Section: Pathology

Original Research Article

EVALUATION OF IMMUNOHISTOCHEMICAL PROFILE OF PATIENTS OF BREAST CARCINOMA AT A TERTIARY CARE CENTRE

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Abstract

Background: Breast cancer represents the most prevalent form of cancer among women globally. Estrogen receptor (ER) and progesterone receptor (PR) are among the most relevant clinical biomarkers that are widely used in stratifying breast cancer cases management. Present study was conducted to evaluate immunohistochemical profile of patients of breast carcinoma at a tertiary care centre. **Materials and Methods:** Fifty archival cases of primary breast carcinoma that underwent subsequent resection or tissue block analysis were identified. Each of these cases was confirmed to be invasive ductal carcinoma. For the assessment of estrogen receptor (ER) and progesterone receptor (PR) status, antigen retrieval was conducted as follows: the tissue sections were deparaffinized and rehydrated using deionized water. Subsequently, they were subjected to heating in a citrate buffer within an electric pressure cooker, followed by a cooling period of 10 minutes before proceeding to immunostaining. The evaluation of ER and PR results was based on the maximum area of staining intensity, and both ER and PR expressions were assessed accordingly. **Result:** A total of 50 patients were enrolled. The mean age of the patients was 45.6 years. 64 percent of the patients were of urban residence. Positive family history of breast cancer was seen in 46 percent of the patients. 48 percent of the patients were of grade 2 while 28 percent of the patients were of grade 3. ER +/ PR +, ER +/ PR -, ER -/ PR + and ER -/ PR – was seen in 36 percent, 18 percent, 16 percent and 30 percent of the patients respectively. Significant correlation of ER and PR status with age and tumour grade was seen. **Conclusion:** Breast cancer incidence is on the rise in developing nations. This malignancy is classified as hormone-dependent, primarily driven by the mitogenic influences of estrogen and progesterone. The status of hormonal receptors is correlated with both the age and tumor grade of patients diagnosed with breast cancer.

INTRODUCTION

Breast cancer represents the most prevalent form of cancer and is the primary cause of cancer-related deaths among women globally. In 2008, around 1.38 million new cases of breast cancer were identified, with nearly half of these cases and approximately 60% of associated fatalities occurring in low-income nations.[1,2] Survival rates for breast cancer exhibit significant disparities across different regions, with a projected 5-year survival rate of 80% in high-income countries, contrasting sharply with rates below 40% in low-income countries.[3]

Research indicates a correlation between hormone replacement therapy (HRT) and the risk of developing breast cancer. The breast cancers associated with HRT are predominantly hormone receptor positive. In comparison to individuals who do not engage in HRT, those who do exhibit an elevated risk of breast cancer.[4,5]

The emergence of molecular technology has introduced novel biomarkers in conjunction with immunohistochemical and serum biomarkers. Immunohistochemical markers play a crucial role in informing treatment strategies, facilitating the classification of breast cancer into biologically distinct subtypes that exhibit varied behaviors, and

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serving as both prognostic and predictive indicators. Key areas of scientific inquiry include steroid hormone receptors, markers associated with tumor proliferation, and factors that contribute to angiogenesis and apoptosis.[6,7] Hormone receptors (ER and PR) and human epidermal growth factor receptor-2 (HER-2) are the most relevant clinical biomarkers that are widely used in stratifying breast cancer cases management. Knowledge of hormone receptors and HER-2 expressions are vital for breast cancer management plans and decision-making.[6,7] Nowadays, immunohistochemical detection of ER and PR is part of the routine work-up of breast cancer, and in some cases of DCIS the presence of ERs is an indication for tamoxifen therapy. There are many scoring systems and many studies have compared their ability to predict treatment response and correlations with outcome. The first scoring system counted the percentage of positive cells and ignored staining intensity.[8,9] Hence; the present study was conducted to evaluate immunohistochemical profile of patients of breast carcinoma at a tertiary care centre.

MATERIALS AND METHODS

Fifty archival cases of primary breast carcinoma that underwent subsequent resection or tissue block analysis were identified. Each of these cases was confirmed to be invasive ductal carcinoma. For the assessment of estrogen receptor (ER) and progesterone receptor (PR) status, antigen retrieval was conducted as follows: the tissue sections were deparaffinized and rehydrated using deionized water. Subsequently, they were subjected to heating in a citrate buffer within an electric pressure cooker, followed by a cooling period of 10 minutes before proceeding to immunostaining. All slides were processed using an automated system, where they were treated with 3% hydrogen peroxide for 5 minutes, incubated with the primary antibody for 30 minutes, exposed to a labeled polymer for another 30 minutes, and then treated with DAB as a chromogen for 5 minutes, concluding with hematoxylin as a counterstain for an additional 5 minutes. The evaluation of ER and PR results was based on the maximum area of staining intensity, and both ER and PR expressions were assessed accordingly. All the results were recorded in Microsoft excel sheet followed by statistical analysis using SPSS software.

RESULTS

A total of 50 patients were enrolled. The mean age of the patients was 45.6 years. 64 percent of the patients were of urban residence. Positive family history of breast cancer was seen in 46 percent of the patients. 48 percent of the patients were of grade 2 while 28 percent of the patients were of grade 3. ER +/ PR +, ER +/ PR -, ER -/ PR + and ER -/ PR – was seen in 36 percent, 18 percent, 16 percent and 30 percent of the patients respectively. Significant correlation of ER and PR status with age and tumour grade was seen.

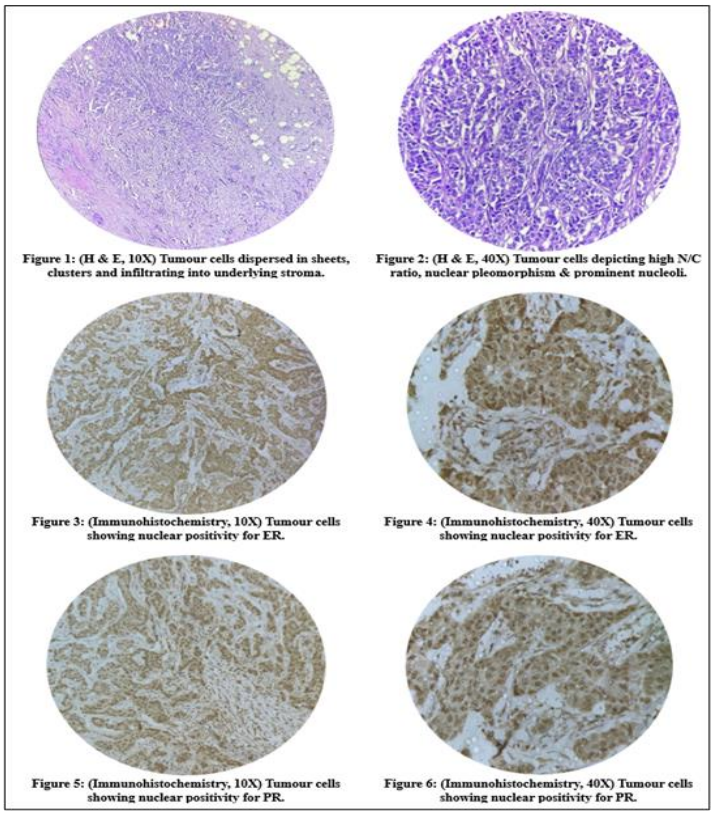

Figure 1: (H & E, 10X) Tumour cells dispersed in sheets, clusters and infiltrating into underlying stroma.

Figure 2: (H & E, 40X) Tumour cells depicting high N/C ratio, nuclear pleomorphism & prominent nucleoli.

Figure 3: (Immunohistochemistry, 10X) Tumour cells showing nuclear positivity for ER.

Figure 4: (Immunohistochemistry, 40X) Tumour cells showing nuclear positivity for ER.

Figure 5: (Immunohistochemistry, 10X) Tumour cells showing nuclear positivity for PR.

Figure 6: (Immunohistochemistry, 40X) Tumour cells showing nuclear positivity for PR.

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Table 1: Demographic details.

Demographic	Number	Percentage
Mean age	45.6 years	
Residence – Rural	18	36
Residence – Urban	32	64
Positive family history of breast cancer	23	46

Table 2: Distribution of patients according to tumour grade

Tumour grade	Number	Percentage
Grade 1	12	24
Grade 2	24	48
Grade 3	14	28
Total	50	100

Table 3: ER/PR receptor status

Tumour grade	Number	Percentage
ER +/ PR +	18	36
ER +/ PR -	9	18
ER -/ PR +	8	16
ER -/ PR -	15	30

Table 4: Correlation of ER/PR status with age and tumour grade

ER/PR status	r-value	p-value
Age	1.223	0.001 (Significant)
Tumour grade	2.712	0.000 (Significant)

DISCUSSION

Breast cancer has a lengthy historical background, with its earliest documentation occurring over 3,500 years ago by the ancient Egyptians around 1500 B.C. Currently, breast cancer ranks as the second most common cancer type and is a major contributor to cancer-related mortality among women in the United States. The American Cancer Society estimates that in 2021, approximately 281,550 women will receive a breast cancer diagnosis, with an anticipated 43,600 fatalities attributed to the disease within the same demographic. Timely detection of breast cancer is essential for effective treatment and favorable outcomes, as patients diagnosed with smaller tumors exhibit significantly improved survival rates and reduced mortality risk.[6-8] Breast cancer is curable if diagnosed at early stage. Traditional morphological prognostic factors include tumor size, tumor grade, and axillary lymph node metastasis. Nowadays, more importance is given to biological molecular prognostic factors because a significant number of patients with early-stage breast cancer harbor microscopic metastasis at the time of diagnosis.[9] Hence; the present study was conducted to evaluate immunohistochemical profile of patients of breast carcinoma at a tertiary care centre.

A total of 50 patients were enrolled. The mean age of the patients was 45.6 years. 64 percent of the patients were of urban residence. Positive family history of breast cancer was seen in 46 percent of the patients. 48 percent of the patients were of grade 2 while 28 percent of the patients were of grade 3. ER +/ PR +, ER +/ PR -, ER -/ PR + and ER -/ PR – was seen in 36 percent, 18 percent, 16 percent and 30 percent of the patients respectively. In a previous study conducted by Ambroise M et al, authors evaluated the estrogen receptor (ER), progesterone receptor (PR) and Her-2 /neu expression in invasive breast carcinomas by immunohistochemistry. It was a retrospective study of 321 female invasive breast carcinomas diagnosed in the Department of Histopathology. The age of the patients ranged from 24 to 99 years, with a mean of 53.8, and the majority of the tumors were T2 (83.8% in range of 2-5 cms), predominantly histological grade 2 (57.3%), followed by grade 3 (33.3%). ER, PR and Her-2/neu expression were seen in 59, 51 and 27% of cases respectively. Triple-negative breast cancer constituted 25 % of our cases. They also found characteristic associations between hormonal receptor and Her-2/neu expression and various clinico-pathological parameters. The hormonal receptor expression appears to be lower in the Indian population compared to the West.[10]

In the present study, Significant correlation of ER and PR status with age and tumour grade was seen. Mlole AT et al determine dthe expression of ER, PR and HER2 in women with breast cancer (BC). Expression of ER, PR and HER2 was determined immunohistochemically. ER, PR and HER2 were expressed in 53.4%, 46.6% and 18.5%, respectively. ER and PR co-expression was present in 42.7% and 37.9% of patients had triple negative breast cancer (TNBC). Age was an independent predictor of expression of ER and PR. The majority of patients in this study had less than 50 years with high tumour grade. Interestingly, most of them had high expression of HER2 with TNBC which are molecular subtypes of BC with poor prognosis.[11] Khabaz MN et al, in another previous study, defined the IHC profile of ER, PR and HER2 in Saudi female breast neoplasms of ductal and lobular types and associations ER, PR and HER2 expression patterns with various clinicopathological factors. ER, PR and HER2 expressions were assessed using IHC staining.

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Ductal carcinomas with a variety of histological grades constituted 88 (88.8%) of total cases. Seventy-four (77.8%), 59 (62.1%), and 35 (36.8%) of ductal carcinomas showed positive staining for ER, PR and HER2, in that order. The remaining breast cancer cases were four (4%) lobular carcinomas and two (2%) mixed form of ductal and lobular types, which were ER+, PR+, and HER2-. Breast cancer expression pattern of ER, PR and HER2 in Saudi female is different from that of Tunisian and Jordanian female populations and closer to the expression pattern of Egyptian, Lebanese, Iraqi and western country females. Furthermore, the present study found two IHC patterns of breast cancer ER+/PR-/HER2+ (5%) and ER+/PR-/HER2- (11.1%), which had not been reported in other Arabic studies. Thus, the rates of IHC expression patterns in breast cancer show some variation among regional female populations.[12]

CONCLUSION

Breast cancer incidence is on the rise in developing nations. This malignancy is classified as hormone-dependent, primarily driven by the mitogenic influences of estrogen and progesterone. The status of hormonal receptors is correlated with both the age and tumor grade of patients diagnosed with breast cancer. Collectively, the findings of this research contribute to the reconsideration of the routine application of hormonal therapy in this patient population.

REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127:2893–2917.
2. Thompson D, Duedal S, Kirner J, McGuffog L, Last J, Reiman A, Byrd P, Taylor M, Easton DF. Cancer risks and mortality in heterozygous ATM mutation carriers. J Natl Cancer Inst. 2005;97:813–822.
3. Seal S, Thompson D, Renwick A, Elliott A, Kelly P, Barfoot R, Chagtai T, Jayatilake H, Ahmed M, Spanova K, et al. Truncating mutations in the Fanconi anemia J gene BRIP1 are low-penetrance breast cancer susceptibility alleles. Nat Genet. 2006;38:1239–1241.
4. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, Baili P, Rachet B, Gatta G, Hakulinen T, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD) Lancet Oncol. 2008;9:730–756
5. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, Vierkant RA, Maloney SD, Pankratz VS, Hillman DW, et al. Benign breast disease and the risk of breast cancer. N Engl J Med. 2005;353:229–237.
6. Waks AG, Winer EP. Breast cancer treatment: a review. JAMA - J Am Med Assoc. 2019;321:288–300
7. Dupont WD, Parl FF, Hartmann WH, Brinton LA, Winfield AC, Worrell JA, Schuyler PA, Plummer WD. Breast cancer risk associated with proliferative breast disease and atypical hyperplasia. Cancer. 1993;71:1258–1265.
8. Barnes DM, Harris WH, Smith P, Millis RR, Rubens RD. Immunohistochemical determination of oestrogen receptor: comparison of different methods of assessment of staining and correlation with clinical outcome of breast cancer patients. Br J Cancer. 1996;74:1445–1451.
9. Fisher ER, Anderson S, Dean S, Dabbs D, Fisher B, Siderits R, Pritchard J, Pereira T, Geyer C, Wolmark N. Solving the dilemma of the immunohistochemical and other methods used for scoring estrogen receptor and progesterone receptor in patients with invasive breast carcinoma. Cancer. 2005;103:164–173.
10. Ambroise M, Ghosh M, Mallikarjuna VS, Kurian A. Immunohistochemical profile of breast cancer patients at a tertiary care hospital in South India. Asian Pac J Cancer Prev. 2011;12(3):625-9.
11. Mlole AT, Yahaya JJ, Othieno E, Kalungi S, Okwi AL. Hormonal Receptors, Human Epidermal Growth Factor Receptor-2 and Triple Negative Immunohistochemical Typing in Women with Breast Cancer in Kampala, Uganda. Int J Womens Health. 2020 Nov 27;12:1109-1123
12. Khabaz MN. Immunohistochemistry subtypes (ER/PR/HER) of breast cancer: where do we stand in the West of Saudi Arabia? Asian Pac J Cancer Prev. 2014;15(19):8395-400.

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