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Mohammad Shahid Iqbal
Department of Pathology, Medicine Program, Batterjee Medical College, Jeddah 21442, Saudi Arabia, shahid.iqbal@bmc.edu.sa

Hussain NA AlAbayah
New Najran General Hospital, Saudi Arabia

Aisha Tabassum
Department of Laboratory Medicine, College of Applied Medical Sciences, Umm al Qura University, Makkah, Saudi Arabia

Ahmad F Arbaeen
Department of Laboratory Medicine, College of Applied Medical Sciences, Umm al Qura University, Makkah, Saudi Arabia

Naif S Sannan
Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud Bin Abdul Aziz University of Health Sciences, Jeddah, Saudi Arabia

See next page for additional authors

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Expression of Estrogen Receptor, Progesterone Receptor and human epidermal growth factor receptor-2 in breast cancer: A two-year retrospective study

Authors

Mohammad Shahid Iqbal, Hussain NA AlAbayah, Aisha Tabassum, Ahmad F Arbaeen, Naif S Sannan, Hasan HH Qadi, Ahmed H Qasem, Mohammed HM Almunajjim, and Sahar F Arbaeen

ORIGINAL ARTICLE

Expression of Estrogen Receptor, Progesterone Receptor and Human Epidermal Growth Factor Receptor-2 in Breast Cancer: A Two-year Retrospective Study

Mohammad Shahid Iqbal [a,*], Hussain Naser Ali AlAbayah [b], Aisha Tabassum [a], Ahmad Fawzi Arbaeen [a], Naif Sami Sannan [c], Hasan Hatem Hasan Qadi [d], Ahmed Hassanain Qasem [a], Mohammed Hussain Mohsen Almunajjim [e], Sahar Fawzi Arbaeen [f]

[a] Clinical Laboratory Sciences Department, College of Applied Medical Sciences, Umm al Qura University, Makkah, Kingdom of Saudi Arabia
[b] New Najran General Hospital, Kingdom of Saudi Arabia
[c] Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud Bin Abdul Aziz University of Health Sciences, Jeddah, Kingdom of Saudi Arabia
[d] Department of Physiology, Faculty of Medicine, King Abdulaziz University, Kingdom of Saudi Arabia
[e] Regional Laboratory and Central Blood Bank, Najran, Kingdom of Saudi Arabia
[f] Ibn Sina National College for Medical Studies, Jeddah, Kingdom of Saudi Arabia

Abstract

Background: **Breast cancer in women is the most frequently diagnosed and lethal form of the disease. A woman's operable invasive breast cancer's hormone receptor subtype is a major long-term prognostic predictor.**

Objectives: **To investigate the expression of estrogen receptor (ER), progesterone receptor (PR), and Her-2/neu in invasive breast cancer and how it relates to clinicopathological prognostic variables.**

Materials and methods: **This study examines all invasive breast cancer patients who were seen between 2019 and 2020 at King Khalid Hospital in Najran. From the laboratory records, the demographic and clinical information, microscopic features, histological grade, lymph node metastases, stage, and final diagnosis, including immunohistochemical results for ER, PR, and Her-2/neu expression, were taken and analyzed in accordance with the goals.**

Results: **Breast cancer type luminal A was the most common. There was a greater prevalence of luminal A type (ER/PR+, Her-2/neu-negative) in older patients compared with the triple negative and Her-2+ subtypes in younger patients. Invasive ductal carcinoma was the most prevalent histopathological type. There was no statistical link between ER, PR, and Her-2/neu receptor expression and any of the breast cancer histological subtypes. The Her-2+ subtype had the highest percentage of grade III lesions, followed by the triple negative subtype. Luminal types A and B were the most common in grade I tumors.**

Conclusion: **In women with operable invasive breast cancer, the hormone receptor subtype is a significant independent prognostic predictor. Proper diagnosis requires regular testing of steroid hormone receptor and Her-2/neu expression.**

Keywords: Breast cancer, Estrogen receptor, Progesterone receptor

1. Introduction

Breast cancer (BC) is the most prevalent type of cancer diagnosed in women and the main cause of cancer death in women worldwide.[1,2] Geographic variation in breast cancer incidence is influenced by ethnic and genetic variances, cultural differences, and global changes in environmental exposures.[3] Its

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* Corresponding author. Department of Pathology, Medicine Program, Batterjee Medical College, 21442 Jeddah, Saudi Arabia.
E-mail address: mmiqbal@uqu.edu.sa (M.S. Iqbal).

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incidence has risen globally in recent decades, with Asian countries having the highest peak, and it is the main cause of cancer fatality in poorer nations.[1,4] cancer of breast is very a common cancer in Saudi Arabian women, with a rising rate of incidence that has reached to 30.4% until 2014. Similar increase in incidence has been reported in a number of nations throughout the globe.[5] Recent profile studies have demonstrated that the prognosis and treatment options for breast cancer vary among patients.[6–9] In the past 50 years, medications have been developed to regulate the estrogen binding ability to its receptor resulting in dramatic increase of longevity for the vast majority of individuals with estrogen receptor positive (ER+) carcinoma of breast.[10] Multiple factors influence the efficacy of chemotherapy, including size of lesion and involvement of nodes, the hormone receptor and Her-2/neu expression. Triple-negative and Her-2-positive breast malignancies respond to chemotherapy better than HR + tumors do.[11] Her-2 amplification or overexpression (human epidermal growth factor receptor-2) is observed in ~15%–25% of breast malignancies.[12] The four-breast cancer molecular subtypes are luminal-A, luminal-B, the triple-negative and the Her-2-enriched type. Breast malignancies classified as Luminal A are ER +, progesterone receptor (PR +), and HER-2-negative and are typically of low grade having most favorable prognosis. Triple positive Luminal B breast tumors are ER +, PR +, and HER-2+, and their prognosis is slightly worse than that of Luminal A. Her-2-enriched breast malignancies are ER-, PR-, and Her-2-positive. These cancers develop more rapidly and they fare poorly compared with luminal tumors, despite the fact that they are often effectively treated with therapies that target the Her-2 protein. Triple-negative breast cancer type are ER negative, PR negative, and Her-2-negative; they are prevalent in younger age groups and are associated with the BRCA1 gene.[13] Immunohistochemistry (IHC) biomarkers correlate with these molecular categories.[14] In clinical practice, the status of hormone receptors has served as a significant biological marker for guiding endocrine therapy for breast cancer.[15] We aim to study the expression of ER, PR, and Her-2/neu in invasive breast cancer patients from the Najran area in Saudi Arabia, as well as their correlation with factors such as patients age, size of tumor, its grade, and histopathological type.

2. Materials and methods

This is a retrospective descriptive analysis of individuals diagnosed with carcinoma breast at a tertiary care centre in Najran over a period of 2 years. The IRB of KACST, Najran, KSA, approved the study (Protocol number 29-03-1434, registration number H-11-N-081). Demographic and clinical data were gathered from laboratory records, together with microscopic characteristics, histological grade, lymph node metastases (based on availability), stage (based on availability), final diagnosis, and immunohistochemical findings for expression of receptors and it was analyzed as per study objective. Accessibility of histopathologically diagnosed invasive breast cancer patient records between January 2019 and December 2020, as well as availability of histological slides, immunohistochemistry (IHC) slides, and complete demographic and clinicopathological data, were the inclusion criteria. Excluded cases lacked sufficient demographic, clinicopathological data and the immunohistochemical results for receptor expression including Her-2/neu.

Statistical Analysis: Version 23 of SPSS was utilized to analyze data. To illustrate numerical data, the mean, standard deviations, range were utilized. The χ^2 test was used to compare categorical variables using their absolute frequencies and percentages. When the probability of significance was less than 0.05 (P 0.05), the results were deemed statistically significant.

3. Results

In the current investigation, 78 cases of breast lesions in total were included. The study group's age ranged from 27 to 98 years, with a mean age of 47.6 ± 14.8 years. Most patients (89.7%) have no prior lesion, and clinical breast cancer was detected in 85.9% of cases. Most of the samples were ultrasound guided tru-cut biopsies. There were 9 (11.55%) grade 1 tumors, 35 (44.87%) grade 2 tumors, and 34 (43.58%) grade 3 tumors (Table 1).

ER/PR+/Her-2 (Luminal A) was the most common tumor subtype identified by immunohistochemistry, with next common types being ER/PR-/Her-2-, ER/PR+/Her-2+ and Her-2 enriched type. Patients with tumors showing ER/PR-with either Her-2+ or Her-2- had considerably smaller tumor sizes (P value = 0.008), whereas those with ER/PR+/Her-2- tended to be statistically significantly older than other groups (P value = 0.001). When compared with the other three kinds, patients with ER/PR-/Her-2- had statistically significantly reduced clinically diagnosed breast cancer (P value = 0.001) as shown in Table 2.

The cases with triple negative type had a significantly greater percentage of grade III lesions

Table 1. Descriptive data of the studied group.

Characteristics	The studied group *N* (%)
Age *(years)*	
Mean ± SD	47.6 ± 14.8
Range	(27–98)
Grade	
I	9 (11.5%)
II	35 (44.87%)
III	34 (43.58%)
Clinical diagnosis	
Breast abscess	4 (5.1%)
Breast mass	7 (8.97%)
Invasive ductal carcinoma	67 (85.9%)
Final diagnosis	
IDC	*57 (73.1%)*
ILC	*11 (14.1%)*
Papillary carcinoma	*1 (1.3%)*
DCIS	*3 (3.8%)*
Metaplastic carcinoma	*3 (3.8%)*
Mucinous carcinoma	*3 (3.8%)*
ER	
Negative	*30 (38.5%)*
Positive	*48 (61.5%)*
PR	
Negative	*39 (50.0%)*
Positive	*39 (50.0%)*
Her2/neu	
Negative	*51 (65.4%)*
Positive	*27 (34.6%)*

Table 1 shows the demographic and descriptive data of 78 cases of breast carcinoma.

whereas Luminal A and Luminal B subtypes exhibited grade I cancers (*P* value = 0.01*). The histology of the lesions did not differ statistically significantly among the different tumor subtypes (*P* value = 0.30). Invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) made up the majority of tumors, accounting for 57 (73.07%) and 11 (14.17%) cases, respectively. (Table 3).

4. Discussion

Breast cancer is a heterogeneous disease whose outcomes vary and depends upon the pathological features, its clinical characteristics, as well as the molecular, and ethnic characteristics of the patient. Disease presentation and prognosis are also influenced by different molecular subtypes and progenitor cell variants Kumar and colleagues.[16] The molecular subtypes are linked to IHC) biomarkers Parise and Caggiano, Ko and colleagues, Sanpaolo and colleagues.[14,17,18] The average age of patients in this study at diagnosis was 47.6 ± 14.8 years. Alnegheimish and colleagues[19] reported a nearly identical result in a study done in Riyadh, Saudi Arabia.[19] However, a slightly older mean age at diagnosis was reported in another study from eastern region Kussaibi.[5] Another Iraqi study reveals a high incidence of cases in the 40–49 age group, despite a mean age of over 50 Mohammed and colleagues.[4] Breast cancer is extremely rare in women younger than 20 and less common in women younger than 30 years of age Sub and colleagues.[1] In USA the average age for first time diagnosis is 60–65 years Kussaibi.[5] Multiple studies have demonstrated that breast cancer patients in

Table 2. Comparing baseline characteristics across the types of breast cancer among the studied group.

Variables	Tumor subtypes				*P* value
	ER/PR+/Her2+ (*n* = 14) (17.19%) Luminal-B	ER/PR+/Her2- (*n* = 36) (46.15%) Luminal-A	ER/PR-/Her2+ (*n* = 13) (16.66%) Her-2 enriched	ER/PR-/Her2- (*n* = 15) (19.23%) Triple negative	
Age (years)					
Mean ± SD	45.5 ± 11.1	57.6 ± 14.8	47.7 ± 8.7	44.5 ± 12.6	**0.001**[a]
Rage	(26–69)	(29–79)	(35–66)	(27–98)	
Tumor size					
≤2	10 (71.4%)	32 (89%)	13 (100.0%)	15 (100.0%)	
2–5	1 (7.1%)	4 (11.0%)	0	0	**0.008**[a]
>5	3 (21.4%)	0	0	0	
Affected side					
Left	10 (71.4%)	19 (52.8%)	6 (46.2%)	6 (40%)	0.3
right	4 (28.6%)	17 (47.2%)	7 (53.8%)	9 (60.0%)	
Clinical diagnosis					
Breast abscess	0	0	0	4 (26.7%)	
Breast mass	0	0	0	7 (46.6%)	**<0.001**[a]
Cancer	14 (100.0%)	36 (100.0%)	13 (100.0%)	4 (26.7%)	

Table 2 shows that the patients with ER/PR+/Her2-tend to be statistically significantly older than other groups (*P*-value = 0.001), but patients with ER/PR-with either Her2+ or Her2-had statistically significantly smaller tumor sizes (*P* value = 0.008). When compared with the other three kinds, patients with ER/PR-/Her2-had statistically significantly reduced clinically diagnosed breast cancer (*P* value = 0.001).

[a] Significant (*P* value < 0.05).

Table 3. Comparing histopathological type and tumor grade across the IHC subtypes of breast carcinoma.

Variables	ER/PR+/Her2+ ($n = 14$) (Luminal-B) (17.19%)	ER/PR+/Her2- (Luminal-A) ($n = 36$) (46.15%)	ER/PR-/Her2+ (Her-2 enriched) ($n = 13$) (16.66%)	ER/PR-/Her2-Triple negative/Basal like) ($n = 15$) (19.23%)	Total ($n = 78$)	*P* Value
Histology						
Ductal	10 (71.42%)	23 (63.88%)	11 (84.61%)	13 (86.66%)	57 (73.07%)	
Lobular	3 (21.42%)	6 (16.66%)	2 (15.38%)	0	11 (14.1%)	0.3
Others	1 (7.14)	7 (19.44)	0	2 (13.33%)	10 (12.82%)	
Grade						
I	1 (7.145)	8 (22.2)	0 (0.0%)	0 (0.0%)	9 (11.5%)	
II	7 (50%)	19 (52.77)	5 (38.46%)	4 (26.66%)	35 (44.87%)	0.01[a]
III	6 (42.85)	9 (25%)	8 (61.53%)	11 (73.33%)	34 (43.58%)	

Table 3 demonstrates that individuals with triple negative breast cancer had a significantly greater proportion of grade III lesions whereas Luminal A and Luminal B sub-types exhibited grade I cancers (*P*-value = 0.01*). There was no statistically significant variation in the histology of the lesions across the various tumor subtypes (p-value = 0.30). Most tumors were Infiltrating ductal carcinoma (IDC), followed by Infiltrating lobular carcinoma (ILC), which made up 57 (73.07%) and 11 (14.17%) cases respectively.

[a] Significant (*P* value < 0.05).

developing nations are diagnosed earlier than their counterparts in the West Kwong and colleagues, Raina and colleagues.[20–22]

In our study, the luminal A-type was more prevalent in elderly compared with triple-negative and Her-2 positive subtypes. Similar findings was reported in an Iraqi investigation Kussaibi.[5]

Variations in racial/ethnic backgrounds, food habits and lifestyles, and environmental factors, could explain the wide range of age incidence found in different research Statista.[23] Her-2 overexpression is linked to an increase in the aggressiveness of cancer breast with reduced ER and PR levels in young patients AlZaman and colleagues.[24] In a study, Estrogen and PR were negative, and Her-2/neu overexpression was observed in good number young patients Albasri and Zhang and colleagues.[25,26] Younger individuals have lower ER and PR mRNA expression as well as higher Her-2/neu expression, according to microarray data of a large breast cancer cohort Anders and colleagues.[27]

In the present study, patients with the Her-2+ subtype had statistically significantly smaller tumors (*P* value = 0.008*). Al-basri[25] reported a greater tumor size, and a higher tumor grade.[25] In another study, TNBC was diagnosed earlier when compared with west, and half of patients had big tumor size and higher grades Kumar and colleagues.[16] The molecular subtyping of breast cancer is now largely regarded as an essential prognostic marker that determines disease prognosis and patient outcome. The type Luminal A was the most common in our cases, while the Her-2+ subtype was the least common. A Saudi study found a comparable prevalence Kussaibi.[5] The triple-negative subtype was the most common, with luminal subtypes accounting for only 28.5% of cases in another study Al Tamimi and colleagues.[28] Our findings on the distribution of molecular subtypes were mainly consistent with other studies. (Table 4).

The correlation among hormone receptor, and Her-2/neu receptor expression and the histopathological type of cancer was not statistically significant in our analysis for any of the types. Similar results have been observed by other researchers Mohammed and colleagues.[4] In our analysis, the incidence of grade II and grade III cancers was almost the same, a finding similar to another study Albasri.[25] At all stages of breast cancer, the histological grade is a measure of predictive value independent of axillary status and tumor size Colomer and colleagues.[34] Mitosis, abnormal patterns, shift of nucleus, and the appearance of chromosomal instability are all linked to the total histological grade of the tumor Colomer and colleagues.[34]

In our investigation, the triple negative subtype showed a significant substantial percentage of grade III lesions than the other groups, followed by the

Table 4. Comparative distribution of molecular sub-types.

Studies	Luminal-A	Luminal-B	Her2/Neu +	Triple- Negative
Mehdi et al.[29]	34.7%	15.95	24.1%	25.3%
Yang et al.[30]	69%	6.0%	8%	18%
Cheng et al.[31]	46.5%	17%	15%	21.5%
Vallejos et al.[32]	49.3%	13.2%	16.2%	21.3%
Fourat et al.[33]	50.7%	13.4%	13.4%	22.5%
Alnegheimish et al.[19]	58.5%	14.5%	12.3%	14.85
Present study	46.15%	17.19%	16.66%	19.23%

Table 4 depicts a comparative distribution of breast cancer subtypes across studies.

Her-2+ subtype. In contrast, grade I tumor was detected in the ER+/PR+/Her-2+and ER+/PR+/Her-2 − subtypes. High histological grade and tumor aggressiveness are connected to Her-2 positive types. Consequently, that's used for analyzing the outcomes of trastuzumab treatment, chemotherapy, and endocrine therapy for predicting of the response Arafah.[35]

Only ER/PR + tumors were found to be of low grade in our investigation, while all other grade cancers were found to be Her-2+ and TNBC. Her-2 overexpression was found to have an association with tumor grade in another investigation, however estrogen and PR overexpression was found to have no correlation. A study reported that breast tumors that overexpress HER-2 form a biological subgroup that is extremely aggressive Colomer and colleagues.[34] However, another study found that patients with a single HR + tumor and which do not overexpress Her-2 fare badly than others Bae and colleagues.[36]

TNBC has a lower probability of axillary lymph node metastases despite being clinically more aggressive Singh and Mukherjee.[37] Approximately half of women showing positive hormone receptor status for cancer may be able to delay axillary staging, while a small percentage might have positive nodes, surprisingly Ruiz and colleagues.[38] Breast cancer status should be determined prior to adjuvant or neoadjuvant therapy for all types of breast cancers, according to current guidelines Parsons and colleagues.[39]

The levels of ER, PR, and Her-2 expression are required to be documented in all pathology reports for patients with primary breast cancer Colomer and colleagues.[34] As a predictor of how well endocrine treatments will work, the HR status is a very important factor in deciding on adjuvant treatment Onitilo and colleagues.[40]

4.1. Conclusions

ER and PR expressions determine a patients hormone receptor status. Her-2 neu is a vital prognostic and predictive breast cancer marker, alongside hormone receptors. In this study, Luminal A type breast cancer was the most common, were more likely to be in older patients while younger patients had the triple negative and Her 2+ subtypes. The commonest histological type was invasive ductal carcinoma. There was not a statistically significant link found between the expression of ER, PR, or Her-2/neu receptors and any of the several histological subtypes of breast cancer. Comparatively, triple negative and Her 2+subtypes exhibited the highest number of grade III lesions. Hormone receptor subtype has persistent prognostic importance in female operable invasive breast carcinoma. Her-2/neu and steroid hormone receptor expression should be routinely examined.

Authorship

The author's contributions as shown below with each author contributing equally towards the manuscript preparation.

Conception and design of the study: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

Methodology: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

Acquisition of data: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

Analysis and interpretation of data: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

Drafting- original draft preparation: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

Revision and final approval: M.I., H.A., A.T., A.A., N.S., H.Q., A.Q., M.A., S.A.

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Conflicts of interest

There is no conflict of interest and no financial issues to be declared with regard to the contents in this article.

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