Significance of the Hormone receptors in the progression of breast cancer among Egyptian women

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ABSTRACT

Breast cancer (BC) ranks second globally in terms of the number of deaths among women. In BC patients, testing for the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (Her-2) is now a routine. In this study, we looked at ER, PR, and HER-2 expression in breast carcinomas and compared it to other Clinicopathological parameters. BC samples (N=96) were obtained while several factors were considered, including age, menopausal status, history of family, size of tumor, grade, lymph node involvement, metastasis, stage of cancer, and the presence of the hormone receptors ER, PR, and Her-2. Breast cancer was associated with ER, PR, and HER-2. Histopathological parameters using SPSS software version 25. Significant relationships existed between ER and age, menopausal status, family history, tumor size, grade, and lymph node involvement. There was no meaningful relationship between ER and metastasis (P = 0.263). Age, menopausal status, history of family, size of tumor, grade, lymph node involvement and metastasis are all significantly associated with PR. Age, menopausal status, size of tumor, grade, lymph node involvement and metastasis showed a strong association with HER-2. Family history and HER-2 were not significantly associated (P = 0.123). Our study discovered a significant relationship between ER, PR, and HER-2 and BC in Egyptian females; these hormone receptors should be considered as significant prognosis indicators for determining individuals who are most likely to develop and advance BC.

Keywords: Breast Cancer; Progesterone Receptor; Estrogen Receptor; Clinicopathological Parameters.

INTRODUCTION

With an estimated 570,000 fatalities in 2015, BC is one of the most prevalent cancers in women globally. More than 1.5 million females globally (25% of all cancer patients) receive a diagnosis of the disease each year (McGuire 2016; Sun et al., 2017) . It is possible for distant organs such as the bone, liver, lung, and brain to be infiltrated by the metastatic, incurable cancer BC. Early disease detection can lead to a greater likelihood of survival and a better prognosis (DeSantis et al., 2016). BC is more common than lung cancer to become the most common disease diagnosed worldwide, accounting for one in every eight cancer diagnoses and 2.3 million fresh instances in adults of both sexes combined. (Sung et al., 2021). In 2020, it was by far the most prevalent cancer in women, accounting for one-quarter of all cancer cases in females. Its prevalence has been rising around the world, especially in transitioning nations. (Heer et al. 2020). According to estimates, 685,000 women died of BC in 2020, accounting for 16% of all female cancer deaths. Because the reaction of public health to this development had previously been insufficient, the World Health Organization (WHO) recently created the Global Breast Cancer Initiative. (Anderson et al., 2021). The majority of female cancer cases in Egypt are BC. It is the root cause of 32% of all female malignancies (Ibrahim, Talima, and Makar 2019). It accounts for 15% of all fatalities worldwide each year and is the main contributor to cancer-related mortality (Bray et al. 2018). Women that are above 50 experienced a considerable increase in BC incidence, with women greater than 70 seeing the highest incidence (Hirko et al. 2013). Throughout the past few years, Egypt's old population has grown, going from 3.7% in 2006 to 9.3% in 2014. The average lifespan has also increased, reaching 76 years for women and 70 years for males (Ibrahim, Talima, and Makar 2019; Zeeneldin et al. 2013). Less than 1% of women under the age of 25 are affected by BC, however as women get older, the frequency increases (Jemal et al. 2009). Although BC has an average age between 60 and 70, it appears to be widespread worldwide (Porter 2009). BC instances are sporadic in the

great majority of cases. Yet, a significant portion of it is brought about by the passing down of specific genetic elements, such as genetic mutations (Rheinbay et al. 2017).

Long-term exposure to estrogen is another contributing factor to BC. This hormone has been linked to the formation of mammary glands as well as the development and progression of BC (Levine 2011). The amount of estrogen in the blood throughout time has been demonstrated to be a significant risk factor for BC. This explains why there is less breast tissue and estrogen in men, which results in a reduced incidence of BC. The cell surface receptors for estrogen and progesterone also contribute negatively to the development of cancer (Wu et al. 2006). Increased exposure to progesterone and estradiol, which was the subject of a study done in the early 1970s, is possibly the most significant risk factor for BC (Feigelson and Henderson 1996; Mohammed Alwan, Tavakol Afshari, and Afzaljavan 2022). It is known that certain types of human breast cancer are influenced by hormones. Estrogen interacts with the ER in the nucleus to regulate breast epithelial cell differentiation and proliferation. Long-term estrogen exposure raises the risk of developing cancer. In healthy breast epithelial cells, the ER controls PR expression (Jensen 1980). Invasive breast cancer is now regularly assessed for the presence of ER, PR, and HER-2 because these markers are thought to be significant prognostic variables (Ambroise et al. 2011). That determine whether a patient is a candidate for endocrine therapy using their ER and PR status (tamoxifen). The transmembrane protein that HER-2 encodes is phosphorylated tyrosine after it interacts with its ligands. It is possible to predict the response to trastuzumab using HER-2 (Gupta 2010; Patnayak et al. 2015) .

Mammography has been proven to drastically lower mortality and is a popular approach for detecting breast cancer. In addition, studies and the application of other screening techniques have been conducted throughout the previous ten years. Magnetic resonance imaging is one such approach and is more accurate than mammography. (DeSantis et al. 2016). BC risk may be increased by a variety of factors, including sex, aging, estrogen, family history, gene mutations, and an unhealthy lifestyle (Majeed et al. 2014).

MATERIALS AND METHODS

From the beginning of June 2019 to the end of May 2021, 96 Egyptian female patients (n=96) enrolled at the National Cancer Institute, Cairo University, participated in this study. Clinical and histological tests have been used to diagnose BC. Clinicopathological information on the patients was documented. The inclusion criteria for BC individuals included age, menopausal status, family history, tumor size, grade, lymph node involvement, metastasis, cancer stage, and hormone receptor status including ER, PR, and Her-2.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 25 was used to analyze the data. Qualitative data were expressed as frequencies and percentages. Differences between groups were considered statistically significant if the p-value was less than 0.05.

RESULTS

Clinicopathological Data of Patients with Breast Cancer

Age, family history, menopausal status, histological type, tumor size, stage, lymph node involvement of the cancer, and metastasis are all reported in the clinicopathological data of BC patients. It also shows the status of hormone receptors such as (ER), (PR), and (HER2 neu).

The statistical relationship between ER and Clinicopathological parameters.

Regarding the relationship between ER and Clinicopathological parameters, our results showed that there is significant correlation between ER and age group, menopausal status, family history, tumor size, grade, and involvement of cancer in a lymph node. Table 1 shows that there was no significant relationship between ER and metastasis (P= 0.263).

The statistical relationship between PR and Clinicopathological parameters.

Age group, menopausal status, family history, tumor size, grade, lymph node involvement, and metastasis were all strongly connected with PR, according to the results of the relationship between PR and BC clinical data (presented in Table 2).

The statistical relationship between HER-2 and Clinicopathological parameters.

Our findings show a strong correlation between HER-2, among other clinicopathological factors, age, menopausal status, tumor size, grade, lymph node

involvement, and metastasis. According to Table 3, there is no significant relationship between HER-2 and family history (P = 0.123).

The statistical relationship between Metastasis and Clinicopathological parameters.

The results of the link between Metastasis and BC clinical data showed a substantial correlation between Metastasis and age group, menopausal status, family history, tumor size, grade, and lymph node involvement (presented in Table 4).

DISCUSSION

Female Egyptians saw 22,038 new instances of breast cancer in 2020, making up 32.4% of all cancer cases with a death rate of 10.3% (Metwally et al. 2021).

Breast cancer risk factors are numerous. The majority of the contributing factors all have one thing in common: extended estrogen stimulation in a genetically susceptible background (Jensen 1980). An important prognostic indicator for invasive tumors is the existence of ER and PR, which is positively correlated with survival. It has been common practice to identify ER, PR, and HER-2 in BC (Ambroise et al. 2011).

The majority of patients in this study (33.3%) were premenopausal (62.5%) and belonged to age group C (40-49). This finding conflicts with earlier research on India (Ambroise et al. 2011; Munjal et al. 2009). According to a number of studies, having your first period before the age of 12 raises your risk of developing BC (Cancer 1996). In addition, compared to women who achieve menopause earlier, those who do so beyond the age of 50 are more prone to develop BC. Every year that passes after the presumptive menopause age results in a rise in the risk of BC of roughly 3% (Rossouw 2002). Prolonged production of ovarian hormones appears to be the mechanism by which late menopause increases the risk of BC. In this investigation, it was discovered that there was a strong correlation between patient age and ER, PR, and HER-2 (P < 0.001) as opposed to the outcomes of other Indian investigations (Kumar et al. 2007; Vaidyanathan et al. 2010). The lymph node status of 96 patients was known. The majority of cases (N2) had lymph node status, and there was a significant connection between lymph node status and ER, PR, and HER-2 (P = 0.001, P = 0.001, and P = 0.012), respectively. This outcome is comparable to that discovered by Vaidyanathan et al(Vaidyanathan et al. 2010) who found that 64.6% of tumors were T2-sized (3.0 cm). The relationship between tumor size and ER, PR, and HER-2 was statistically significant (P = 0.001, P = 0.001, and P = 0.022, respectively). Comparing this result to that of Ambroise et al (Ambroise et al. 2011).

In total, we found positive results for 67.7% ER, 58.3% PR, and 55.2% HER-2. Compared to the rest of the globe, Africa has a lower prevalence of BC positive people. Western studies have noted 70–80% ER and 60–70% PR in the context of invasive ductal carcinoma, respectively (Ambroise et al. 2011; Horii et al. 2007; Jirström et al. 2005; Li, Daling, and Malone 2003)

CONCLUSION

BC is a chronic, complex illness of global importance that is the main cause of mortality and morbidity in women. This is what drives us to look for novel medicinal approaches and pest-control strategies. It is important to conduct campaigns that aime at the elderly to inform them about BC early detection and how to acquire access to healthcare. To entice older women to seek medical attention, emphasis must be made on enhancing treatment outcomes and incorporating them into social media. Advertisements should tell seniors that there is ahigh life expectancy worldwide and that ailments that are diagnosed early are easily treatable.

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Table 1: Statistic relationship of ER with Clinicopathological parameters.

Clinicopathological parameters		ER		P-Value
		Negative	Positive	
menopausal status	Post	18	18	0.004
	Pre	13	47	
Family history of breast cancer	Negative	28	44	0.017
	Positive	3	21	
Tumor size	T2	12	50	0.001
	T3	16	11	
	T4	3	4	
Grade	G1	1	8	0.002
	G2	11	41	
	G3	19	16	
Stage	I	2	10	0.001
	II	10	42	
	III	15	9	
	IV	4	4	
Lymph nodes invasion	N1	3	11	0.001
	N2	9	40	
	N3	19	14	
Metastasis	M0	27	61	0.263
	M1	4	4	
Age group	(A) 20-29	0	2	< 0,001
	(B) 30-39	3	25	
	(C) 40-49	10	22	
	(D) 50-59	14	10	
	(E) 60-69	4	6	

Table 2: Statistic relationship of PR with Clinicopathological parameters.

Clinicopathological parameters		PR		P-Value
		Negative	Positive	
menopausal status	Post	8	28	0.003
	Pre	32	28	
Family history of breast cancer	Negative	23	49	0.001
	Positive	17	7	
Tumor size	T2	36	26	< 0,001
	T3	3	24	
	T4	1	6	
Grade	G1	6	3	< 0,001
	G2	30	22	
	G3	4	31	
Stage	I	5	7	< 0,001
	II	32	20	
	III	3	21	
	IV	0	8	
Lymph nodes invasion	N1	6	8	< 0,001
	N2	30	19	
	N3	4	29	
Metastasis	M0	40	48	0.013
	M1	0	8	
Age group	(A) 20-29	2	0	< 0,001
	(B) 30-39	17	11	
	(C) 40-49	15	17	
	(D) 50-59	3	21	
	(E) 60-69	3	7	

Table 3: Statistic relationship of HER2 with Clinicopathological parameters.

Clinicopathological parameters		HER2 neu		P-Value
		Negative	Positive	
menopausal status	Post	11	25	0.030
	Pre	32	28	
Family history of breast cancer	Negative	29	43	0.123
	Positive	14	10	
Tumor size	T2	34	28	0.022
	T3	8	19	
	T4	1	6	
Grade	G1	5	4	0.017
	G2	29	23	
	G3	9	26	
Stage	I	6	6	0.006
	II	30	22	
	III	7	17	
	IV	0	8	
Lymph nodes invasion	N1	7	7	0.012
	N2	28	21	
	N3	8	25	
Metastasis	M0	43	45	0.008
	M1	0	8	
Age group	(A) 20-29	2	0	< 0,001
	(B) 30-39	14	14	
	(C) 40-49	18	14	
	(D) 50-59	5	19	
	(E) 60-69	4	6	

Table 4: Statistic relationship of Metastasis with Clinicopathological parameters.

Clinicopathological parameters		Metastasis		P-Value
		M0	M1	
menopausal status	Post	28	8	< 0,001
	Pre	60	0	
Family history of breast cancer	Negative	64	8	0.088
	Positive	24	0	
Tumor size	T2	62	0	< 0,001
	T3	25	2	
	T4	1	6	
Grade	G1	9	0	< 0,001
	G2	52	0	
	G3	27	8	
Stage	I	12	0	< 0,001
	II	52	0	
	III	24	0	
	IV	0	8	
Lymph nodes invasion	N1	14	0	< 0,001
	N2	49	0	
	N3	25	8	
Age group	20-29	2	0	< 0,001
	30-39	28	0	
	40-49	32	0	
	50-59	20	4	
	60-69	6	4	

Table 5: Different study groups' receptor status

Study group	ER positivity %	PR positivity %	HER-2 positivity %
(Desai et al. 2000)	32.6	46.1	—
(Dutta et al. 2008)	24	30	46.3
(Ambroise et al. 2011)	59	51	27.10
(Vaidyanathan et al. 2010)	50.2	46.9	43.2
(James et al. 2008)	—	—	29.0
(Munjal et al. 2009)	41.1	41.1	40.2
(Patnayak et al. 2015)	47.6	48.8	29.6
This study	67.7	58.3	55.2

أهمية مستقبلات الهرمون في تطور سرطان الثدي بين النساء المصريات

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الملخص العربي

يحتل سرطان الثدي المرتبة الثانية عالمياً من حيث عدد الوفيات بين النساء. في مرضى سرطان الثدي أصبح اختبار مستقبلات هرمون الاستروجين ومستقبل البروجسترون ومستقبل عامل نمو البشرة البشري 2 أمرًا روتينيًا الآن في سرطان الثدي. في هذه الدراسة نظرنا في تعبير ER وPR وHER-2 في سرطان الثدي وقارناه بالمعايير السريرية المرضية الأخرى. الطريقة: تم الحصول على 96 عينة للمرضى مع مراعاة عدة عوامل بما في ذلك العمر وحالة سن اليأس وتاريخ الأسرة وحجم الورم والدرجة ومشاركة العقدة الليمفاوية والورم الخبيث ومرحلة السرطان ووجود مستقبلات الهرمون ER وPR وHer-2. ارتبط سرطان الثدي بـ ER وPR وHER-2. المعلمات النسيجية المرضية باستخدام الإصدار 25 من برنامج SPSS. النتائج: توجد علاقات مهمة بين ER والعمر وحالة سن اليأس وتاريخ العائلة وحجم الورم ودرجته ومشاركة العقدة الليمفاوية. لم تكن هناك علاقة ذات مغزى بين ER والورم النقلي (P = 0.263). العمر وحالة انقطاع الطمث وتاريخ الأسرة وحجم الورم والدرجة وتورط العقدة الليمفاوية والورم الخبيث كلها مرتبطة بشكل كبير بالعلاقات العامة. أظهر العمر وحالة انقطاع الطمث وحجم الورم والدرجة ومشاركة العقدة الليمفاوية والورم الخبيث ارتباطًا قويًا بـ HER-2. لم يرتبط تاريخ العائلة وHER-2 بشكل كبير (P = 0.123). الخلاصة: اكتشفت دراستنا علاقة مهمة بين ER وPR وHER-2 وسرطان الثدي في الإناث المصريات. يجب اعتبار مستقبلات الهرمون هذه بمثابة مؤشرات تشخيص مهمة لتحديد الأفراد الأكثر عرضة لتطور وتقدم سرطان الثدي.

الكلمات الاسترشادية: سرطان الثدي، مستقبلات البروجسترون، مستقبلات هرمون الاستروجين، المعلمات السريرية المرضية.