

Axillary Lymph Node Involvement in Primary Invasive Breast Carcinoma in a Center in Baghdad Province

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Abstract

Introduction: Breast carcinoma is the most common malignancy in women and it has become a major health problem affecting women worldwide. In Iraq, breast carcinoma is still a major cause of health morbidity and mortality in women. Axillary lymph node metastasis is considered the most important factor affecting prognosis and management in patients with breast cancer. **Objective:** This study aimed to evaluate lymph node metastasis in cases of primary invasive breast carcinoma and to find if there was any association among lymph node involvement with type, grade, and tumor stage. **Materials and Methods:** This was cross-sectional study of 100 female patients with primary invasive breast carcinoma aged 25–88 years, which collected from the archive of the educational laboratory in Baghdad Medical City, Baghdad, Iraq from April 2018 to December 2020. Male patients were excluded from this study. **Results:** A total of 100 patients were included in this study; all were women with primary invasive breast cancer with different histopathological types (80% of cases were invasive ductal ca. NOS). The age range of the patients was between 25 and 88 years. A significant correlation was observed between lymph node stage and tumor pathological stage (tumor size). **Conclusions:** Most cases of primary invasive breast carcinoma had axillary lymph nodes metastasis, with a strong correlation between lymph node stage and tumor size. However, no association was found with tumor grade or tumor type that could be related to the small sample size of this study.

Keywords: Axillary lymph node, breast carcinoma, primary invasive

INTRODUCTION

Breast carcinoma is the most common malignant tumor and is the second most common cause of carcinoma death in women, with more than 1.7 million cases occurring worldwide annually.^[1] In Iraq, breast cancer has remained the most common cancer affecting women and the most common cause of morbidity and mortality in Iraqi women.^[2] It forms 19.70% of all malignant tumors and was responsible for 34.06% of female cancers in 2018; the total number of affected women was 6094 according to cancer registry report in Iraq for 2019, showing an increase in the number of cases as compared with 2017 when the number of cases was 5851.^[3] Breast cancer is the first cause of cancer death in women responsible for 24.6% of deaths among other cancers in women.^[3] Prevalence of breast cancer in Iran was 9.7 per 1000 in 2002. The incidence rate among Iranian women is 17%, which ranked the first.^[4] In the United States, approximately 230,000 new cases are diagnosed annually and approximately 40,000 patients die from the disease each year.^[1] The incidence

is high in North America and northern Europe (92 new cases per 100,000 women/year), intermediate in southern European and Latin American countries, and low in most Asian and African countries (but rising rapidly in recent years in some of these countries). Most of these cases have been early stage, measuring less than 2cm in diameter and/or DCIS.^[5,6] However, in some regions of the world (North America, Western Europe, and Australia) breast cancer mortality is now declining, which has been attributed to the combined effects of earlier diagnosis and improved therapy.^[7,8] Breast cancer comprises multiple histological entities that thought to have various biological behaviors. Invasive ductal carcinoma not otherwise specified constitutes the most common type and estimated to be around 70%. Other types comprise the

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resting percentages.^[9] There are approximately 17 special types of breast cancer that analyzed, each thought to have a different biological behavior.^[9] Risk factors for breast cancer include increasing age, early menarche, late menopause, late age of the mother for the first pregnancy, null parity, obesity, long-term use of the combined oral contraceptive tablets, and the presence of some genetic mutations such as BRCA1 and BRCA2 mutations that may cause cancer at earlier age.^[10,11] Axillary lymph node metastasis is one of the most important prognostic parameters.^[12] In addition to the sharp difference in survival rates between patients with positive and negative nodes, the survival rate also depends on the level of axillary node involved (low, medium, or high), the absolute number (fewer than four versus four or more), the amount of metastatic tumor, and the presence or absence of extra nodal extension.^[12] There is no clinical significance to the presence of “micro metastases” (>0.2 to ≤ 2 mm) or “isolated tumor cells” (≤ 0.2 mm) as shown in the NSABP (National Surgical Adjuvant Breast and Bowel Project) B32 trial.^[13] This study aimed to evaluate involvement of axillary lymph nodes in cases of primary invasive breast carcinoma in female patients, and to find out any correlation among the number of involved nodes (nodal stage) with tumor histological types, grades, and tumor pathological stage (tumor size).

MATERIALS AND METHODS

Pathology reports of a 100 female patients who underwent mastectomy for removing breast masses were collected from the archive of the teaching laboratories of Baghdad Medical City from April 2018 to December 2020. This study was performed on cases of female patients diagnosed with primary invasive breast carcinomas; all of them underwent different procedures of mastectomies with axillary clearance (60 radical mastectomies, 35 modified radical mastectomies, 3 quadrantectomies, and 2 nipple-sparing mastectomies).

The histopathology reports included age of the patients, type and site of the surgical procedures, and tumor characteristics that include (tumor histological type, grade that is obtained according to Bloom-Richardson (Nottingham) scoring system,^[14] and tumor stage according to AJCC TNM staging.^[4] Half of the cases were sent for immunohistochemically study. The inclusion criteria of the study were female patients, histopathological type, histopathological grade, lymph node stage, and tumor stage. The exclusion criteria of the study were M stage, male patients, and women with no completed reports. The patient's age and tumor histological type, grade, stage, and nodal stage were shown in terms of frequency, percentage, mean, and standard deviation. The correlation was done using the chi-square and Fisher's exact tests. A value of $P \leq 0.05$ was considered statistically significant. The statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS) software program (IBM).

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with the patient's verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee (approval number 2065, dated December 29, 2020).

RESULTS

This was a cross-sectional study of 100 female patients. The age range of the patients was between 25 and 88 years with a mean and standard deviation (SD) of age (51.97 ± 12.39) years. The patients were divided into three age groups: <30 years, 30–60 years, and >60 years. The highest proportion (73 patients, 73%) was in 30–60 years' age group. Fifty-one patients presented with stage II (tumor size >2 but ≤ 5 cm) (51%) followed by 20 patients (20%) with stage III, and 15 patients (15%) with stage I and 14 patients (14%) with stage IV in order of frequency, according to the TNM staging system. Approximately 59% of the studied cases had grade II tumor, 33 cases (33%) had grade III tumor, whereas grade I tumor was in 8 (8%) of cases (which is obtained according to Bloom-Richardson [Nottingham] scoring system). Axillary lymph node metastasis occurred in 74 (74%) of the cases with different grades, types, and stages. Twenty six of them

Table 1: Variables distribution

Variables	Frequency	Percentage
Age (years)		
<30	4	4
31–60	73	73
>60	23	23
Type of surgery		
Radical mastectomy	59	59
Modified radical mastectomy	35	35
Nipple sparing surgery	2	2
Quadrantectomy	4	4
Tumor stages		
T1	15	15
T2	51	51
T3	20	20
T4	14	14
Tumor grade		
G1	8	8
G2	59	59
G3	33	33
Lymph node stage		
No nodes involved	26	26
1–3 nodes involved	24	24
4–9 nodes involved	24	24
≥ 10 nodes involved	26	26

came with stage III (pN3≥10 involved nodes) lymph node metastasis [Table 1].

Invasive ductal carcinoma (NOS) was the most common histological type (80 cases, 80%) followed by invasive lobular carcinoma (7 cases, 7%), whereas mucinous and micropapillary carcinomas were the least common histological type (1 case, 1%) [Figure 1].

Correlations were done to search for significant association between lymph node stage (no. of involved lymph nodes) with tumor histological type, tumor grade, and tumor stage (tumor size) [Tables 2-4].

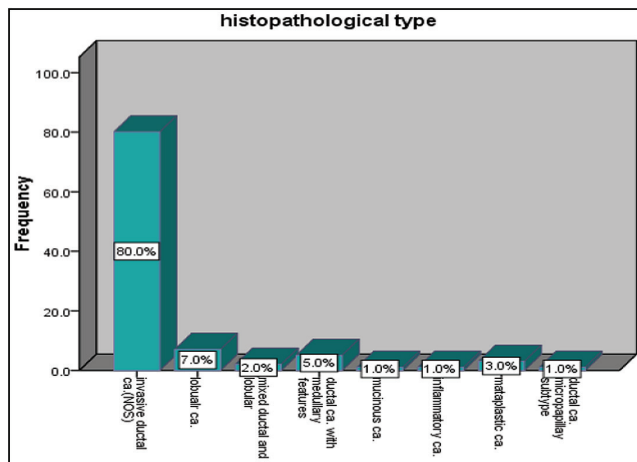


Figure 1: Distribution of histological types of breast carcinoma in cases studied

The correlation between the tumor pathological stage (tumor size) and lymph nodes stage (no. of involved nodes), there is a significant association between them, 9 patients (60%) of cases with stage I tumor (≤ 2 cm in greatest dimension) had no axillary lymph nodes metastasis, 17 patients (33.3%) of cases with stage II tumor (>2 cm but ≤ 5 cm in greatest dimension) had stage I lymph nodes metastasis (1–3 involved lymph nodes), 8 patients (40%) of cases with stage III (> 5 cm in greatest dimension) had stage II nodal metastasis (4–9 involved nodes) and 11 patients (78.6%) of cases with stage IV tumor had stage III lymph nodes metastasis.

DISCUSSION

In this study, we collected the data of 100 patients who were diagnosed with primary invasive breast carcinoma. Axillary lymph node metastasis occurred in 74% of the cases (74 patients of 100). Approximately 80% of cases were invasive ductal ca. NOS. The most common grade and tumor stage were 59% and 51%, respectively. These results are close to the results of other separate studies. One of them was published in 2019 in Tehran University Medical Journal, which was done on 167 patients with breast cancer. Approximately 70% of them had lymph nodes metastasis, 93.4% had invasive ductal ca., and 52.1% came with grade II tumor.^[15] The other study was done in Duhok, Iraq published in 2019 which was done on 479 patients with breast cancer. Approximately 87.7% of them had invasive ductal carcinoma, 47.2% had stage II tumors, and most of them came with axillary lymph

Table 2: The correlation between the tumors histological types and lymph nodes stage (no. of involved nodes)

			TNM lymph node stage				Total
			No lymph nodes involved	1–3 involved nodes by tumor	4–9 involved nodes by tumor	10 and more involved nodes by tumor	
Histopathological type	Invasive ductal ca. (NOS)	Count (%) within histopathological type	22 (27.5)	17 (21.2)	22 (27.5)	19 (23.8)	80 (100.0)
	Lobular ca.	Count (%) within histopathological type	2 (28.6)	3 (42.9)	0 (0.0)	2 (28.6)	7 (100.0)
	Mixed ductal and lobular	Count (%) within histopathological type	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	2 (100.0)
	Ductal ca. with medullary features	Count (%) within histopathological type	2 (40.0)	1 (20.0)	1 (20.0)	1 (20.0)	5 (100.0)
	Mucinous ca.	Count (%) within histopathological type	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
	Inflammatory ca.	Count (%) within histopathological type	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
	Metaplastic ca.	Count (%) within histopathological type	0 (0.0)	2 (66.7)	0 (0.0)	1 (33.3)	3 (100)
	Ductal ca. micropapillary subtype	Count (%) within histopathological type	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Total			26 (26.0)	24 (24.0)	24 (24.0)	26 (26.0)	100 (100.0)

P value = 0.309 (>0.05) which is not significant

No significant association found as shown in the table

nodes metastasis.^[16] Other separate studies in Malaysia, China, Jordan, Turkey, and Tunisia also revealed that invasive ductal carcinoma is the most common type.^[17-21] This study agrees with Mohammed *et al.*^[16] which showed no significant association between tumor type and lymph nodes involvement (nodal stage), whereas it disagrees with Al Soudi *et al.*^[13] and Keihanian *et al.*,^[17] which showed in their studies a significant relationship between lymph nodes metastasis and tumor type as most cases of lymph nodes metastasis occurred with invasive ductal carcinoma. Approximately 59% of the cases came with grade II tumor which is close to Wu *et al.*,^[13] 55% of cases (of 1325 patients) came with grade II tumor which is close to Keihanian *et al.*,^[22] and 52% of cases (of 167) came with grade II. Axillary lymph nodes metastasis occurred in 74%, 74.7%, and 70% of the cases in each of these studies, respectively. Wu *et al.*^[13] and Keihanian *et al.*^[22] revealed a significant correlation between these two factors as nodal metastasis increases with higher tumor

grade. However in this study, there was no significant correlation as even percentages of each grade came with different lymph node stages agreeing with Mohammed *et al.*'s^[16] study. These differences in the study's results can be related to variations in sample size, racial, and genetic differences. Approximately 51% of cases in this study had stage II tumors (tumor size 2–5 cm), which is close to studies of Keihanian *et al.*^[13] (58.7%), Wu *et al.*^[16] (54%), and Mohammed *et al.*^[22] (47.2%). These studies showed a strong association between tumor size and lymph nodes metastasis which affect patients survival. The tumors larger than T2 are related to the patient's lower chance of survival. This study showed a significant correlation between tumor size and lymph nodes metastasis, as larger tumor size (higher T stage) is associated with higher lymph nodes stage ($P = 0.000$). Tseng *et al.*'s^[23] study performed on 1325 patients with breast carcinoma in Taiwan showed a larger tumor size in cases with involved nodes than cases with noninvolved nodes. Study done by Soerijomatarata

Table 3: The correlation between the tumor grades and lymph nodes stage (no. of involved nodes)

			TNM lymph node stage				Total
			No lymph nodes involved	1–3 involved nodes by tumor	4–9 involved nodes by tumor	10 and more involved nodes by tumor	
Histopathological grade	Grade 1	Count (%) within histopathological grade	3 (37.5)	2 (25.0)	2 (25.0)	1 (12.5)	8 (100.0)
	Grade 2	Count (%) within histopathological grade	15 (25.4)	13 (22.0)	14 (23.7)	17 (28.8)	59 (100.0)
	Grade 3	Count (%) within histopathological grade	8 (24.2)	9 (27.3)	8 (24.2)	8 (24.2)	33 (100.0)
Total		Count (%) within histopathological grade	26 (26.0)	24 (24.0)	24 (24.0)	26 (26.0)	100 (100.0)

P value = 0.968 (>0.05) which is not significant

No significant association found as shown in the table

Table 4: Association between lymph nodes pathological stage and tumor pathological stage

			TNM lymph node stage				Total
			No lymph nodes involved	1–3 involved nodes by tumor	4–9 involved nodes by tumor	10 and more involved nodes by tumor	
TNM tumor stage	Stage 1	Count (%) within TNM tumor stage	9 (60)	3 (20.0)	3 (20.0)	0 (0.0)	15 (100.0)
	Stage 2	Count (%) within TNM tumor stage	13 (25.5)	17 (33.3)	12 (23.5)	9 (17.6)	51 (100.0)
	Stage 3	Count (%) within TNM tumor stage	3 (15.0)	3 (15.0)	8 (40.0)	6 (30.0)	20 (100.0)
	Stage 4	Count (%) within TNM tumor stage	1 (7.1)	1 (7.1)	1 (7.1)	11 (78.6)	14 (100.0)
Total		Count (%) within TNM tumor stage	26 (26.0)	24 (24.0)	24 (24.0)	26 (26.0)	100 (100.0)

P value = 0.000 (<0.05) which is significant

The correlation between the tumor pathological stage (tumor size) and lymph nodes stage (no. of involved nodes), there is a significant association between them, 9 patients (60%) of cases with stage I tumor (≤ 2 cm in greatest dimension) had no axillary lymph nodes metastasis, 17 patients (33.3%) of cases with stage II tumor (> 2 cm but ≤ 5 cm in greatest dimension) had stage I lymph nodes metastasis (1–3 involved lymph nodes), 8 patients (40%) of cases with stage III (> 5 cm in greatest dimension) had stage II nodal metastasis (4–9 involved nodes) and 11 patients (78.6%) of cases with stage IV tumor had stage III lymph nodes metastasis

et al.^[24] showed that tumors with equivalent size, mortality increases with the increase in number of involved nodes. Small sample size of the study, lack of control group, and incomplete patients data were among the limitations of our study. Therefore, a study with larger sample size and presence of control group for more accurate investigations of lymph nodes metastasis in breast carcinoma are required.

CONCLUSION

Axillary lymph nodes involvement is presented in most cases with primary invasive breast carcinoma. The number of these involved nodes correlates strongly with tumor stage (size of the tumor).

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Conflicts of interest

There are no conflicts of interest.

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