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Hormonal receptor status and lymph nodes involvement in breast cancer: a retrospective study

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Abstract

Hormonal status and lymphatic invasion are two important prognostic factors among cases of breast cancer. This study aims to assess and evaluate the hormonal receptor status and lymph node involvement among female breast cancer patients in Duhok city, Kurdistan region, Iraq. A retrospective cross-sectional study was conducted, involving 156 diagnosed cases of breast cancer who had undergone surgical treatment and laboratory investigations at Azadi Teaching Hospital and Duhok Private Hospital for 30 months. Hormonal status (ER, PR, HER2 enriched, and Ki67), luminal staging, and lymphatic invasions were analyzed using SPSS version 26. Invasive ductal carcinoma not otherwise specified accounted for 87.8% of the total sample, with Luminal A being the most common form (42.31%), followed by Luminal B (37.17%). The prevalence of hormonal status among cases of breast cancer with lymphatic invasion was ER 42.5%, PR 41.2%, HER2 enriched 21.01%, and Ki67 36.8%; however, these differences were not statistically significant (P values: 0.586, 0.65, 0.253, and 0.469, respectively). In conclusion, invasive ductal carcinoma is the most common histological type of breast cancer, and the most frequent biological form is Luminal A. A significant number of breast cancer cases with positive lymphatic invasion show positive hormonal receptor levels; however, the number of lymphatic invasions is not correlated with the type of hormonal receptor positivity

Keywords: Breast cancer; Hormonal receptor; Lymph nodes; Retrospective.

1. Introduction

Breast cancer is the second most common malignancy and the second leading cause of cancer-related mortality among females worldwide. Each year, more than one in ten women are diagnosed with breast cancer. [1] Although the disease often progresses silently, it can be detected at an early stage through screening methods, which are routinely implemented in Western countries. Despite the availability of these screening programs, delayed presentation remains common due to various factors such as feelings of embarrassment, fear of a cancer diagnosis and its potentially fatal outcome, reliance on alternative therapies, concerns about abandonment by partners, disfigurement, or apprehension about treatment itself. [1, 2]

The incidence of breast cancer is anticipated to rise further, particularly in low- and middle-income countries, due to factors such as delayed pregnancies, earlier onset of menarche, reduced breastfeeding, physical inactivity, and unhealthy dietary habits [3]. Local and national studies indicate that breast cancer is the most frequently recorded malignancy among all cancers, accounting for 21.2% of cases according to the latest Iraqi Cancer Registry update. Notably, breast cancer in this region tends to occur in younger age groups, with a mean age at diagnosis of 52.8 years [4-6].

Several Risk factors of breast cancer are present and they are subdivided into modifiable and non-modifiable factors. Non-modifiable risk factors include; female gender, older age group (80% account for those older than 55 years of age), positive family history, genetic mutations such as BRCA1 and BRCA2, CDH1, PTEN and STK11, ethnicity, delayed pregnancy, early menarche and late menopause and sedentary life style has been associated with breast cancer [7,8].

The advancement in the diagnosis of diseases has recommended the benefit of analyzing Tumor markers among patients for therapeutic and prognostic factors. The most commonly analyzed tumor markers in breast cancer are estrogen receptors (ER), progesterone receptors (PR) and Her-2/neu receptors; thus, hormonal status assessment is an essential and integral part of breast cancer assessment [9, 10]. Additionally, Lymph node status, involvement among patients with breast cancer, acts as an independent and additive factor for prognosis among these cases and can be used as a decision-making tool in the adjuvant chemotherapy [11,12]

This study aimed to assess and evaluate the hormonal receptor status and lymph nodes involvement among

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female breast cancer patients in Duhok city, Kurdistan region, Iraq.

2. Materials and Methods

2.1. Study design

This study was conducted as a retrospective cross-sectional study collecting data from diagnosed cases of breast cancer who underwent surgical treatment and laboratory investigations.

2.2. Study setting and duration

The information was collected and extracted from the medical records of the Surgery and Pathology departments at Azadi Teaching Hospital and Duhok Private Hospital over 30 months from January 2022 to June 2024.

2.3. Study population and inclusion criteria

A total of 156 female patients diagnosed with histopathological evidence of breast cancer and who underwent surgical operation were enrolled in the study.

2.4 Data collection

Each case was retrieved from the patient's individual clinic file. Information regarding lymph node status and hormonal receptor status was recorded in each case sheet. Patients' contact details were used to obtain any missing information. Cases with missing or lost results were labeled as "not done" for any reason; consequently, 15 cases were excluded from the study.

2.5. Variables and definitions

The study focused on the hormonal status—including Estrogen Receptors (ER), Progesterone Receptors (PR), Ki67, and HER2—in each case, along with the number of axillary lymph nodes involved following surgical resection and the histopathological type of breast cancer. Finally, cases were classified into biological subtypes according to established guidelines: Luminal A, Luminal B (HER2 Positive), Luminal B (HER2 Negative), HER2-enriched, and Triple Negative [13].

The data were later analyzed based on the hormonal status of their ER (estrogen receptor), PR (progesterone receptor), HER2 (human epidermal growth factor) receptors, and Ki67 involvement (the cases were regarded as positive if Ki67 was > 14%, otherwise regarded labeled as negative) of each patient was categorized into one of eight (ER/PR/HER2) groups as well as the number of lymph nodes involved (less than 5 LNs, 5-10 LNs and more than 10 LNs) after surgical resection.

2.6. Ethical approval

The study protocol was approved by the Scientific Committee of the College of Medicine, University of Duhok, and the Research Ethics Committee of the Duhok Directorate General of Health (Reference number: 31072024-6-65, dated July 31, 2024).

2.7. Statistical analysis

All data were analyzed using SPSS version 26. Frequency tables were generated, and the chi-square test was employed to examine the relationship between the number of lymph nodes resected and hormonal receptor status. A p-value of less than 0.05 was considered statistically significant. The correlation between lymph node involvement and hormonal receptor status was specifically assessed using the chi-square test. Of the total cases, 10 were excluded due to unknown lymph node status. Additionally, cases lacking hormonal receptor data were excluded to ensure a purified and unbiased analysis.

3. Results

The hormonal status of the patients diagnosed with breast cancer is shown in Table 1. ER was positive in 70.5% of the cases, PR was positive in 64.7%, HER2 was positive in 31.4% and Ki67 was found high in 56.4% of the cases.

Table 2 demonstrates positive lymph node status among patients with breast cancer who underwent lymph node removal. Nearly 54.5% of the patients had < 5 lymph nodes positive upon removal, 12.2% of the cases had 5 – 10 lymph nodes positive, while only 5.7% of the cases had > 10 lymph nodes positive among the removed lymph nodes. Additionally, nearly 21.2% of the cases had no lymph node involvement and 6.4% of the cases had missing data on lymph node involvement.

The majority of cases (87.8%) were diagnosed as invasive ductal carcinoma not otherwise specified, while 1.9% were identified as invasive lobular carcinoma. Ductal carcinoma in situ (DCIS) and no residual tumor accounted for 0.6% and 7.0% of cases, respectively. These findings are summarized in Table 3.

Table 4 describes the hormonal status among patients

Table 1. Hormonal receptor and biomarkers-defined breast cancer subtypes.

Hormonal Receptors	No. of Cases	Percentage
ER		
Positive	110	70.50%
Negative	44	28.20%
Not done	2	1%
PR		
Positive	101	64.70%
Negative	53	33.90%
Not done	2	1%
HER2		
Positive	49	31.40%
Negative	104	66.70%
Not done	3	1.90%
Ki67		
High	88	56.40%
Low	67	43.00%
Not done	1	0.60%

Table 2. Number of lymph nodes involved after surgical resection.

	No. of Cases	%
< 5	85	54.5
5 - 10	19	12.2
> 10	9	5.7
Not involved	33	21.2
Lost data	10	6.4
Total	156	100.0

Table 3. Histologic types of breast lesions from histopathological reports.

Types of Breast Cancer	No. of Cases	Percentage
Invasive ductal carcinoma (NOS)	137	87.8
Invasive lobular carcinoma	3	1.9
Ductal carcinoma in situ (DCIS)	1	0.6
No residual tumor	11	7.0
Other types (e.g., mucinous carcinoma)*	4	2.6
Total	156	100

Table 4. Relation of hormonal status to the lymph nodes.

Hormonal Status	Category	Not Involved	< 5 Nodes	5 to 10 Nodes	> 10 Nodes	Total	P-value
ER	Negative	18	11	6	3	38	0.586
	Positive	39	40	11	6	96	
PR	Negative	22	15	5	3	45	0.650
	Positive	35	38	13	5	91	
Her2	Negative	40	42	6	4	92	0.253
	Positive	17	18	7	4	46	
Ki67	Negative	16	23	6	2	47	0.469
	Positive	37	31	11	7	86	

and its relation to the positivity of cancer-involved lymph nodes. The correlation of ER, PR, HER2-enriched and Ki67 was found to be statistically non-significant, P value > 0.05. The prevalence of ER positive among cases with lymphatic invasion (LI) was 42.5% while PR prevalence was found to be 41.2%, HER2 enriched was 21.01% and Ki67 was 36.8%.

Table 5 demonstrates the biological classification of cases of breast cancer based on hormonal status. Luminal A was found to be the commonest, 42.31% followed by Luminal B (Her Positive and Negative), 37.17%. HER2-enriched cases accounted for 12.82% of the cases and triple-negative negative accounted for 7.7% of the total cases.

Table 5. Biological classification of breast cancer.

Types	No. (%)
Luminal A	66 (42.31)
Luminal B (Her2 Negative)	40 (25.64)
Luminal B (Her2 Positive)	18 (11.53)
HER2 enriched	20 (12.82)
Triple Negative	12 (7.7)
Total	156 (100)

4. Discussion

The breasts, which contain milk-producing cells, are a pair of glands of variable size and density located superficial to the pectoralis major muscle. Breast cancer is the most common cancer among females and the second leading cause of cancer-related death in women worldwide. [1] Over the past three decades, both the incidence and mortality rates of breast cancer have increased, largely due to improvements in cancer registration and detection, as well as changes in the risk factor profile [3]. This study aims to identify the hormonal receptor status and lymph node involvement among diagnosed cases of breast cancer.

Histological classification of breast cancer has prognostic significance [14]. The commonest form of breast cancer is adenocarcinoma; furthermore, of the histological types documented is invasive ductal carcinoma, with literature documenting up to 88.9% of the cases [15, 16]. In a local study, it accounted for 89.1% [17]. Similarly, in this study, the commonest histological type was Invasive Ductal carcinoma, 87.8%. This was followed by those cases with no residual tumor, 7%, which have achieved complete pathological response following neoadjuvant chemotherapy.

Further classification of Breast cancer depends on immunohistochemical expression of hormone receptors into Luminal A, B, HER2 enriched and Triple Negative, which is of diagnostic and prognostic value [17-19]. Luminal A represents the commonest gene subtype, 50-60% of all cases, it is characterized by genetic expression of ER/PR positivity and HER2 negativity with a low cellular proliferation index (Ki-67 <14%) [18, 20]. In this study, Luminal A accounted for majority of the cases, 42.3% of all cases and Luminal B accounted for 36% of the cases and the second most common form. Nevertheless, in a local study, Mohammed (2021). found Luminal-B as the commonest molecular subtype [17]. HER2, also known as Human Epidermal Growth Factor Receptor 2, c-erbB-2, is one of the important oncogenic factors for breast cancer, located on chromosome 17 and is seen in nearly 20% of primary breast cancer cases. The protein produced by HER2 gene belongs to EGFR of Tyrosine kinase family. The overexpression of this gene indicated poor clinical outcomes [7]. In this study, 12.82% of the samples were HER2 enriched and only 7.7% were triple negative, which in fact shows a poor prognostic index [21].

Lymphatic status among cases of breast cancer has a significant prognostic factor [11-12] as lymphatic invasion worsens the prognosis [22-23]. Hormonal status can be of predictive value for lymphatic invasion among patients with breast cancer [24]. In this study, only 21.2% had no

lymphatic involvement, while the majority, 54.5% had less than 5 lymphatic invasions. Additionally, although the hormonal status and lymphatic invasion are of prognostic significance, the correlation of the type of hormonal receptor positivity and the number of lymphatic invasions per case was found statistically non-significant, indicating that hormonal status, when taken individually, does not have a role in the number of lymph node involvement.

This study highlights the predominance of invasive ductal carcinoma and Luminal A subtype among breast cancer patients in Duhok, Kurdistan region, Iraq. While a significant proportion of cases demonstrated both positive hormonal receptor status and lymphatic invasion—factors known to influence prognosis—no statistically significant correlation was found between the type of hormonal receptor positivity and the number of lymph nodes involved. These findings emphasize the heterogeneity of breast cancer and the importance of comprehensive pathological and molecular profiling for optimal prognostication and management. Further large-scale, prospective studies are recommended to validate these results and explore additional prognostic factors in this population.

Limitations of the study

This study was conducted as a retrospective analysis of the sample; a prospective study would provide more accurate data. The cases were collected based on their presence in the clinic, a cross-sectional form of sample collection.

Conflict of interest

Not applicable.

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