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EFFECT PATIENTS' AGE AND ABO BLOOD GROUPS WITH TUMOR MARKERS IN BREAST CANCER IN KERBALA'A GOVERNORATE

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ABSTRACT

Breast cancer affects 13% of women worldwide at the moment. Despite the fact that breast cancer incidence rises with age, the earlier a diagnosis is made, the higher the death rate. We go over age-related aspects that impact the diagnosis, therapy, and management of breast cancer, examining the key ideas and pointing out important areas that need further investigation. We are studying age as a worker in breast cancer diagnosis, hormone factors and the effect of the blood type on the disease. The results showed that estrogen and progesterone hormonal rise in ages older than the 50 yeasr. But noticed that the Ki67 is rising at the ages of less than 49, as statistics showed clear moral differences. While the results showed that there is no clear role for employees Her2/neu, BCL2 and their relationship with age. As for the effect of the blood type, the results showed that the most injured women with breast cancer carry the blood type A, followed by the blood type O.

Keywords : breast cancer , ER, PR , Her2/neu , Bcl2, Ki67 and ABO blood group.

INTRODUCTION

According to Carey *et al.* (2006), breast cancer is a diverse disease with multiple biological subgroups. According to Runowicz *et al.* (2016), 246 600 new instances of breast cancer are expected to be diagnosed in 2016. Breast cancer is the most prevalent tumor type identified in American women. Cancer cells' DNA and RNA are similar to the creature from which they originated, yet they are not the same. This clarifies the reason the immune system, especially if it is compromised, does not frequently identify them (Sharma *et al*. 2010).

The cells lining the ducts are where most breast malignancies start (ductal tumors). Some (lobular cancers) develop in the cells lining the lobules, although a tiny percentage start in the other tissues (Jagsi *et al* 2019).

It is divided into four biological subgroups according to the expression of human epithelial growth factor receptor 2 (HER2) and the status of hormone receptors. These subtypes include basal-like, HER2-enriched (without ER expression) subtype, and luminal types A and B. (Perou *et al* , 2000). ER+ and/or PR+/HER2− status, low-grade tumor, and a favorable prognosis are the hallmarks of luminal A, the most prevalent subtype of breast cancer (Perou *et al* 2011, Blows *et al* 2010, Carey *et al* 2007). In clinical practice nowadays, a surrogate classification consisting of five categories based on histology and genetic characteristics is frequently employed. (Nadia , *et al* 2019)

In order to perform its biological action, estrogen binds to estrogen receptors (ERs), which are mostly made up of nuclear ERs (ERα and ERβ) and membrane ERs (mainly G protein–coupled receptors). Through these receptors, estrogen predominantly controls cancer stem cells (CSCs) (Kumar *et al* 1987). The prognosis is better for patients whose tumors are ER positive. These tumors are thought to be hormone-dependent and can be treated with tamoxifen or other medications that modify the way estrogen acts in the body. Three distinct ERs mediate the effects of estrogen: (1) the nuclear receptor ERα, which is responsible for around 75% of breast cancers (Siersbaek *et al*., 2018); (2) the nuclear receptor ERβ; and (3) the cytoplasmic G protein-coupled estrogen receptor 1 (GPER) (Huang *et al*., 2015). ERα and ERβ have similar mechanisms of action and have common

structural features with five distinct domains (A/B, C, D, E, and F) (Gérard *et al.,* 2018). Luminal A and B cancers are distinguished by Ki-67, a nuclear marker of cell proliferation. Based on a multigene expression assay, luminal A-like tumors among ER-positive/HER2 negative breast cancers are identified as PgR positive, low Ki67 breast cancers with low recurrence risk. Luminal B-like tumors, on the other hand, were initially discovered by Gerdes et al. in the early 1980s. They are characterized as tumors with a negative or low positive reaction for PgR, high Ki67 (≥20%) index, and significant recurrence risk (Goldhirsch, *et al* 2013). It has been repeatedly demonstrated that the proliferation marker Ki-67 is an independent predictor and prognostic factor in early breast cancer (Urruticoechea *et al,* 2005). Chemotherapy works better for breast cancer with high Ki-67 expression (Jones *et al* 2010). The majority of the protein is moved to the surface of cellular chromosomes during mitosis, however during interphase, the Ki-67 antigen is only found in cell nuclei. (Cuylen *et al* , 2016). One of the proteins in the bcl family that controls apoptosis is the BCL2 protein. The bcl-2 gene codes for the Bcl-2 protein. Animal models have shown its carcinogenic potential (McDonnell and Korsmeyer, 1991). It also has an anti-apoptotic effect, which prevents cell death and prolongs cell life (Vaux *et al.,* 1988). Breast cancer cells and normal breast epithelial cells both commonly express Bcl-2, which is known to be increased by estrogen. (Leek *et al*, 1994). According to studies (Silvestrini *et al.,* 1994), Bcl-2 expression in breast cancer has been shown to favorably correlate with differentiated indicators or good prognostic characteristics such ER/PR expression, HER2 negative, slow proliferation, small tumor size, and more. Bcl-2 targeted therapy appears to be a promising treatment option for a variety of malignancies, according to mounting data. The majority of research have found that Bcl-2 expression indicates a positive prognosis for the patient. When considering the therapeutic regimen, In patients undergoing endocrine therapy, Bcl-2 has been demonstrated to be a good predictor of clinical success; however, this is not the case for patients getting local-regional treatment alone. (Sung, H. et al. 2020).

METHOD AND MATERIAL

fifty patients newly diagnosed with breast cancer attended the Breast Cancer Early Detection Center at Al-Husseini Hospital in Karbalaa city . Samples were collected from July to December 2022. The patients were diagnosed clinically by the consultant. The medical staff in the center that was based on the clinical examination,Ultrasound, mammography, immunological tests, and under

Supervising these employees, the information sheet (Appendix) was filled out. The technique known as immunohistochemistry (IHC) uses the idea that antibodies bind selectively to antigens in biological tissues to identify antigens inside the cells of a tissue segment. One can visualize the binding of the antibody to the antigen in several ways. Enzymes that catalyze color-producing reactions include horseradish peroxidase (HRP) and alkaline phosphatase (AP). IHC is a commonly used method in many clinical and research facilities because It enables the distribution and localization of specific cellular components within cells within the relevant tissue context to be seen. To locate antigens, a variety of IHC techniques are available. Additionally, the blood type of the study ladies was looked into.

RESULT

ER with the age of the patients: The results showed that the percentage of nuclear expression of the estrogen receptor in the age group (29-49) years is 1.071, and this group has less expression than the second age group, which includes ages over 50 years, as the percentage of expression for this receptor increased to 1.27, as shown in the figure (1).

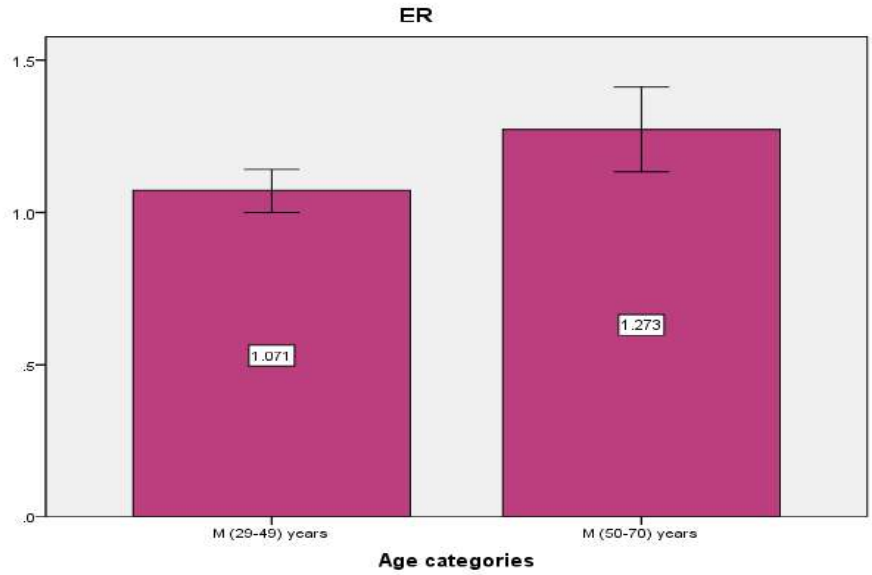


Figure 1: relationship of ER with the age in the patients with malignant breast cancer

PR with the age of the patients:

We finding that the expression of progesterone receptor protein in the tumor tissue in the first age group reached 1.286, while in the second age group, which includes ages over 50 years, the expression of the progesterone receptor in the tumor tissue increased until it reached 1.455, as shown in Figure (2)

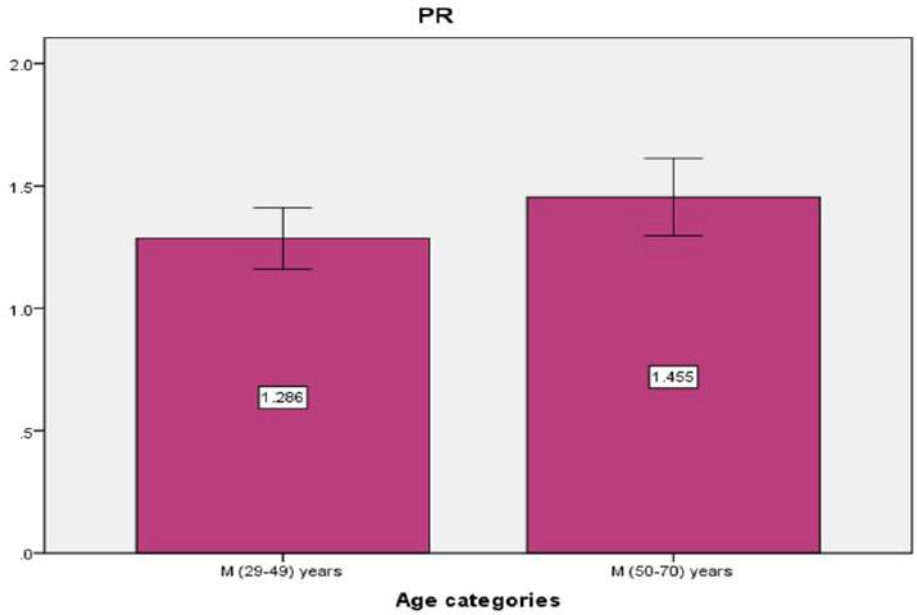


Figure 2 : relationship of PR with the age in the patients with malignant breast cancer.

Her2- neu with the age of the patients:

As for the tumor marker her2-neu and its relationship to the age of patients with malignant breast cancer, the results showed that the percentage of expression of this tumor marker in tissue reached 1.929 in the age group under 50 years, while in the other age group over 50 years, the percentage Its expression decreased slightly and reached 1.909, as shown in Figure (3)

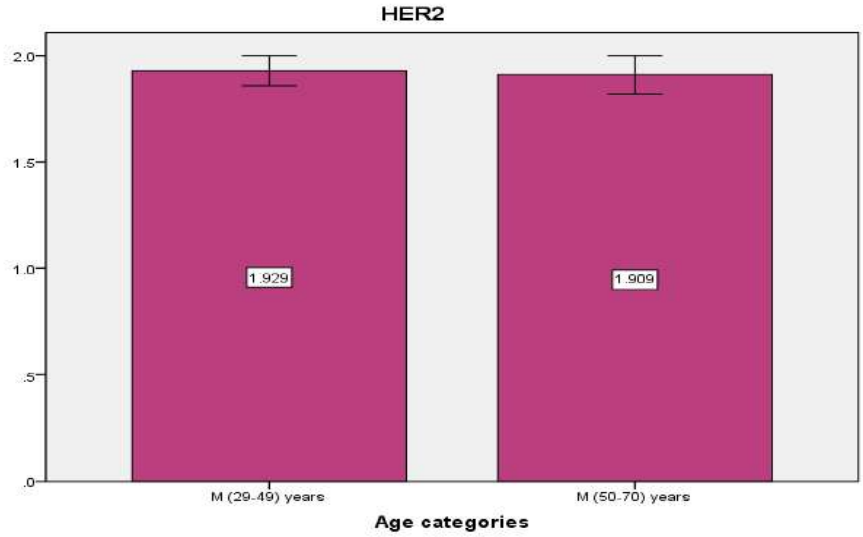


Figure 3: relationship of Her2-neu with the age in the patients with malignant breast cancer.

KI67 with the age of the patients:

In this study, histological sections were examined and the percentage of tumor cellular expression of the tumor marker Ki67 was examined in each of the two age groups. It was found that the percentage of Ki67 in the first age group, which includes ages under 49 years, reached 42.54%, while in the second age group, which includes ages older than the first, the expression percentage decreased until it reached 26.55. The results also showed that there were clear significant differences between the two age groups, with the p value = 0.014, as shown in Figure 4.

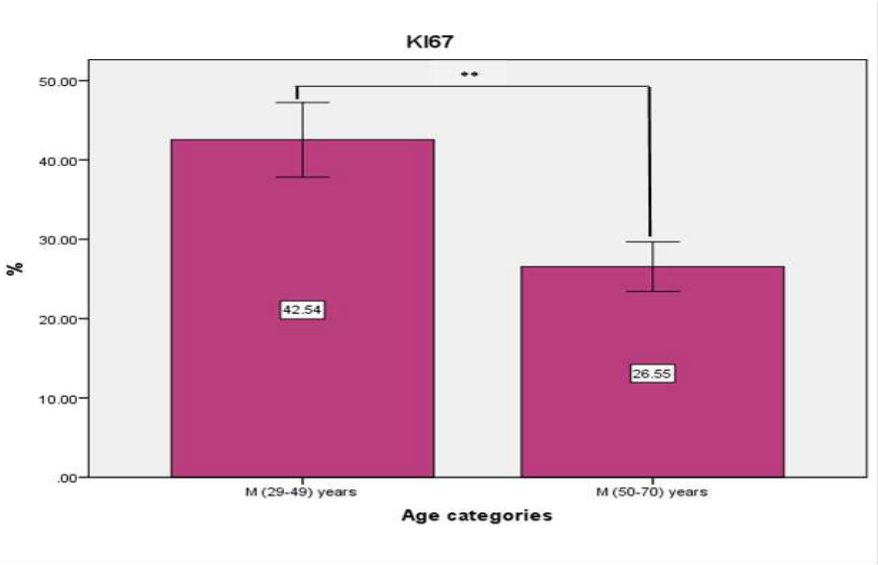


Figure 4-9: relationship of Ki67 with the age in thewomen with malignant breast cancer.

Bcl2 with the age of the patients:

The tumor marker BCL2 is considered the last tumor marker whose relationship to the age of patients with malignant breast cancer has been studied. We showed that the tumor tissue expression of this marker in the first age group reached 1.357, and this value was very close to the expression rate of this marker in the second age group (50-70 years), as it decreased very slightly, reaching 1.364, as shown. In Figure (5).

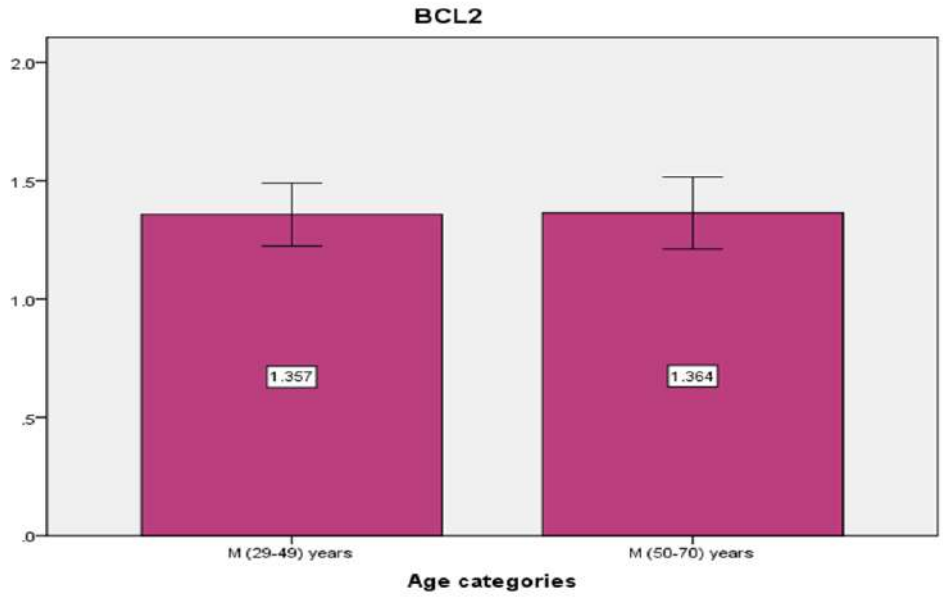
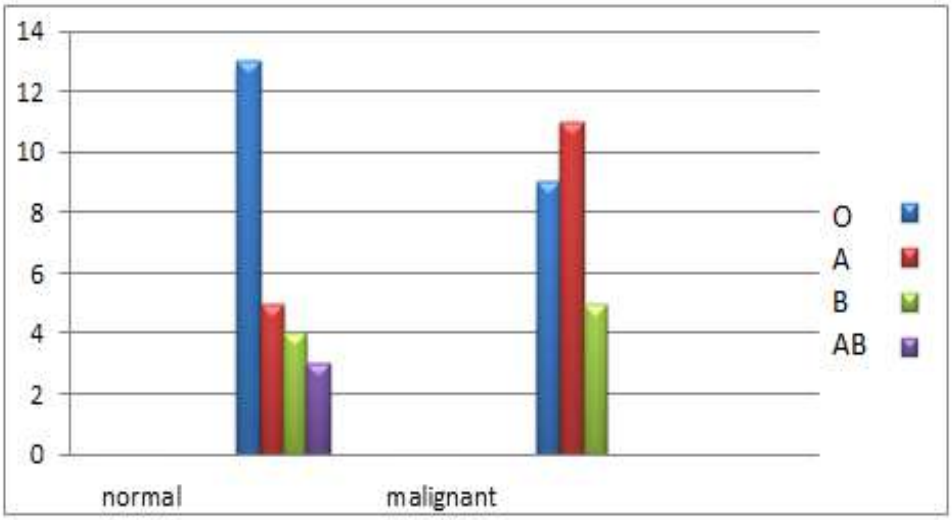


Figure 5: relationship of Bcl2 with the age in the patients with malignant breast cancer

The relationship of blood group with type of cancer

In this study, we investigated whether blood type has an effect on the development of breast cancer or not? The results showed that the highest percentage of women with malignant breast cancer were blood type A 44%, followed by blood type O 36%, and finally blood type B 20%.



DISCUSSION

Estrogens are steroid hormones that control several target tissues in the human body, including growth, differentiation, and function.. Estrogen receptors (ER) α and β, members of the large nuclear receptor superfamily, mediate the biological effects of the hormones. These receptors function as transcription factors that are activated by ligands. According to the traditional mechanism of ER activity, estrogen binds to nucleus-based receptors, which then dimerize and bind to certain response elements (EREs) found in target gene promoters. A conformational shift brought about by hormone interaction also occurs in the receptors' ligand binding domain, which makes it possible to recruit co-activator proteins. (Nilsson *et al* 2001).

This result of the estrogen receptor is agree with (AlZaman, *et al* , 2016) they found Older women were more likely to be estrogen receptor (ER) positive. Many studies have reported that younger age is an independent factor for poor prognosis in breast cancer (Lobbezoo *et al 2013).* ER positivity increased with rising age (Azizun-Nisa,*et al* , 2008).

This study's findings, which support those of Shah et al. (2022), who discovered a statistically significant correlation between age and PR, show that women with breast cancer who are older than 50 have higher PR levels. There was a substantial correlation between PR status and age between 41 and 50 years. Significant differences were seen between younger (27–39 years old) and older (40–80 years old) ages in another investigation. In a research by Pourzand et al. (2011), women between the ages of 27 and 39 had breast cancer that was PR-positive. The lesser sample size, racial variance, and various age groups could be the source of the discrepancy. Our study's findings also confirmed that cancers that form in different age groups have distinct biological characteristics, which calls for more investigation in this area. Our research showed that while there was no significant correlation with HER2/neu status, there was a substantial association between age and ER and PR status. According to Shah et al. (2022) the current study's findings are in agreement. The current study's findings conflict with research that established how early life affects hormone receptors. Our findings aligned with the research conducted by Nishimura et al. (2010) and Madani et al. (2016), which indicated that women under 50 years old had higher rates of increased expression of the tumor marker Ki67 in their tumorous breast tissue compared to their older counterparts. According to a study, age and the proportion of cells in BC that are positive for Ki-67 are strongly correlated. (Sahin *et al,*1991).

Furthermore, we discovered no association between age and the bcl2. The Chi-square test revealed no statistically significant variations in BCL2 expression with respect to the age of the patients ($p > 0.05$), which is consistent with the findings of Heba et al., 2020 and Holmqvis et al., 1999.

It is yet unknown how Bcl-2 contributes to the onset and spread of breast cancer. It has been reported that ductal carcinomas exhibit both overexpression and absence of Bcl-2 expression.

According to a number of studies, including Sultan Ayoub Meo et al. (2017), blood groups "A" (45.88%), "O" (31.69%), "B" (16.16%), and "AB" (6.27%) have higher incidences of breast cancer. The blood group "AB" has the lowest correlation with breast cancer, while blood group "A" has the greatest.

Comparably, (Akin and Altundag 2018) discovered that blood group A made up 43.7%, blood type O made up 33.8%, blood group B made up 14.7%, and blood group AB made up 7.9%. However, there are statistically insignificant variations in the way blood types are related to breast cancer risk.

However, (Sahar et al., 2013) they discovered a strong association between the ABO group type and breast cancer, with blood group type having the highest frequency and proportion of patients with breast cancer..

CONCLUSION

The current findings suggested that the Ki-67 level in patients with breast cancer may be a useful biomarker for treatment and follow-up. Standardizing Ki-67 assessment and clarifying its therapeutic role should be the main goals of future research. decision-making. Also, from a genetic standpoint, blood type may have an impact on the development of the disease.

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