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Breast cancer histology and hormonal status characterization in Libyan patients; a sample from middle region

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Abstract

Background: Breast cancer, has increased in developed and developing countries among females, and in Libya, often diagnosed at advanced stage. This study conducted to evaluate histological features and hormonal status of breast carcinoma in Libyan females.

Materials and Methods: This retrospective study was performed at Sirte Oncology Centre, Sirte, Libya. Demographic characteristics, such as age, sex, marital status recorded. Histopathology examination provided the histologic type, grade, tumor size, stage, lymph node status, site of metastasis and hormonal status. Data were obtained and analyzed using SPSS software version18.0.

Results: A total of 74 breast cancer patients of which 72 (97.3%) were females and 2 (2.7%) were males. Majority of the cases occurred in the 5th decades. Invasive ductal carcinoma of no specific type was the most commonly diagnosed type of breast carcinoma accounting 95.9% of total cases, invasive lobular, ductal and lobular carcinoma and malignant phylloides were the second most common types. Majority of cases (57.4%) diagnosed with grade III tumors and 60 % of cases were found at advanced invasive and metastatic stage of breast cancer. Most of cases showed positive hormonal receptors (both ER and PR positive) (67.2%) while triple negative (ER, PR, and Her2Neu negative) cases were found to be the rarest group (1.6%).

Conclusion: Invasive ductal carcinoma was the most common histological type of breast cancer in Libyan patients, commonly diagnosed with a higher grade and at advanced stage. As hormonal status carries a hope of benefit from hormonal treatment, so our study places the significance of early detection, histo-pathological informations and hormonal status in an appropriate treatment strategy.

Key words: Breast carcinoma; invasive ductal carcinoma; hormonal status; Libya.

Introduction:

Breast cancer is the commonest cancer in female worldwide [1], and accounting 20% of total cancers among Libyan females [2, 3, 4, 5, 6, & 7]. There are many risk factors of breast cancer including patient aging, female gender, genetic mutations and presence of family history of breast cancer at a young age, menstrual history either early menarche or late menopause, older age at first live childbirth, prolonged hormone replacement therapy and history of exposure to therapeutic chest wall irradiation. In addition to presence benign proliferative breast disease and increased the mammographic densities. The commonest proliferative pathological abnormalities of the breast are limited to the ductal and lobular epithelium [8]. The incidence of breast cancer has been rising up in low- and middle-income countries in the

last few years, and the majority of women diagnosed in advanced stage for many reasons, including lack of awareness on early detection and barriers to health services [9 and 10]. In Libya, the diagnosis delay is a major problem lead to advanced stages of cancer and potentially a high mortality, many social, medical and other patient –related factors play role in this delay [11]. According to WHO, the hope for a reduction of mortality in breast cancer is screening and early detection with adequate, efficient treatment of the breast cancer cases [9 & 10]**.** We aim in this study to review and highlight the main demographic characteristics and clinic-pathological features of 74 Libyan patients diagnosed as having breast cancer and trying to conclude the important points for health strategies to reduce risk of increased breast cancer among Libyans.

Patients and Methods:

Data for this study were retrieved from the center-based breast cancer registries. A total of 74 cases diagnosed as breast carcinoma based on histopathological examination from the year 2013 to 2020, by qualified pathologist. The medical records were retrieved and studied retrospectively with regards to variables of interest included age at diagnosis, sex, marital status, AJCC stage, histologic grade, nodal status, site of metastasis & tumor markers (estrogen receptor (ER), progesterone receptor (PR), and Her-2/neustatus). Demographic data at the time of presentation and histopathological details were analyzed. Data routinely recorded on the patient's file sheet by the examining physician at the center included demographic data while data on tumor characteristics and nodal status were obtained by a surgical pathology examination of the tissue. Abdominal ultrasound and chest X-rays, CT chest and abdomen and bone scan were carried out to exclude metastases. All cases were confirmed histopathologically on the excised tumours and the type of carcinoma was determined based on the WHO classification and histopathological grading of the tumor was based on Scarff Bloom Richardson's (SBR) grading system while the TNM staging system (tumor, node, and distant deposits) of the American Joint Committee on Cancer (AJCC) was employed in recording the clinical stage of the disease [12]. Cases without confirmed histopathology diagnosis were completely excluded.

Statistical Methods:

All categorical variables were analyzed on a personal computer running SPSS for windows (Statistical Package for Social Sciences) Release 18, where descriptive statistics of qualitative variables, the frequency distribution procedure was run with calculation of both the number of cases and percentages and for descriptive statistics of quantitative variables, the mean, median and range were used to describe central tendency and dispersion.

Results:

A total number of 74 cases (n = 74) of breast cancers of which 72(97.3%) were females and 2 (2.7%) were males, suitably registered in the records with some clinical information and diagnosis, that was histologically confirmed. The age of the patients ranged between 27 and 76 years (mean = 47.72 years) and the median age of presentation was 46.50 years of age. Majority of the cases occurred in the 5th decades (40–50 years) (Fig. 1) & most of the patients (82.4%) were married while single and divorced and widow comprising only 9.5% and 4.1% respectively. The common histological variant of breast cancer (BC) recorded was infiltrating ductal carcinoma (IDC, not otherwise specified (NOS)) comprising of 95.9% of cases followed by other less common types,

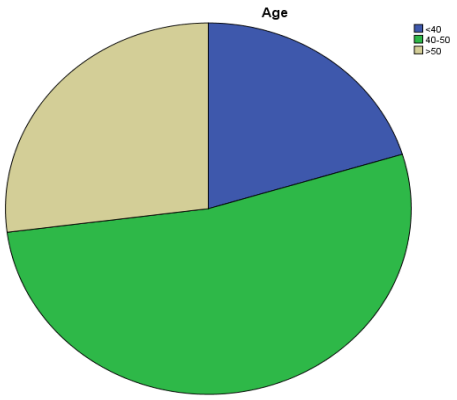

Figure 1. Patients' age distribution

these were invasive lobular, ductal and lobular carcinoma and malignant phylloides (1.4% each) [Table 1]. Forty - seven patients had information regarding tumor grade at diagnosis, one case (2.1%) showed Grade I of Nottingham modification of Bloom Richardson System, nineteen cases (40.4%) showed Grade II, while twenty - seven cases (57.4%) showed Grade III, respectively [Table 1]. Information regarding the pathological T stage was available in 65 patients, the most common pathological T stage was T2 (47.7%) followed by T4 (30.8%), T3 (18.5%), and T1 (3.1%) and data regarding nodal stage of the tumour were available for fifty patients, the most common pathological nodal stage was N0 (44%) followed by N1 (34%), N2 (16%) and N3 (6%), [Table 1].

Table1. Tumor clinico-pathological characteristics of patients with breast cancer:

Variables	Cases	%
Histopathology (n=74) *		
IDC	71	95.9
ILC	1	1.4
Mixed (IDC/ILC)	1	1.4
Malignant phylloides	1	1.4
Tumor grading (n=47) *		
I	1	2.1
II	19	40.4
III	27	57.4
Primary Tumor Size (n=65) *		
T1	2	3.1
T2	31	47.7
T3	12	18.5
T4	20	30.8
No. of nodes positive (n=50) *		
0	22	44
1-3	17	34
4-9	8	16
>9	3	6
Tumor biomarkers (n= 64) *		
ER positive	4	6.3
Her2 positive	3	4.7
ER & Her2 positive	2	3.1
PR, ER & Her2 positive	11	17.2
ER & PR positive & Her2 negative	43	67.2
PR, ER & Her2 negative	1	1.6

*** valid cases**

Based on the staging criteria described in [Table 2], data regarding pathological staging was available in fifty-five out of 74 Libyan patients with breast cancer, only twenty - two cases (40 %) were diagnosed in early stages of invasive cancer (stages 1 and 2), and the remaining 33 cases (60 %) were classified as advanced invasive and metastatic stage of breast cancer in 14 and 19 cases, respectively, the sites of distant metastasis included lung, liver, lymph node and bone. Pathological tumor, node, and metastasis (TNM) staging showed most common group was anyTanyNM1 (34.5%) followed by pT2N0M0 (23.6%) [Table 2]. Information regarding the evaluation of the immunohistochemical markers—ER, PR, and Her2neu was available in 64 cases, where both ER and PR positive and Her2Neu negative were found to be the commonest group comprising 67.2% (43/64) of all the cases followed by triple positive (ER, PR, and Her2Neu positive); 17,2% (11/64). Triple negative (ER, PR, and Her2Neu negative) were found to be the rarest group comprising 1.6% (1/64) of all the cases [Table 1].

Table 2: TNM staging among the breast cancer patients:

Stage (n=55)*	Cases	%
Stage 1 T1N0M0	 2	 3.6
Stage 2A T0N1M0 T1N1M0 T2N0M0	 - - 13	 - - 23.6
Stage 2B T2N1M0 T3N0M0	 5 2	 9.1 3.6
Stage 3A T2N2M0 T3N1M0 T3N2M0	 4 4 1	 7.3 7.3 1.8
Stage 3B T4 any NM0 Any T N3M0	 4 1	 7.3 1.8
Stage 4 Any T any N M1	 19	 34.5

*** valid cases**

Discussion:

The present study showed that the incidence of breast cancer is high in females and rarely detected in males, this result does not differ significantly from other study that found 1.6% incidence of male breast cancer [13] & inconsistent with study reported 50.1% of male patients diagnosed with breast cancer in western Libya [7]. The occurrence of breast cancer in our study is strongly associated with young age with nearly 73% of cases arising in individuals who are 50 years or younger, in concordance with other reported study [14]. The mean age of disease get diagnosed was about 47.72, is similar to other studies [14, 15, 16]. In the recent study invasive ductal carcinoma NST is the commonest histological type of breast carcinoma accounting 95.9% of the total cases, in concordance with other reports [16, 17, 18, 19, 20 & 21] and also consistent with other study showed that, the commonest histological types of the breast cancer cases in Libya, Nigeria and Finland, was non-specific variety of invasive ductal carcinoma [14]. The current study reported three-second common cancers, in contrast to others, only lobular carcinoma was found to be second most frequent type of breast cancer [14, 16, 18 & 22]. Histological grading was based on Nottingham modification of the Scarff Bloom and Richardson's grading system.

The extent of tubular formation, nuclear size and pleomorphism, and mitotic activity are the parameters measured. Each of the three elements was assigned with a score 1 to 3 and the final grade is obtained by the summation of each individual scores resulting in a total score between 3 and 9 which indicate the degree of differentiation, well differentiated (grade I) scores 3 to 5, moderately differentiated (grade II) scores 6 to 7 and poorly differentiated (grade III) scores 8 to 9 [23]. In current study, the majority of tumors were poorly differentiated grade III accounting 27 (57.4 %) of total cases followed by 19 (40.4%) tumors with moderately differentiated grade II and one (2.1%) tumor with well differentiated grade I, the higher tumor grade percentage (grade III) was higher than other reports, where they show that, grade II tumors were the most frequent tumor comprising 62.3% of total tumors observed [14] & Zeeneldin et al observed grade II tumors were most frequent comprising 76.6% of total tumors [17]. According to the AJCC TNM staging criteria, the majority (47.7%) of tumors belonging to T2 (more than 2.0 to 5.0 cm) stage, followed by T4 (30.8%) (tumor growing to chest wall or skin), T3(18.5%), (more than 5 cm), and T1 (3.1%). (up to 2 cm). A study observed that, the majority of (44.1%) cases with T2 stage that correlate with our results [8]. Interestingly, another performed study showed over 90% of breast cancer patients are diagnosed at stage II or later [15]. Similarly, other studies also observed highest frequency of tumors with T2 stage [24, 25 & 26]. In this study highest frequency of tumors belonged to N0, N1 & N2 stages respectively that explained as no cancer was found in the lymph nodes or only areas of cancer smaller than 0.2 mm are in the lymph nodes, involving 1 to 3 nodes, and involving 4-9 nodes respectively (no available data regarding each N stage) this consistent with other studies have shown N0

stage as the most common stage followed by N1, N2 respectively [18, 19, 26 & 27].
Our study showed that, 33 cases (60 %) were classified as advanced invasive and metastatic stage of breast cancer. In contrast to other study reported that, the majority of cases (48.5%) diagnosed at earlier stages of cancer (stage I and II). However, the large percentage of patients in advanced stages indicates delayed presentation and late diagnosis in developing countries, and lack of screening mammogram, especially the majority of cases is young age [16]. A study stated that, the main factor in planning of breast cancer treatment is hormone receptor status, where cancers with both ER and PR negative have poorer prognosis than with either ER or PR positive, in addition, ER+, PR+, HER2- tumors have the best prognosis and more likely to response to hormone therapy while ER- PR- HER2+ and ER- PR- HER2- tumors are poorly differentiated, and have poor prognosis, and are least likely to respond to hormone therapy [28]. In the current study, the evaluation of the immunohistochemical markers—ER, PR, and Her2neu was done in 64 cases and the majority have a good prognosis as predicting to response to hormonal therapy, where both ER and PR positive and Her2Neu negative were found to be the commonest group (67.2%) & Triple negative (ER, PR, and Her2Neu negative) were found to be the rarest group comprising 1.6%, this is in concordance with study [29] reported cases with $HR^+/HER2^-$ type (48.5%) as the commonest, and cases with $HR^-/HER2^-$ type (triple-negative [TN]) (15.5%) as rarest one, and inconsistent with study were found Triple negative (ER, PR, and Her2Neu negative) to be the commonest group comprising 39.4% followed by ER and PR both positive (34.50%) and the triple positive (ER, PR, and Her2neu positive; 26.06%.) was the rarest group [30].
Interestingly, other study conducted by Kakarala *et al.*, where observed that incidence of ER, PR negative breast cancer were increased in India and Pakistan [26].
It should be considered that, this study has limitations; small sample size and incomplete data for some variables, as data collected during early establishment of the centre, however, the findings of this study added to present knowledge about histology and hormonal status characterization of breast cancer in middle region of Libya.

Conclusion:

The current study has provided the information about the histo-pathological features of breast cancer cases in middle region and showed that, the invasive ductal carcinoma (NST) is the most common histological type of breast cancer, diagnosed with a higher grade and presenting at advanced stage.
Taking preventive diagnostic measures as basic education and awareness of the women's health, self-breast examination, and clinical breast examination and screening programs are important to identify breast cancer cases at early stages, in addition to emphasizing on prognostic significance of breast biomarkers as hormonal receptors and Herceptin in all breast cancer cases. Since the study was conducted when the centre is just established, further study in the same setting using a larger sample is recommended.

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