BREAST CANCER IN NINEVEH 2020; A DESCRIPTIVE STUDY

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ABSTRACT

Background: According to GLOBOCAN 2020 data, breast cancer is currently one of the most frequently diagnosed malignancies and the fifth cause of cancer-related deaths, with an anticipated 2.3 million new cases worldwide. The WHO estimates that 19.6 million DALYs are attributable to breast cancer, with 2.26 million new cases in 2020, cancer of breast will be the most commonest diagnosed malignancy in women worldwide. **Aim of the study:** To describe the situation of breast CA among the patients in Mosul. **Patients and Methods:** Case-series study design was chosen to achieve the study objectives and conducted in Oncology and Nuclear Medicine Hospital in Mosul. The data collection, analysis, and writing will be planned to be over one year, starting in January 2020 to December 2020. Data was gathered by analyzing special cancer registration forms for each of the 178 women in the sample who had breast cancer then reviewing the patients' files in the Cancer Control Division at the Oncology and Nuclear Medicine Hospital in Mosul. **Results:** The (40-49 years) age group is 30.9%, 76.9% of them are lived in Mosul center, 89.0% are housewife, and the positive family history presents only in 3.4%, tumor size 2-5 cm is the commonest. Absence of the LN involvement occurs in 26.9%, most prevailed type of breast CA is IDC representing 79.0%. The unilateral side is commonest in 45.0% and 43.0% respectively. Most of them were in stages 2 and 3 representing 35.0% and 44.0% respectively. Stage 2B is found in 20.8%. Ki-67 found positive in 32.1%, HER2 marker positive in 35.9%, positive PR found in 35.9%, and positive ER is found in 37.0%, most frequent operation done is mastectomy in 43.8%, the axillaries clearance in 78.1%, Chemotherapy in 91.0%, radiotherapy 51.1%, hormonal 37.1%, and targeted therapy 13.0%. **Conclusion:** The breast CA is commonest CA affecting adult age group women in Mosul mainly in housewife with minor role of family history.

KEYWORDS: Breast CA, Descriptive study, Nineveh.

INTRODUCTION

The northernmost province of Iraq, Nineveh, is the second-largest after Baghdad (the capital). The Central Organization for Statistics estimates its population in 2011 to be 3,270,422 and that its area is equal to 37,323 square kilometers.[1]

According to GLOBOCAN 2020 data, breast cancer is currently one of the most frequently diagnosed malignancies and the fifth cause of cancer-related deaths, with an anticipated new cases of 2.3 million worldwide.[2]

The WHO estimates that malignant neoplasms cause 107.8 million Disability- Adjusted Life Years known as (DALYs) for women worldwide, of which 19.6 million DALYs are attributable to breast cancer.[3] With 2.26 million [95% UI, 2.24-2.79 million] new cases in 2020, cancer of breast will be the most commonest diagnosed malignancy in women worldwide.[4]

In addition to being the most prevalent, breast cancer also kills more women from cancer than any other type. Breast cancer caused 684,996 deaths worldwide [95% UI, 675,493-694,633] at a rate of 13.6/100,000 adjusted for age.[3] Although industrialized regions had the greatest incidence rates, Asia and Africa together

accounted for 63% of all deaths in 2020[3,4] In high-income nations, the majority of breast cancer patients survive; nevertheless, this is not the case for many low- and middle-income nations' women.[5]

Breast cancer mortality/incidence ratio (MIR), used as a proxy for 5-year survival rates,[6] was 0.30 globally in 2020.[3] In countries with developed healthcare systems (Hong Kong, Singapore, Turkey), the 5-year survival rate for localized and 75.4% for regional cancer, respectively, was determined by the clinical extent of the disease. The survival rates for localized and regional breast cancer in less developed nations (Costa Rica, India, Philippines, Saudi Arabia, Thailand) were 76.3% and 47.4%, respectively.[7]

Stages of breast cancer
The size, kind, and depth of the tumor cells' penetration into the breast tissues were all factors in determining the stages of breast cancer.[8] Stage 0 indicates non-invasive tumors, whereas stage 4 refers to invasive tumors. Descriptions of those tumor stages are:

Stage 0: The ductal cell carcinoma in situ tumor stage is an example of a non- invasive tumor stage in which both cancerous and non-cancerous cells are contained within the boundaries of the area of the breast where the tumor first appears and there is no evidence of their invasion of the tissues around that area (DCIS).[9]

Stage 1: This stage is characterized as an invasive form of breast cancer, and microscopic invasion is still conceivable. It falls into two categories: stage 1A as, well as, stage 1B. Category 1A refers to tumors up to 2 cm in size with no lymph nodes implicated, whereas stage 1B refers to a small cluster of cancer cells larger than 0.2 mm discovered in a lymph node nearby.[10]

Stage 2: There are also two categories in Stage 2: 2A and 2B. Stage 2A depicts a tumor that is identified in the sentinel or axillary lymph nodes but not in the breast. The tumor can range in size from less than 2 cm to more than 5 cm. Stage 2B, however, states that the tumor may exceed 5 cm in size but cannot reach the lymph nodes of axilla.[11]

Stage 3: Three subclasses—3A, 3B, as, well as, 3C—have been created from it. Stage 3A describes no tumor in the breast, but it can be found in four to nine lymph nodes in the axilla or in sentinel lymph nodes, while stage 3B describes a lump of any size that has resulted in an ulcer or swelling on the breast's skin and has extend up to 9 axillary or to sentinel lymph nodes. Stage 3B can be described as inflammatory breast CA since the breast's skin to become red, warm, and swollen. Stage 3C, however, refers to the spread of the tumor to ≥10 axillary lymph nodes, as well as to the lymph nodes above and below the clavicle.[12]

Stage 4: This stage of cancer is advanced and metastatic,

and it depicts how the disease has progressed to several body organs, including the lungs, bones, liver, brain, and others.[13]

Critically important clinical variables, such as tumor size, nodal status, stage distribution at the time of initial diagnosis, hormonal receptor status, percentage of women presenting with distant metastasis, and percentage of patients treated with radical mastectomy versus breast conservation surgery, are not accurately documented in hospital records in Iraq.[14]

Numerous investigations into the clinicopathologic features of breast CA in Iraq have revealed that ethnic variance in the population has an impact on incidence, stage, therapy, and survival.[15] Therefore, understanding how the characteristics ofbreast cancer patients from Iraq differ from the global trends for this illness may help with better treatment and early detection. In order to ascertain whether the patients' presentations differ from those in earlier studies, this study is intended to provide information about patients seen at the National Center for Cancer over the previous year. The results of earlier studies have shown that patients' presentations vary across different timeframes. The majority of earlier research had a limited emphasis and minimally focused on other types of data. For example, when a study gave clinical data but had insufficient information regarding the patients' sociodemographic status, or vice versa. Therefore, we collected information on patients' sociodemographic characteristics, clinical, histopathologic, and molecular data, nutritional condition (as measured by body mass index [BMI]), and whether or not they self-examined their breasts (BSE). In comparison to earlier studies, this one provides a more thorough description of Iraqi patients.[16]

In addition, the availability of solid clinical and pathological data is essential for improved management of BC in guiding decision-making (particularly from a variety of pharmacological possibilities). Histologic and prognostic criteria are necessary for pathological research. At this time, the three prognostic factors in clinical and pathological examination are the size of the main tumor, the degree of axillary lymph node involvement, and the histological grade.[17] One of the most significant prognostic tools for predicting spread or overall survival for operable BC is lymph node status. Both the Nottingham grading system and TNM staging system incorporate it.[18] Most of the time, the chance of a BC recurrence increases with the number of involved positive lymph nodes.[19] Similarly, tumor size plays a significant role in predicting BC outcomes and is unrelated to lymph node metastasis.[18] Consistent evidence suggests that the Union for International Cancer Control's traditional prognostic classification is based in part on a tumor's size (UICC).[20] According to the findings, as the main tumor grows larger, the prognosis or chance of survival decreases.[19] The histologic grade is used to assess the aggressiveness of a tumor in a

similar manner. It offers predictive data for a variety of tumor types, including BC.[17]

PATIENTS AND METHODS

Administrative agreement: The administrative agreement will be obtained from Directorate of Health in Nineveh.

Study setting: The present study was conducted in Oncology and Nuclear Medicine Hospital in Mosul.

Study design: Case-series study design was chosen to achieve the study objectives.

Data Collection Period: The data collection, analysis, and writing will be planned to be over one year, starting in January 2020 to December 2020.

Data Collection Tool: Data was gathered by analyzing special cancer registration forms for each of the 178 women in the sample who had breast cancer then reviewing the patients' files in the Cancer Control Division at the Oncology and Nuclear Medicine Hospital in Mosul.

Statistical analysis: The data collection is done by Microsoft Excel 2007.

RESULTS

Table (1) shows the distribution of the study sample according to age group intervals and demonstrates that the disease is more frequent in the age group 40-49 years (30.9%) followed by the age group 50-59 years (25.3%). The age group 20- 29 years shows the least frequencies that is only 2.2% of the disease.

Table (1): The distribution of the study sample according to age group intervals.

Age groups intervals	No.	%
20-29 years	4	2.2
30-39 years	30	16.9
40-49 years	55	30.9
50-59 years	45	25.3
60-69 years	29	16.3
≥70 years	15	8.4
Total	178	100.0

Figure (1) shows the distribution of the breast CA according to geographical locations and demonstrates that 76.9% are lived in Mosul sector and the remaining 23.1% live in other sectors.
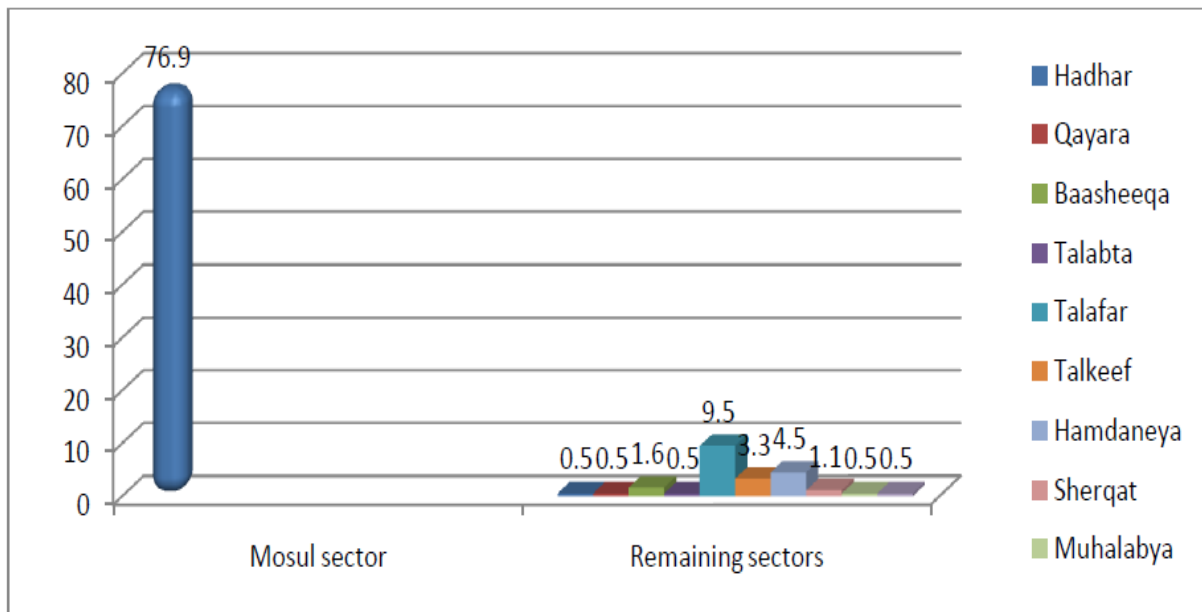

Figure (1): The distribution of the breast CA according to geographical locations.

Figure (2) shows the distribution of breast CA according to occupations and displays that 89.0% of the patients are housewife, 6.0% are employee, and 5.0% are retired.
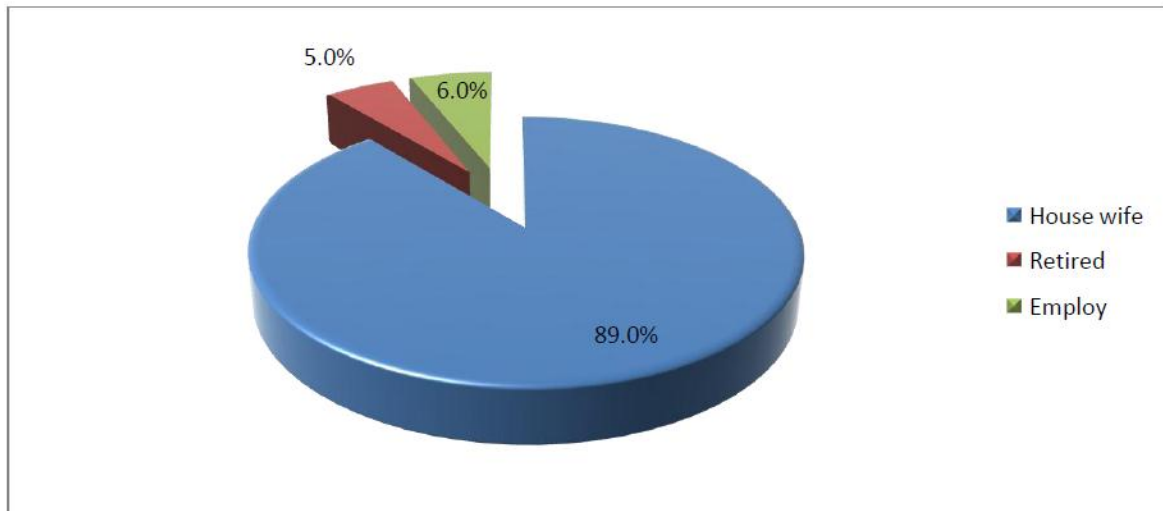
Figure (2): The distribution of breast CA according to occupations.

Figure (3) demonstrates the family history of breast CA and shows that it presents only in 3.4% and absent in 87.1% while it is unknown in 9.5% of cases.
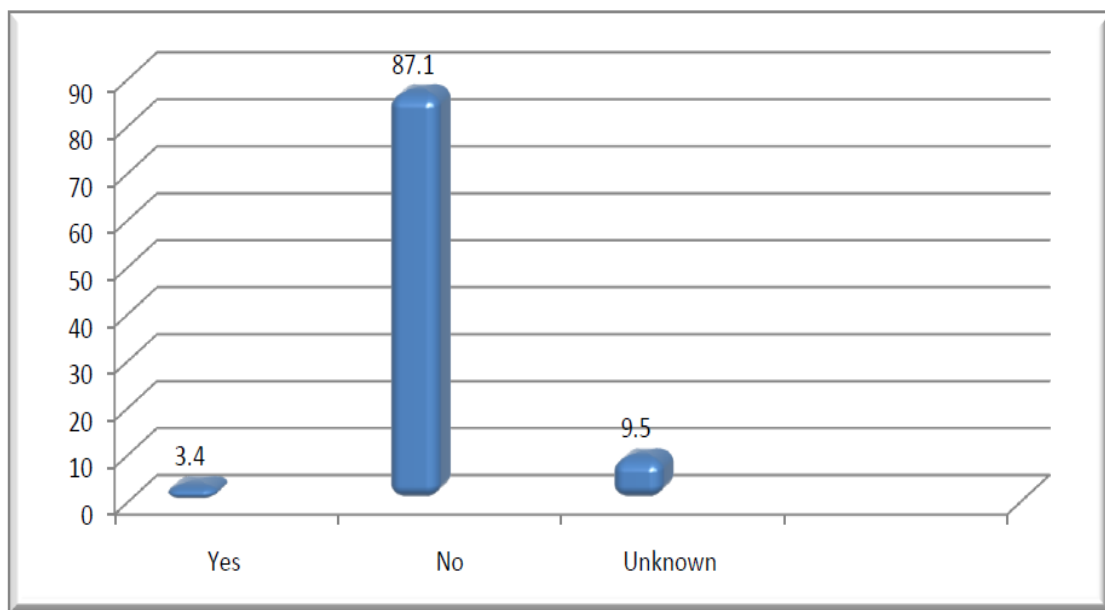

Figure (3): The family history of breast CA.

Table (2) demonstrates the tumor size and no. of LN and shows that the tumor of 2-5 cm is the most frequent size found in the patients in 92(51.7%). The size below 2 cm presents in 26(14.6%), more than 5 cm presents in 21(11.8%), while 39(21.9%) are with unknown size.

Regarding the no. of LN, 48(26.9%) of the patients have no LN involvement. One LN involvement found in 38(21.3%) of the patients, while more than 10 LN involvement found in 4(2.3%). Unknown LN found in 40(22.5%).

Table (2): The tumor size and no. of LN.

		No.	%
TumorSize	<2 cm	26	14.6
	2-5 cm	92	51.7
	>5 cm	21	11.8
	Unknown	39	21.9
No. of LN	No LN	48	26.9
	1	38	21.3
	2	11	6.2
	3	7	3.9
	4	6	3.4
	5	6	3.4
	6	4	2.3
	7	10	5.6
	8	1	0.5
	9	3	1.7
	>10	4	2.3
	Unknown	40	22.5
Total		178	100.0

Table (3) demonstrates the tumor characteristics and shows that the most frequent type of breast CA is IDC representing 79.0% of cases followed by ILC in 8.0%. The least frequent types are Medullary 0.5% and Pleomorphic 0.5%. The unilateral side whether left or right is the main common side in 45.0% and 43.0% respectively. Most of the breast tumor is found in stages 2 and 3 representing 35.0% and 44.0% respectively. In situ stage found only in 1.6% while the most common stage is 2B which found in 37(20.8%).

Table (3): The tumor characteristics.

Tumor characteristics		No.	%
Types	Adeno carcinoma	11	6.0
	DCIS	5	3.0
	IDC	141	79.0
	ILC	14	8.0
	Unknown	3	2.0
	Medullary	1	0.5
	Mucinous	2	1.0
	Pleomorphic	1	0.5
Sides	Bilateral	3	2.0
	LT	80	45.0
	RT	77	43.0
	Unknown	18	10.0
Grades	1	6	3.0
	2	61	35.0
	3	79	44.0
	4	7	4.0
	Unknown	25	14.0
Stages	In situ	3	1.6
	1	16	9
	2A	41	23
	2B	37	20.8
	3A	32	18
	3B	24	13.6
	4	17	9.5
	Unknown	8	4.5

Table (4): Shows the frequencies of tumor markers and demonstrates that Ki-67 found positive in 57(32.1%), negative in 67(37.6%), and unknown in 54(30.3%). HER2 marker is found positive in 64(35.9%), negative in 63(35.4%), and unknown in 51(28.7%). Positive PR found in 64(35.9%), negative PR found in 62(34.8%), and unknown result found in 52(29.3%). Positive ER is found in 66(37.0%), negative in 60(33.8%), and unknown in 52(29.2%).

Table (4): The frequencies of tumor markers.

Tumor Markers		No.	%
ki-67	Negative	67	37.6
	Positive	57	32.1
	Unknown	54	30.3
HER2	Negative	63	35.4
	Positive	64	35.9
	Unknown	51	28.7
PR	Negative	62	34.8
	Positive	64	35.9
	Unknown	52	29.3
ER	Negative	60	33.8
	Positive	66	37.0
	Unknown	52	29.2

Table (5) demonstrates the frequencies of operation's types and axillaries clearance and shows that the most frequent operation done is mastectomy in 78(43.8%), the MRM done in 50(28.1%), lumpectomy in 7(3.9%), and quadrectomy done in only 1(0.6%) of the cases while it unknown in 42(23.6%).

The axillaries clearance is performed in 139(78.1%) and unknown in 37(20.8%) while not in 2(1.1%) not performed.

Table (5): The frequencies of operation's types and axillaries clearance.

Treatment		No.	%
Operation types	Mastectomy	78	43.8
	MRM	50	28.1
	Lumpectomy	7	3.9
	Quadrectomy	1	0.6
	Unknown	42	23.6
Axillariesclearance	No	2	1.1
	Yes	139	78.1
	Unknown	37	20.8

Table (6) demonstrates the types of treatment and shows that the chemotherapy was used in 91.0% of cases, radiotherapy in 51.1%, the hormonal in 37.1%, and the targeted in 13.0% only.

Table (6): The types of treatment.

Treatment		No.	%
Chemotherapy	Yes	162	91.0
	No	5	2.8
	Suggested	3	1.7
	Unknown	8	4.5
Radiotherapy	Yes	91	51.1
	No	38	21.3
	Suggested	24	13.5
	Unknown	25	14.1
Hormonaltherapy	Yes	66	37.1
	No	38	21.3
	Suggested	5	2.8
	Unknown	69	38.8
Targeted	Yes	23	13.0
	No	96	54.0
	Suggested	0	0.0
	Unknown	59	33.0

DISCUSSION

Breast CA is the commonest tumor in women, and the major cause of death. This study was performed in order to make a descriptive study for breast cancer patients in Mosul.

The most frequent affected age in this study was 40-49 years in 30.9% of the sample. Similarly, in a study done in north of Iraq conducted by Molah Karim *et al*,[21] in 2015, the most common mean age was 49.4 years. Moreover, the 40-49 age groups showed highest breast cancer patient (44.7%), with mean age of cases were 45±5.7 years in a case control study done by Al-Mukhtar.[22] in Mosul city.

While Al-Saigh *et al*.,[23] study found that the highest incidence of breast cancer was between the ages 51 ≥ 60 years representing 35.8%. The incidence of breast CA overall Iraq was 126.037 for 50-59 years and for 60-69 years were 122.218, while the age group of 40-49 years was 87.275 from 2000-2019.[24]

In the current study, 76.9% of patients were lived in Mosul sector while the 23.1% were lived outside the center. Al-Khursani *et al*.,[25] study conducted in Najaf, reported that according to the residency of the breast CA 44(59.0%) of caseswere from urban, and 31(41.0%) from the rural area. Additionally, another study Ali *et al*.,[26] involving Kurdish women with breast CA found that 198(58.6%) were lived in urban compared to 140(41.4%) in rural.

Housewife found in 89.0% of the present study sample which agreed with the results of Al-Khursani *et al*., [25] study in which the housewife form found in 59(79.0%) of women having breast CA and 10(13.0%) in teachers women while 5(7.0%) in different occupational status and only 1(1.0%) in doctors. Additionally, in the study conducted by Ali *et al*., [26] study unemployed patients found in 255(75.4%) while employed in 83 (24.6%).

The family history was found positive in only 3.4% of the current sample which was lower than other studies as Alwan *et al*., study [15] where it was positive in 18.7%. Also in Ali *et al*.,[26] study, the positive family history found in 54 out of 338 representing 15.9% of cases and 34/338 among controls with odd ration of 1.7.Moreover, the distribution of breast CA according to family history show 11(15.0%) has first degree of family history, 7(9.0%) has second degree and7(9.0%) has third degree while 50(67.0%) without family history.[25]

The current study found that breast CA of 2-5 cm is the most frequent size accounting for 92(51.7%) of cases. The size below 2 cm presents in 26(14.6%), bigger than 5 cm presents in 21(11.8%). Similarly, the most frequent tumor size was 2-5cm as in Al Zobair *et al*., study.[27] which found that 244 out of 350 breast CA within the size of 2-5 cm representing 69.7%. Furthermore, Oluogun *et al*., study.[28] found that (51.9%) had tumor sizes ranging 2–5 cm (pT2) and some (39.1%) with >5 cm (pT3) were all at palpable stages.

Concerning the no. of LN, the present study found that 48(26.9%) of the patients have no LN involvement, 38(21.3%) had one LN involvement, while more than 10 LN involvement found in 4(2.3%). This result was parallel to that of Al Zobair *et al*., study.[27] which includes 350 women with breast CA in Mosul that found that one LN involvement in 97(27.7%) of the cases. Another study observing lymph node metastasis confirmed that 261 (76.1%) were negative, 77 (22.4%) were one LN.[28]

Regarding the type of breast CA among the present sample, it found that 79.0% of cases were IDC and 8.0% were ILC. The least frequent types are Medullary 0.5% and Pleomorphic 0.5%. The similar outcomes were reported by Al-Esawi study,[29] in which 292 patients involved, the invasive ductal carcinoma was found in 88.0% of cases, the invasive lobular in 3.1%, Medullary 6.8% and Mucinous 2.1%. The histopathological

subtypes are shown in Tareq *et al.,* study.[16] with invasive ductal carcinoma being the most common subtype (83.17%).

In the present study, the unilateral side whether left or right is the main common side in 45.0% and 43.0% respectively. In contrary, the tumor in the right side (66.35%) was significantly higher than the left side in the study conducted by Al-Saigh *et al.,*[23] in Mosul. Other preceding studies showed that the bilaterality rates and left side predominance of tumor.[30-32]

Different stages of breast CA were found in the current study; the stages 2 and 3 were 35.0% and 44.0% respectively which parallel to that of Tareq *et al.,* study.[16] in which 42.9% of the patients were identified with stage III and 25% with stage IV. Another Iraqi study[33] confirmed the late presentation, finding that 47 percent of patients experienced an advanced illness stages when they first appeared, with only 9.8 percent having stage I. In a recent study published in 2018,[34] 50.5% of patients had tumor stage III or IV. A study carried out in Maysan province at the south of Iraq reported that stage II was the commonest (52.9%) then stage III (29.4%), which also indicates that most of the patients presented with advanced-stage disease.[35] Another study [36] conducted in 2010 in the Northern region of Nigeria included 103 patients and showed that most (62%) presented with advanced-stage disease.

The commonest stage found in this study was 2B which account for 37(20.8%) while the In situ stage found only in 1.6%. The study conducted by Alwan *et al.,*[37] in 2010 including 570 females found that the molecular subtype with the highest proportion was luminal A. Moreover, in a recent study, luminal A was the commonest type in 47.4% of the patients, luminal B in 13.7%, human epidermal growth factor receptor 2 (HER2)–enriched cancer in 10.7%, and triple-negative in 14.7%.[38]

Ki-67, HER2, PR, and ER tumour marker positivity was noted in this investigation. Many studies on breast CA have reported that overexpress Ki-67 in more than 20%–50% of cells are at a high risk of developing recurrent disease, showing a statistically significant correlation with clinical outcomes, such as disease-free survival or overall survival[39,40] The ki-67 was found to be positive in 32.1% of case. According to the findings of previous studies, the over- expression of the HER2 protein and gene was associated with aggressive tumour characteristics, such as early tumour relapse, axillary node positivity, high tumour grade, and large tumour size, and was detected in 35.9% of the sample in the current study. However, the expression of HER2 in primary cancers and relapsing/metastasizing tumours varied between 0% and 34%.[41,42] A positive oestrogen receptor status in breast cancer is linked to a good response to hormone therapy, a good prognosis, a long disease-free survival, and overall survival.[43]

Additionally, 35.9% of the current sample tested positive for the PR marker. In 37.0% of the patients, ER was discovered. Previous results.[44,45] showed that ER was connected to very late tumour relapse. It is common knowledge that different cancers, individual tumours, and the main tumour and its metastases all exhibit varied patterns of ER expression.

The most frequent procedure for breast CA is a mastectomy, or breast removal surgery, which accounted for 43.8% of cases. Modified radical mastectomy made up 28.1% of the sample in this study, while lumpectomies and quadruplectomies accounted for 3.9% and 0.6% of cases, respectively. The parallel finding found in AlGaithy *et al.,* study.[46] conducted among the Saudi women diagnosed with breast CA and 18.2% of the sample underwent mastectomy and 70.8% modified radical mastectomy. In another study done by *et al.,*[47] involved 1606 women with breast CA operated on, there were 60.9% mastectomy patients and 39.1% lumpectomy.

In the current cases, the lymph node clearance was completed in 78.1% of the cases. The foundation of the theory is the discovery of the first "sentinel" lymph node that lymphatic flow reaches. So, only patients with confirmed node positivity are subjected to axillary dissection. Internal mammary lymph nodes rarely fail locally, but in about 10% to 20% of patients with axillary node-negative disease, they appear to have underestimated prognostic relevance. As a result, systemic therapy with early breast CA might be discontinued. However, there is currently no reason to perform a standard parasternal dissection.[48]

Chemotherapy, radiotherapy, hormonal, and targeted therapy all were recorded in the present study to be used in the treatment of breast CA in 91.0%, 51.1%, 37.1%, and 13.0% respectively. The adjuvant situation of early breast CA treatment is an exciting field where one has to combine many various emerging modalities. These have contributed to a decline in breast CA mortality over the last decades, despite the excess breast CA incidence.[49] Breast surgery, radiotherapy (RT), chemotherapy (chemoT), hormonotherapy (HT), and targeted agents are all being used together concomitantly or sequentially with the aim to achieve local and distant control and improve survival. With this goal being reached more and more often nowadays, quality of life emerges as another issue of pivotal importance considering their use and their impact on the patient's other-than breast CA–related mortality.[50]

CONCLUSION

The breast CA is common type of CA affecting adult age group women in Mosul mainly in housewife with minor role of family history.

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