

Factors Affecting the Development of Breast Cancer in Men: A Review

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Abstract: *Breast cancer is a malignant tumor that begins with breast cells and may grow to invade the surrounding tissues .This disease is not limited to women, as the male's breast tissue may have precancerous changes. The factors leading to precancerous changes are similar in Both sexes .Men are also prone to breast cancer, but few men disclose to people that they have this disease embarrassing because it is common that breast cancer is limited to women only. Male breast cancer(MBC) is a rare type of cancer that forms in the breast tissue of men, breast cancer affects more elderly men, although it may occur at any age, and men who have been diagnosed with breast cancer at an early stage have a good chance of being cured. The causes of breast cancer in men may not be entirely clear, However, it appears that there are men who are more likely to develop breast cancer than other men.Breast cancer is like other types of cancer, so there must be factors and causes that lead to its appearance in both sexes, and some of them may be unknown, but there are a number of genetic, environmental and other factors that increase the risk of developing this disease, we will address them here*

Keywords: *Breast Cancer in Men, Factors*

1. Cancer

Cancer is defined as the increase in the growth of abnormal cells in any part of the body, these cells are known as malignant cells or cancer cells, and these cells are also able to move to normal body tissues. The name of the disease is cancer in a tissue through the name of the same tissue that witnesses this type From the growth of these cancer cells, for example lung cancer,Prostate cancer and breast cancer(1).

2. What is breast cancer?

It is a cancer that forms in the breast tissue, in which the malignant and cancerous cells grow abnormally in the breast tissue, and it is the most common cancer in women that may cause death,It occurs in both sexes, but its occurrence in men may be rare, and either occurs in the ducts through which the milk is transported to the nipple or the lobules in which the milk is manufactured(2).Figure1 shows the anatomy of male breast tissue.

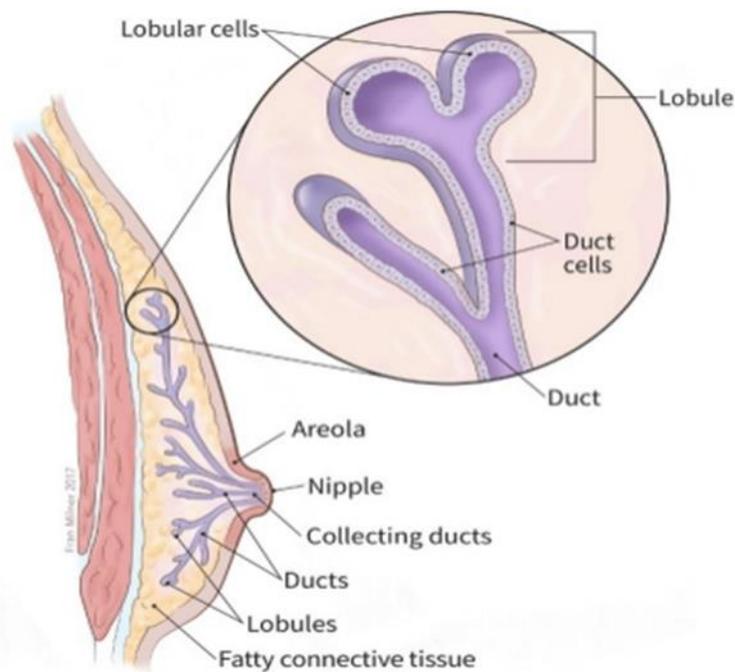


Fig. 1: anatomy of Breast tissue in men(3)

3. Do men get breast cancer?

When we hear about breast cancer, women immediately come to mind, but hey, men are also susceptible to breast cancer, but few men reveal to people that they have this disease embarrassing because it is common that breast cancer is limited to women only, this is not true, but there are statistics of the American Cancer Society (American Cancer Society) For the year 2019, about 2,670 men were diagnosed with breast cancer and about 500 died. It is true that breast cancer in men is very rare, but the mortality rate from it is higher compared to women due to late diagnosis and lack of awareness of it, as is the case with breast cancer in women(4).

Male breast cancer (MBC) is a rare type of cancer that forms in the breast tissue of men(5).

3.1. Symptoms of breast cancer in men

The disease ranges in symptoms from a mild tumor to a node to a malignant tumor, as the stages of the disease follow the following rates: the first stage 37%, the second stage 21%, the third stage 33% and the fourth stage 9%(6).

The most common symptoms are the presence of a tangible, painless lump, sore skin, and shrinkage of the nipple in addition to its secretions in up to 75% of cases, as in women, and because the tissues are smaller in the breast of men, the nipple often has a role in the early stages of the disease, as the breast may be affected male left more than the right breast(7).

3.2. Signs and symptoms of breast cancer in men include:-

- A painless lump or an increase in thickness of breast tissue-
- Changes in the skin of the breast, such as pitting, wrinkling, redness or peeling
- Changes in your nipples, such as redness or scaling, or a nipple orientation inward-
- Discharge from the nipples(8).



Fig. 2:Breast cancer in men(7)

4. What are the causes of breast cancer in men?

The growth of normal body cells naturally leads to cancer, although some causes of cancer are almost unknown, but there may be cancer triggers related to the environment or lifestyle, and the genetic makeup may have an effective effect on the events of the disease, as it may Cancer is caused by a combination of these factors(1).The cause of male breast cancer is not clear, doctors know that male breast cancer occurs when some breast cells divide faster than healthy cells ,the accumulating cells form a tumor that may spread (metastasize) to neighboring tissues, lymph nodes, or other parts of the body(9).

Breast cancer is rare in men, as it constitutes 0.5-1% of all breast cancer patients, and the reason for the decrease in the incidence rate in males is the relatively small amount of breast tissue compared to women in addition to the difference in the hormonal environment,The incidence of infection is similar in both sexes(10).Most of the causes of infection in males are related to either an increase in the level of the hormone estrogen or a defect in the testicle(11).

1-Age and The elderly: Age is one of the important factors that contribute to the occurrence of breast cancer ,breast cancer affects more men than the elderly, although it may occur at any age (5).The risk of this disease increases with increasing age, It is often detected in men at the age of 60 years (12).Studies have shown that the highest incidence of breast cancer in males is between the ages of 52-71 during the years 1973-2000, and the maximum incidence of the disease was at the age of 71 years(13).

2-Genetic reasons: Which include:-

A-Family history of breast cancer: As is the case in women ,the risk of contracting the disease increases if one of the relatives (blood relatives) suffers from breast cancer, as it was found that one out of every five cases of this disease had a relative of a male or female with this disease(14).And studies have shown that approximately 15-20% of breast cancer cases in men are due to their positive family history of this disease(15).

B- Klinefelter's syndrome: Several studies have shown men with this syndrome they are at higher risk of breast cancer than normal men, and this genetic syndrome occurs when a male is born with more than one copy of the X chromosome. Klinefelter's syndrome causes abnormal growth of the testicles, and as a result these men

secrete lower levels of male hormones (androgens) and more levels of hormones Femininity (estrogen)(14,16). Where studies have Klinefelter's shown that the risk of breast cancer increases by 20-50 times in males with syndrome, and their mortality is similar to that of females(17).

C-Genetic predisposition: Various studies have proven that men have a mutation in the gene(BRCA2) are more susceptible to this disease, as well as the occurrence of the mutation in BRCA1,this gene may lead to breast cancer in men with lower levels of the first gene. The risk of developing the disease increases in BRCA2 males by 6% over their lifetime, compared to 0.1% in normal males(18).Also, mutations in the genes (CHEK2) and (PTEN) can lead to some types of breast cancer in men(14).

3-Endocrine factors: Which include:-

A-Exposure to Estrogen: The imbalance that occurs in the level of the estrogen / testosterone balance in the body as a result of the ingestion of exogenous estrogen by transgender people and when taking estrogen-related medications, such as use hormone therapy for prostate cancer, The risk of developing breast cancer increases (16).

B-Liver disease: The liver plays an important role in the metabolism of the sex hormone through formation associated proteins that are responsible for transporting these hormones in the blood, Liver diseases such as Cirrhosis have high hormone level estrogen, which increases the risk of breast cancer(14).

Liver disease for benign breast growth (gynecomastia),However, it has been shown that there is no significant relationship between breast cancer and male gynecomastia(11).

C- Obesity: Studies have shown that obesity increases the risk of breast cancer for women and men alike, as fat cells in the body convert male hormones (androgens) into female hormones (estrogens), and this indicates the presence of high levels of estrogen in the bodies of obese men(14).

D-And other reasons which are related with- Endocrine factors: The risk of breast cancer in men increases by about twelve times with increased testicular dysfunction as a result of congenital inguinal hernia, orchietomy, infertility, orchitis and mumps that affects males in adulthood(19).The risk of developing breast cancer is also increased in patients who suffer from excessive prolactin secretion due to pituitary tumors(20).

4-Radiation exposure: Exposure to radiation increases the incidence of breast cancer for both sexes(21)As the few times the chest X-ray is not harmful, the more harmful it increases with the exposure to it(22).A man who has previously been exposed to radiation in the chest area, for example, treating cancer in the chest area, such as lymphoma, has a higher risk of developing breast cancer(14).Also to use high doses of radiation therapy as a way to treat gynecomastia in men increases the chance of breast cancer by about seven times(23).Therefore, many health institutions are still using radiotherapy and very low cost to treat this problem in males, but the danger lies in long-term exposure to this type of treatment(24).It also increased the risk of breast cancer by about eight times among the 45,880 male atomic bomb survivors, depending on the extent of exposure(25).

5-Alcohol consumption: Abuse increases the risk of many types of cancer and is the third most important risk factor for cancer(3).Excessive consumption of alcoholic drinks negatively affects and harms the health of the liver and thus increases the risk of breast cancer in men (12,14), as we have shown above.A European study of a group of centers on 74 cases of breast cancer and 1,432 natural or controlled cases of the population showed that there is a strong relationship between alcohol consumption and the risk of breast cancer,the risk of breast cancer increases by 16% for every 10 grams of alcohol a day(26).

6-Occupation: That the working environment of men has a great influence in raising the degree of disease or not, for example men who work in environments with high temperatures are more likely to develop breast cancer than others, such as blast furnaces, rolling mills and steel works,There are also some occupations that increase the risk of contracting the disease, such as working in soap factories or perfumes, or being exposed to oil emissions or exhaust fumes(27).Where the vapors of these polycyclic aromatic hydrocarbons (PAH), in the exhaust emissions are the causes of carcinogenicity(11).The risk of exposure to electromagnetic fields has also been proven, even to a limited extent(28).

Table(1) shows the risk factors & ratios for developing breast cancer in men(11).

Table I: Effect of risk factors on developing breast cancer in men.

Risk Factors	Feature	Relative risk
1-Lifestyle Alcohol Obesity Gynecomastia	2	
	Higher economic status	1.8
2.5 2-Genetic 50-60 Klinefelter's syndrome	Family history 20-50	BRCA2
3-Endocrine Bilateral orchiectomy	Undescended test Mumps aged >20 Liver damage	12 12 4
4-Occupation High temperatures	2.5 exhaust emissions	2
5-Radiation exposure electromagnetic fields	Chest wall radiotherapy	7

5. How does a man protect himself from getting this type of cancer?

Most cases of breast cancer in men are unknown to the cause, so there is no specific way to prevent this disease, but there are some healthy practices that will reduce the risk of infection if they are followed:(3).

1-Maintaining a healthy weight: The risk of obesity is linked to the risk of developing many types of cancer, including breast cancer, for men and women alike, so the American Cancer Society recommends maintaining a healthy weight and avoiding habits that increase weight and obesity and work on a balance between food and physical activity(14).

2-Role of food in the prevention of cancer: Adhering to a diet rich in vegetables and fruits helps prevent types of cancer in general, as it has been shown that vegetables such as garlic, onions and leeks are of great benefit in preventing cancer, being rich in cancer-preventing preventive elements as well as containing vitamins C, D, E, and dietary fibers(1).

3-Avoid or limit alcohol: It is known that alcohol abuse increases the risk of developing types of cancer, including breast cancer, as we mentioned earlier, even a small amount of it is not without risk as it is the third most important risk factor for cancer. Drink more than two alcoholic drinks a day(14).

4-Be physically active: Several studies have shown that the practice of vigorous or moderate physical activity greatly reduces the risk of breast cancer for females and males, as well as the case for other types of cancer, Therefore, the American Cancer Society urges adult males and females to engage in physical activity and get a minimum of 150-300 minutes of moderate activity or 150 minutes of vigorous physical activity per week, and exceeding the maximum of 300 minutes is ideal(14).

6. Diagnosing of breast cancer in men

Male breast cancer is diagnosed in advanced stages of the disease, unlike women, where more than 40% of sick men are in the third or fourth stage of the disease when they visit the doctor, and the lack of breast tissue in males may lead to an early stage of injury to the chest wall of the disease(29).

The doctor may run some diagnostic tests and procedures, such as:-

1-Clinical breast examination: The doctor uses his fingertips to examine the breast and the surrounding area for any nodes or other changes. The doctor examines the size and texture of the patient's nodes, and their position on the skin and muscles(9).

2-Mammography (MG): Despite the small size of the male breast, it is possible to perform a mammogram, which will enhance the clinical examination (30).

3-Ultrasonography (USG): Using an ultrasound (ultrasound transducer), which uses sound waves to form images(10).

4-Biopsy taking a sample of breast cells for testing (biopsy): Biopsy is the only sure way to confirm a breast cancer diagnosis. When a biopsy is taken, your doctor uses a dedicated needle, guided by X-rays or other imaging device, to take a sample of tissue from the affected area ,The biopsies taken are sent to the laboratory for analysis, where experts can determine whether these cells are cancerous or not,The biopsy is also analyzed to determine the type of cancer cells in the breast, the stage of the cancer, and whether these cancer cells possess hormonal receptors or any other receptors that may affect the treatment options(9).

7. Treatment of breast cancer in men

Early detection and prompt treatment is one of the most important strategies in reducing and reducing the mortality rate from breast cancer (14). Men diagnosed with breast cancer at an early stage have a good chance of a cure (8).

Most men consider the issue of early detection that is a problem for them, as many of them may not notice the emergence or presence of lumps in the breast area, or their visit to the doctor may only be when the lumps develop and become larger, and the reason for the increase in the percentage of deaths from this disease in males is due to a few awareness and failure to diagnose the disease early, unlike women, the diagnosis is often at advanced stages (10). Treatment usually includes surgery to remove breast tissue, He may recommend other treatments, such as chemotherapy, radiation therapy (4). To determine treatment options, the doctor takes into account the patient's stage of cancer and general health, Treatment for male breast cancer often involves surgery and may include other treatments as well, They can be explained below :-

1-Surgery: aims to remove the tumor and the tissues surrounding the breast. Actions on me include:

A-Removal of all breast tissue (mastectomy):- The surgeon removes all breast tissue, including the nipple and brown areola.

B-Removing a few lymph nodes for testing (sentinel lymph node biopsy):- The doctor identifies the lymph nodes that are the first place for possible cancer cells to spread. These few lymph nodes are removed and analyzed. If cancer cells are not detected, there is a high chance that breast cancer has not spread. If detected, lymph node removal is added to the test(9).

2-Radiation therapy: For radiation therapy usedHigh-energy beams,such as X-raysand protons, to kill cancer cells. In cases of breast cancer in men, radiation therapy can be used after surgery to get rid of any cancer

cells remaining in the breast, chest muscles, or armpits, In radiation therapy, radiation is emitted from a giant device that moves around the body, focusing the radiation energy on specific areas of the chest(10).

3-Hormonal therapy: Most men with breast cancer have tumors that are sensitive to hormones. A doctor may recommend hormonal therapy if the cancer is hormone-positive, Hormonal treatment for male breast cancer often includes tamoxifen, and the effectiveness of other hormonal therapy drugs used in breast cancer for women has not been proven when used in men(11).

4-Chemical treatment: For chemical processing we use drugs to kill cancer cells, these drugs may be administered by injection into a vein in the arm, or in the form of pills, or both. The doctor may recommend chemotherapy after the surgery to eliminate any cancer cells that have spread outside the breast, chemotherapy may be an option for men with advanced breast cancer(10).

References

- [1] Kumari M.(2020).Nutrition in cancer.*ResearchGate* GmbH.
- [2] (ESMO)European Society for Medical Oncology(2018)Breast Cancer: Guidefor Patients, Via Ginevra 4, Lugano 6900, Switzerland.
- [3] American Cancer Society.(2020) Cancer Facts & Figures 2020. Atlanta., Ga:American Cancer Society.
- [4] <https://annabaa.org/arabic/authorsarticles/249188>.
- [5] <https://www.albayan.ae/health/articles-studies/2017-12-03-1.3119061>.
- [6] Ribeiro GG., Swindell R., Harris M., Baerjee S., Cramer A.(1996). A review of the management of the male breast carcinoma based on an analysis of 420 treated cases. *Breast* ;5:141–146.
[https://doi.org/10.1016/S0960-9776\(96\)90058-2](https://doi.org/10.1016/S0960-9776(96)90058-2)
- [7] <https://www.mayoclinic.org/ar/diseases-conditions/male-breast-cancer/symptoms-causes/syc-20374740>, Mayo Clinic Foundation for Medical Education and Research. all rights are reserved 1998-2020.Mayo Foundation for Medical Education and Research (MFMER).
- [8] American Cancer Society. (2018). Signs and Symptoms of Breast Cancer in Men.<https://www.cancer.org/cancer/breast-cancer-in-men/detection-diagnosis-staging/signs-symptoms.html>.
- [9] <https://www.mayoclinic.org/ar/diseases-conditions/male-breast-cancer/diagnosis-treatment/drc-20374745>.
- [10] Yalaza, M.; Inan, A. and Bozer, M.(2016)Male Breast Cancer.*Journal of Breast Health*, v.12(1):1-8.
<https://doi.org/10.5152/tjbh.2015.2711>
- [11] Fentiman, J.S.(2009). Male breast cancer: A review. *Ecancer*, 3:140.
<https://doi.org/10.3332/ecancer.2009.140>
- [12] Jafari M., Olfatbakhsh A. and Rezaei-Kalantari K.(2017). Male breast cancer. A review of risk factors and clinical and radiological features., *Multidisciplina.Cancer Investigation*, 1:1-6
- [13] Crew KD., Neugut AI., Wang X., Jacobson JS., Grann VR., Raptis G., Hershman DL.(2007). Racial disparities in treatment and survival of male breast cancer. *J.Clin. Oncol.*;25:1089–1098.
<https://doi.org/10.1200/JCO.2006.09.1710>
- [14] American Cancer Society. (2018). Risk factor of breast cancer in men. <https://www.cancer.org/cancer/breast-cancer-in-men/causes-risks-prevention/prevention.html>.
- [15] Basham VM, Lipscombe JM, Ward JM et al (2002) BRCA1 and BRCA2 mutations in a population-based study of male breast cancer *Breast Cancer.Res.*, R2.1:4 . .
<https://doi.org/10.1186/bcr419>

- [16] Cutuli B., Lacroze M., Dilhuydy JM., Velten M., De Lafontan B., Marchal C., Resbeut M., Graic Y., Campana F., Moncho-Bernier V.(1995). Male breast cancer: results of the treatments and prognostic factors in 397 cases. *Eur. J. Cancer*;31A:1960–1964.
[https://doi.org/10.1016/0959-8049\(95\)00366-5](https://doi.org/10.1016/0959-8049(95)00366-5)
- [17] Price WH, Clayton JF, Wilson J, Collyer S and De Mey R (1985). Causes of death in X chromatin positive males (Klinefelter’s syndrome) *J.Epidemiol Community Health* 39 330–6.
<https://doi.org/10.1136/jech.39.4.330>
- [18] Friedman LS, Gayther SA, Kurosaki T et al (1997). Mutation analysis of BRCA1 and BRCA2 mutations in a male breast cancer population *Am. J. Hum. Genet.* 60 313–9.
- [19] Thomas DB, Jimenez LM, McTiernan A et al (1992) Breast cancer in men: . risk factors with hormonal implications.*Am. J. Epidemiol*135: 7,34–48.
<https://doi.org/10.1093/oxfordjournals.aje.a116360>
- [20] Volm MD, Talamonti MS, Thangavelu M et al (1997) Pituitary adenoma and bilateral male breast cancer:an unusual association*J. Surg. Oncol.* 64 74–8.
[https://doi.org/10.1002/\(SICI\)1096-9098\(199701\)64:1<74::AID-JSO14>3.0.CO;2-W](https://doi.org/10.1002/(SICI)1096-9098(199701)64:1<74::AID-JSO14>3.0.CO;2-W)
- [21] Lenfant-Pejovic M-H, Mlika-Cabanne N, Bouchardy C et al (1990). Risk factors for male breast cancer: a Franco-Swiss case-control study. *Int.J. Cancer* 45 661–5.
<https://doi.org/10.1002/ijc.2910450415>
- [22] Olsson H and Ranstam J (1988) Head trauma and exposure to Prolactin-elevating drugs as risk factors for male breast cancer.*J. Natl. Cancer Inst*,80: 679.
<https://doi.org/10.1093/jnci/80.9.679>
- [23] Sasco AJ, Lowenfels AB and Pasker de Jong P (1993). Epidemiology of male breast cancer: a meta-analysis of published case-control studies and discussion of selected etiological factors. *Int. J. Cancer* 53 539–49.
<https://doi.org/10.1002/ijc.2910530403>
- [24] Dicker AP (2003) The safety and tolerability of low-dose irradiation for the management of gynaecomastia caused by antiandrogen monotherapy *Lancet Oncol* 4:30–6.
[https://doi.org/10.1016/S1470-2045\(03\)00958-6](https://doi.org/10.1016/S1470-2045(03)00958-6)
- [25] Ron E, Ikeda T, Preston DL et al (2005) Male breast cancer incidence among atomic bomb survivors *J. Natl. Cancer Inst.* 97 603–5.
<https://doi.org/10.1093/jnci/dji097>
- [26] Guenel P, Cyr D, Sabroe S et al (2004) Alcohol drinking may increase the risk of breast cancer in men:a European population-based case-control study *Cancer Causes Control* , 15 :571–80.
<https://doi.org/10.1023/B:CACO.0000036154.18162.43>
- [27] Hansen J (2000) Elevated risk for male breast cancer after exposure to gasoline and vehicular combustion products.*Am. J. Ind Med.*37: 349–52.
[https://doi.org/10.1002/\(SICI\)1097-0274\(200004\)37:4<349::AID-AJIM4>3.0.CO;2-L](https://doi.org/10.1002/(SICI)1097-0274(200004)37:4<349::AID-AJIM4>3.0.CO;2-L)
- [28] Loomis DP (1992) Cancer of breast among men in electrical occupations.*Lancet*.339:1482–3.
[https://doi.org/10.1016/0140-6736\(92\)92078-T](https://doi.org/10.1016/0140-6736(92)92078-T)
- [29] 16-Donagan WL., Redlich PN., Lang PJ., Gall MT.(1998). Carcinoma of the breast in males. *Cancer* ;83:498–509.
[https://doi.org/10.1002/\(SICI\)1097-0142\(19980801\)83:3<498::AID-CNCR19>3.0.CO;2-R](https://doi.org/10.1002/(SICI)1097-0142(19980801)83:3<498::AID-CNCR19>3.0.CO;2-R)

- [30] Chen L, Chantra PK, Larsen LH, Barton P, Rohitopakarn M, Zhu EQ, Bassett LW.(2006). Imaging characteristics of malignant lesions of the male breast. *Radiographics*;26:993–1006.
<https://doi.org/10.1148/rg.264055116>