that vitamin D deficiency is common among mammary neoplasms and the risk of developing breast cancer increases by decreasing the level of vitamin D.

Duration of sleep

There is a relationship between sleep duration and breast cancer. Compared to women with normal sleep duration, women with longer sleep duration may be at an increased risk of developing breast cancer. However, in this study, this association was not seen in women with shorter sleep time.[135] Xiao et al[136] stated that short sleep duration is associated with an increased risk of hormone receptor-positive breast cancer. The findings of a retrospective cohort study showed that insomnia is associated with an increased risk of developing breast cancer (adjusted HR, 1.43; 95% CI, 1.10–1.84).[137] Another study showed that different aspects of sleep, such as sleep duration and quality, are associated with an increased risk of aggressive breast tumors, and the severity of this association depends on the race of people.[138] The duration of sleep does not affect the prognosis in people who have been saved from cancer.[139] The result of a prospective cohort study did not show any relationship between sleep and breast cancer.[140]

Other risk factors

Air pollution

The result of a study showed a relationship between air pollution and the incidence rate of breast cancer in postmenopausal European women.[141] Wei et al[142] stated that breast cancer is more common in urban areas and areas with high levels of pollution. The result of 15 cohort studies from nine European countries also reported an association between air pollution and the incidence rate of postmenopausal breast cancer in European women.[143]

Night work

The result of a study showed that overnight working is associated with an increased moderate risk of developing breast cancer, and this connection is stronger in women who have been working for more than 20 years.[144] Exposure to artificial light at night sharply reduces the level of melatonin and is

thought to increase the risk of developing breast cancer.[145] This reduction in melatonin production leads to an increase in the levels of reproductive hormones such as estrogen, which is effective in the development of hormone-sensitive breast tumors.[146] The result of a meta-analysis showed that shift work increases the risk of breast cancer by up to 48%.[147]

Socioeconomic status

One of the issues that have been discussed in more detail in recent studies is the role of socioeconomic status in the incidence rate of breast cancer. In various studies, there was a relationship between high socioeconomic status and breast cancer.[36,148] Breast cancer is higher in women with higher socioeconomic status, which can be due to the direct effects of important risk factors such as paralysis, and older age at the first childbirth and during menopause.[149] In addition, sedentary lifestyle and a high-fat diet in this social class can directly and indirectly affect the menstrual cycle of women.[36] On the one hand, access to care and prevention, diagnosis, and prevention of breast cancer is also higher in these women.[150] The educational level[49] and employment status (OR, 0.32; CI, 0.19–0.56)[53] are among the most important socioeconomic variables that affect the incidence rate of breast cancer. Researchers believe that employed women generally have higher income and are more likely to use health insurance. In addition, the economic situation can contribute to the person's willingness to spend money on medical care.[53] Due to differences in lifestyle, diet, and environmental factors, living in urban areas is associated with an increase in the risk of developing breast cancer.[53] In the low social class, lower levels of vitamin C, retinol and beta carotene, and high level of fat intake can be found, which is associated with changes in levels of estrogen and prolactin hormones in the incidence of breast cancer.[151] Socioeconomic status can significantly alter the outcome of patient in cases of relapse and death. In addition, researcher considers the socioeconomic status as an important indicator of disease-free survival and overall survival.[151] The socioeconomic status is associated with the clinical course[152] and survival rate (7% absolute difference in overall survival, $P<.001$; 4% cancer-specific survival, $P<0.001$).[153]

Diabetes

Diabetes can affect the incidence of breast cancer by interfering with biological mechanisms or through its effects on screening and treatment.[154] The results of the studies show that diabetes is associated with the risk of breast cancer progress among postmenopausal women and those with higher BMI (OR, 4.928; 95% CI, 2.1–11.3).[155] Findings of a meta-analysis revealed that women with diabetes (especially those with type II diabetes) are at 20% increased risk of developing breast cancer.[156] Researchers suggest that in postmenopausal women and in people with BMI of greater than 26 kg/m^2, the levels of blood glucose, insulin, and IGF-1 patterns are associated with an increased risk of developing breast cancer.[157] The use of metformin can improve the overall survival rate in people with breast cancer and type II diabetes.[158] According to EPIC, in addition to endocrine factors, in women with higher levels of IGF-1 and insulin-like growth factor binding protein-3 (IGFBP-3) than normal, the risk of developing breast cancer is significantly increased, and this association is stronger in those whose tumors are detected after the age of 50 years (highest vs lowest quintile OR, 1.38 [95% CI, 1.02–1.86], $P=0.01$, and 1.44 [95% CI, 1.04–1.98], $P=0.01$, respectively).[159] The control of HbA1C below 7% can improve the outcome of women with breast cancer.[160]

Radiation

A large population-based case–control study found that the risk of developing breast cancer in women, who are faced with radiation due to the history of previous cancer treatment (OR, 3.55; 95% CI, 1.47–8.54), screening or tuberculosis (OR, 2.49; 95% CI, 1.82–3.40), or pneumonia monitoring (OR, 2.19; 95% CI, 1.38–3.47), is two to three times higher.[161] On the other hand, those who have been treated with radiation due to childhood cancer and people who are being treated with the whole-lung irradiation are at the highest risk of developing breast cancer. The researchers in this study have pointed to this issue and emphasized that the mortality associated with breast cancer in these individuals is significantly higher (standardized incidence ratio [SIR], 43.6; 95% CI, 27.2–70.3).[162] However, in addition to chest radiations, people who have been treated after surviving a sarcoma (SIR, 5.3; 95% CI, 3.6–7.8) or leukemia (SIR ,4.1; 95% CI, 2.4–6.9) are at higher risk of developing breast cancer at younger age, which can be due to high-dose alkylator and anthracycline chemotherapy.[163]

Conclusion

Cancer imposes a huge burden on people around the world.[164] This study investigated the epidemiological aspects and the risk factors associated with breast cancer in the world. The trace of breast cancer as one of the most common form of cancer and causes of mortality among women is seen all over the world, and the mortality rate of breast cancer is higher in less developed countries. The findings of this study showed

that various factors affect the incidence of breast cancer, of which genetic factors, environmental factors, and lifestyle are the most important ones, and also many factors such as parities, lactation, and exercise play important roles in reducing the risk of this disease.

Disclosure

The authors report no conflicts of interest in this work.

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