

# Bilateral Breast Cancer: Clinical Presentation and Pathological Characteristics in Iraqi Patients

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## ABSTRACT

**Background:** Conflicting findings in the literature have been reported regarding the incidence and characteristics of bilateral breast cancer. Histologic lobular type of breast cancer in the index breast, having positive family history for breast cancer, diagnosis of first cancer at early age and BRCA genetic mutations are considered risk factors for developing bilateral breast cancer.

**Aim of the study:** To assess the demographic, clinical and pathological characters of bilateral breast cancer among a sample of Iraqi patients diagnosed with breast cancer.

**Patients and Methods:** This study is a descriptive retrospective comparative study which included 1161 patients histopathologically diagnosed to have breast cancer. Data was taken from clinical patients records as apart of competent information system data base developed by the National Cancer Research Center, Baghdad University in collaboration with the Referral Center for Early Detection of Breast Tumors, Medical City Teaching Hospital.

**Results:** Bilateral breast cancer constituted 4.4% of all breast cancer cases in the current study (51 cases out of 1162 cases). Significant differences were noted between Unilateral and Bilateral breast cancer patients with respect to patients age, family history of breast cancer, stage of the disease, histologic types and grade of the tumor ( $p < 0.05$ ). Bilateral breast cancer was more common among patients with positive family history of breast cancer, who are under the age of 50 years and presented at more advanced stages than those with unilateral breast cancer. Invasive lobular carcinoma and well differentiated tumor grades were significantly more encountered among patients with bilateral breast cancer. On the other hand, there were no statistical differences between the two groups regarding marital status, history of lactation, hormonal intake, tumor size, lymph nodes involvement, skin changes, Estrogen, Progesterone and Her2/neu contents of the tumors.

**Conclusion:** Bilateral breast cancer tends to affect patients with positive family history of breast cancer, at younger ages and more advanced stages than those with Unilateral breast cancer. Invasive lobular carcinoma and well differentiated tumor grades were significantly more encountered among those with bilateral breast involvement. Careful identification of Iraqi patients with bilateral breast cancer through prompt diagnosis and early detection is mandatory to guide management protocols and ensure effective therapy.

**Keywords:** Unilateral, bilateral, breast, cancer, clinical, pathological, Iraq.

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## INTRODUCTION

Breast cancer is the commonest cancer in Iraq<sup>[1-2]</sup>, often diagnosed at relatively late stages (II and IV) among middle aged females<sup>[2-5]</sup> and registered as the first killer among all other Iraqi female malignancies<sup>[1,2]</sup>. Breast cancer has different biological, clinical and pathological features related to different gene profiles of the disease which influence the plans of treatment and prognosis<sup>[3,6-8]</sup>. Risk for developing breast cancer include sedentary life style, alcohol consumption, radiation exposure, early menarche, late menopause, postmenopausal hormonal intake, positive family history of breast cancer and previous involvement of one breast with the disease<sup>[7-9]</sup>.

It has been reported that bilateral breast cancer is an important entity which comprises an overall incidence of 4–20% among patients with breast cancer<sup>[10,11]</sup>. Lobular type of breast cancer in the index breast, having positive family history for breast cancer, diagnosis of first cancer at early age and BRCA genetic mutations are suspicious risk factors for developing bilateral breast cancer<sup>[10,12]</sup>. Nevertheless, there has been conflicting evidence in the literature on the impact of bilateral breast cancer in the management of patients affected with the disease.

With the objective of developing national protocol guidelines for cancer management, this study was designed to address the prevalence of Bilateral breast cancer among

Iraqi female patients focusing on their demographic, clinical and pathological characteristics as compared to those presenting with Unilateral breast cancer.

## PATIENTS AND METHODS

This study is a descriptive retrospective comparative study that included 1161 patients histopathologically diagnosed with breast cancer. The reported data was obtained from an established information system developed by the second author based on clinical records of patients referred to the Breast Cancer Early Detection Center, Medical City Hospital, Baghdad and the National Cancer Research Center, University of Baghdad over the period from 2014 to 2016.

The studied variables included age of the patient, marital status, history of lactation, hormonal intake, tumor size, lymph node status, family history of breast cancer, stage of the disease at presentation, skin involvement, tumor histopathologic type and grade, Estrogen, Progesterone and Her2 contents of the primary tumor.

Demographic, clinical and pathological features of the two groups were compared statistically using frequency and chi Square Test. P values less or equal to 0.05 were considered significance. The study was approved by the Ethical committee of the National Cancer Research Center of Baghdad University following Helsinki declaration.

RESULTS

Bilateral breast cancer cases constituted 4.4% of all diagnosed breast cancer cases in our study (51 cases) out of a total sample size of 1162 cases (Figure 1).

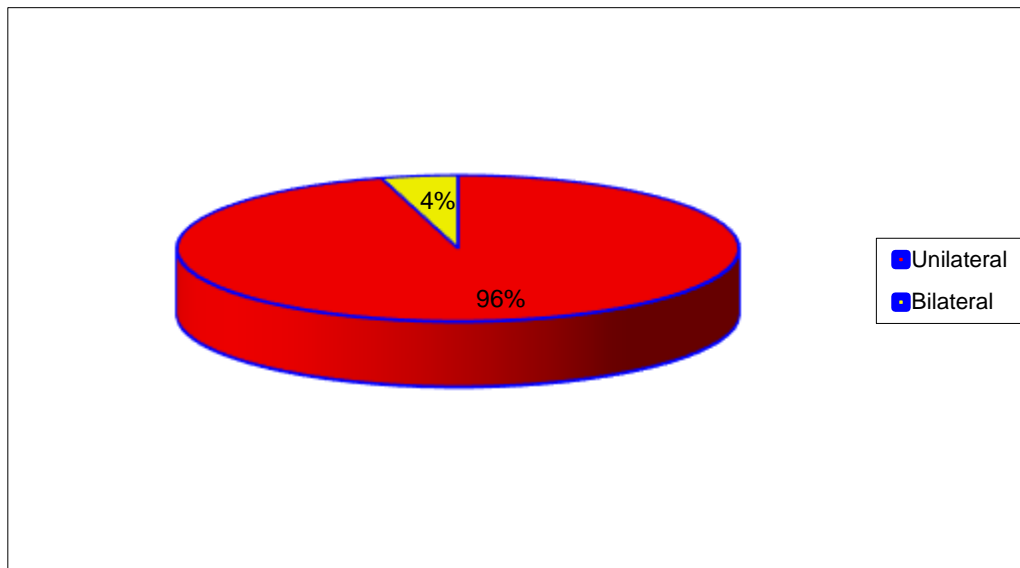


Figure 1: Rate of Bilateral breast cancer among the total examined cases in the study.

Table (1) showed that there were significant differences between the two groups regarding the age of the patients and the family history of the disease ( $p < 0.05$ ). Patients under the age of 50 years and family history were more statistically encountered among the Bilateral than the

Unilateral group (58.8% versus 46.1% and 31.3% as opposed to 18.5% respectively). On the other hand, no statistical differences were displayed between the two groups regarding marital status, history of lactation and hormonal intake.

Table 1: Demographic features among patients with Unilateral and Bilateral breast cancers.

Variables	Unilateral Group		Bilateral Group		Chi square
	No	%	No.	%	p value
<b>Age Category</b>					
20-34	4.6%	52	0%	0	0.0469
35-49	462	41.5%	58.8%	30	
50-64	477	42.9%	29.4%	15	
65 and above	120	10.8%	11.7%	6	
Total	100%	1111	100%	51	
<b>Marital Status</b>					
Married	979	88.1%	42	82.3%	0.648
Unmarried	108	9.7%	13.7%	7	
Widowed	1%	12	1.9%	1	
Divorced	12	1%	1.9%	1	
Total	100%	1111	100%	51	
<b>Lactation</b>					
Yes	501	53.1%	60.9%	25	0.327
No	46.8%	441	39%	16	
Total	942	100%	100%	41	
<b>Hormonal Intake</b>					
Yes	23.8%	219	15.7%	6	0.252
No	76.1%	700	84.2%	32	
Total	100%	919	100%	38	
<b>Family History</b>					
Yes	18.5%	203	31.3%	16	0.023
No	81.4%	890	68.6%	35	
Total	100%	1093	100%	51	

\*The sample size was not the same for all the studied variables due to the differences in the availability of complete valid data for each variable.

Table 2: Clinical presentation of patients with Unilateral and Bilateral breast cancers.

Variables	Unilateral		Bilateral		Chi square
	No	(%)	No	(%)	p value
Lymph Node					
N 0	32.2%		162	28%	7
N1	31.2%		157	12%	3
N2	20.4%		103	32%	8
N3	13.7%		69	20%	5
N x	2.3%		12	8%	2
Total	100%		503	100%	25
Clinical Stage					
Stage 0	5	1.2%	0	0%	0.0371
Stage I	42	9.8%	3	13.6%	
Stage II	210	49.2%	4	18.2%	
Stage III	33.5% 143		11	50%	
Stage IV	27	6.3%	4	18.2%	
Total	427	100%	22	100%	
Skin Changes					
Yes	37.8%		390	39.5%	17
No	62.1%		641	60.4%	26
Total	100%		1031	100%	43

Clinically, Table (2) revealed that there were no significant differences between the two studied groups with respect to the lymph node status or the skin changes overlying the affected breast tumor. Nevertheless, a statistical variation was illustrated regarding the stage of breast cancer at

diagnosis. Patients with Bilateral breast cancer more significantly presented with advanced stages III and IV breast cancer as opposed to those with Unilateral disease (68.2% versus 39.8% respectively).

Table 3: Pathological characteristics among patients with Unilateral and Bilateral breast cancers.

Variables	Unilateral		Bilateral		No.	Chi square
	No.	(%)	(%)			p value
Histologic Type						
Invasive ductal	85.1%		412	65.2%	15	
Invasive lobular	6.4%		31	13%	3	
Others	8.4%		41	21.7%	5	0.034
Total	100%		484	100%	23	
Histologic Grade						
Well differentiated	4.4%		18	17.6%	3	0.031
Moderately differentiated	72.8%		295	52.9%	9	
Poorly differentiated	22.7%		92	29.4%	5	
Total	100%		405	100%	17	
T Status						
T0	2.5%		13	0%	0	0.896
T1	17.3%		88	16%	4	
T2	59.8%		303	60%	15	
T3	14.8%		75	16%	4	
T4	4.3%		22	8%	2	
TX	.9%		5	0%	0	
Total	100%		506	100%	25	

While histopathological examinations of the breast cancer specimens in both groups showed no statistical variations regarding tumor sizes, significant differences were observed concerning tumor histological types and grades ( $p < 0.05$ ). Table (3) clearly illustrated that patients

presenting with Bilateral cancers exhibited significantly higher rates of lobular carcinomas than those with Unilateral (13% versus 6.4%) and more frequent well differentiated tumor grades (17.6% versus 4.4%).

**Table 4:** Estrogen, Progesterone Receptors and Her2/neu status among Unilateral versus Bilateral breast cancer groups.

Variables	Unilateral (%)	No.	Bilateral (%)	No.	Chi square p value
<b>Estrogen Receptor</b>					
Positive	68.8%	329	61.9%	13	0.503
Negative	31.1%	149	38%	8	
Total	100%	478	100%	21	
<b>Progesterone Receptor</b>					
Positive	66.8%	320	66.6%	14	0.989
Negative	33.1%	159	33.3%	7	
Total	100%	479	100%	21	
<b>Her2/neu</b>					
Positive	29.5%	135	25%	5	0.662
Negative	70.4%	322	75%	15	
Total	100%	457	100%	20	

Table (4) demonstrated that there were no differences in the hormone receptor contents (Estrogen and Progesterone) and Her2/neu over expressions of the breast cancer specimens among the two studied groups.

## DISCUSSION

Bilateral breast cancer is not uncommon. It has been reported that the frequency of bilateral breast cancer ranges between 1.4-11.0% among all breast cancers (13). In this study bilateral breast cancer constituted 4.4% of all diagnosed breast cancer cases. Whereas that rate was very close to those reported in earlier studies from Iraq (4,5) and worldwide (14-16), it was relatively higher than the frequencies documented in other studies (10,17). At clinical presentation, our patients presenting with bilateral breast cancer were significantly younger than those with unilateral disease; the peak age frequency occurred in patients between 35-49 years. That was consistent with other reports which found that most of the bilateral breast cancer cases were detected in the fourth decade of life (14, 18) and that the median age of presentation was around 42 years (19).

A positive family history of breast cancer was displayed in 31.3% of patients with bilateral breast involvement in this study; significantly more common than in those with unilateral disease. That was in agreement with the findings reported by earlier researches (10,13,20-22) which confirmed that family history is considered one of the known risk factors for developing the disease.

The roles of the stage and grade of breast cancers, their histological types and immunohistochemical subtypes, as prognostic markers, have been well investigated in the clinicopathological profiles of Iraqi patients affected by the disease (3-6,8,23-27). However, compared to patients with

unilateral breast involvement in this study, bilateral breast cancer patients presented significantly with more advanced stages (III and IV). Although such finding was supported by previous studies (10,27), other investigators illustrated that bilateral breast cancers could be diagnosed at earlier stages (14); most probably reflecting inclusion bias and/or ethnic disparities.

Lobular carcinoma has long been considered as a risk factor for bilateral breast cancer (10,11,28). In the current study, the displayed rate among the bilateral group was twice more common than that observed among patients with unilateral breast cancer. In general it has been documented in the literature that patients with positive family history of breast cancer, lobular carcinoma, ER-negative tumors, and younger age at breast cancer diagnosis have the greatest risk for developing BBC (21,22).

Focusing on the correlation between bilateral breast cancer and the grade of the tumor, our results displayed that the affected patients had more frequent well differentiated tumor grades whereas few other reports revealed that the latter often present with worse histologic grade (10). Contrary to other studies which considered positive Her2/neu and negative hormone receptor tumor contents as risk factors for developing bilateral breast cancer (14,21,22), in the current work no differences were noted between unilateral and bilateral breast cancer patients with respect to Estrogen, Progesterone receptors and Her2 contents of the primary tumors; probably attributable to racial differences.

In line with other studies, no significant differences were observed between the two groups concerning lymph nodes status, overlying skin changes, history of hormonal intake, lactation and overlying skin involvement (29-30).

## CONCLUSION

Bilateral breast cancer is not uncommon among Iraqi female population. It tends to affect patients with positive family history of breast cancer, at younger ages and more advanced stages than those with Unilateral breast cancer. Invasive lobular carcinoma and well differentiated tumor grades were significantly more encountered among those with bilateral breast involvement. Careful identification of Iraqi patients with bilateral breast cancer through prompt diagnosis and early detection is mandatory to guide management protocols and ensure effective therapy.

#### ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

#### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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