Demographic and Clinicohistological Profiles of Women Diagnosed with Breast Cancer at Al-El Wiya Maternity Teaching Hospital / Baghdad: A Retrospective Study

Zaynab S. Abdulghany[1*], Najim Al-Kalidy[2], Maeda H. Mohammad[1], Noor H. Ismail[1]

[1]Lecturer, Iraqi Center For Cancer And Medical Genetics Research / Mustansiriyah University / Baghdad /Iraq,
[2]Consultant General Surgeon Women tumor center at Al-El Wiya maternity teaching hospital/Baghdad / Iraq

Abstract

Knowing the incidence of, breast cancer, diagnosis, and treatment methods given a strategic approach for community awareness and rapid management. This study was aimed to: Estimate the demographic pattern including age, marital status, number of children, mass location, lactation, using contraceptive and smoking habit and to estimate the pattern of BC risk factors including family history, histological type, grading, and staging. The retrospective cross-sectional descriptive design was utilized. A total of 282 confirmed breast cancer female patients for the years 2016 to 2018 were included. Overall result showed that the age of Breast cancer female patients ranged from (25-80) years with a mean (49.12±0.67). Most Breast Cancer cases were diagnosed with infiltrating ductal carcinoma (73.4%). The percentage of the discovered tumor was dominating the right side of the breast (52.8%). Also, 11% of BC females were diagnosed with stage IIa. And 31.2 % of BC cases were diagnosed as grade II. However, 20.2% of the cases were having a family history with breast cancer. Most of the cases (94.7%) were did not checked for biomarker testing, just 12 cases (4.3%) were positive ER. And 3.9% of cases tested for PR only 11 cases were positive. While negative results for HER2/neu was only in 9 cases (3.2%). Current study validates scientific knowledge about BC in Baghdad. Each year, the incidence rates increase especially for age above 49.

***Keywords**: Iraqi breast cancer, awareness, early detection, biomarkers, retrospective, ductal carcinoma*

Introduction

Cancer incidence looks like a scale of diatonic, the increasing faced by increasing in society age and unhealthy lifestyles and premature death that would reduce the country's productivity. According to data published by the Globocan site that in the 2030 year about 13 million people may die from cancer incidence worldwide, three-quarter of them may be in low income and middle-income countries [(1)]. The breast cancer new cases increasing gradually and stand at the top first rank among other cancer in Iraq depending to the Annual report of the Iraqi cancer registry and this affected the community population [(2)].

Corresponding author:
Zaynab S. Abdulghany
Lecturer, Iraqi center for cancer and medical genetics research / Mustansiriyah University.
Email: zaynab.saad@iccmgr.org

The Iraqi national program for early detection of breast cancer, which was initiated since 2001, in an attempt to down-stage this disease at the time of presentation. Since then, specialized centers and clinics for early detection of breast tumors have been established in the major hospitals in all Iraqi provinces. Most screening and biological detection techniques simplify the early diagnosis of breast cancer; immunohistochemistry for biomarkers detection [(2)], ELISA for blood assay analysis [(3)], and the golden standard method is the presence of screening programs using mammography as an imaging technique [(4,5)]. Still, self-breast screening is the major easy early detection method [(5)]. All these techniques were present in the Iraq strategy of screening programs.

The innovation of several genetic factors has been found to detect breast cancer for example; BRCA1 and BRCA2 were the most important tests, followed by MYC and P53. These tests are available, more specific

but very costly for in low come countries, as in Iraq [6]. Then adventure of new assays for gene detection using mammaprint and Oncotype DX [7] but still not very widely in use.

Pieces of information about the incidence rate of breast cancer are important in planning health issues. In Iraq, the respective nesses of the present project were largely unclear partly due to inconsistency in data collection, an outcome that may be linked to the absence of a true cancer registry. This study was aimed to:

1. Estimate the demographic pattern including age, marital status, number of children, mass location, lactation, using contraceptive and smoking habit

2. Estimate the pattern of BC risk factors including family history, histological type, grading, and staging.

3. Due to lack of biomarker data for almost patient data here not shown in the result. Assess the pattern of BC characteristics, including HER2/ neu status, estrogen and progesterone receptor status, CA15-3, CEA, P53, and Ki-67 biomarkers.

Methods

A descriptive – retrospective study has been conducted by using an information system data base from Al-Alwyia / oncology unit/ breast cancer center/ Baghdad /Iraq. In order to obtain representative data of patients, these data were collected during women visiting the center for checkup and examination for any breast problems 2016, 2017, and 2018 years. A total of 282 patients were included during these years.

The patients were asked for several pieces of information and each patient has his own file according to the Iraqi Cancer Registry, the list of questions contains age, number of children, using the contraceptive, side of the mass, smoking habit, family history with breast cancer, marital status and lactation. Then the data of results from their consequence visiting the center were collected and included: mammography result, FNA test, type of tissue, histological result, TNM, the grade of tissue, BI-RADs, and the result of biomarkers (ER, PR, Her2/neu, P53, Ki-67, CEA, CA15-3, AFP, and Keratin).

Statistical Analyses

Statistical analyses were run using SPSS software for Windows (version 24; IBM SPSS). The variables that were significant in the univariate analysis were included in the multivariate model. The data were analyzed and the frequency and the percentage were calculated accordingly. All of the statistical tests were $P<0.05$ indicated a significant difference.

Ethical statement

The present study was approved by the Research Ethics Committee of the cancer research center and according to the ethical standards laid down by the declaration of Helsinki. The ethical committee was obtained from the Health Research Unite and protocol Review Committee in the Ministry of Health / Baghdad / Iraq.

Results

The demographic characteristics of the patients were presented in Table 1, and their age distribution was presented in figure- 1. The main clinical features and the histopathological features were shown in Tables 1, 2, and 3, respectively. In total, 282 cases of women diagnosed with breast cancer were included in this study from 2016-2018 years. The age at diagnosis of the women was ranged from 25-80 years old with a mean of 49.21 (SD+0.67) years. The majority of the age group was 45-55 years and represented 31.1%.

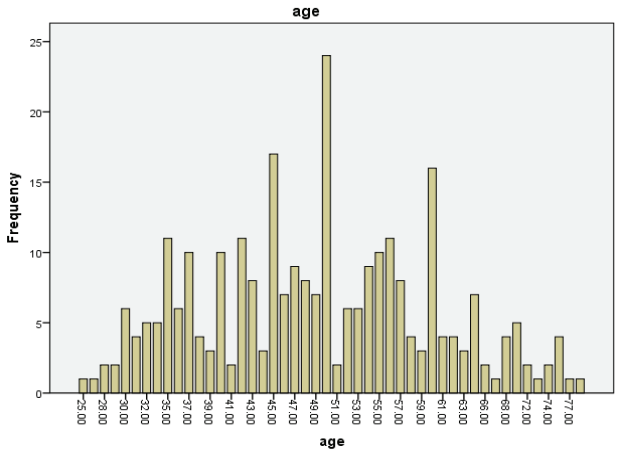

Figure 1: Patients age distribution during 2016-2018 years and age ranged from (25-80) years.

Generally according to data collected and summarized in table 1, increasing in frequency of

patients age. However, the range of 45-55 years was recorded as the highest incidence rate, about 31.1% (88) of total patients compared to other age ranges.

Table 1: frequency distribution of patients according to age

Patient age (Year)	No. of patient	Frequency (%)
25-35	37	13.2
35-34	74	27.9
45-55	88	31.1
55-65 and above	83	29.6

In table- 2, illustrate the socio-demographic characteristics and clinical history of 282 female patients diagnosed with breast cancer. The peak frequency occurred among the age group 25-80 years. Selected equal patient age above and under 49 years were 141 females. About 65.6% of them were determined as married and 44 % were having less than four children. Also, 52.8% having a mass on their right side of the breast. Their history of lactation was recorded in 70.2%, on the other hand, 72.7% doesn't take contraceptive pills and 90.4% doesn't have a smoking habit.

Table 2: socio-demographic characteristics of female patients with breast cancer.

Variable	Frequency (n.)	Percentage (%)
Age group		
Mean ± SD (49.21±0.67)	141	50
<49	141	50
>49	282	100
Total		
Marital status		
Single	25	8.9
Married	185	65.6
Widow	41	14.5
Divorced	17	6
Total	268	95
Missing data	14	5
Number of children		
0	37	13.1
<4	124	44
>4	113	40.1
Total	274	97.2
Missing data	8	2.8
Mass location		
Left	130	46.1
Right	149	52.8
Total	279	98.9
Missing data	3	1.1
Lactation		
Yes	198	70.2
No	65	23
Total	263	93.3
Missing	19	6.7
Using contraceptive		
Yes	22	7.8
No	205	72.7
Total	227	80.5
Missing data	55	19.5
Smoking habit		
Yes	18	6.4
No	255	90.4
Total	273	96.8
Missing data	9	3.2

Next, the histological trend and grade of common pathological type between patients with breast cancer were represented in table- 3. The predominant tumor histological patterns were: invasive ductal carcinoma 207 (74.4%), metastatic carcinoma 20 (7.1%), and invasive lobular carcinoma 13 (4.6%). On the other hand, the histological tumor grade was available for 121 patients (42.9%). The common grade was II in 88 patients (31.2%), grade III 25 (8.9%), and grade I 8 (2.2%). Also, stage II a recorded in 31 patients (11%), stage IIb in 22 (7.8%) followed by stage III c in 17 (6%).

While tested biomarkers faced almost missing data during recording follow up. The main problem for patients following up, and missing data recorded to reach 94% of the tested cases (data not shown). Even several types of biomarkers were available but need more following up documentation, and more control.

Table 3: Histological features of patients with breast cancer.

Variable	Frequency	Percentage (%)
Family history with BCA		
Yes	57	20.2
No	218	77.7
Total	4276	97.9
Missing data	6	2.1
Histological diagnosis		
Benign	14	5
Ductal carcinoma	207	73.4
Lobular carcinoma	13	4.6
Metastatic carcinoma	20	7.1
Total	254	90.1
Missing data	28	9.9
Grade		
I	8	2.8
II	88	31.2
III	25	8.9
Total	121	42.9
Missing data	161	57.1
BI-RADs		
I, II, III	21	7.4
IV, V	81	28.7
Total	102	36.2
Missing data	180	63.8
Staging		
Stage Ia	9	3.2
Stage Ib	3	1.1
Stage IIa	31	11
Stage IIb	22	7.8
Stage IIIa	12	4.3
Stage IIIb	4	1.4
Stage IIIc	17	6
Stage IV	4	1.4
Total	102	36.2
Missing data	180	63.8

In an attempt to classify patients according to median age into those who above 49 years old and those who lower than 49 years old and data presented in the table- 4. Significant statistical differences were noticed regarding using contraceptive pills, smoking habits, marital status, and the number of having children. Patients <49 years age utilize significantly more contraceptive compared to those above 49 years old (P<0.024), the smoking habit was noticed in women >49 years old significantly more than those <49 years old (P<0.026). While the older age >49 years was prefer breastfeeding significantly higher than <49 years old (P<0.08), the number of having children >4 was significantly in <49 years old (P<0.044). The frequency of unmarried (single) women <49 years old was a significantly higher number than above 49 years old.

Table 4: demographic characteristics of the patients under study according to age (>49 years versus <49 years):

Patients characterization	Age <49 year	Age >49 year	P-value
Mass location			
Left	65	65	1.0
Right	74	75	
Using contraceptive			
Yes	17	5	0.024
No	105	100	
Family history			
Yes	31	26	0.459
No	106	113	
Smoking habit			
Yes	4	14	0.026
No	132	123	
Lactation			
Yes	94	104	0.08
No	39	26	
No. of children			
>4	70	54	0.044
<4	54	67	
Marital status			
Single	14	11	0.00
Married	111	74	
Widow	4	37	
Divorced	8	9	

On the other hand, couldn't notice any statistical differences in respect to the clinicopathological data including histological tissue type, stage group, and tissue grading as presented in table-5. But patients under 49 years old were in stage two (a, b, and c) recorded in 18, 17, and 11 patients respectively. And grade II recorded in 51 patients under 49 years old.

Table 5: Clinical characteristics of the patients diagnosed with breast cancer under study according to age (>49 years versus <49 years)

Patients characterization	Age <49 year	Age >49 year	P-value
Stage group			
Ia	4	5	
Ib	3	0	
IIa	18	13	
IIb	17	5	0.12
IIIa	5	7	
IIIb	1	3	
IIIc	11	6	
IV	1	3	
Grading			
I	4	4	
II	51	37	0.77
III	16	9	

In table- 6, the comparison between tumor grading and staging was recorded in 93 patients, significant differences (P<0.001) was shown between grading and staging; grade II/ stage IIa was higher in 28 patients. There were significant statistical differences as shown in table- 7, in comparing tumor histological type and grading (P<0.002). Ductal carcinoma has a higher number of patients among other types and stage IIa and stage IIb was recorded in 21 patients for both.

Table 6: Comparison between grading and staging

Variable	Grade I	Grade II	Grade III	Total	p-value
Stage Ia	2	7	0	9	
Stage Ib	0	1	0	1	
Stage IIa	1	28	1	30	
Stage IIb	1	19	2	22	
Stage IIIa	0	5	7	12	0.001
Stage IIIB	0	0	1	1	
Stage IIIC	0	9	8	17	
IV	0	0	1	1	
Total	4	69	20	93	

Table 7: comparison between histological types and grading

Variable	Benign	Ductal carcinoma	Lobular carcinoma	Metastatic carcinoma	total	p-value
Stage Ia	0	9	0	0	9	0.002
Stage Ib	0	2	0	1	3	
Stage IIa	3	21	6	0	30	
Stage IIb	0	21	0	1	22	
Stage IIIa	0	11	0	1	12	
Stage IIIB	0	1	2	1	4	
Stage IIIC	0	11	4	2	17	
IV	0	1	1	1	3	
Total	3	77	13	7	100	

Discussion

Breast cancer with estrogen receptor ER +ve accounts for three quarter percent of western women while Arab women have a majority in ER -ve expression with 20%, 30%, and 9.3% in the UAE, Saudi women, and Lebanese women respectively compared to 9% in European women (9%) [10].

Women in low- income countries especially as presented in the review of Munzone E (2014) [11], the study was focusing on Africa region were women seek treatment in advanced stages or when the tumor spread to other organs and care has a relief aspect in these women; while in comparison to European countries very few women were diagnosed in late stages of cancer. In Kenya and Uganda for example in the study, all women were diagnosed at a late stage and assumed to be associated with high mortality rates [11].

The tests for breast cancer which are commercially available and currently used in the clinical practice were: the Oncotype DX test (Genomic Health, Redwood, CA, USA), the MammaPrint test (Netherlands Cancer Institute™ and Agendia™, Netherland), and the Prosigma one (NanoString Technologies, Seattle, WA, USA) very expensive and not very widely in use in our country (Iraq especially in Baghdad). The Oncotype DX test represent the most widely used molecular test in the therapeutic decision-making and predictive for endocrine responsiveness in hormone receptor-positive breast cancers with 0–3 positive nodes, also it is recommended by both the National Comprehensive Cancer Network (NCCN) and the St. Gallen Consensus [7].

In comparison between Arabic women and the United States, the recording average age of newly diagnosed breast cancer was high and estimated at 60 years old and these are the result of increases in the age specifically in the status of ER^+/PR^+ in post-menopausal US women [12]. While in Northern Iraq the status of incidence at age is different, it was recorded to be less 50 years old in Sulaimaniyah for Kurdish people [13],

the authors suggested that the increase in the age rate of breast cancer in Iraq and other Middle-East countries was might be the increased establishment of new cancer centers for early detection.

In the present retrospective study, results were parallel to published records and gives an idea about disease diagnosis and incidence rates that would help to ensure accurate records and next to proper disease diagnosis and management in the future. For sure, more studies with more significant periods and risk factors were required to explain more accurate findings.

Breast cancer management programs require multi-disciplinary teams starting from surgery, radiation and chemotherapy and that will need more resources and related expertise to identify genes associated with breast cancer that would need more accurate procedures and expenses a lot [14].

In Iraq, a preliminary analysis study carried by Alwan 2016, 855 patients were recruited and the study findings were: 35% of the women were diagnosed at the age of 45-54 years old, their history of lactation and hormonal therapy was reported in 48 %, and 20.5% respectively. Only 18.5 % of the group with breast cancer family history. Depending on TNM classification, 9.8% stage I of the disease and 46% at stage II and IV. Infiltration ductal carcinoma was the most common pathology about 67% (the same of this study findings), followed by ductal carcinoma, lobular carcinoma, and malignant tumor 13.6%, 18.5 %, and 7 % respectively [15].

In a recent study carried by Alwan and her team work 2019, 1172 females have participated in their study from Baghdad city. They found that the main age was 51 years old and the patient's groupage under 50 years demonstrated about 46.8%. Participants with breast cancer family history were recorded in 18.7%. Stages I-IV were recorded in 12%, 47.5%, 31.9% and 8.6% respectively. The frequency of age at diagnosis was significantly estimated higher among younger women under 50 years old. Alwan and her colleague give a conclusion that "breast cancer in Iraq represent an advanced disease at the time of diagnosis that justifies the necessity to promote public awareness educational campaigns to strengthen our national early detection programs" [16].

Limitations

There were several limitations while collecting data in this study: 1) most of the results of the biomarker were not included in patents file records, 2) also most of the FNA result not included, 3) the most importantly missing the follow-up of each patient that undergo surgery and 4) wither patients started chemotherapy or hormonal therapy cycles. These limitations might effects Iraqi cancer registration processes for breast cancer future information also affects planning for the new strategy of facilities, Mammography and MRI devices have the ability to detect small mass and in situ breast cancer that might be helpful in early detection programs.

Also, the unavailability of breast cancer mortality records was faced during data collection, it would be a predictor of effects caused by any disease or complications. Asian countries as mentioned in the study [17] don't have proper records and data of incidence rate and mortality were collected from hospital-based registries and records.

Source of Funding: Self

Conflict of Interest: Nil

Ethical Clearance: taken for this study from the Iraqi Center for Cancer and Medical Genetics Research/ Mustansiriyah University, and conducted according to the criteria set by the declaration of Helsinki

References

1. Globocan: counting the toll of cancer. Editorial September 2018. Lancet. 2018. 391: 1023-1075
2. Annual report. Iraqi Cancer Registry 2016. Iraqi Cancer Board, Ministry of Health and Environment, Republic of Iraq.
3. Alwan NAS. Iraqi Breast Cancer: A Review on Patients' Demographic Characteristics and Clinico-Pathological Presentation. J Facul Med. 2010. 52 (1):105-110
4. Nofech-Mozes S, Vella ET, Dhesy-Thind S, Hagerty KL, Mangu PB and Termin S. Systemic review on hormone receptor testing in breast cancer. AIMM. 2012. 20: 214-263.
5. Haddad FG, Kourie HR and Adib SM. Trends in mammography utilization for breast cancer screening in a middle-eastern country: Lebanon

2005-2013. Cancer Epidemiol. 2015. 39: 819-824.

6. Mustafa M, Nornazirah A, Salih F, Illzam E, Suleiman M and Sharifa A. Breast cancer: detection markers, prognosis and prevention. IOSR J of dental and medical sciences. 2016. 15(8):73-80.
7. Miller AB and Baines CJ. The role of clinical examination and breast self-examination. Prev Med. 2011. 53:118-120.
8. Serena Bertozzi, Ambrogio P. Londero, Luca Seriau, et al. Biomarkers in breast cancer. Chapter 1. Book: biomarker: indicator of abnormal process. 2018. By Ghousia Begum. Inteun Open. India
9. Albain KS, Barlow WE, Shak S, Hortobagyi GN, Livingston RB, Yeh IT, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, estrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial. The Lancet Oncol. 2010. 11:55-65.
10. Chouchane L., Boussen H. and Sastry KSR. Breast cancer in Arab populations: Molecular characteristics and disease management implications. Lancet Oncol. 2013. 14: e417–e424.
11. Munzone E. Highlights from the 9th European breast cancer conference, Glasgow, 19-21 March 2014. Ecancer medical sciences. 2014. 8:426-432.
12. Runnak MA, Hazha MA, Hemin HA, Wasan AA, Rekant RA and Michael HD. A population- based study of Kurdish breast cancer in Northern Iraq: hormone receptor and HER2 status. A comparison with Arabic women and United Stats SEER data. BMC Women's Health. 2012. 12:16.
13. Runak MA, Hassan AH, Dana Majid RA, Hassan HA, Muhealdeen DM, Mohammed HA and Hughson MD. Breast cancer in Iraq is associated with a unimodally distributed predominance of luminal type B over luminal type A surrogates from young to old age. BMC Women's Health. 2017. 17(1):27.
14. Mushhid Ghancheh, Zahra Pournamdar and Hamid Salehiniya. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pacific Journal of Cancer Prevention. 2016. 17 (cancer control in Western Asia Special issue): 43-46.
15. Alwan N. Breast cancer among Iraqi women: preliminary findings from a regional comparative breast cancer research project. J of Global Oncology. 2016. 2 (5):255-258.
16. Alwan NA, Tawfeeq FN and Mallah NA. Demographic and clinical profiles of female patients diagnosed with breast cancer in Iraq. J of Contemporary Medical Sciences. 2019. 5 (1):14-19.
17. Mubarik S, Malik S, Wang Z, Li C, Fawad M and Yu C. Recants insights into breast cancer incidence trends among four Asian countries using age-period- cohort models. Cancer Management and Research. 2019. 11: 8145-8155.