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COMPARISON OF MALE AND FEMALE BREAST CANCER CHARACTERISTICS IN SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS PROGRAM REGISTRIES

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Abstract

The prevalence and incidence of breast cancer in today's era is a remarkable health concern in both sexes. Male breast cancer constitutes a small fraction of reported cases but its impact should not be underestimated. The escalating number of male breast cancer and its distinctive characteristics call for a comprehensive analogy with its female counterpart. The purpose of this study is to conduct comparative analysis of male and female breast cancer, focusing on various variable factors such as race, age, and Surveillance, Epidemiological, and End Results Program (SEER) historical stage and to make a substantial difference to the broader understanding of breast cancer. This study was conducted under the approach of observational and retrospective study entailing 2021–2022-year cases from SEER registries of 9, 13, and 17. The key variables examined in the study are age, race, tumor size, and lymph node. The results showed that reported cases of male breast cancer are almost 1% around the world. The study includes 5494 male cases (0.7%) and 835,805 female cases (99.3%). The investigation's findings highlight that the mean age of males with breast cancer is 65.8 years. They also have low-grade tumors and a higher incidence of estrogen receptor positivity in comparison to females. Clearly, variations in attributes are noticeable amidst diverse categories, emphasizing the requirement for directed interventions. This research highlights the infrequency of male breast cancer occurrences, demonstrating the necessity for further investigation to enhance early detection and treatment. The discoveries of the inquiry supplement the broader appreciation of breast cancer and furnish acuities into potential fields for enhancing patient care.

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1. INTRODUCTION

Among all new and previous diseases, cancer is still considered to be one of the main causes of mortality worldwide [1]. Breast cancer is lagging behind lung cancer and is the second most common cancer worldwide. It is the 5th leading cause of death. In women, breast cancer has the highest prevalence, incidence, and mortality rate [2]. Breast cancer in females is common in both developed and developing countries, but it is more frequent in countries with low income and economic instability. As of 2020, one in eight women was affected by breast cancer in high-income countries [3]. Breast cancer in males, known as male breast cancer (MBC), is a very uncommon and rare disease. Less than 1% of cases of male breast cancers are reported worldwide. Breast carcinomas have some common characteristics in males and females, but there are also several prominent differences. However, much research has not been done on MBC since cases of MBC are rare [4]. Breast cancer is known to be a multifactorial disease. Many factors affect the incidence of breast cancer. Due to this, the incidence rate of breast cancer is different in different parts of the world [5]. High-income countries have shown a progressive decrease in the breast cancer mortality rate due to the presence of more advanced and better diagnosis as well as treatment methods [6]. Unfortunately, there is no decrease or fall in the incidence rate of breast cancer [7]. The reason behind this increase in the incidence rate of breast cancer might be due to an increase in diagnostic methods and a lack of effective prevention measures [8].

Data collected from the Surveillance, Epidemiology, and End Results Program (SEER) in 2015 showed that the incidence of male breast cancer was 1.1:100,000 men [9]. In the US, 2550 men were diagnosed with breast cancer in 2018. However, 480 of them died of breast cancer. The incidence rate of male breast cancer has soared in the last few years [10].

The Global Cancer Observatory GLOBOCAN 2018 status report on the incidence and mortality rate of cancer shows that breast cancer is the second most frequently diagnosed malignancy, as it accounts for more than 11.6% of all female cancers [11]. Globally, the incidence and mortality rate of breast cancer in women is rising [12]. As age increases, breast cancer incidence and mortality rates also increase. More than 90% of new breast cancer cases occur in women above the age of 40 due to hormonal alterations, menopausal transition, and age-related changes in breast tissue like size, shape, loss of firmness and fullness [13].

The clinical manifestation of breast cancer is similar in males and females [14]. Infiltrating ductal carcinoma is the most common type of breast cancer found in women [15, 16]. Milk ducts, which carry milk from the lobules to the nipple, are the site of origin of infiltrating ductal carcinoma (IDC). Ninety percent of men also have the same carcinoma [17]. The remaining 10% of men have in situ carcinoma [18]. Infiltrating lobular carcinoma, medullary lesions, and tubular or neuroendocrine tumors are as scarce as in her teeth in men [19].

Radiation therapy, targeted endocrine or molecular therapy and cytoreductive surgery are some treatment approaches for female breast cancer [20]. Radical mastectomy and modified radical mastectomy were mainly used for loco-regional management. However, now they are not used. Because there is new and better management approach available which is breast-conserving surgery with irradiation. It is used for early-stage breast cancer. After lumpectomy, whole breast irradiation was performed to eliminate potential cancerous cells. It yields results similar to mastectomy [21]. Breast cancer has a heterogeneous nature, which is the main obstacle in treatment, as its nature determines the therapeutic or treatment method [22]. BRCA (Breast cancer gene) gene's mutation, Cell-cycle checkpoint kinase encoding gene CHEK2(checkpoint kinase 2), PALB2 (partner and localizer of *BRCA2*) are the main culprit of male and female breast cancer. *PTEN* mutations and the androgen receptor mutations are mainly involved with occurrence of male breast cancer.

The risk of male breast cancer also increases with single-nucleotide polymorphisms in *CYP17* (Cytochrome P450 17 α- hydroxylase / 17, 20 lyase), RAD51 paralog B (Radiation damage repairing protein), *and* chromosomes 2q35, 5p12, 6q25.1, 10q26.13, and 16q12.1.

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In the last few years, female breast cancer awareness, screening, diagnosis and treatment options have improved due to multiple effective measures. However, male breast cancer research is still limited. Hence, the management and treatment of male breast cancer is based on all those clinical measures and practices that were developed for treating female breast cancer [23]. Several studies have revealed that for male breast cancer, overall survival (OS) estimates are markedly lower than for female breast cancer. This is due to lack of techniques for early diagnosis, screening, and better treatment methods. In addition to this, in males with breast cancer there are higher chances of developing other accessory comorbidities and neoplasms (colon cancer, prostate cancer). Death rate from these comorbidities is also very high in men [24, 25]. This stresses the need for early diagnosis, screening, and better treatment methods. It has been proven that in males with breast cancer, there are higher chances of developing other accessory comorbidities and neoplasms (colon cancer, prostate cancer). In addition, the death rate from these comorbidities is also very high in men [26].

2. MATERIALS AND METHODS

A research study can be designed to investigate and compare the age, tumor size, race, grade, SEER historical stage, lymph node status, and presence and absence of estrogen receptor of breast cancer in both female and male subjects.

2.1. Study Design

The study adopted an observational and retrospective design to compare breast cancer cases between females and males. Data were collected from various sources, including cancer registries, hospital databases, and medical records of breast cancer patients. The study period encompassed a specified timeframe 2021-2022, to capture recent cases.

2.2 Data Collection:

Data were gathered from patients who had been diagnosed with breast cancer, regardless of sex.

Patients with complete and comprehensive medical records were included in the study, whereas patients with missing or incomplete data were excluded from the analysis.

2.3. Study Participants:

The study included both female and male patients diagnosed with breast cancer.

2.4. Variables of Interest:

Prevalence: The number of breast cancer cases in females and males within the specified period.

Age: The age at which most of the cases were reported, with categories of 70+ years, 50-69 years, 40-49 years and <40 years.

Race: The ethnic group of the breast cancer patients (Black, White, and others)

Tumor size: The measurement of a tumor resulting from the uncontrolled and excessive growth of cells. (≤ 2.0 cm, > 2.0 cm and others)

Lymph node status: This refers to whether the cancer cells have undergone metastasis and spread to the vicinity of the lymph nodes.

SEER historical stage: This classification categorizes cancer into a variety of stages. These stages are based on the extent of metastasis. This helps in the prognosis and treatment of cancer. It includes stages such as localized (no metastasis), regional (metastasis toward nearby tissues/lymph nodes), distant (spread to distant organs/lymph nodes), and un staged (insufficient information to detect the extent of metastasis).

Cancer grade: A characteristic employed to describe the phenotype of the cancer cells along with their resemblance/similarity to the noncancerous cells under a microscope. This includes low-grade (well differentiated) and high-grade poorly differentiated).

Estrogen receptor: Estrogen Receptor Alpha (ERα), Estrogen Receptor Beta (ERβ), and G Protein-Coupled Estrogen Receptor (GPER) are proteins found in and on the surface of breast cells, playing an important role in the hormone estrogen response. This aids in diagnosis, prognosis, and treatment. It has two main categories: ER positive breast cancer (which has ER receptors) and ER-negative breast cancer (which has no ER receptors).

2.5. Data Analysis:

Descriptive statistics were used to summarize age, tumor size, race, grade, SEER historical stage, lymph node status, and presence and absence of estrogen receptors.

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2.6. Limitations:

Rarity of Male Cases: Due to the rarity of male breast cancer cases, the sample size may be limited.

Retrospective Nature: Since the study is retrospective, some data might be missing or incomplete.

Data Bias: The study might face biases inherent to retrospective data collection and analysis.

2.7. Ethical Considerations:

Patient Confidentiality: Patient data were anonymized and kept confidential during data collection and analysis.

Ethical Approval: Ethical approval was obtained from the relevant Institutional Review Board (IRB) or ethics committee to ensure patient rights and data confidentiality.

In summary, this research aims to provide a comprehensive comparison of breast cancer between females and males, focusing on various aspects, such as age, tumor size, race, grade, SEER historical stage, lymph node status, and presence or absence of estrogen receptor. The study's methodology involves retrospective data collection, thorough analysis, and ethical considerations to ensure the validity and integrity of the findings.

3. RESULTS

The current series of SEER registries presents an overall comparative analysis, wherein male breast cancer patients account for a sample size of 5494, which is a mere 0.7% of the total number of breast cancer patients. The comparison can be observed in Table 1. The remaining 99.3% of patients were female. The female breast cancer patients had a mean and median age of approximately 67, while the median age for male patients was 67. This study aims to compare several variables, such as age, race, size, lymph node status, SEER historical stage, grade, and estrogen receptor status, between male andfemale breast cancer patients.

Table 1. Comparison of Male and Female Breast Cancer Characteristics in SEER Registries.

Characteristics	Male	Female
Sample size	5,494	835,805
Percent of total no.	0.7%	99.3%
Age, years		
Mean	65.8	61.3
Median	67	61
Tumor size , cm		
Mean	2.4	2.2
Rate per 100,000	1.1	142.7
Variable		
Age, years		
70+	2,323	260,993
50-69	2,497	377,660
40-69	524	148,713
<40	150	48,439
Race		
White	4,616	711,904 (2.3 × 10^-14)
Black	611	67,945
Other / unknown	1,871	293,953
Tumor size, cm		
≤ 2.0	2,005	351,891
> 2.0	1,618	189,961
Other/ unknown	1,871	293,953
Lymph node status		

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Negative	1,836	316,406
Positive	1,348	156,921
Other/ unknown	2,310	362,478
SEER historical stage		
In situ	555	121,909
Local	2,321	420,723
Regional	2,036	225,161
Distant	380	43,371
Other / unknown	202	24,641
Grade		
Low	2,242	320,711 (.01)
High	1,440	224,656
Other / unknown	1,712	290,438
Estrogen receptor		
Positive	2,576	344,406
Negative	212	100,152
Other / unknown	2,706	391,247

*Contrast the characteristics of breast cancer among both gender with different characteristic values. The data used for this analysis are primarily derived from the SEER 9, 13, and 17 registries. The table comprises several crucial elements, such as the sizes of the sample, the distribution of age, the size of the tumor, and the rates of occurrence per 100,000 individuals. The present study reached a conclusive conclusion that male breast cancer patients tend to have low-grade tumors and estrogen receptor positivity more often than female patients. Additionally, there were significant differences in these characteristics between male and female breast cancer patients based on variables such as race and grade. The genetics mechanism is shown in Figure 1.

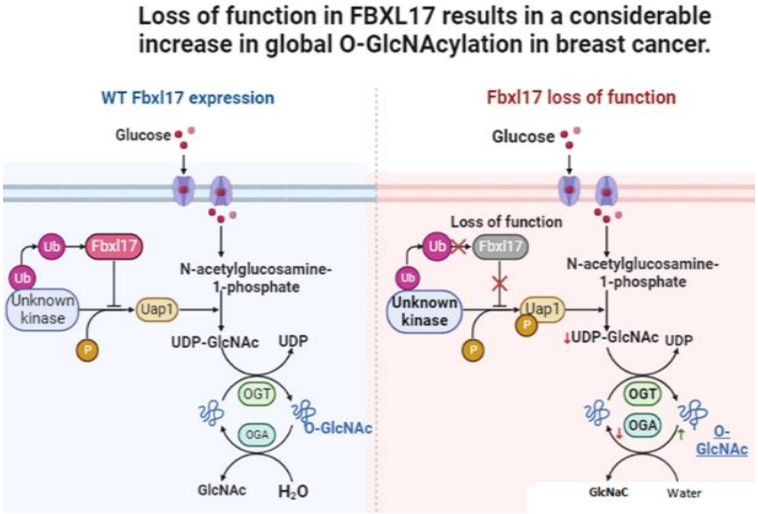

Fig. 1. FBXL17 and its role in breast cancer created with BioRender.com

FBXL17 is a gene that encodes a protein that participates in the ubiquitin-proteasome system, which plays a critical function in protein degradation within cells. O-GlcNAcylation is a post-translational modification in which a sugar molecule known as O-GlcNAc is appended to proteins, impacting their functionality and stability.

A decline in the function of the FBXL17 gene leads to an increase in O-GlcNAcylation levels in breast cancer. This could suggest that FBXL17 normally functions to govern O-GlcNAcylation levels, and its

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loss of function could contribute to the altered protein modifications noted in breast cancer cells.

4. DISCUSSION

Female Breast Cancer is an extensive form of cancer that affects women more than men. Although Male Breast Cancer is rare, the mortality rate among men with breast cancer is noteworthy [27]. The current study also favored the fact that male breast cancer is a rare event in males, as only 0.7% of males had breast cancer. This dissimilarity in mortality rates accentuates the significance of timely detection and improved treatment approaches for Male Breast Cancer. The occurrence of breast cancer corresponds with age, with the risk rising in older individuals. It is worth mentioning that male breast cancer patients are commonly diagnosed at a more advanced age than their female counterparts [28, 29]. The current study also indicates that as age progresses, the incidence of breast cancer increases. In males, only 150 cases of breast cancer were reported among males younger than 40 years, and 48,439 cases were reported for females of the same age group.

In a study conducted by Anderson, W., *et al.*, in 2008, qualitative interactions between age and race were observed in breast cancer patients. It was found that the incidence of breast cancer was higher in black women than in white women younger than 40 years of age. The reverse was true for women older than 40 years [30]. The same results were observed in the present study, which means that Black women have a lower incidence of breast cancer (67,945 cases) than White women (711,904) for all age groups.

Crew *et al.* in 2007 analyzed male breast cancer cases for different treatment options. Among the 510 males, there were 456 white men and 34 black men. This indicates that the incidence of breast cancer in males has racial disparities [31]. The present study also showed that more white men (4616 cases) had reported breast cancer than black men 611 cases).

The current study showed that most of the cases reported of breast cancer had no lymph node involvement (1836 males and 316,406 females), whereas 1348 male patients and 156921 female patients had positive lymph node status. This is true with the study of Unal, B., *et al.*, in 2009 stating that of the 309 patients, 80 (25.9%) had four or more positive axillary lymph nodes [32]. The clinical manifestations of breast cancer are generally similar between men and women, including the types of carcinomas found, as previously stated in research. MBC being detected at earlier stages with smaller tumor sizes and a lower probability of lymph node involvement and distant metastases is highly unlikely [33, 34]. This indicates the need for heightened awareness and early detection efforts for MBC. Treatment approaches developed for FBC are frequently applied to MBC due to limited research that is specific to male patients [35].

Previous inquiries into the examination of breast cancers in males and females on a massive population basis have produced captivating insights into their origin and prognosis. The similarity in incidence rate trends for breast cancer among both men and women suggests shared risk factors. Second, the descriptive patterns indicate that male breast cancer exhibits similarities with the ER-positive type of female breast cancer that presents itself later in life [36]. Although strides have been made in the management of breast cancer, the rates of death for males have persisted stubbornly high [37, 38]. In the study under discussion, the number of females reported to have estrogen receptors was higher than that of ER-negative females, as only 100,152 females had no estrogen receptors compared to 344,406 ER-positive females.

5. CONCLUSIONS

This investigation offers a comprehensive comparative examination of the characteristics of breast cancer across the sexes. The research highlights the significance of timely detection and enhanced approaches, particularly for male breast cancer, owing to its relatively inferior rates of overall survival. The exploration exposes the variations in tumor features, age distribution, and estrogen receptor status between male and female patients with breast cancer. According to the study, females are likely to be affected by breast cancer.

Ultimately, the findings contribute to the broader understanding of breast cancer and underscore the need for continued research to enhance outcomes and quality of life for both male and female patients.

Conflict of interest: The authors show no conflict of interest regarding this research article.

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ETHICAL APPROVAL STATEMENT

Give the statement, and details of the committee who approved.

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