Clinicopathological Characteristics of Breast Cancer: A local Institutional Experience

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Abstract:

Background and aim of the work: Breast cancer (BC) is the most prevalent type of cancer among Egyptian women. This study was undertaken to evaluate the clinic-pathological profile of BC patients at South Egypt Cancer Institution (SECI), a tertiary-care cancer center at Upper Egypt.

Methods: This one year prospective study included all BC patients registered at our institution from the first of February 2022 up to the end of January 2023. All studied participants were subjected to detailed data collection about demographic, clinical, pathological characteristics, and treatment details.

Results: We included 75 adult females with newly diagnosed non-metastatic BC, with a mean age of 47.05±11.94 years (range; 25- 74 years). The majority of the studied cases (76%) underwent modified radical mastectomy (MRM). Infiltrating ductal carcinoma (92.0%) was the most common histopathological subtype. 69.3% and 30.7% had tumor grade 2 and 3 respectively. Patients had relatively large tumors at presentation (> 2 cm in 84% of patients). Positive nodal metastasis was documented in 82.7% patients. As regard to biological sub types; luminal A, luminal B (HER2-positive), luminal B (HER2-negative), HER2 amplified and triple negative breast cancer was found in 33.3%, 25.3%, 16%, 12% and 13.3% respectively. 52.0% positive for lymphovascular invasion, and 62.7% positive for perineural invasion. The TNM (AJCC-7th edition) stage distribution was stage I (4.0%), stage II (49.3%), and stage III, (46.7%). During the study period 11 cases (14.7%) show disease progression and one case (1.3%) died.

Conclusion: This is a comprehensive data from a single tertiary-care cancer center in Egypt. Thus, dominance of young age and positive nodal metastasis at diagnosis represented the two main features of BC among studied Egyptian women. There is a great need for ongoing public health education programs to enhance awareness about cancer and encourage for national BC screening program.

Keywords: Breast cancer, metastasis, clinic-pathological characteristics.

Introduction:

In 2022, there were 2.3 million women diagnosed with breast cancer and 670,000 deaths globally. Moreover, it is the primary cause of cancer-related mortality among females, accounting for about 680,000 deaths [1].

Despite the disparity in incidence rates between industrialized and developing nations [1], BC is still the most frequent form of female cancer in Egypt, with an age-specific incidence rate of 48.8/105. Approximately 46,000 incident cases are forecasted in 2050 [2]. The World Health Organization statistics have alarmingly

revealed the high incidence of breast cancer among Egyptian Women, which constitutes 35% of all women cancer cases.

The clinical and pathologic characteristics of breast cancer vary. The choice of therapy and the patient's prognosis are influenced by various factors, including age, tumor size, involvement of axillary nodes, histologic grade, hormone receptor status, and human epidermal growth factor receptor 2 (HER2)/neu amplification [3]. Thus, the main aim of the current study is to document the clinic-pathological characteristics of breast cancer at our institution.

Patients and Methods:

Patients:

The present study was a one year prospective cohort study included 75 adult females with newly diagnosed non-metastatic BC patients who attended to the Medical Oncology Department, South Egypt Cancer Institute, Assiut University, Egypt in the period from February 1st, 2022 and January 31st, 2023. The study was approved by the institutional Review Board (IRB no: 584). An informed written consent was obtained from all studied cases before enrolment in the present study.

The data regarding demographics, complete clinical characteristics, pathological characteristics, stage determination, and complete pathologic response were obtained from our medical records. Male patients, pregnant or lactating women, patients with other malignant cancers, mentally diseased patients who cannot cooperate well in the current study, and those refused to participate in the present study were excluded.

Laboratory investigations including (complete blood count (CBC), liver and renal function tests, and calcium level) were also done for all cases. Base line investigations for stage I are CXR, abdominal US and Bilateral breast sonomammogram, Breast MRI (optional) with special consideration for mammographically occult tumors, and consider additional imaging studies only in the presence of signs and symptoms of metastatic disease.

Base line investigations for stage II & III are Bilateral breast sonomammogram, MSCT chest & Pelvi-Abdomen and bone scan, and also in follow up.

All patients were followed for at least one year to determine disease progression or metastasis.

End points of the study

The primary endpoint of the current study was to determine the clinic-pathological characteristics of BC at our institution. Secondary end point was the patient's outcome (overall survival (OS), and disease free survival (DFS)).

Statistical analysis:

SPSS (statistical package for the social sciences; SPSS Inc., Chicago, IL, USA) version 22 was used for all statistics. When applicable, percentages (number of instances) and frequency distributions (percentages) were used to statistically describe the data along with means, standard deviations (SD) and median (range) for quantitative data. Kaplan-Meier's method with log rank test was used for disease free survival analysis. P-value set significant at 0.05 level.

Results:

Demographic Data of the studied breast cancer cases:

Study of demographics of our patients revealed that the mean age of the studied cases was 47.05±11.94 years with an age range from 25-74 years. Most patients 90.7% were married, 6.7% were singles and only 2.7% were widows. More than half (61.3%) were urban residence. Regarding Menopausal status, 52% of cases were postmenopausal while 48% were premenopausal. Positive family history of breast cancer was documented in 36% of studied cases; 17% first degree, and 19.0% second degree (Table 1).

Table (1) Demographic data of the studied BC cohort

Variable name	N=75	
Age (years)		
• Mean ± SD	47.05 ± 11.94	
• Median (range)	46 (25 – 74)	
Marital status		
• Single	5	(6.7)
• Married	68	(90.7)
• Widow	2	(2.7)
Residence		
• Rural	29	(38.7)
• Urban	46	(61.3)
Menopausal status		
• Premenopausal	36	(48.0)
• Postmenopausal	39	(52.0)
Family history		
• Negative	48	(64.0)
• Positive	27	(36.0)

Tumor Characteristics

Table 2 lists tumor characteristics of the studied cases and pathological details. The incidence of left breast cancer was slightly more than the right side (56% VS 42.7%), the most common site for both was the upper outer quadrant (41.3%). About 24% of patients underwent BCS and 76% of patients underwent MRM. The pathological type IDC was about nine folds of infiltrating lobular carcinoma (ILC) (92 % vs. 8%). Majority of cases (69.3%) had tumor grade 2 while 30.7% had tumor grade 3.

Patients had relatively large tumors at presentation (more than 2 cm in 84% of patients). Node negative was in 17.3% of the patients whereas node positive was in 82.7% of the patients.

As regard to biological sub types; luminal A, luminal B(HER2-positive), luminal B(HER2-negative), HER2 amplified and triple negative breast cancer was found in 33.3%, 25.3%, 16%, 12% and 13.3% respectively.

About half of patients (52%) were positive for lymphovascular invasion, and more than half (62.7%) had positive perineural invasion. Regarding to tumor stag; 49.3% were stage II, 46.7% were stage III and only 4% of patients were stage I.

Lines of treatment

Table (3) states data about lines of treatment of the studied cases. Seventy patients in our study received chemotherapy. Regarding type of chemotherapy; 58.6% of patients received AC/Taxanes and 35.7% of patients received AC/Taxanes and herceptin while 5.7% of patients received FEC. Fifty-six patients received endocrine therapy, 55.4% of them were treated with letrozole, while 44.6% of them received tamoxifen. In our study, sixty – seven patients (89.3%) received radiotherapy and only eight cases (10.7%) not received radiotherapy.

Disease free survival among the studied non-metastatic BC cases:

Table 4 shows that; at 12 months follow-up; tumor size, nodal metastasis, progesterone receptors, and HER2-neu receptors were shown to affect the disease free survival among the studied participants.

- Tumor size; at 12 months of follow-up, disease free was 100.0% in patients with tumor size <2 cm, 91.6% in patients with tumor size 2-5 cm and 70.7% in patients with tumor size > 5 cm (P= 0.003).
- Nodal metastasis; at 12 months of follow-up, disease free was 100.0% in patients with no nodal metastasis, 85.3% in patients with N1, 95.5% in patients with N2 and 45.5% in patients with N3 (P= 0.005).
- Progesterone receptors; at 12 months of follow-up, disease free was 75.8% in patients with negative PR, and 97.8% in patients with positive PR (P<0.001).
- HER2-neu receptors; at 12 months of follow-up, disease free was 93.1% in patients with negative HER2-neu receptors, and 82.1% in patients with positive HER2-neu receptors (P=0.044).

Discussion:

Breast cancer (BC) is one of the most prevalent cancers and a significant health concern among Egyptian women [4]. The disease is still the most frequent type of cancer among Egyptian women, with an age-specific incidence rate of 48.8/105, and approximately 46,000 incident cases are expected in 2050 [2].

The current study was aimed to study the clinic-pathological characteristics of breast cancer at our institution which might provide meaningful details about the demographics, disease's histology, stage, and as well as the type of BC surgery. The study included 75 adult female patients with a mean age of 47.05±11.94 years (range; 25-74 years).

Two main interesting findings in the current study is that; first, the Egyptian BC patients was significantly younger that the Western counterparts with a mean age of 47.1 years and 48% being premenopausal at diagnosis. This finding was supported by the recent Egyptian meta-analysis of Azim et al. (2023) who revealed that the mean age of the studied participants was 50.4 years and 57% were premenopausal/perimenopausal at diagnosis.

Of note, in the US-based SEER data [5] and the Japanese Breast Cancer Society registry [6], the median age at diagnosis was 63 years and 59.7 years, respectively. This age pattern in Egypt could be explained by the population pyramid distribution, with only a minority of the female population (8%-9%) older than 60 years [4]. By contrast, a similar age pattern is seen in other developing countries, such as China, where mean age at presentation is 53 years [7].

Positive family history of breast cancer was documented in 36% of studied cases. This is not a surprising result as it is well known that family history is one of the most well-known factors that have a major impact on breast cancer risk, with an odds ratio of 1.71 (95% CI 1.59–1.84) [8]. Another study using a large patient cohort showed that women with two or more relatives having a history of breast cancer have a 2.5-fold (95% CI 1.83–3.47) increased risk of developing breast cancer [9]. Based on the available data, it is recommended that a family history of breast cancer be considered as a critical screening factor in the prevention of breast cancer.

Furthermore, there was a low rate of BCS utilization in our study, representing only 24% of total BC cases. This rate for BCS was higher than that reported by Azim et al. (2023) who observed that only 15% of the included BC patients undergo BCS; however, a clear trend to increased BCS rates and decreased MRM rates were observed over time. Of note, in the Korean study, 67.4% were treated with BCS among 22,395 invasive cancer cases diagnosed in 2017 [10].

Patey's mastectomy is the most commonly performed surgical treatment at the South Egypt Cancer Institute in Egypt. The limited adoption of conservative surgery for the treatment of early breast cancer cases could be explained by clinicians' lack of confidence in their patients' compliance with specified radiation regimens and regular follow-up. Other reasons for the desire of mastectomy include the fear and inconvenience of radiotherapy, as well as the the belief that survival may be reduced if mastectomy is not performed [11).

However, according to new practice guidelines, women with early stage invasive BC who are suitable for BCS should be given the option of BCS or a MRM. As a result, each patient must make their own decision, and all patients should be thoroughly informed of their alternatives, including the risks and advantages of each surgery. Women should be advised that breast irradiation is an element of BCS. Furthermore, women must be advised that if the excision margins are positive, they may require further surgery [12).

Table (2) Tumor characteristics among the studied BC cases (n=75)

Tumor characteristics		N	(%)
Tumor location	Upper outer quadrant	31	(41.3)
	Lower outer quadrant	19	(25.3)
	Upper inner quadrant	12	(16.0)
	Lower inner quadrant	12	(16.0)
	Retro areolar	1	(1.3)
Laterality	Right	32	(42.7)
	Left	42	(56.0)
	Bilateral	1	(1.3)
Type of surgery	MRM	57	(76.0)
	BCS	18	(24.0)
Type of pathology	IDC	69	(92.0)
	ILC	6	(8.0)
Histo-pathological grade	Grade 2	52	(69.3)
	Grade 3	23	(30.7)
Tumor size (cm)	< 2 cm	12	(16.0)
	2-5 cm	49	(65.3)
	> 5 cm	14	(18.7)
Stage (N)	Negative (N0)	13	(17.3)
	Positive (N1-N3)	62	(82.7)
	▪ N1	29	(38.7)
	▪ N2	22	(29.3)
	▪ N3	11	(14.7)
Stage (M)	M0	75	(100.0)
ER	Positive	55	(73.3)
	Negative	20	(26.7)
PR	Positive	45	(60.0)
	Negative	30	(40.0)
HER_2NEU	Positive	28	(37.3)
	Negative	47	(62.7)
Ki67	Median (range)	20 (2 – 80)	
Biological type	Luminal A	25	(33.3)
	Luminal B (HER2-positive)	19	(25.3)
	Luminal B (HER2-negative)	12	(16.0)
	HER2-positive	9	(12.0)
	Triple Negative Disease	10	(13.3)
LVI	Yes	39	(52.0)
	No	36	(48.0)
Perineural invasion	Yes	28	(37.3)
	No	47	(62.7)
Clinical staging	I	3	(4.0)
	II	37	(49.3)
	III	35	(46.7)

Data are presented as median (range), or number (percentage).
AR, Androgen receptor; ER, Estrogen receptor, PR, Progesterone receptor, LVI, lymphovascular invasion. HER2 was considered positive in cases with IHC score 3 + or gene amplification detected by FISH or SISH.

Table (3): Lines of treatment received by the studied Breast Cancer cases (n=75):

Lines of treatment		N	(%)
Type of CTH (n=70)	FEC	4	(5.7)
	AC & Taxol	41	(58.6)
	AC & Taxol & H	25	(35.7)
Type of hormonal treatment (n=56)	TAM	25	(44.6)
	Femara	31	(55.4)
Radiotherapy (n=67)	Yes	67	(89.3)
	No	8	(10.7)

Qualitative data are presented as number (percentage).

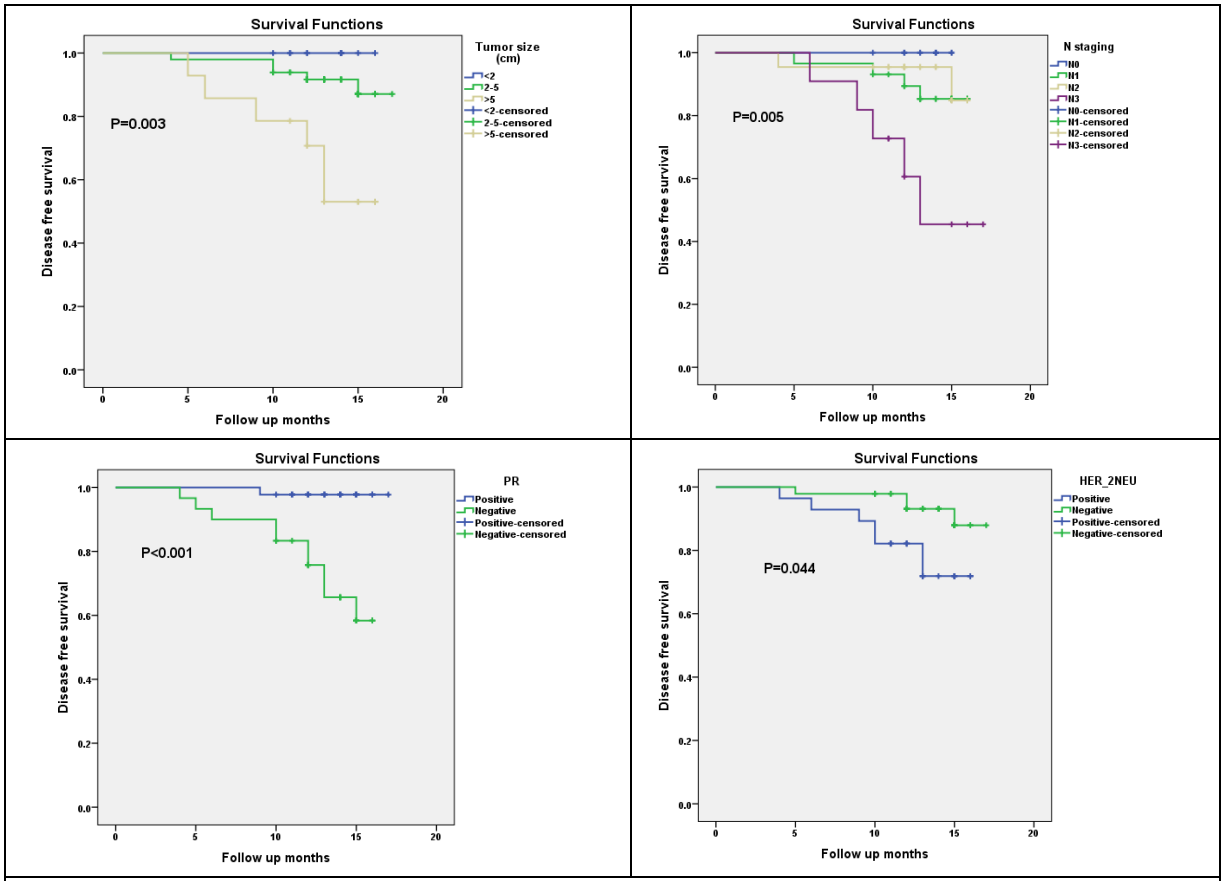

Figure 1 Disease free survival curves according to the clinic-pathological details of the studied BC cases.

Table (4) Disease free survival according to the clinic-pathological details of the studied BC cases

	DFS (one year)	
	Estimate ± SE	**P value**
Age		0.059
• < 45	73.4 ± 8.3%	
• ≥ 45	95.0 ± 3.4%	
Tumor size (cm)		**0.003**
• < 2 cm	100.0 ± 0.0%	
• 2-5 cm	91.6 ± 4.0%	
• > 5 cm	70.7 ± 12.4%	
N staging		**0.005**
• N0	100.0 ± 0.0%	
• N1	85.3 ± 6.8%	
• N2	95.5 ± 4.4%	
• N3	60.6 ± 15.7%	
Estrogen receptors		0.107
• Negative	78.9 ± 9.4%	
• Positive	92.5 ± 3.6%	
Progesterone receptors		**<0.001**
• Negative	75.8 ± 8.0%	
• Positive	97.8 ± 2.2%	
HER2-neu receptors		**0.044**
• Negative	93.1 ± 3.9%	
• Positive	82.1 ± 7.2%	
Ki67		0.452
• Low (0 – 15%)	92.5 ± 5.1%	
• Intermediate (16 – 30%)	85.2 ± 6.8%	
• High (>30%)	88.0 ± 8.1%	
Biological subtypes		0.143
• Luminal A	91.4 ± 5.8%	
• Luminal B (HER2-positive)	89.5 ± 7.0%	
• Luminal B (HER2-negative)	100.0 ± 0.0%	
• HER2-positive	66.7 ± 15.7%	
• Triple Negative Disease	87.5 ± 11.7%	
LVI		0.512
• Yes	89.5 ± 5.0%	
• No	88.4 ± 5.5%	
Perineural invasion		0.485
• Yes	89.3 ± 5.8%	
• No	88.8 ± 4.7%	
Clinical stages		0.699
• Stage 1	100.0 ± 0.0%	
• Stage 2	85.8 ± 5.9%	
• Stage 3	91.4 ± 4.7%	
Family history		0.989
• Negative	87.1 ± 4.9%	
• Positive	92.6 ± 5.0%	

Significance defined by $p < 0.05$.

The histological type was mainly invasive ductal carcinoma (IDC) in 92.0%, and invasive lobular carcinoma (ILC) in six cases (8.0%). Similar to that found in other series [3, 13-15].

The second striking finding in our study is that Egyptian patients were more frequently presented with advanced stages (stage III disease: 46.7%, stages T2: 65.3%, T3: 18.7%, and positive nodal metastasis: 82.7%). The fact that no case had stage I at first diagnosis suggests that our society's women are not receiving adequate health education about the risk of developing BC. Women who have first-degree relatives with BC should be adequately informed about the necessity of breast self-examination (BSE) and routine annual mammography beginning at the age of ≤ 35 years. It is widely recognized that a patient's chances of disease recurrence and mortality depend on the number of cancer-positive regional lymph nodes at the time of diagnosis [11]. Thus, despite advancements in therapy, a worse rate of survival is a result of this increased occurrence of advanced stages. This emphasizes the value of early detection as a strategy to improve the prognosis of disease in Egypt.

Of note, in the California Cancer Registry [16] and the Chinese population [7], the incidence of stages III was 13% and stage IV was 20%. However, younger patients were also presented with more advanced stages in a recent (2022) SEER report [17].

In our cohort 73.3%, 60.0%, and 13.3% patients had ER/PR positive BC, and TNBC respectively, that is similar to the recent Egyptian meta-analysis [4]. The Indian study of Gogia et al. revealed an increase in prevalence of TNBC (28%) [3], another Indian study revealed that 23% of the studied cohort had TNBC [18].

Moreover, our study had pointed to another factor that may contribute to the poorer prognosis in the Egyptian population, which is the higher prevalence of more aggressive biological subtypes. This was evident for the HER2+ subtype, where it represented 37.3% of BC in Egyptian females, compared with 14% in SEER reports [19, 20].

Furthermore, it is well known that lymphovascular invasion (LVI) and, to a much lesser extent, perineural invasion are one of the biologic prerequisites of systemic spread and metastases [21]. In our studied cohort; 52.0% and 37.3% suffered from LVI, and PNI, respectively.

Survival analysis was also conducted to investigate the independent factors that could affect patient's outcome and we observed that at 12 months follow-up; tumor size, nodal metastasis, progesterone receptors, and HER2-neu receptors were shown to affect the disease free survival among the studied participants. In addition, younger aged patients had poorer outcome compared to those aged ≥45 years, with borderline significance (P=0.059).

In line with the current finding, several studies have shown that younger patients with BC carry poorer prognosis. A study by Azim et al found that patients with BC <40 years had poorer relapse-free survival even after adjustment for BC subtype, tumor size, nodal status, histologic grade, and treatment modality (hazard ratio (HR)=1.34; 95% CI=1.10-1.63; P=0.004) [22]. This highlights age as an independent predictor of biological aggressiveness, which may contribute (along with advanced stage) to the poor outcome observed in Egyptian patients with BC.

In 2014, Alieldin et al. study revealed similar finding as author reported that the recurrence rates were significantly higher among young women 44.2% compared to 34.5% in older women. Five year DFS in young women was 38.9% compared to 48.6% but not reach statistical significant result (P=0.19) as observed in the current study. Thus, author concluded that young age was not found to be an adverse independent prognostic factor for DFS, however, positive axillary lymph nodes (pN2-pN3), larger tumor size (pT3-pT4), hypertension, lobular carcinoma type and lack of adjuvant systemic treatment as independent factors associated with poor DFS [23], which is similar to that founded in the current study.

Conclusion:

Our study showed that the main challenges facing breast cancer care in Egypt are younger age, and the late stage at first presentation, which ultimately lead to reduced effectiveness of therapy and higher mortality rates. Lack of health awareness in Egyptian women about the early warning signs of BC and the importance of early consultation are the most important reasons for this. Thus, we recommend for adapting ongoing public health education programs to enhance awareness about BC and encourage them for participating in the current national BC screening program.

Competing interests:

The authors declare that they have no competing interests.

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Ethics approval and consent to participate:

The protocol was approved by the Institutional Review Board of South Egypt Cancer Institute, Assiut University (approval number: 584, 21 March 2022 date of approval).

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