

Treatment Follow up in Patients Diagnosed with Breast Cancer in Iraq

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ABSTRACT:

BACKGROUND:

Breast cancer is the most common malignancy affecting the Iraqi population. As many cases are still detected in advanced stages of the disease, regular follow-up of the diagnosed and treated patients is crucial to manage therapy-related complications and limit loco-regional recurrences.

OBJECTIVE:

To report the clinicopathological features, the offered treatment options and the recurrence rates among a sample of Iraqi female patients followed up after diagnoses with breast cancer.

PATIENTS AND METHODS:

A retrospective study design was followed enrolling a sample of 154 female patients diagnosed with breast cancer at a referral center for early detection of cancer in Baghdad, Iraq during a six month period (from January to July 2019). All cases with histopathologically confirmed invasive breast carcinoma were included in the study if they had reliable valid data related to their demographic, clinical, pathological and follow up status (for at least two years).

RESULTS:

The peak age frequency for breast cancer occurred in the fifth decade of life. Family history was observed in 18.2% of patients. The most common histological type was invasive ductal carcinoma (92.9%) while 46.8% of the patients presented in advanced clinical stages (III and IV). ER and PR and HER2 were positive in 66.2%, 63.6% and 36.4% of the cases respectively. Surgery was prescribed in 95.5% of the patients; 83.8% underwent modified radical mastectomy. Chemotherapy, Radiotherapy, Hormonal and Biological therapy were received by 92.2%, 66.9%, 64.9% and 32.4% of patients respectively. Overall, discontinuation of the treatment was observed in 8.4% while recurrence was recorded among 10.1% of the patients.

CONCLUSION:

Frequent regular follow up of patients diagnosed with breast cancer is crucial to achieve better prognosis. Continuous monitoring of the response to therapy and coordination through multidisciplinary follow-up care are essential recommendations to avoid risks of local and regional recurrences.

KEYWORDS: Breast, Cancer, Treatment, Follow up, Iraq.

INTRODUCTION:

Breast cancer is the most common malignancy among the Iraqi population and the essential cause of cancer related mortality among Iraqi women. It constitutes nearly one third of the registered female cancers being the second killer after cerebrovascular disease and responsible for about 11.3% of cancer related mortality in general and 22.3% of deaths from cancer among women⁽¹⁻²⁾.

Up to the present time a non-negligible proportion of Iraqi females are still diagnosed with that disease in the premenopausal age

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groups; presenting with late stages and unfavorable prognosis^(1,3-7). Numerous reports clearly illustrated that screening and early detection of breast cancer in middle and low income countries could significantly reduce mortality when coped with appropriate treatment⁽⁸⁻¹¹⁾

A critical advancement in the treatment of breast carcinoma has been the realization that the presence of hormone (estrogen and progesterone) receptors in the tumor tissues is associated with better response to hormone therapy and chemotherapy.

BREAST CANCER IN IRAQ

The treatment of breast cancer needs both local and systemic approaches to be effective; thus, should comprise surgery, radiation, chemotherapy, hormonal and targeted therapy according to the type and extent of the disease⁽¹²⁾. Follow-up of the diagnosed and treated patients is crucial to detect early recurrences, manage therapy-related complications and provide psychological support⁽¹³⁾.

AIM OF THE STUDY :

The aim of this study was to report the clinicopathological features, the offered treatment options and the recurrence rates among a sample of female patients followed up after diagnoses with breast cancer at a referral center for early detection of cancer in Iraq.

PATIENTS AND METHODS:

A retrospective study design was followed enrolling a sample of 154 Iraqi female patients diagnosed with breast cancer who were referred to the Main Referral Center for Early Detection of Breast Tumors, Oncology Teaching Hospital in Baghdad during a six month period (from January to July 2019).

Inclusion criteria:

All female patients with histopathologically confirmed diagnosis of invasive breast carcinoma who have reliable valid data recorded in their file case sheet questionnaires related to their demographic, clinical, pathological and follow up status (for at least two years).

Exclusion criteria:

Cases with non-invasive in situ carcinoma and those with missing data.

Demographic, Clinical and Pathological Data:

Age of the patient at the time of diagnosis, marital status, age at first delivery, history of lactation, family history of breast or any other cancer, histologic type of mammary carcinoma, grade of breast cancer, size of the tumor, stage of the disease at presentation according to TNM classification, Estrogen Receptor (ER), Progesterone Receptor (PR) and HER2 overexpression.

Treatment Data:

Treatment options (Surgery, Chemotherapy, Radiotherapy, Hormonal, or Biological); types of surgery (breast-conserving surgery, simple mastectomy, modified radical mastectomy, radical mastectomy); completeness of treatment after initiation, and follow up of patients to exclude recurrence (through full history, physical examination, imaging and pathological laboratory tests).

Statistical analysis:

The reported information was analyzed using Statistical Package for Social Sciences (SPSS) version 25; figures presented as mean, standard deviation and ranges. Categorical data were represented by frequencies and percentages. Chi square test was used to assess the association between recurrence of malignancy and stage of disease. A level of P value less than 0.05 was considered significant.

RESULTS:

Table (1) shows that the age of the patients ranged from 25 to 75 years with a mean of 47.15 years and a standard deviation (SD) of ± 9.15 years. The highest proportion of patients (46.1%) was in the fifth decade of life (40 – 49 years).

Table 1: Distribution of patients by age

Age (Year)	No. (n=154)	Percentage (%)
< 30	5	3.2
30 – 39	27	17.5
40 – 49	71	46.1
50 – 59	37	24.0
60 – 69	13	8.4
≥ 70	1	0.7

In this study, the majority of patients were married (85.7%). More than half of the patients (58.4%) had more than three children, while only (16.9%) of them were nulliparous (Table 2).

Only (16.4%) of them delivered their first child over the age of 30 years. Family history of breast cancer was noted in (18.2%) of the patients while history of lactation was recorded in (72.7%).

Table 2 : Demographic and reproductive features of the study population

Variable	No. (n=154)	Percentage (%)
Marital status		
Currently married	132	85.7
Single	15	9.7
Divorced or widowed	7	4.6
Number of children		
No children	26	16.9
1 – 3	38	24.7
> 3	90	58.4
Age of 1st delivery n= 128		
< 20	32	25.0
20 – 29	75	58.6
≥ 30	21	16.4
Family history of cancer		
Positive for breast cancer	28	18.2
Positive for other cancers	14	9.1
Negative	112	72.7
History of lactation		
Yes	112	72.7
No	42	27.3

Table (3) illustrates the distribution of patients by certain pathological features. Overall, (41.6%) of the masses measured < 2 cm and the most common histological type was invasive ductal carcinoma (92.9%). It was noted that stage II and III were diagnosed in the majority

of cases (45.4% and 42.2% respectively) while (78.6%) of the tumors were diagnosed as Grade 2. Estrogen and progesterone receptors were positive in about two thirds of cases (66.2% and 63.6% respectively), while HER2 was positive in (36.4%).

Table 3: Distribution of patients according to the pathological characteristics

Variable	No. (n=154)	Percentage (%)
Tumor Size		
< 2	64	41.6
2 – 5	62	40.3
>5	28	18.2
Histological type		
Invasive ductal carcinoma	143	92.9
Invasive lobular carcinoma	6	3.9
Others	5	3.1
Breast Cancer Stage		
I	12	7.8
II	IIA	43
	IIB	27
III	IIIA	39
	IIIB	4
	IIIC	22
IV	7	4.6
Grade		
1	6	3.9
2	121	78.6
3	27	17.5
Estrogen Receptor		
Positive	102	66.2
Negative	52	33.8
Progesterone Receptor		
Positive	98	63.6
Negative	56	36.4
HER2		
Positive	56	36.4
Negative	98	63.6

Regarding treatment, (63%) of the patients was still continuing therapy at the time of the study (Table 4) whereas incomplete therapy was noted in (8.4%). Table (5) displays that the majority of the patients underwent modified radical

mastectomy (83.8%) while Table (6) shows that Chemotherapy was received in (92.2%) of cases, on the other hand, Surgery, Radiotherapy, Hormonal and Biological therapy were applied on 95.5%, 66.9%, 64.9% and 32.4% respectively.

Table 4 : State of therapy during the period of the study

Final state of therapy	No. (n=154)	Percentage (%)
Complete	44	28.5
Continuous	97	63.0
Incomplete	13	8.4

Table 5: Intention of surgical treatment

Intention of Surgery	Description	No. (n= 154)	Percentage (%)
1	1-Not prescribed	3	1.9
3	3-Breast conserving surgery	5	3.2
5	5-Simple mastectomy	7	4.5
6	6-Modified radical mastectomy	129	83.8
7	7-Radical mastectomy	6	3.9
9	9-Unknown	4	2.6

Table 6 : Type of the offered therapy

Type of Therapy	No. (n=154)	Percentage (%)
Surgery	147	95.5
Chemotherapy	142	92.2
Radiotherapy	103	66.9
Hormonal	100	64.9
Biological	50	32.4

The prevalence of recurrence of malignancy among the studied patients was 10.1%. Table (7) reveals the association between composite stage at breast cancer presentation and the disease recurrence.

The recurrence of malignancy was significantly increasing as the stage of cancer advance with the highest rate recorded stage IV (33.3%, P= 0.017)

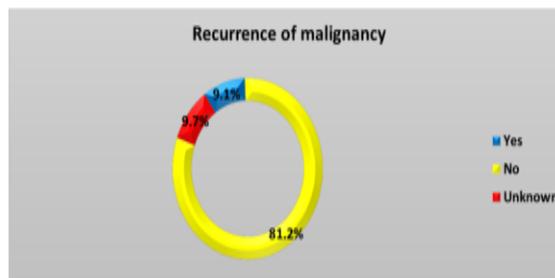


Figure 1: Recurrence of malignancy

Table 7: Correlation between composite stage at breast cancer presentation and disease recurrence

Stage	Recurrence of Malignancy		Total (%) n= 139	P- Value
	Yes (%) n= 14	No (%) n= 125		
I	0 (0)	11 (100.0)	11 (7.9)	0.017
IIA	0 (0)	39 (100.0)	39 (28.1)	
IIB	2 (8.0)	23 (92.0)	25 (18.0)	
IIIA	4 (11.8)	30 (88.2)	34 (24.5)	
IIIB	1 (25.0)	3 (75.0)	4 (2.9)	
IIIC	5 (25.0)	15 (75.0)	20 (14.4)	
IV	2 (33.3)	4 (66.7)	6 (4.3)	
Total	14 (10.1)	125 (89.9)		

DISCUSSION:

In this study the peak age distribution of breast cancer was displayed in the fifth decade of life; confirming what was reported in earlier surveys from Iraq^(1-3,5-7,9,11,14); The significantly younger age at presentation of that disease among Iraqi females compared to the British and other Western patients emphasizes the urgent need of promoting public awareness and screening programs in our country focusing on the target population at risk^(9,15-18). The national breast cancer control plan should be strictly applied among patients revealing family history of the disease.

The relatively high rate of positive family history of breast cancer noted in this study is consistent with the findings reported in several earlier studies conducted at the same referral center^(6,14,18,19) and slightly higher than those recorded in other studies from Iraq⁽²⁰⁾. Likewise, the analyzed clinical features of the patients and the pathological characteristics of their breast cancer were comparable to the results illustrated in previous studies carried out on Iraqi patients suffering from the disease⁽³⁻⁷⁾.

The advanced stages at the time of detecting breast cancer among our affected female population reflect the dilemma of access to care and management of breast cancer in developing countries^(3-7,9-11,14). The relatively low hormone receptor contents and high HER2 overexpression of breast cancers, which are constantly demonstrated in numerous studies on our patients^(3,5,7,21), as compared to their western counterparts⁽³⁾, compel comprehensive assessment of the breast cancer surrogate subtypes as a principal approach to the effective treatment.

In this study the rates of patients who received Chemotherapy and Radiotherapy were significantly higher than those reported in previous studies^(22,23) probably attributed to the fact that the studied patients were treated in a specialized breast cancer center affiliated to a major Medical City Teaching Hospital in the capital Baghdad. Good response was found to all types of treatment.

It is observed that during the period of the study 8.4% of the patients did not continue their treatment protocols.

Discontinuation of therapy is mostly attributable to either severe side effects that avoided continuation, patient death, carelessness or due to psychological reasons often encountered when the patients reach to desperate stages^(24,25).

Primary surgical treatment was prescribed to the majority of the patients in this study; most of them underwent modified radical mastectomy (83.8%) while breast conserving surgery was carried out in only 3.2%; the rate of the latter being significantly lower than what has been reported in other studies^(26,27). Regrettably, modified radical mastectomy is still the standard mode of surgical treatment in Iraq^(7,14) and other developing Arab countries^(10,28) where most of the patients are still diagnosed at advanced stages and access to modern radiotherapy approaches is still limited. It has been reported that modern radiation therapy is currently practiced in only few comprehensive cancer centers in the Arab world; emphasizing the importance of investment in that field⁽²⁸⁾. In a critical review on the surgical management of breast cancer it was highlighted that mastectomy is still adopted worldwide as a principal therapeutic procedure⁽²⁹⁾. No significant relationship was found between the type of surgery and the response to treatment. Follow up of the studied population showed that recurrence was registered among 10.1% of patients; slightly higher than the reported rate in a previous breast cancer research project from Iraq and lower than the frequencies displayed by other local study^(14,26).

The comparatively lower recurrence rates which are recorded in the western literature are obviously related to the earlier stages at presentation of breast cancer in those societies and the accompanied optimum follow-up management⁽³⁰⁾.

CONCLUSIONS:

Continuous frequent regular follow up of the Iraqi female patients who are diagnosed with breast cancer is crucial to achieving better prognosis, specifically in those presenting with advanced stages. Identifying the individuals at risk through early detection, continuous monitoring of the response to therapy and coordination of the multidisciplinary follow-up care between the oncologists, surgeons, radiologists and pathologists are essential recommendations to avoid risks of local and regional recurrences.

REFERENCES:

1. Iraqi Cancer Board (2016). Results of the Iraqi Cancer Registry 2015. Baghdad, Iraqi Cancer Registry Center, Ministry of Health, 2018.
2. Annual Statistical Report 2016. Planning Directorate, Ministry of Health/Environment, Republic of Iraq, 2017. Available from: <https://moh.gov.iq/upload/ule/ar/513.pdf>.
3. Alwan, N, Kerr D, Al-Okati D, et al. Comparative study on the clinic-pathological profiles of breast cancer among Iraqi and British patients. *The Open Public Health Journal*. 2018; (11): 177–191
4. Alwan NAS, Tawfeeq F, Maallah M et al: The Stage of Breast Cancer at the Time of Diagnosis: Correlation with the Clinicopathological Findings among Iraqi Patients. *J Neoplasm*, 2017; Vol. 2 (3:22); 1-10.
5. Alwan NAS, Mualla F, Naqash M et al: Clinical and Pathological Characteristics of Triple Positive Breast Cancer among Iraqi Patients, *Gulf Journal of Oncology*, 2017; 25: 6-15.
6. Alwan NAS.,Tawfek FN.,Mallah NAC, Demographic and clinical profiles of female Patients diagnosed with breast cancer in Iraq. *Journal of Contemporary Medical Science*, 2019; 5 (1): 14-19.
7. Alwan NAS. Tumor Characteristics of Female Breast Cancer: Pathological review of Mastectomy Specimens Belonging to Iraqi Patients .*World Journal of Breast Cancer Research*, 2018; 1 (1): 1-3.
8. Rosai and Ackerman's Surgical Pathology, Elsevier, eleventh edition, 2018, chapter36 Breast pp (1434-1527)
9. Alwan N: Establishing Guidelines for Early Detection of Breast Cancer in Iraq. *Int J. of Advanced Research*. 2015; 3 (12): 539-555
10. Sankar R, Alwan N & Denny L: "How Can We Improve Survival from Breast Cancer in Developing Countries?" *Future Medicine, Breast Cancer Management*, 2013, 2 (3): 179-183.
11. Alwan NAS, Kerr D. Cancer Control in War-Torn Iraq, *The Lancet Oncology*, 2018; 19 (3): 291-292
12. Goldhirsch A, Wood WC, Coates AS, et al. Strategies for subtypes dealing with the diversity of breast cancer: Highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011, *Ann Oncol*. 2011; 22 (8):1747-1736
13. Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E,Zackrisson S, Cardoso F. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology*. 2015 Sep 1; 26 (suppl_5):v8-30.
14. Alwan NAS. Breast Cancer Among Iraqi Women: Preliminary Findings From a Regional Comparative Breast Cancer Research Project. *Journal of Global Oncology*, 2016; 2 (5): 255-258.
15. Alwan NAS and Al-Attar: Evaluating the Effect of an Educational Teaching Model on the Knowledge about Breast Cancer among Female University Students in Iraq., *JJ Cancer Sci. Res*. 2016, 2 (1): 026.
16. Alwan NAS, Alattar W, Mallah N, Hassoun T: Baseline Needs Assessment for Breast Cancer Awareness and Management among Paramedical Health Care Providers in Iraq. *International Journal of Science and Research (IJSR)*, 2017; 6 (7): 1515-1520.
17. Alwan NAS, Al-Attar WM, Al Mallah N. Baseline Needs Assessment for Breast Cancer Awareness among Patients in Iraq, *International Journal of Science and Research (IJSR)*, 2017; 6 (1): 2088 – 2093.

18. Alwan NAS: Clinical and Pathological Characteristics of Familial Breast Cancer in Iraq, *Chronicle Journal of Cancer Science*, 2017; 1 (1): 002.
19. Alwan NAS. Family History among Iraqi Patents Diagnosed with Breast Cancer, *IJSR*, 2017; 6 (2): 868-872.
20. Majid RA, Mohammed HA, Saeed HM, Safar BM, Rashid RM, Hughson MD. Breast cancer in kurdish women of northern Iraq: incidence, clinical stage, and case control analysis of parity and family risk. *BMC women's health*. 2009; 9 (1):33.
21. Alwan NAS, Tawfeeq FN, Muallah FH. Breast Cancer Subtypes among Iraqi Patients: Identified By Their ER, PR and HER2 Status. *Fac Med Baghdad*, 2017; 59 (4): 304-307.
22. Alawad AS, ALkathum MA, Alwahed AA. A Retrospective Study of Relapsed Breast Cancer Cases During Follow-Up in Merjan. *Medical Journal of Babylon*. 2009;6 (1): 130-7.
23. Onitilo AA, Engel JM, Greenlee RT, Mukesh BN. Breast cancer subtypes based on ER/PR and Her2 expression: comparison of clinicopathologic features and survival. *Clinical Medicine & Research*. 2009 Jun 1; 7 (1-2):4-13.
24. Anthony FY, Yadav NU, Lung BY, Eaton AA, Thaler HT, Hudis CA, Dang CT, Steingart RM. Trastuzumab interruption and treatment-induced cardiotoxicity in early HER2-positive breast cancer. *Breast cancer research and treatment*. 2015; 1; 149(2):489-95.
25. Talima S, Kassem H, Kassem N. Chemotherapy and targeted therapy for breast cancer patients with hepatitis C virus infection. *Breast Cancer*. 2019; 15;26 (2):154-63.
26. Tlefih AJ. Non-Metastatic Breast Cancer: Clinical Presentation and Patterns of Surgical Treatment. *Al-Kindy College Medical Journal*. 2009; 5 (1):40-6.
27. Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. *Journal of the National Cancer Institute*. 2002; 3;94 (7):490-6.
28. El Saghir N, Khalil MK, Eid T, et al. Trends in epidemiology and management of breast cancer in developing Arab countries: A literature and registry analysis. *International Journal of Surgery*, 2007; 226-233.
29. Lazaraviciute G, Chaturvedi S. Mastectomy—A Critical Review. *Open Journal of Clinical Diagnostics*, 2017; 7: 58-66.
30. American Society of Clinical Oncology. The state of cancer care in America. A report by the American Society of Clinical Oncology. *J. Oncol. Practice*, 2014; 10: 119-142.