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Demographic, Clinical, and Histopathological Characteristics of Breast Cancer among Females in Karbala City

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Abstract

Background: Breast cancer is considered an important public health topic owing to its high incidence, occurrence, and death rate. It is a multi-faceted disease with both environmental and genetic causal factors. It is the first of the 10 most popular tumors triggering public concern in Iraq, compensating for 20% of all cancers and approximately 33 % of the total female cancers. This study aimed to study the demographic characteristics of female individuals identified recently as having breast cancer with the clinical features as tumor characteristics, and stage at time of diagnosis.

Methods: A descriptive cross-sectional study was accomplished in the early detection of breast cancer clinic. Seventy women recently diagnosed as having breast cancer were included in the study. Purposive sampling was done, all women attending the clinic and recently identified with breast cancer based on clinical examination, imaging findings, and confirmed by histopathological assessment were included. The data was collected for those patients including; demographical, clinical, and histopathological findings, and were statistically analyzed.

Results: The mean age of females who participated in the study was 52.2±10.5 years. A positive family member's history of carcinoma of the breast was reported in (21.4%) of patients. Most patients presented with a painless palpable mass (74.3%). Stage II breast carcinoma was the predominance stage while invasive ductal carcinoma was the most common histological type (74.3%).

Conclusions: At the time of diagnosis, a considerable majority of female breast cancer patients have locally progressed disease, with the most common complaint being a painless breast lump.

Key words: breast cancer, invasive ductal carcinoma, immunohistochemistry.

Introduction

Breast cancer (BC) has been identified as an important public health concern because of its high incidence, commonness, and fatality rate [1] and it is the most common registered malignancy among females in developed countries [2]. BC is a group of diseases that result in the creation of a swelling or mass due to atypical changes and divisions of the breast tissue cells [3]. It is a complex disease, having both environmental and genetic causes [4].

In Iraq, it ranks first among the most prevalent ten tumors causing public concern, contributing to 20% of all cancers and nearly 33% of female malignancies, with an incidence of 22% per 100,000 female population [5]. Throughout 2016, almost 900 women died due to breast cancer, making it the top leading cause of cancer-related deaths among Iraqi women (around 23%) and the second major cause among both genders (12%) after bronchogenic cancer [6]. Many breast malignancies originate from elements of the epithelium and are known as carcinomas, a complex group of lesions that vary in microscopic appearance and biological activity [3, 7]. Typically, treatment choices and prognosis of disease were determined by multiple factors including the immunohistochemistry (IHC) markers such as estrogen and progesterone receptor (ER and PR) as well as human epidermal growth receptor 2 (HER2), alongside the tumor size, grade, and lymph node involvement [8].

A large percentage of women with breast cancer are diagnosed as a result of self-discovered masses (25 %) are self-examined and eighteen percent are discovered accidentally) or symptoms and approximately forty percent are detected during mammography screening [9]. Diagnosis of breast cancer is achieved by a combination of clinical examination

and imaging, and it is long-established through histopathological examination [10]. Information on clinical and histopathological features and demographic distribution of newly diagnosed breast cancer in females, as well as the distribution of molecular subtypes, is inadequate for Kerbala individuals.

This study aims to gain a better understanding of the disease to improve prevention, diagnosis, treatment, and overall patient care, by examining the demographic characteristics of individuals recently diagnosed with breast cancer to promote the implementation of early detection strategies and preventive measures.

Materials and Methods

Patients

A descriptive cross-sectional study was accomplished in the Early Detection of Breast Cancer Clinic, Imam Al-Hussein Medical City, Karbala Province, Iraq from the 1st of September 2020 to the 30th of April 2021. Seventy women recently diagnosed with breast cancer were selected and enrolled in the study. All women attending the Early Detection of Breast Cancer Clinic and recently identified with breast cancer grounded on clinical examination, imaging findings, and confirmed by histopathological assessment were included. Patients with metastatic breast cancer, missing data, and loss of follow-up results were excluded from the study.

This study made use of an information sheet that was well constructed. It contains questionnaires for demographical records, finding of clinical examination, and measurements of anthropometric parameters (height, weight, and BMI). Data from imaging procedures (ultrasound and mammography), and histopathological tests were obtained and documented from patient's files.

A comprehensive history was taken from each patient regarding personal data, reproductive and menstrual history. History of present illness focused on symptoms like the presence of palpable lump or pain or tenderness in the breast or nipple discharge. Purposive sampling was used; all of the women included in this study underwent digital mammography and breast ultrasound. Wherever a biopsy was indicated following clinical and radiological examinations, a true-cut biopsy was performed under ultrasound guidance. The tumors were classified according to the (American Joint Committee on Cancer's Staging System for Breast Cancer, Eighth Edition) [11-12].

Ethical consideration

The study was conducted in line with the code of ethics in research of the Ministry of Health. The ethical committee of the Karbala Training and Human Development Center has approved the protocol of this study. Oral consent was obtained from all those who agreed to participate in this study.

Statistical analysis

Statistical analysis is carried out in this study using the SPSS (Statistical Package for Social Science) program, version 22, and Microsoft Excel Worksheet 2019. Categorical variables were expressed as frequencies and percentages whereas continuous variables were expressed as mean and standard deviation (M ± SD).

Results

A total of 70 females newly diagnosed with breast cancer were enrolled in this study, the age, anthropometric, and demographic data were summarized in Tables 1 and 2. The age of females who participated in this study ranged from 31 to 75 years with a mean of 52.2±10.5 and the predominant age group was 40 years and older females 59 (84.3%). The study population was categorized according to their BMI into four groups; only 27 patients (38.6 %) were within the normal BMI range which means that about two-thirds of them were either overweight or obese. Approximately a quarter of the included patients resided in rural regions, and the great majority of them (91.4%) were unemployed. Over 70 % of those newly diagnosed with BC had been married while 20% of all patients were widowed, however, just 2.9% were unmarried or separated altogether.

In Table 3, the menstrual and reproductive history of the studied group was listed, the average date of 1st menstrual period in females enrolled in the current study was 13.4±1.01year, and the regular female monthly cycle was reported in 57 (81.4%) of patients. Cessation of menstruation was documented in more than half of patients (55.7%) with a mean age of menopause was 51.1±1.3 years.

Table 1. Age and body mass index distribution of females newly diagnosed with breast cancer (n=70)

	Variables	N (%)	Mean ± SD
Age (years)	< 40	10 (14.3%)	36.2±2.5
	≥ 40	60 (85.7%)	54.9±8.8
	Total	70 (100%)	52.2±10.5
BMI (kg/m2)	< 25	27 (38.6%)	22.8±1.4
	25-29.9	29 (41.4%)	27.2±1.08
	30-35	11 (15.7%)	32.3±1.7
	>35	3 (4.3%)	37.5±2.4
	Total	70 (100%)	26.8±4.2

Table 2. Demographic characteristics of females detected with malignant breast disease (n=70)

Variables		Frequency (%)
Address	Urban	51 (72.9)
	Rural	19 (27.1)
Occupation	House Wife	64 (91.4)
	Employee	6 (8.6)
Educational Status	Illiterate	25 (35.7)
	Primary School	27 (38.6)
	Secondary School	16 (22.8)
	University	2 (2.9)
Marital status	Single	2 (2.9)
	Married	52 (74.2)
	Widowed	14 (20.0)
	Divorced	2 (2.9)

A confirmed positive history of BC in one or more family members was shown in 21.4% of patients while a positive history of cancer rather than breast was reported in 48.6% of females' relatives. A history of usage of oral contraceptive drugs was documented in patients 21.4% of patients with an average duration of consumption was 4.2±2.2 years. A small proportion of the patients 14.3% had never been pregnant while the mean number of children in mothers diagnosed with BC was 4.4±2.1 children.

Table 3. The menstrual and reproductive history of the studied group (n=70)

Variables		Frequency (%)
Onset of Menarche (years)		**70 (100%)**
Mensural cycle	Regular Irregular	57 (81.4) 13 (18.6)
Menopause (years)	Yes No	39 (55.7) 31 (44.3)
Positive History of Breast Cancer (family members)	Yes No	15 (21.4) 55 (78.6)
Positive History of any Cancer (family members)	Yes No	34 (48.6) 36 (51.4)
Use of Oral contraceptive pills "years"	Positive Negative	15 (21.4) 55 (78.6)
Child feeding	Breast feeding Bottle feeding Mixed feeding No feeding	25 (35.7) 22 (31.4) 13 (18.6) 10 (14.3)
Parity	Nulliparous Multiparous	10 (14.3) 60 (85.7)
Age at first delivery	Nulliparous Multiparous	10 (14.3) 60 (85.7)

In Table 4, the clinical presentation of the patients and tumor characteristics were registered, where the majority of patients 74.3% showed a painless palpable mass, whereas a quarter of patients 25.7% reported pain as their main symptom at the time of diagnosis. Discharging nipples was observed in 15.7% of patients, in addition; abnormal skin manifestations were seen in 7.1% of women. In the context of histopathological characteristics of cancer, the most prevalent form was invasive ductal carcinoma 74.3%, subsequently followed by invasive lobular carcinoma 14.3% and ductal carcinoma in situ 11.4%. Grade II tumor was commonly observed in 48.6% of patients and subsequently recorded in grade III in 40.0% and grade I in 11.4%. According to the tumor, half of the cases were stage II 50.0% followed by stage I in 28.57% of cases and stage III was the less existing tumor stage which was noticed in only 12.86% of cases.

Table 4. Clinical presentation and tumor Characteristics of newly diagnosed female breast (n=70)

Findings		No. (%)
Symptoms of presentation	Palpable mass Pain	52 (74.3) 18 (25.7)
Nipple discharge	Present No discharge	11(15.7) 59 (84.3)
Skin changes	Present No changes	5 (7.1) 65 (92.9)
Histopathological classification	IDC ILC DCIS	52 (74.3) 10 (14.3) 8 (11.4)
Grade of tumor	Grade I Grade II Grade III	8 (11.4) 34 (48.6) 28 (40.0)
Breast cancer stage	Stage 0 Stage I Stage II Stage III	6 (8.57) 20 (28.57) 35 (50.0) 9 (12.86)

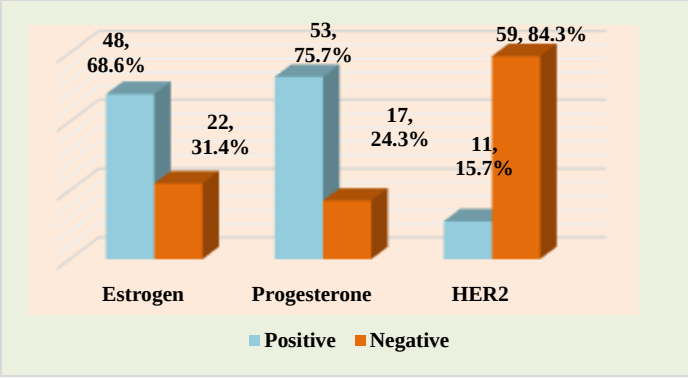

Figure 1. The proportion of tumor receptors expression (immunohistochemistry) of breast cancer women PR: progesterone receptors, ER: estrogen receptors, HER2: human epidermal growth factor receptor 2

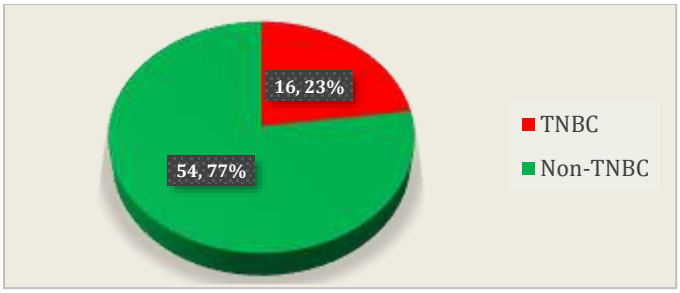

Figure 2. The proportion of Triple Negative Breast Cancer (TNBC) in newly diagnosed women participated in the study.

DCIS: ductal carcinoma in situ; IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma
The percent of the three major tumor receptors expression was illustrated in Figure 1 below, the majority of cases expressed positive both for estrogen and progesterone receptors 48 (68.6) % and 53 (75.7 %) respectively. On the other hand, 59 (84.3 %) of cases had negative HER2 receptor expression. And based on these data, less than one third16 (22.9 %) of all cases were triple-negative breast cancer. The percent of the three major tumor receptors expression was illustrated in Figure 1 below, the majority of cases expressed positive both for estrogen and progesterone receptors 48 (68.6) % and 53 (75.7 %) respectively. On the other hand, 59 (84.3 %) of cases had negative HER2 receptor expression. And based on these data, less than one-third 16 (22.9 %) of all cases were triple negative breast cancer (Figure 2).

Discussion

The current research was directed to survey the epidemiological, clinical, and pathological trends of females newly diagnosed with breast cancer registered in Kerbala Province in the Middle Euphrates Area of Iraq. The high rise in the incidence of breast cancer among women in the Eastern Mediterranean Region including Iraq is believed to be related to the presence of certain risk factors such as early menarche, late menopausal time, nulliparity, no breastfeeding, advanced female age at the time of delivery of first child, use of exogenous hormones, obesity and changes in socioeconomic characteristics [13]. In the current study, the average age at the moment of breast cancer detection was 52.2±10.5 years which is nearly identical to the findings of previous published articles accomplished in Iraq [6, 14] when their mean age was 50 and 51 years respectively. Regarding the countries bordering Iraq, the results were fairly similar, the mean age of Jordanian females with breast cancer at the time of diagnosis was 51 years [15], 48 years in the Kingdom of Saudi Arabia [16], 49.48 years in Iran [17] and 51 years in Turkey [18]. On the other hand, western countries revealed a higher average age at the date of cancer discovery; based on the American Cancer Society only 20 % of women diagnosed recently with breast cancer were younger than 50 years old [19]. This disagreement might be attributed to the Arab "and neighboring regions" having a younger age population [20]. About two-thirds of patients in the current study were either overweight or obese (BMI >25). An increasing review of studies displayed an amplified hazard of obesity on breast cancer [21-22], it's approximately (30 %) higher in women who have a BMI more than 31 (m2/Kg) in contrast to those having a BMI equal to 20 m2/Kg [23-24]. Clinically, breast cancer occurs most frequently as a breast mass; our study more than (75%) of women present as palpable breast lumps however, retraction of the skin, inversion of the nipple, variations in the size and form of the breasts, breast skin discoloration, discomfort or pain, skin redness and/or edema, and local lymph node mass are general signs of breast cancer [25-26]. In our study, invasive ductal carcinoma was the most common histological subtype, comprising (74.3%) of all cases followed by ILC, these results are consistent with previous Iraqi studies confirming IDC as the most common histological type of breast cancer [24, 27]. The degree of differentiation aids in further adjusting the treatment's effectiveness for patients along with the histological subtype. In the present study, (grade II) and (grade III) breast cancer compromised a majority of cases (48.6%) and (40%) respectively, these findings are reliable with earlier Iraqi study, in which grade II and grade III constituted (58%) and (36%) of cases correspondingly [14]. The main staging system for breast cancer used in clinical settings is the American Joint Committee on Cancer (AJCC) staging system [28]. In the current study, stage II cases represent half of all cases (50%), former Iraqi studies also revealed a similar result with stage II reported as (40.4%) [29], (45%) [14], and (47.5%) [27]. A possible explanation for this presentation is that most Iraqi women come from middle-income backgrounds, in this study most women were housewives (91.4%) and had low educational levels, only 25.8% had secondary school degree or higher education, and those with a high socio-economic status typically pursue private health facilities that we can't catch them and that was in agree with a recent study from Iraq [30]. Another point is that more than quatre 27.1% lived in rural areas with decreased facilities for screening and diagnosis so to promote care and

reduce related mortality in Iraqi women, early detection and diagnosis of breast cancer is needed. Owing to the lack of targeted therapy, triple-negative breast cancer has been associated with a high mortality rate [31] in this study the percent of TNBC was 15.7% and was consistent with others [32] when they found that 15.6% of cases have TNBC. On the other hand, hormone-positive breast cancer was shown to more predominant in this study with ER 68.8% and PR 75.7% and it is well documented that these patients have a higher survival rate than hormone-negative breast cancer, in the meantime positive receptor's BC have advantages from hormonal therapy [24].

Conclusion

at the time of breast cancer detection, a high percentage of breast cancer patients in Kerbala Province have locally advanced cancer with the most prevalent symptom being painless breast swelling. The commonest cancer stage was stage II and grade 2 at the moment of detection of cancer. We recommend making screening facilities easily accessible, particularly in underserved areas, with focusing on higher-risk populations, specifically women with a family history of the disease.

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References

1. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. Breast Cancer: Targets and Therapy. 2019;11:151.
2. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin D, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. International journal of cancer. 2019;144(8):1941-53.
3. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes & diseases. 2018;5(2):77-106.
4. Yeo SK, Guan J-L. Breast cancer: multiple subtypes within a tumor? Trends in cancer. 2017;3(11):753-60.
5. Alwan N, Tawfeeq F, Maallah M, Sattar S, Saleh W. The stage of breast cancer at the time of diagnosis: correlation with the clinicopathological findings among Iraqi patients. J Neoplasm. 2017;2(3):22.
6. Alwan NA, Tawfeeq FN, Mallah NA. Demographic and clinical profiles of female patients diagnosed with breast cancer in Iraq. Journal of Contemporary Medical Sciences. 2019;5(1):14-9.
7. Masood S. Breast cancer subtypes: morphologic and biologic characterization. Women's Health. 2016;12(1):103-19.
8. Gao JJ, Swain SM. Luminal a breast cancer and molecular assays: a review. The oncologist. 2018;23(5):556.
9. Seely J, Alhassan T. Screening for breast cancer in 2018—what should we be doing today? Current Oncology. 2018;25(Suppl 1):S115.
10. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio I, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2019;30(8):1194-220.
11. Kalli S, Semine A, Cohen S, Naber SP, Makim SS, Bahl M. American joint committee on cancer's staging system for breast cancer: what the radiologist needs to know. Radiographics. 2018;38(7):1921-33.
12. Cserni G, Chmielik E, Cserni B, Tot T. The new TNM-based staging of breast cancer. Virchows Arch. 2018;472(5):697-703.
13. Alwan NA. Breast cancer among Iraqi women: Preliminary findings from a regional comparative Breast Cancer Research Project. Journal of global oncology. 2016;2(5):255.
14. Abood RA. Breast cancer in basra oncology center: a clinico-epidemiological analysis. Asian Pacific journal of cancer prevention: APJCP. 2018;19(10):2943.
15. Abdel-Razeq H, Mansour A, Jaddan D. Breast cancer care in Jordan. JCO global oncology. 2020;6:260-8.
16. Al Diab A, Qureshi S, Al Saleh KA, Al Qahtani FH, Aleem A, Algamdi M. Review on breast cancer in the Kingdom of Saudi Arabia. Middle-East J Sci Res. 2013;14(4):532-43.
17. Nafissi N, Khayamzadeh M, Zeinali Z, Pazooki D, Hosseini M, Akbari ME. Epidemiology and histopathology of breast cancer in Iran versus other Middle Eastern countries. Middle East Journal of Cancer. 2018;9(3):243-51.
18. Özmen V, Özmen T, Doğru V. Breast Cancer in Turkey; An analysis of 20.000 patients with breast cancer. European journal of breast health. 2019;15(3):141.
19. Society AC. Breast cancer facts & figures 2019–2020. Am Cancer Soc. 2019:1-44.
20. World Health Organization. World Health Statistics 2016 (OP): Monitoring Health for the Sustainable Development Goals (SDGs). World Health Organization; 2016 Jun 8.21.
21. Argolo DF, Hudis CA, Iyengar NM. The impact of obesity on breast cancer. Current Oncology Reports. 2018;20(6):1-8.
22. Lee K, Kruper L, Dieli-Conwright CM, Mortimer JE. The impact of obesity on breast cancer diagnosis and treatment. Current oncology reports. 2019;21(5):1-6.
23. Al-Rawaq KJ, Al-Naqqash MA, Jassim MK. Molecular Classification of Iraqi Breast Cancer Patients and Its Correlation with Patients' Profile. Journal of the Faculty of Medicine Baghdad. 2016;58(3):197-201.

24. Alawadi A, Al-Naqqash M, Al-Nuaimi D. Time to Progression of Early Versus Advanced Breast Cancer in Iraq. Prensa Med Argent. 2020;106:171.
25. Al-Amri AM. Clinical presentation and causes of the delayed diagnosis of breast cancer in patients with pregnancy associated breast cancer. Journal of family & community medicine. 2015;22(2):96.
26. Zgajnar J. Clinical presentation, diagnosis and staging of breast cancer. Breast Cancer Management for Surgeons: Springer; 2018:159-76.
27. Alwan N. Tumor characteristics of female breast cancer: Pathological review of mastectomy specimens belonging to Iraqi patients. World J Breast Cancer Res 2018; 1 (1). 2018;1006.
28. Keung EZ, Gershenwald JE. The eighth edition American Joint Committee on Cancer (AJCC) melanoma staging system: implications for melanoma treatment and care. Expert review of anticancer therapy. 2018;18(8):775-84.
29. Mohammed NH, Al-Taie A, Al-Sultany FH. Assessment of Predictive Confounders for the Prevalence of Breast Cancer among Iraqi Population: A Retrospective Study from Baghdad, Iraq. International Journal of Pharmacological and Pharmaceutical Sciences. 2019;13(4):145-9.
30. Abedalrahman SK, Ali BM, Al-Khalidy NAI, Al-Hashimi AS. Risk factors of breast cancer among Iraqi women. Journal of Contemporary Medical Sciences. 2019;5(3).
31. Bianchini G, Balko JM, Mayer IA, Sanders ME, Gianni L. Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. Nature reviews Clinical oncology. 2016;13(11):674.
32. Mutar MT, Goyani MS, Had AM, Mahmood AS. Pattern of presentation of patients with breast cancer in Iraq in 2018: A cross-sectional study. Journal of global oncology. 2019;5:1-6.