

Susceptibility and Sexual Dimorphism in the Human Cancers

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Abstract

Women have more chances of developing breast cancer during their life time than men, reasons may be due to different hormonal milieu and the higher number of breast cells responsible for dense breasts. In cancer epidemiology, gender difference in cancer susceptibility is one of the most consistent findings. In general, men are more likely to develop cancer than women; however, especially women are more susceptible to breast cancer.

Keywords: sexual dimorphism; cancer; hormone replacement therapy (HRT); hematologic malignancies

Introduction

Breast cancer starts when cells in the breast begin to grow out of control. It can start in one or both breasts. Breast cancer cells usually form a tumour that can often be seen on a mammogram [1] or ultrasound or felt as a lump. Though, it can develop both in males and females, more common in females. There has been a sharp rise in the number of breast cancer cases, especially in urban areas. A diet high in fats, obesity, late marriage, no or fewer children, and little or no breastfeeding – are considered to be the reasons for the higher incidence of breast cancer in women. Simply being a woman is the main risk factor for developing breast cancer [2, 3]. Women have many more breast cells than men, the main reason they develop breast cancer more often is because their breast cells are constantly and in different concentrations exposed to the female hormones' estrogen and progesterone, which promote cell growth [4,5] Though both breasts are equally exposed to sex steroids, still breast cancer occurs more frequently in the left breast than in the right. The left breast is 5%-10% more likely to develop cancer than the right breast. Experts are still not sure why left-sided breast cancer appears to be more common. Over the years, researchers have made various hypotheses to try to explain it, such as the larger size of the left breast. [6] According to a 2017 study, research has repeatedly shown that the upper outer quadrant of the breast is the most common site of breast cancer occurrence. That would be the part of the breast nearest the armpit [7]. In general risk factors for developing cancer include the following:

- Age – the risk of developing cancer increases with age
- Lifestyle factors – these include smoking, weight, diet, how active you are, sun exposure and sunbed use, and how much alcohol is consumed per day basis [8-13]. Cancer epidemiological surveys showed that men are more prone to cancer than women; in fact, one in two men will develop some form of the disease in a lifetime, compared with one in three women. The gender difference in cancer susceptibility is one of

the most consistent findings in cancer epidemiology. Hematologic malignancies are generally more common in males and this can be generalized to most other cancers.

Susceptibility Towards Cancers

Cancer susceptibility in females versus males is the increased risk of developing cancer because of sexual dimorphism exists between the genders. Their genetic makeup and different hormonal milieu make them react to cancers differently. i.e., their susceptibility towards cancer is also different. They do secrete different hormones, which may support cell proliferation [14, 15]. Both males and females will have BRCA1 and BRCA2 genes. [16]. The function of the BRCA genes is to repair cell damage and keep breast, ovarian, and other cells growing normally. On mutation these genes don't function normally and breast, ovarian, prostate, and other cancer risk increases. Men who have an abnormal BRCA2 gene have a higher risk of breast cancer than females. The proteins encoded by mutated BRCA1 and BRCA2 have their perceived value to the cancer biology field. [17,18]

Asymmetry in breast size

The breast is one of the body's major paired organs. One breast may have a different percentage of true breast tissue versus fatty tissue, and may therefore react to hormonal changes differently; it is not abnormal to have different-sized breasts [19] It happens when breasts react abnormally to hormones during the developing stage, infancy, or puberty. The tissue structures in each can be different. This is why many people get breast cancer in just one breast. For reasons that are unknown, clinical data shows that breast cancer develops more frequently in the left breast than in the of right breast. Scientists have given reason breast cancer occurs more often in the left breast, and have floated some suggestions such as,

- The left breast is usually larger than the right, which could mean denser breast tissues (a risk factor for breast cancer).
- Breastfeeding (which can reduce breast cancer risk) may be preferred on the right side.

Existing literature indicated that when a woman develops unilateral breast cancer, it is roughly 5% to 13% more likely to grow in the left breast than in the right breast. On the other hand, some authors have suggested that left-sided breast cancer may lead to worse survival rates and higher chances of cancer recurring [20]. In addition to left breast cancer also raises additional heart-related risks because of heart position, particularly for older patients, such as heart damage and worse survival outcomes.

Most common cancers in females

There are 5 most common cancers in females. The five main types of gynecologic cancer are: cervical, ovarian, uterine, vaginal, and vulvar. Globally, breast cancer is the most common cancer in women [21]. Among other risk factors, hormonal factor is the most important factor [22]. The female hormone estrogen produced by the ovaries at puberty can sometimes stimulate breast cancer cells. The risk of developing breast cancer may rise slightly with the blood levels of estrogen in the female body. For example, if the person started having periods at a young age and experienced menopause later than average, the person will have been exposed to estrogen over a longer period of time. In the same way, not having children or having children later in life [23] may slightly increase the risk of developing breast cancer because exposure to estrogen is not interrupted by pregnancy. On the other hand, having a baby but not breastfed also a big risk factor [24, 25]

Hormone replacement therapy (HRT):

All types of HRT can increase the risk of breast cancer, except for applying estrogen-containing creams in the vagina. There is no increased risk of breast cancer if one takes for short periods, however, for longer than 1 year, one has a higher risk of breast cancer than women who never use HRT [26]. The increased risk of breast cancer falls after stopping taking HRT, but some increased risk remains for more than 10 years compared to women who have never used HRT. Contraceptive pill: Research shows that women who take the contraceptive pill have a slightly increased risk of developing breast cancer, especially the progestogen-only pill. Newer research shows taking the progestogen-only pill slightly increases the risk of breast cancer, similar to the combined contraceptive pill [27]. However, the risk starts to decrease once you stop taking the pill, and your risk of breast cancer is back to normal 10 years after stopping. Obesity: If any female has experienced menopause and is overweight or obese, she may be more at risk of developing breast cancer. Obesity has been linked to several common cancers including the breast [28, 29] this is thought to be linked to the amount of estrogen in the body, as being overweight or obese after menopause causes more estrogen to be produced.

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