WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 14, 39-49. Research Article ISSN 2277–7105

IMMUNOHISTOCHEMISTRY PROFILE OF FEMALE BREAST CANCER IN BASRAH CITY FROM (2021-2023) SCIENTIFIC COUNCIL OF THE ARAB BOARD OF ANATOMIC PATHOLOGY

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Article Received on
28 May 2024,

Revised on 18 June 2024,
Accepted on 08 July 2024

DOI: 10.20959/wjpr202414-33245

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ABSTRACT

Introduction: Breast cancer is the commonly diagnosed cancer in females, leading cause of female cancer death worldwide Molecular classification of Breast cancer based on Estrogen receptors, progesterone receptors and Her2neu receptors expression which have significant inference for prognosis. **Aim:** The study aim to evaluate the hormonal receptor status in female breast cancer and assess the relationship with cancer grade and type. **Methodology:** Atotal 500 Cases of breast cancer were collected from governmental and private laboratories reports were collected; the study period was conducted from January 2021 to December2023. Data analyzed according to age, grade, histological type and immunohistochemical profile. Recurrent cases and cases with incomplete information were not included in the analysis. **Results**: Invasive ductal carcinoma (not otherwise specified) accounted for 94.2% of all cases in our analysis, with the majority of patients (32%) being between the ages of 51 and 60. The majority of these cases were grade III. Hormone receptor positivity was found to have an inverse relationship with HER 2/neu status. Compared to Grade III tumors, the majority of low-grade cancers were ER+PR+. **Conclusion:** There was a significant statistical association (p=0.003) between the grade of breast cancer and (ER, PR, Her2neu). When the possibility of statistical association between type of cancer and (ER, PR, Her2neu), it was found that there was no any significant statistical association between the two factors (p=0.277), may be because not all cases of breast cancer with different histopathologic subtypes were included in this study.

INTRODUCTION

Breast cancer is the leading form of cancer among women globally, with over 1 million new cases diagnosed annually.[1]

Breast cancer varies significantly in its biological characteristics, and patients who share similar diagnostic and clinical prognostic factors may experience notably different clinical results.[2]

Breast cancer survival depends on detecting it early, providing timely and suitable treatment, and considering genetic predisposition.[2]

The Health Surveillance Secretariat states that women between the ages of 50 and 69 years are the group most at risk of sickness. Yet they encounter considerable obstacles in their quest for secondary cancer prevention measures.[3]

The majority of invasive carcinoma of breast are originate from the ducts(over 90%). specifically Invasive ductal carcinoma of no special type not otherwise specified (NOS) which accounts for 60%–80% of all breast carcinoma cases.[4]

The two sub groups of Luminal breast carcinoma (ER-positive, HER2/neu negative with low proliferation and ER-positive, HER2/neu negative with high proliferation), as well as HER2/neu positive and basal- like are the molecular subtypes of breast carcinoma, these sub types are predictive of clinical outcomes and response to treatment.

Among them, the basal like subtype has the poorest prognosis.[5]

The best approach is thought to be to Classifying breast carcinoma patients into subgroups based on patterns of gene expression patterns in tumor tissue. However, its clinical and research utility is limited due to the high cost and technical challenges associated with carrying out gene activity profiling by use of paraffin-embedded samples. Therefore, immunohistochemistry now used to classify breast carcinoma.[6]

In contrast to gene expression activity, access to immunohistochemistry is easy, not require specified education, allows for analysis of large tumor area easily, requires less time for interpretation and is relatively cost- effective.[7]

The immunohistochemical classification is as follows:[6]

- The subtype1= positive for HER2/neu positive and ER/PR
- The subtype2= HER2/neu negative, ER/PR positive
- The subtype3= HER2/neu positive, ER/PR negative
- The subtype4= negative for HER2/neu and ER/PR

The above categorization provide predictive therapeutic information. A lot of clinical, pathological and molecular factors, such as histopathological type, tumor grade, size, lymph node involvement, and status with respect to the Estrogen receptor(ER), Progesterone receptor(PR) and (HER-2nue) gene ,all impact the prognosis and course of treatment for breast carcinoma.[8,9]

Currently, it is recommended as standard practice to determine hormone status using biopsy specimens Currently, ER status is considered the most influential predictive marker in breast cancer treatment ,despite ER and PR being interdependent variables.[4]

PR holds equal importance to ER in predicting the prognosis of breast cancer as it is expressed in 60-70% of invasive cancers.[10] HER 2neu a proto-oncogene that is amplified and over expressed in 15-25% of breast carcinoma cases and it is linked to a poor prognosis.[11]

Presently, these indicators are widely employed to guide management strategies and predict prognosis of disease in relation to clinical and pathological factors, including status of lymph node, size of tumor, grade, histopathological characteristics, and surgical edges.[12],[13]

More than 70% of breast tumors exhibit activity of estrogen and progesterone in the tumor center, making them suitable for antiestrogen therapy.[14]

And about 20% of tumors display amplifying HER2 and could potentially advantage from adjuvant treatment with trastuzumab directed target therapy. This treatment can be given alone or in conjunction with chemotherapy, to reduce the risk of recurrence by fifty percent.[15],[16]

The current study conducted immunohistochemical analysis to assess Human epidermal growth factor receptor-2 (HER2/neu), progesterone receptor and estrogen receptor expressions, and subsequently analyzed their statistical relationships with tumor type and

grade.

METHODOLOGY

In Basrah, Iraq, from January 2021 to December 2023, across- sectional study was conducted. All histopathological information for primary breast cancer released by histopathology departments of all major governmental hospitals and from pathological private laboratories were collected in the governorate and analyzed, totaling 500 Cases. The data collected included information on age, grade, histological type, and immunohistochemical profile. Only newly diagnosed cases were used in this analysis, Recurrent cases and cases with incomplete information were not included.

RESULTS

Among 500 case of breast cancer, the most frequent affected age group had been was between 51 to 60 years old represent (32%) of all cases as shown in below table(1).

Table 1: Age distribution of the study sample.

Age group (Year)	Frequency	Percent
21-30	14	2.8
31-40	71	14.2
41-50	152	30.4
51-60	162	32.4
61 or older	101	20.2
Total	500	100.0

It is clear that the most frequent type of breast cancer in this study was invasive ductal carcinoma (not otherwise specified) (94.2%). As shown In figure (1).

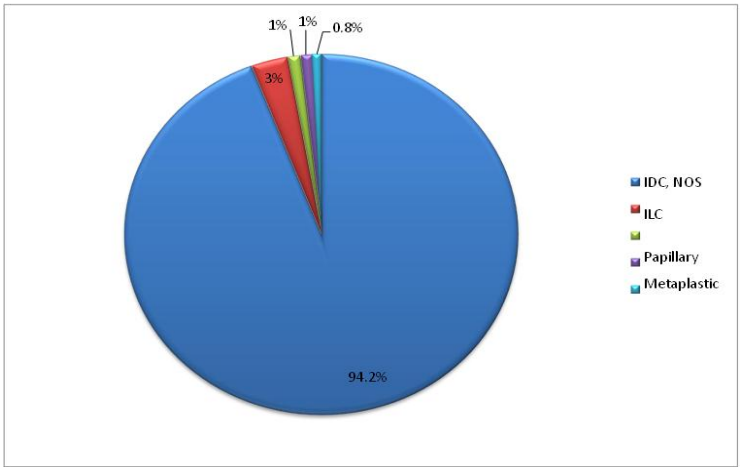

Figure 1: The frequency of different histological types of breast cancer in the study sample.

About 50.6% of all cases of breast cancer are present with high Grade (grade III), as shows in Table (2).

Table 2: Grade distribution of breast carcinoma throught the research participants.

Grade	Frequency	Percent
I	12	2.4
II	235	47.0
III	253	50.6
Total	500	100.0

The distribution of (ER, PR, Her2neu) among cancer patients in the study, Table (3), shows that the most frequent one is hormones positive + Her2neu negative which represent(63.4%).

Table 3: Distribution of (ER, PR, Her2neu) among cancer patients in the study.

Net (ER, PR, Her2neu)	Frequency	Percent
Hormones positive + Her2neu negative	317	63.4
Triple negative	86	17.2
Hormones negative + Her2neu positive	51	10.2
Triple positive	46	9.2
Total	500	100.0

When the possibility of statistical association between type of cancer and (ER, PR, Her2neu), it was found that there was no any significant statistical association between the two factors (p=0.277), as shown in figure (2).

Where A=Triple positive, B=Triple negative,

C=Hormone positive Her 2nue negative, D=Hormone negative Her2nue positive

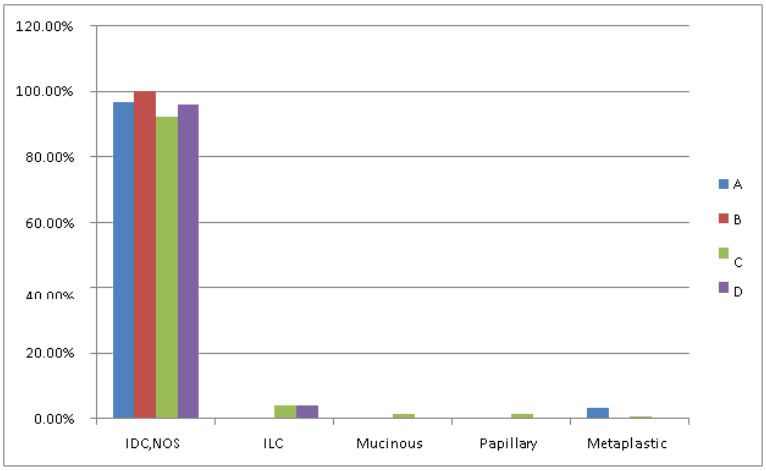

Figure (2): The association between histological type of breast cancer and (ER, PR, Her2neu)

* Fisher's Exact Test

There was a significant statistical association (p=0.003) between the grade of breast cancer and (ER, PR, Her2neu). As show in figure (3)

Where hormones receptors expression more in low grade ductal carcinoma grade (I and II) while when increasing the grade(III) the hormones receptors expression is low.

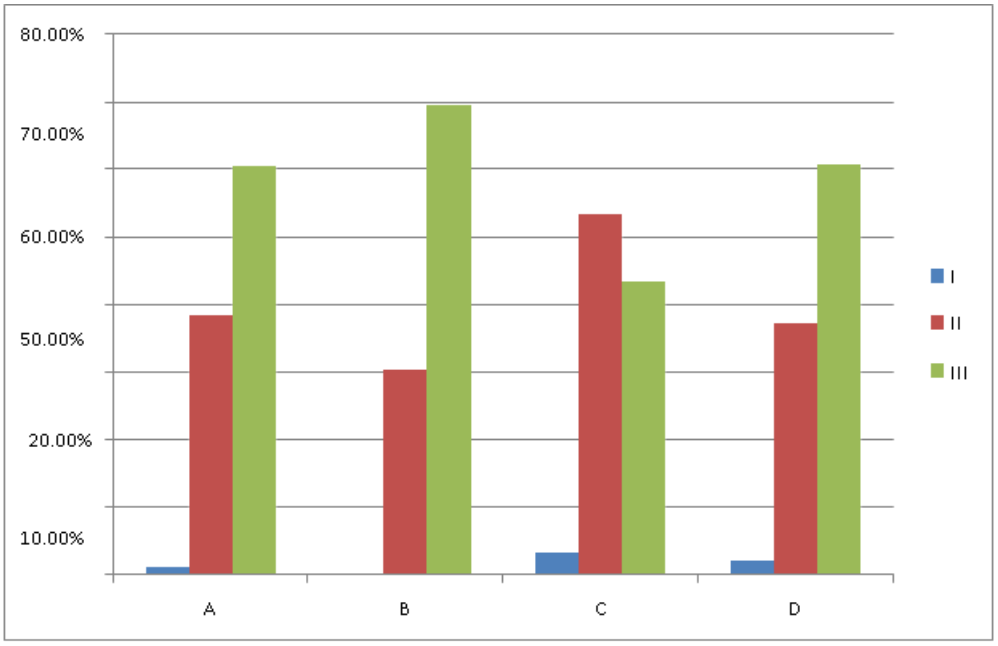

Figure 3: The correlation of the grade of breast cancer with (Her2neu, ER, PR).

* Fisher's Exact Test

DISCUSION

Breast cancer is the leading cancer among women worldwide, and early detection significantly increases chances of cure. Traditional factors like tumor size, grade, and axillary lymph node involvement are key for prognosis, but there is growing emphasis on molecular biological factors in prognosis assessment today.

Breast cancer's biological prognostic indicators encompass: HER2/neu, ER, PR, Ki67, p53, plasminogen activators & inhibitors, and others.

ER, PR and HER2/neu are the most significant predictive and prognostic indicators.[17]

The 500 patients with breast carcinoma in the current study had a mean age of presentation was 51.7 years. most common age group was 51 to 60 years(32%)years, these findings align

closely with *Maryam Sadat Hosseini, Maliheh Arab, Behzad Nemati Honar, Giti Noghabaei, Nazanin Safaei, Tahereh Ghasemi, Farah Farzaneh, Tahereh Ashraf Ganjoie* research outcomes which show breast cancer is increasing up to 50- 54 age group in Iran, and 55-59 age group in Iraq followed by a reduction in older age while an steady increasing pattern in all ages happens in the US.[18],[19],[20]

Invasive Ductal carcinoma (IDC) specifically IDC/ NOS (no special type),constituted most common histopathological form in 471 (94.2%) cases. similar predominant findings of IDC/ NOS were reported in research conducted by Sofi *et al[*21] (80.30%), Aziz un Nisa *et al*[22] (85.8%), Pallavi Shrigondekar *et al [23*] (93.2%), Suvarchala S B *et al* [24] (93.7%)and Bhagat Vasudha M *et al*[25] (94.8%).I have not found a study that proves the opposite of these results.

Only 12 (2.4%) cases In our research had Grade I tumor, whereas majority 253(50.6%) cases had grade III tumor which were followed by 235(47.0%) cases with grade II tumor, similar finding were reported by Pallavi Shrigondekar *et al [*23] where the most common presentation of breast carcinoma present with high Grade(grade III) tumor.

In our current study, the majority (63.4%) of tumors tested positive for ER and PR while a smaller percentage (10.2%)were HER2neu negative, These results are similar to findings from studies done by Ayadi *et al*.,[26] Ahmed *et al*.,[27] and Vasudha *et al*.[28] conversely, studies done by Lal *et al*.,[29] Moser Emliroise *et al*.,[30] Vaidhyanatha *et al*.,[31] and Munjal *et al*.[32] reported a higher incidence of Her-2/neu positivity. There is considerable variability in the expression of ER, PR & HER2/neu across different studies on breast carcinoma, likely influenced by diverse population characteristics.[33-34]

In our study, we did not observe a strong correlation between Hormone receptor expression and the histological type of breast carcinoma (ductal, lobular, etc), this finding aligns with similar results reported by Cherry Bansal, Aarti Sharma1, Mukta Pujani2, Meenu Pujani3, Kiran Lata Sharma1, AN Srivastava4, US Singh5.[35]

Tumor grade and hormone receptor positivity were found to be inversely correlated , tumors with Grade I mainly positive for ER and PR, while tumors with Grade III mostly negative for both ER and PR.

The presence of ER or PR Expression typically correlate with improved prognosis.[24] Women with breast tumors containing hormone receptor proteins should receive adjuvant hormonal therapy, irrespective of factors like menopausal circumstances, age, tumor size, location or involvement of.[23]

In Asian countries, the prevalence of hormone receptor-positive breast cancer is lower compared to Western countries, where more than half of tumors express hormone receptors.[23]

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