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EVALUATION SEXUAL HORMONES IN BREAST CANCER WOMEN PATIENTS

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Abstract:

Among women, breast cancer is the prevailing malignant neoplasm. At 22% of all cancers in females, it is greater than twice as typical as cancers in other areas of the female body. In breast carcinomas, immunohistochemistry (IHC) is presently the universally recognized method for identifying estrogen (ER) and progesterone (PR) receptors. The history of progesterone and progesterone receptors (PR) in breast tumors is both renowned and contentious. As endocrine treatments for breast cancer advanced from oophorectomy to anti-estrogens, it became evident in the 1970s that the mere existence of estrogen receptors (ER) was not a reliable indicator of treatment response. Protein PR, controlled by estrogen, has emerged as the initial prognostic and predictive indicator of the response to endocrine treatments. The gold standard for predicting functional, targetable endoplasmic reticulum (ER) in breast cancers continues to be established today. PRs were later characterized as intricately organized transcription factors that control various physiological activities in breast cancer cells.

Keywords: Breast cancer (BC), estrogen receptor (ER) progesterone receptor (PR), androgen receptor (AR), immunohistochemistry (IHC), terminal end-buds (TEBs), endoplasmic reticulum (ER)

INTRODUCTION

Breast cancer (BC) is a disease characterized by significant heterogeneity in terms of both histology and molecular profiles. It remains the most prevalent cancer globally. Hormonal signals regulate the breast's development. Therefore, breast cancer significantly depends on hormones. In breast cancer, expressing GALNT7, a glycosyltransferase, is associated with estrogen receptor (ER), progesterone receptor (PR), and HER2-dependent alterations, which have potentially prognostic consequences. Human breast cancer's etiology remains mostly unclear.

Principal variables seem to be genetic predisposition, hormone impacts, and environmental factors. Nevertheless, established progesterone receptor (PR), the ER and HER2 are crucial indicators used in the prognosis and molecular subtyping differentiation of breast cancer [1]. ER, PR and Androgen-Receptor (AR) are steroid receptor superfamily members [2,5]. Once these receptors associate with their corresponding hormones, they become active and operate as transcription factors by linking to the promoter regions of their target genes. Without the hormone, they can nonetheless be activated by phosphorylation generated by other kinases. Hereditary risk factors are found in a mere (1-15) % of breast cancer cases [7]. Several hormonal interaction factors contribute to an elevated susceptibility to breast cancer in humans. The occurrence of breast cancer is 100 times more frequent in females than in males, and a woman's procreative history is a major risk factor for the disease [8,9]. Research indicates that an early start to menstruation and a late onset of menopause, both of which extend the interval of exposure to ovarian steroids, are associated with a higher risk.

Conversely, undertaking bilateral oophorectomy at a young age is linked to a lower risk (5). While breast cancer evolution and progression require low physiological levels of ovarian steroids, the risk is significantly diminished when a young woman has a full-term pregnancy, during which she is exposed to high levels of ovarian steroids [11,12]. Women who have a full-term pregnancy before age 20 have their breast cancer risk reduced by half compared to that of nulliparous women. Lactation appears to have little significance in this regard (13), and there is no documented association between terminated pregnancy and lower risk (11). While early full-term pregnancy offers enduring protection against breast cancer, there is evidence to suggest that pregnancy occurring after the age of 35 leads to an increased risk [11,12,14]. Hence, the timing of the initial full-term pregnancy mainly influences the extent of immunity against breast cancer resulting from parity, not merely by its simple presence. The global prevalence of breast cancer differs, and the disparities in breast cancer rates among migrants offer significant scientific evidence for the influence of environmental factors on the development of the disease (15). Nutrition is regarded as a significant environmental factor influencing the chance of developing breast cancer. Dietary fats and phytochemicals, which modify the structure

of the breast epithelium through a variety of mechanisms, are the primary nutritional components that are substantially linked to the risk of breast cancer[16]. A diverse range of dietary items consumed by humans can influence the levels of endogenous hormones and perhaps alter the risk of developing breast cancer—experimental manipulation of estrogen and progesterone levels to simulate pregnancy for breast cancer prevention.

During the latter part of the 19th century, it was observed that women with breast cancer who had their ovaries surgically removed had a higher survival rate for a significant number of patients. Nevertheless, the exact process responsible for this enhancement remained without clarity, and Beatson initially ascribed it to Nevertheless, the exact process responsible for this enhancement remained without clarity, and Beatson first ascribed it to the interference of nerve links between the ovarian and breast tissues [17]. In the 1960s, identifying estrogen and progesterone receptors in breast tissue confirmed the existence of a traditional ligand-receptor path, where epithelium cells in the breast react to the effects of the hormone progesterone and estrogen. The molecular processes estrogen attaches to its receptor have been rigorously established. Oestradiol penetrates the epithelial cells in the breast and attaches to its receptor located within the nucleus.

Consequently, a conformational alteration occurs, leading to the dimerization of oestradiol with other receptors, activating genes that respond to estrogen. Two distinct estrogen receptor (ER) conformations, α and β, are encoded by separate genes, ESR 1 and ESR 2, respectively. Although the clinical importance of ER-α is well-established, the therapeutic relevance of ER-β is still unclear. Therefore, the acronym ER denotes the α isoform for the rest of this review. Progesterone interacts with nuclear receptors in a manner analogous to estrogen. This protein is stated in two distinct isoforms, PRB and PRA, similar to the ER.

Contrary to the endoplasmic reticulum (ER), these isoforms are synthesized by a similar (PR gene), with the sole difference given that (PRA) is a version of (PRB) that has been shortened. Compared to older patients, younger people are more prone to being ER negative(ER-). According to the United States SEER cancer registries, the incidence of ER-positive (ER+) breast cancer increases with age; however, this increase decreases beyond the age range of 50 to 54 years.

Conversely, the rates of breast cancer according to ER age did not rise after the age range of 50-54 years. The PR role in breast cancer is still a complex and controversial topic. Although the incidence of ER+ breast cancer rises with age, there is no apparent trend in PR, and the PR+ rate is consistent across all age ranges [21]. Compared to ER+ breast cancers, PR+ breast cancers are less common. Twenty percent of ER+ breast tumors in the SEER breast cancer registries are PR-positive as well [22].

Empirical studies conducted on mice without the estrogen receptor (ER) and progesterone receptor (PR) have demonstrated that the combined influence of estrogen and progesterone is essential for the appropriate development of the mammary gland. In particular, estrogen (ER) stimulates the initial development of milk ducts that extend into the mammary fat pad originating from the nipple. In contrast, the isoforms of estrogen/ER and progesterone/PR are responsible for developing terminal end buds (TEBs) or acini at the duct ends, which will function as the milk-producing structures in the mammary gland during lactation. EGF and IGF-1, two essential hormones, promote the development of terminal end-buds in the breast during average growth and facilitate the enlargement of ducts and the branching of the breast initiated by estrogen and progesterone. Estrogen-induced stimulation of PR isoform expression depends on the presence of EGF [27]. This observation implies the presence of significant intercommunication between (EGF) receptors (EGFR) and their family members (erbB2), as well as both insulin receptors. One further constraint in comprehending the function of progesterone in the context of breast cancer, namely regarding uncontrolled proliferation, is that normal proliferating breast epithelial cells lack steroid hormone receptors. [28].

Obesity is a significant health issue in industrialized nations; 280,000 US adults die each year from obesity-related causes (29). Associated with a multitude of metabolic illnesses, including endocrine, cardiovascular, and gastrointestinal diseases, this pathophysiology is likely implicated in the pathogenesis of several malignancies, including colon, prostate, and breast cancers (23). Empirical evidence unequivocally establishes that obesity significantly raises the likelihood of experiencing breast cancer in women who have reached menopause (24,25). Furthermore, obesity is linked to higher rates of breast cancer recurrence and morbidity (26). An observed mechanism that could elucidate the correlation between obesity and the development of hormone-dependent breast cancer is the excessive generation of estrogens by adipose tissue resulting from increased androgen conversion (27). Furthermore, adipose tissue can produce and release several additional substances known as adipokines, including leptin, adiponectin, resistin, and interleukins (28

The categorization of breast cancers adheres to the guidelines set by the World Health Organisation (WHO), which undergoes periodic revisions to enhance patient care [10]. The categorization of tumors is essential for malignancy ranking and the selection of the optimal therapy to overcome the sickness. As an illustration, the existence or nonexistence of hormone receptors dictates, from several aspects, the necessity for hormone therapy or targeted treatments. An essential factor in classifying breast tumors is their molecular profile, as outlined by Perou et al. in 2000 [11]. We investigated the molecular-level heterogeneity of breast tumors by measuring the varying expression of critical genes. By analyzing the gene expression profile. Breast cancer is categorized into four primary groups: basal-like triple-negative tumors, which account for around 10% of breast cancer cases; luminal A (50–60% of cases); luminal B (10% of cases); and human epidermal growth factor receptor 2 (HER2)-positive (20% of cases). Identified as a normal-like subtype, this subgroup exhibits resemblances to the luminal A group but carries a more unfavorable prognosis. The subgroup above makes up 10% of the total luminal A cell population. Immunohistochemistry markers, such as ERα, PR, and HER2, are frequently used in standard clinical practice to differentiate many tumor classifications. These tumor

identification biomarkers can take the role of transcriptome data in the correct correlation of the many forms of breast cancer to predict therapy and outcome. Luminal cell carcinomas, characterized by ERα, exhibit the least aggressiveness. Although both types may have PR, only type B features HER2 expression. In contrast to luminal A malignancies, which have poor proliferative potential, luminal B tumors exhibit greater aggressiveness. This can be attributed to the elevated expression of genes associated with the cell cycle and cell proliferation, such as Aurora kinase A and KI-67. Furthermore, luminal B malignancies exhibit reduced expression of luminal-associated genes, including FOXA1 and PR [12–14]. Luminal B cancers have higher frequencies of p53 mutations (29% and 12%, respectively) than do luminal A tumors. Expression of ERα and PR receptors are absent in HER2-positive tumors. The upregulation of the HER2 receptor triggers the activation of more signaling pathways, including PI3K/AKT (phosphoinositide 3-kinases/protein kinase B) or Ras/MAPK (mitogen-activated protein kinases), leading to enhanced overall survival and cell propagation. This phenomenon promotes the formation of metastases and renders this form of breast cancer more severe compared to luminal cancers [9]. Consequently, basal-like tumors lacking the key biomarkers (ERα, HER2, and PR) were classified as triple negative compared to the other groups. The expression of gene features of this particular subtype of breast cancer encompasses keratin 17, keratin 5, integrin-B4, laminin, and an elevated expression of genes associated with propagation, including amplification of CDK6, MYC, and CCNE1.

Furthermore, Breast cancer that is triple-negative is distinguished by modified DNA reparation mechanisms, including the removal of BRCA2, PTEN, and MDM2 genes, as well as a high frequency of TP53 mutations. These tumors exhibit greater aggressiveness and heterogeneity, characterized by a high proliferation index, histological grade, and local and distant recurrence rate. Consequently, their prognosis is quite unfavorable [15,16].

The occurrence of breast cancer is influenced by various risk factors due to the intricate molecular mechanisms involved in its development. These are associated with heredity, lifestyle, hormone exposure, dietary and alcohol intake, thinness, and environment [30,31,32]. Less than 10% of breast cancers are causally linked to genetic and inherited factors. In this scenario, most patients had a genetic alteration in Breast Cancer-Associated genes 1 and 2 (BRCA1 and BRCA2), which work to repair DNA and activate cell cycle checkpoints. Changes in these genes lead to chromosomal instability and disrupt checkpoint regulation, therefore facilitating the growth of tumors [33]. One of the most significant hazards associated with breast cancer is exposure to hormones. The risk of breast cancer is elevated by prolonged exposure to both endogenous and exogenous estrogen [34]. Menopausal hormone therapy, consisting of estrogen and progestin, has been linked to an increased risk of invasive and in situ breast tumors.

Regarding androgens, evidence is conflicting and does not demonstrate a correlation between circulating androgen levels and the likelihood of developing breast cancer [36]. Nevertheless, McNamara et al. demonstrated that elevated levels of total testosterone in the bloodstream seem to elevate the risk in women before menopause [37]. A high blood testosterone level in postmenopausal women may also serve as a significant prognostic indicator for the return of breast cancer [38]. Environmental factors, including ionizing radiation, air pollution, heavy metals, and extended contact with substances including insecticides, organochlorine pesticides, polycyclic aromatic hydrocarbons, organic solvents, and polychlorinated biphenyl are widely recognized as significant contributors to the development of breast cancer [39,40]. The risk factors are more widespread in industrialized nations, characterized by delayed first pregnancies, diminished prevalence of breastfeeding, increased use of hormone therapies, and more sedentary lifestyles. This accounts for the increased rate of breast cancer in developed countries regardless of the less extensive implementation of screening programs. Nevertheless, the evolving lifestyles in emerging nations and Asia are causing a rise in the occurrence of breast cancer and, as a result, in the death rate related to breast cancer. Thus, it is crucial to undertake prevention and early detection programs to effectively combat the advancement of this malignancy, particularly in developing nations [41].

Clinical laboratory testing for erythropoiesis (ER) and prolactin originally measured the levels of hormone receptors in breast cancer textiles using radiolabelled ligand-binding assays (LBAs). For this, it was necessary to use well-frozen textile from the tumor, which was subsequently homogenized and combined with predetermined amounts of radiolabeled oestradiol. The receptor-bound radiolabeled oestradiol was isolated from the unbound ligand using dextran-coated charcoal. The quantity of bound ligands was determined using the Scatchard methodology [42]. An advantage of this specific study method was its ability to estimate the number of receptors found in the tumor quantitatively. Nevertheless, it had many drawbacks, such as the need for considerably larger quantities of properly frozen tissues than those utilized for the initial diagnosis, the risks associated with utilizing radiolabeled ligands, and its technological complexity. Furthermore, the test was susceptible to producing false-positive outcomes due to the requirement of using homogenized tissue in the LBA, which could include invasive tumors, in situ tumors, and healthy glands. Histogeneity of endoplasmic reticulum (ER) appearance in the homogenized textile utilized for testing may lead to false-negative outcomes. Introducing receptor-specific antibodies in ELISA-based techniques was an advancement, enabling quantitative analysis without the need for radiolabeled ligand materials. Furthermore, it has other similar constraints to the LBA [44]. An ideal assay would be one that could also evaluate the expression of the endoplasmic reticulum (ER) and progesterone receptor (PR) in the invasive tumor component used for the diagnosis. It was clear that an immunohistochemistry test was the most appropriate method. Nevertheless, before the early 1990s, commercial antibodies targeting ER were accessible in an immunohistochemical test on tissues fixed with formalin and processed with paraffin, yielding low-quality results [45,46]. However, it was only with the introduction of heat-produced epitope recovery by [47] that antibodies targeting ER became accessible for application in an immunohistochemical test on textile sections preserved with formalin [48,50]. Following this, other research has confirmed this immunohistochemical

method's technical and clinical validity for evaluating endoplasmic reticulum (ER) and progesterone receptor (PR) in clinical samples. The results of these studies have shown a strong association with the well-established lymphocyte-binding assays [49,51,52]. Further, clinical trials have shown that immunohistochemistry-based response prediction to hormone treatment is more precise than the earlier LBA [53,54]. Thus, at the beginning of the new century, most clinical laboratories adopted immunohistochemistry as the most reliable method to perform ER and PR testing on patient samples. Based on LBA research showing that patients receiving hormone treatment fared better when their tumors had higher levels of receptors than when there was less ER. The immunohistochemical assay remains a valuable tool for clinicians to estimate the receptor present. However, a major drawback of the immunohistochemistry method is that it does not easily enable a quantification estimate of the staining concentration and quantity of immunohistochemically colored invasive tumors using image analysis tools is a costly and limited practice. Instead, a commonly used semi-quantitative method involves the pathologist assessing the stained intensity and proportion of invasive tumor cells under a microscope [35,58,59]. From this perspective, it is crucial to establish the threshold where the tumor is classified as receptor-positive, indicating that the patient is probably will get advantages from hormone treatment. Below this threshold, alternative therapies should be explored. Currently, the recommended threshold is a cut-point of 1% for the percentage of invasive tumors that show positive staining for hormone receivers, while less than 1% is deemed negative [59]. It appears that quantifying the ER and PR immunohistochemistry data has extra prognostic relevance. It is a more accurate indicator of mortality risk specific to breast cancer compared to merely determining ER positivity. The widespread application of immunohistochemistry in diagnostic laboratories as a diagnostic tool and the wide variety of commerce reagents and antibodies have resulted in challenges during unification. This issue has been especially worrisome with predictive tests, such as those for HER2, ER, and PR, which need a certain level of quantitative evaluation. The presence of significant variability in the PR and ER assays' sensitivity, which may lead to false negative outcomes, prompted the implementation of rigorous quality assurance (QA) procedures in clinical laboratories. These programs aim to monitor the results and mitigate the incidence of mistakes. If quality assurance procedures are not implemented, it will unavoidably result in the reporting of false-negative results and the denial of hormone therapy to patients due to incorrect test results [56,57,61]. Most laboratory accreditation systems require that laboratories implement these quality assurance standards or give proof that deviations from these guidelines do not negatively impact the accuracy and quality of test outcomes for predictive indicators such as PR and ER.

RESULTS

First: statistical analysis of the hormone (progesterone)

1- Testing the distribution of data for the patient sample: Looking at Table No. (1), it was found that the data is distributed normally, as the Kolmogorov-Smirnova test value appeared equal to (.098) and a probability value (=.200 Sig), which is greater than the significance level (0.05). The Shapiro-Wilk test also showed a value of (.960) and a probability value of (=.548 sig), which is greater than the significance level of (0.05), which indicates the moderation of the data.

Table (1):

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
patpatients	.098	20	.200*	.960	20	.548

2- Testing the distribution of data for the healthy sample: Looking at Table No. (2), it was found that the data is distributed normally, as the Kolmogorov-Smirnova test value appeared equal to (.085) and with a probability value (=.200 Sig), which is greater than the significance level (0.05). The Shapiro-Wilk test also showed a value of (.971) and a probability value of (=.782 sig), which is greater than the significance level of (0.05), which indicates the moderation of the data.

Table(2):

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
control	.085	20	.200*	.971	20	.782

Evaluation of the sex hormone (progesterone) in breast cancer patients:

After verifying the data moderation, a parametric test (t-test) was conducted between two independent samples to test the following hypothesis: Null hypothesis (H_0): No significant differences exist in the average levels of the sex hormone (progesterone) between breast cancer patients and controls.

Alternative hypothesis (H_1): Significant differences exist in the average levels of the sex hormone (progesterone) between breast cancer patients and healthy controls.

By looking at Table No. (3), we notice that the value of the t-test is equal to (.118), and the probability value is (.907 sig=), which is greater than the level of significance (0.05), which leads to not rejecting the null hypothesis and therefore there are no significant differences between Average levels of the sex hormone (progesterone) in breast cancer patients and healthy controls

Table3

I		t	df	Sig. (2-tailed)
PROGESTERONE	Equal variances assumed	.118	38	.907

Second: Statistical analysis of the hormone (estradiol)

1- Testing the distribution of data for the healthy sample: Looking at Table No. (4), it was found that the data is distributed normally, as the Kolmogorov-Smirnova test value appeared equal to (.117) and a probability value (=.200 Sig), which is greater than the significance level (0.05). The Shapiro-Wilk test also showed a value of (.969) and a probability value of (=.732 sig), which is greater than the significance level of (0.05), which indicates the moderation of the data.

Table(4):

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
control	.117	20	.200*	.969	20	.732

2- Testing the distribution of data for the patient sample: Looking at Table No. (5), it was found that the data is distributed normally, as the Kolmogorov-Smirnova test value appeared to be equal to (.222) and with a probability value (=.111 Sig), which is greater than the significance level (0.05). Likewise, the Shapiro-Wilk test value appeared to be equal to (.843) and with a probability value (=.204 sig), which is greater than the significance level (0.05), which indicates the lack of moderation of the data.

Table (5):

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
patpatients	.222	20	.111	.843	20	.204

Evaluation of the sex hormone (Estradil) in breast cancer patients:

After confirming the moderation of data, a parametric test (t-test) was conducted between two independent samples to evaluate the following hypothesis: Null hypothesis (H_0): No significant differences exist in the average levels of the sex hormone (estradiol) between breast cancer patients and controls. Alternative hypothesis (H_1): Significant differences exist in the average levels of the sex hormone estradiol between breast cancer patients and healthy people. By looking at Table No. (6), we notice that the value of the t-test is equal to (7.575), with a probability value of (0.000 sig=), which is smaller than the significance level of 0.05, resulting in the rejection of the null hypothesis, and thus there are significant differences between the means The level of the sex hormone (Estradiol) in breast cancer patients and healthy people, with an average of (132.92500)

Table (6): Test of Independent Samples

t	df	Sig. (2-tailed)	Mean Difference

Estradiol	Equal variances assumed	7.575	38	.000	132.92500

DISCUSSION

Cancer of the breast is a diverse and adaptable disease characterized by numerous latent genetic and epigenetic alterations. Molecular categorization provides important information for assessing several features of breast cancer in addition to the histological diagnosis, such as differences in disease progression, survival rates, and reaction to therapy across patient groups. This classification relies on the expression of estrogen receptor (ER), progesterone receptor (PR), and HER2, categorizing breast cancer into four molecular subtypes: luminal A, luminal B, HER2-enriched, and basal-like. Notwithstanding these accomplishments, there is a general agreement on the need to develop novel biomarkers for the early identification of breast cancer. (ESR1 and PGR Gene Promoter Methylation and Correlations with Oestrogen and Progesterone Receptors in Ductal and Lobular Breast Cancer).

Contemporary global recommendations for metastatic hormone therapy (MHT) suggest the addition of a progestogen to estrogen treatment in peri and postmenopausal women who have an undamaged uterus to protect the endometrium.2,27–29. However, prolonged use of combined estrogen-progestogen treatment has been linked with a raised breast cancer risk. The controversy around (compound) bioidentical hormones has significantly intensified in recent years 30 to 32. Evaluation of the impact of micronized progesterone on breast cancer risk: a comprehensive analysis.

Evaluation of estrogen receptor representation in breast cancer is generally recognized for its biological, prognostic, and predictive significance. However, the additional utility of assessing progesterone receptor representation is debatable. 7, 8. It has been postulated since the 1970s that the expression of PR is linked to the reaction to hormonal therapies in ER+ breast cancer. This is because it is believed that the simultaneous production of ER and PR indicates a functionally intact pathway for estrogen response. An analysis of observational studies revealed that the absence of PR expression was linked to a poorer overall outcome in ER+ breast tumors (11, 12, 13, 14, 15). These findings indicated that assessing the PR rank in ER+ breast cancer could be utilized to direct medical treatment, as elevated PR expression levels may pinpoint a specific group of ER+ patients who are most likely to benefit from hormone therapy 16. Immunohistochemistry (IHC) detection of ER is a modest prognostic indicator of clinical outcome in breast cancer but a reliable predictor of response to tamoxifen-based treatment. Recent studies have shown that endoplasmic reticulum (ER) expression is found in around 70% of breast tumors. Therefore, obtaining a precise and dependable ER result is crucial for hormone therapy. A noteworthy finding in our investigation was the presence of ER-/PR+ in just one out of 137 malignant patients. Olivotto et al. similarly reported similar results, observing that just 192 total cases with ER-positive cells had PR+ cells faintly positive immunostaining. In contrast, 21 Colomer *et al*. found ER+/PR+, ER+/PR–, ER–/PR+, and ER–/PR– in 46%, 19%, 7%, and 28% of cases, respectively, contradicting these findings. Within the current investigation, we also identified 6.4% of cases belonging to the ER-ve and PR+ve group, therefore highlighting the significance of this subgroup among breast cancer patients. Subsequently, it has been proposed that PR status is linked to a healthy state and general survival separately. Specifically, patients with PR-positive, ER-positive cancers have a better prognosis than those with ER-positive, PR-negative tumors, which are better than those with ER-negative, PR-negative tumors. 22. Therefore, it may be deduced that hormone receptor testing was positive in two-thirds of breast cancer patients. Evidence of ER, and PR positivity suggests excessive production of progesterone and estrogen in breast-cancer. The presence of ER- and PR+ groups was also noted in a considerable proportion of breast cancer patients. Early-age group breast cancer patients exhibited ER negativity, but higher-age group patients displayed PR negativity-evaluation of the relationship between estrogen and progesterone receptor expression in breast cancer.

CONCLUSION

To comprehend the molecular processes of estrogen and progestogens and their effects on the growth of breast cancer cells, we examined prior research on progesterone and estrogen receptors in breast cancer cells, together with their corresponding signaling pathways. The hormone receptors exerted significant influence on the growth of breast cancer cells, both through genomic and non-genetic mechanisms. Moreover, the biological roles of estrogen and progesterone metabolites were also associated with the growth of breast cancer cells, but this facet of research necessitated additional investigation. The impact of menopausal hormone therapy on the growth of breast cancer cells: an analysis of the involvement of estrogens, progestogens, and their metabolites

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