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BREAST CANCER AND ITS CAUSES: A COMPREHENSIVE REVIEW OF ETIOLOGY, RISK FACTORS, PATHOGENESIS, PREVENTION, AND PUBLIC HEALTH IMPLICATIONS

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ABSTRACT

Breast cancer is the most frequently diagnosed cancer in women and remains a leading cause of cancer-related death worldwide. Its development is multifactorial, involving a complex interaction of genetic susceptibility, hormonal exposure, reproductive history, environmental influences, and modifiable lifestyle factors.

Hereditary mutations, particularly in BRCA1 and BRCA2, contribute substantially to risk in a smaller proportion of patients, while age, family history, obesity, alcohol intake, physical inactivity, and prolonged exposure to endogenous or exogenous estrogen influence a much larger population. The disease burden continues to increase globally, highlighting the need for early recognition of risk, effective screening strategies, and lifestyle-based prevention.

This review explores the major causes of breast cancer, explains biological mechanisms that underlie carcinogenesis, and discusses preventive and clinical implications. The paper is intended as a detailed academic review suitable for undergraduate, postgraduate, or nursing and medical coursework.

KEYWORDS: Breast cancer; etiology; risk factors; BRCA1; BRCA2; hormones; obesity; alcohol; reproductive factors; prevention.

INTRODUCTION

Breast cancer is a malignant disease that originates from the epithelial cells of the breast, most commonly from the ducts or lobules. It is not a single disease but a group of biologically distinct subtypes with different causes, behaviour's, and outcomes. The burden of breast cancer has increased

steadily across both developed and developing nations, making it one of the most important public health concerns of the 21st century. The causes of breast cancer are best understood as a combination of non-modifiable and modifiable risk factors. Non-modifiable factors include age, sex, family history, inherited gene mutations, and certain reproductive characteristics. [(1)]
Modifiable factors include obesity, alcohol use, inactivity, hormone therapy, and some environmental exposures.
Although no single factor explains every case, the cumulative effect of these influences is central to disease development .This review provides a detailed overview of the causes of breast cancer, including genetic, hormonal, reproductive, lifestyle, and environmental contributors. It also highlights current prevention approaches and the importance of risk-based screening.[(2)]

Epidemiology and burden

Breast cancer is the most commonly diagnosed cancer among women worldwide and remains a major cause of mortality. In 2022, global estimates showed more than 2.3 million new cases, and the burden is projected to rise further in coming decades .
The increasing burden reflects population aging, changes in reproductive patterns, urbanization, obesity, alcohol use, and unequal access to screening and treatment.
The disease affects women more often than men, but male breast cancer also occurs and is important in hereditary syndromes. Most cases are diagnosed after age 50, but younger women can also be affected, especially those with strong family history or inherited mutations.
incidence is generally higher in regions with better screening systems, while mortality is disproportionately higher in low-resource settings due to delayed diagnosis and limited treatment access .
These epidemiologic trends make risk-factor awareness essential not only for clinicians but also for public health planning.[(3)]

Genetic causes

Genetic predisposition is one of the most important causes of breast cancer. Inherited pathogenic variants in BRCA1 and BRCA2 significantly increase lifetime risk and are strongly associated with hereditary breast and ovarian cancer syndromes. These genes normally help repair damaged DNA, so mutations reduce genomic stability and allow malignant transformation to occur.[(4)]
Other high- and moderate-penetrance genes also contribute to inherited susceptibility, including TP53, PALB2, CHEK2, ATM, PTEN, and CDH1. The likelihood of a hereditary component is higher when breast cancer appears at a young age, occurs in multiple close relatives, affects both breasts, or is associated with ovarian cancer or male breast cancer in the family.Although hereditary mutations account for only a minority of cases, they are clinically important because they justify enhanced screening, genetic counselling, and sometimes preventive surgery or chemoprevention.

Family history and inheritance

Family history is a strong indicator of inherited or shared environmental risk. Women with a first-degree relative, such as a mother, sister, or daughter, diagnosed with breast cancer have a higher lifetime risk than women without such history.

The risk increases further when more than one relative is affected, when the cancer occurs at a younger age, or when the family includes both breast and ovarian cancer cases.

Family history may reflect inherited gene variants, but it can also represent shared reproductive, hormonal, dietary, or environmental exposures.

Therefore, the presence of a family history should trigger a more detailed risk assessment rather than being viewed as a simple yes-or-no factor. In clinical practice, family history is often the first clue that a patient may benefit from genetic testing and intensified surveillance.[5]

This makes accurate family history taking a key part of breast cancer prevention.

Hormonal causes

Hormonal exposure plays a central role in breast cancer causation. Breast tissue is highly responsive to estrogen and progesterone, and prolonged exposure to these hormones increases the chance of cellular proliferation and DNA damage.

Early menarche and late menopause lengthen the lifetime window of hormonal stimulation, which is why both are associated with increased risk.[6]

Endogenous hormones are not the only concern. Exogenous hormonal exposures, such as postmenopausal hormone replacement therapy and some oral contraceptive use, can also affect risk depending on formulation, duration, and age at use.

The relationship is especially relevant for postmenopausal women taking combined estrogen-progestin therapy for long periods .

Hormonal singling also influences the biology of estrogen receptor-positive cancers, which represent a major clinical subtype. This connection between causation and tumour biology explains why endocrine therapies are effective in many patients.

Reproductive causes

Reproductive history is strongly linked with breast cancer risk because it affects cumulative hormonal exposure and breast cell maturation. Early age at first menstruation, late age at first full-term pregnancy, nulliparity, and short or absent breastfeeding are associated with increased risk . These patterns are more common in many modern societies where childbearing is delayed and family size is smaller.

Pregnancy induces terminal differentiation in breast tissue, which appears to lower susceptibility to malignant transformation.

Breastfeeding also provides a protective effect by reducing estrogen exposure and promoting structural changes in breast cells. Conversely, women who never become pregnant or who have their first child later in life tend to have higher lifetime risk, especially if other factors such as obesity or family history are present.

Reproductive factors do not cause cancer in isolation, but they are important components of long-term risk profiling.[7]

Lifestyle causes

Lifestyle choices are among the most important modifiable contributors to breast cancer risk. Obesity, especially after menopause, is strongly associated with higher risk because adipose tissue becomes a major source of estrogen production.

Excess body weight is also linked to insulin resistance, inflammation, and altered immune singling, all of which may support tumour development. Physical inactivity is another important risk factor. Regular exercise helps regulate body weight, insulin sensitivity, sex hormones, and inflammatory pathways, which may explain its protective role.

Alcohol consumption has a consistent dose-related association with breast cancer; even moderate intake can slightly raise risk, and heavier intake increases it further.

Smoking is also implicated, particularly with long-term exposure and early initiation, although the association is less consistent than for alcohol or obesity.These modifiable factors are especially important because they provide realistic targets for prevention at both individual and population levels.[8]

Diet and nutrition

Diet is often discussed as a cause of breast cancer, although the evidence is more complex than for obesity or alcohol. A diet high in calories, saturated fat, and ultra-processed foods may contribute indirectly by promoting weight gain and metabolic dysfunction.

In contrast, diets rich in fruits, vegetables, fiber, and whole grains may support general health and lower cancer risk indirectly through weight control and improved metabolic status.

Some reviews have suggested that certain dietary patterns may influence estrogen metabolism and inflammatory pathways, but the evidence is not always consistent across populations.

This means nutrition should be viewed as part of an overall lifestyle pattern rather than as a single isolated cause. Nutrition is particularly relevant in public health because it can be addressed through education, community interventions, and policy.

Overall, diet matters most when it contributes to obesity, poor metabolic health, or excess alcohol intake.

Environmental and occupational causes

Environmental factors may contribute to breast cancer, although the evidence is often less direct and more difficult to quantify. Prior radiation exposure to the chest, especially during childhood or early adulthood, is a well-established risk factor. This is particularly relevant for women treated with chest radiation for lymphoma or other cancers at a young age.

Other suspected environmental contributors include endocrine-disrupting chemicals, night-shift work, and chronic exposure to air pollution or industrial pollutants, though the strength of evidence varies. Night-shift work may interfere with melatonin production and circadian rhythm, potentially influencing estrogen singling and cell-cycle regulation.

Occupational exposures remain an area of ongoing research, and current evidence supports caution but not overstatement .Environmental causes likely interact with genetic vulnerability and lifestyle behaviour's rather than acting alone.[9]

Biological mechanisms

The pathogenesis of breast cancer involves accumulation of genetic and epigenetic damage that disrupts normal cell-cycle regulation, DNA repair, apoptosis, and tissue architecture. Carcinogenesis often begins with mutations in critical genes followed by clonal expansion of abnormal cells.

Over time, these cells acquire additional changes that allow invasion, metastasis, and treatment resistance.

Breast cancers are biologically heterogeneous. Hormone receptor-positive tumours often develop in the setting of cumulative estrogen exposure, HER2-positive cancers involve receptor overexpression and aggressive proliferation, and triple-negative cancers often show stronger links with hereditary mutations and younger age at diagnosis. This heterogeneity explains why a single causal pathway cannot explain all breast cancers.

Understanding molecular mechanisms is essential because risk factors often influence specific biologic pathways, which in turn affects treatment response.[10]

Risk assessment

Risk assessment combines personal, reproductive, family, and genetic information to identify women who may benefit from enhanced surveillance or prevention. Important risk markers include age, early menarche, late menopause, nulliparity, obesity, alcohol use, prior radiation, benign breast disease, family history, and known genetic mutations.

Risk models can help estimate lifetime probability of developing breast cancer and guide decisions about mammography, MRI screening, genetic counselling, and preventive therapy. Women at high risk may require earlier and more frequent screening than the general population.

Risk assessment is especially valuable because many women are unaware that their family history or reproductive history may place them at elevated risk. In practice, this approach supports personalized prevention rather than a one-size-fits-all model.[11]

Screening and early detection

Screening does not prevent breast cancer, but it reduces mortality by finding disease at an earlier and more treatable stage. Mammography remains the cornerstone of population screening, while MRI may be added for high-risk individuals such as BRCA mutation carriers. Earlier diagnosis is associated with improved survival and less extensive treatment.

Awareness of warning signs is also important. A new lump, nipple discharge, skin dimpling, breast asymmetry, or changes in skin texture should be evaluated promptly. Screening access remains uneven across countries, which contributes to late-stage presentation in many regions. Public education on screening is therefore a major part of reducing breast cancer burden.[12]

Prevention strategies

Prevention focuses on lowering modifiable risk and identifying high-risk individuals early. Maintaining a healthy body weight, exercising regularly, limiting alcohol, avoiding unnecessary hormone therapy, and breastfeeding when possible are widely recommended strategies. These measures do not eliminate risk but can reduce it meaningfully.

For women with strong family history or pathogenic mutations, prevention may also include genetic counselling, enhanced imaging, chemoprevention, or risk-reducing surgery.

Prevention must be tailored to the individual because the balance of benefits and harms varies by age, mutation status, and personal preference. At the population level, prevention is most effective when combined with education, access to screening, and timely treatment.[13]

Public health importance

Breast cancer is not only a medical issue but also a public health challenge. Rising incidence and uneven survival across regions show the need for better prevention, early detection, and equitable treatment access.

Public health programs should address obesity, alcohol use, physical inactivity, and delayed diagnosis while also supporting family-history-based risk assessment. Countries with limited resources often face delayed detection because screening programs are less available and awareness is lower.

In such settings, simple interventions such as community education, primary care training, and referral pathways can improve outcomes significantly. The global response to breast cancer must therefore combine clinical care with prevention policy. A strong public health strategy can reduce both mortality and long-term healthcare costs.[14]

CONCLUSION

Breast cancer develops through a complex interaction of inherited, hormonal, reproductive, lifestyle, and environmental factors. Some causes, such as BRCA mutations and radiation exposure, are strongly established, while others, such as diet and occupational exposures, are less direct but still relevant. Because many important risk factors are modifiable or identifiable early, prevention and screening remain central to reducing disease burden.

A better understanding of breast cancer causes supports personalized risk assessment, targeted prevention, and earlier diagnosis. Continued research, public awareness, and equitable access to care are essential for reducing the global impact of this disease.(15)

REFERENCES

1. Centre's for Disease Control and Prevention. Breast cancer risk factors [Internet]. Atlanta: CDC; 2025 [cited 2026 May 23]. Available from: https://www.cdc.gov/breast-cancer/risk-factors/index.html
2. Fakhri N, Chad MA, Lahkim M, Houari A, Dehbi H, Belmouden A, et al. Risk factors for breast cancer in women: an update review. Med Oncol. 2022;39(12):197.
3. National Cancer Institute. Breast cancer [Internet]. Bethesda (MD): NCI; 2025 [cited 2026 May 23]. Available from: https://www.cancer.gov/types/breast
4. World Health Organization. Breast cancer [Internet]. Geneva: WHO; 2026 [cited 2026 May 23]. Available from: https://www.who.int/news-room/fact-sheets/detail/breast-cancer
5. International Agency for Research on Cancer. Breast cancer [Internet]. Lyon: IARC; 2026 [cited 2026 May 23]. Available from: https://www.iarc.who.int/cancer-type/breast-cancer/
6. National Cancer Institute. Treatment for breast cancer [Internet]. Bethesda (MD): NCI; 2025 [cited 2026 May 23]. Available from: https://www.cancer.gov/types/breast/treatment
7. Zhang Y, et al. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies: an updated review. Front Oncol. 2021;11:1-19.
8. Fakhri N, Chad MA, Lahkim M, Houari A, Dehbi H, Belmouden A, et al. Risk factors for breast cancer in women: an update review. Med Oncol. 2022;39(12):197.
9. Alqahtani A, et al. Breast cancer: a review of risk factors and diagnosis. 2024.
10. Jayant B, et al. Comprehensive review of breast cancer risk factors, diagnosis, screening, and treatment methods. 2024.
11. Global patterns and trends in breast cancer incidence and mortality across 185 countries. Nat Med. 2025;31:1-10.
12. International Agency for Research on Cancer. Breast cancer cases and deaths are projected to rise globally [Internet]. Lyon: IARC; 2025 [cited 2026 May 23]. Available from: https://www.iarc.who.int/news-events/breast-cancer-cases-and-deaths-are-projected-to-rise-globally/

13. Modifiable risk factors for breast cancer: insights from systematic review. J Public Health Nurs. 2024.
14. The etiology of breast cancer. PubMed. 2022.
15. Causes and risk factors of breast cancer, what do we know for sure? Cancers (Basel). 2024;16(8):1583.