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A Comprehensive Study of Invasive Breast Cancer in Egyptians: Histological Subtypes and Prognostic Indicators

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ABSTRACT

Background: Breast cancer (BC) is the most commonly diagnosed malignancy among women globally and in Egypt, representing 25.4% of new female cancer cases in 2018.

Aim: This study aimed to assess clinicopathological features of invasive BC in Egyptian women and identify key prognostic indicators.

Materials and methods: A retrospective analysis was conducted on 373 cases of histologically confirmed invasive BC retrieved from archives of Pathology Department, Faculty of Medicine, Benha University, between March 2019 and July 2024. Ethical approval was obtained, and data were anonymized.

Results: Patients showed that 50.7% were over 50 years old. Invasive carcinoma of no special type was the predominant histologic subtype (78.8%). Most tumors were grade II (62.7%), with pT2 and pN1 stages reported in 46.1% and 35.4% of cases, respectively. Luminal A was the most frequent molecular subtype (47.7%). Significant correlations were found between molecular subtypes and hormone receptor expression, age > 50, lymphovascular invasion, and pT & pN stage. No significant association was observed with tumor grade or histologic type.

Conclusion: Egyptian women with BC tend to present at a younger age compared to those in developed countries. The higher incidence of advanced stage of lymph node metastasis at the time of diagnosis highlights the importance of early cancer detection program, increased public awareness, and access to individualized treatment strategies in Egypt.

Keywords: Breast cancer, Egyptian women, Prognostic indicators.

INTRODUCTION

Breast cancer (BC) remains a major global health burden and is the leading cause of cancer-related deaths among women. According to World Health Organization, over 2 million new cases are diagnosed annually, representing nearly one-quarter of all female cancers. Despite advancements in screening and treatment, BC still leads to over 600,000 deaths each year [1]. In Egypt, according to National Cancer Institute cases registry, BC is the commonest cancer with a percentage of 32.04% of cancer cases. It is also considered first cause of cancer related deaths accounting for 21.6% among females [2].

Invasive breast carcinoma (IBC) is most common and aggressive form of BC, characterized by ability to invade surrounding breast tissue and metastasize to distant organs such as lymph nodes, bones, liver, and lungs [3]. IBC incidence varies geographically and demographically. In developed countries, incidence rate is higher due to widespread use of mammographic screening, which facilitates early detection. However, mortality rates are disproportionately high in developing regions where access to healthcare and early detection programs is limited [4, 5]. The risk of developing IBC is influenced by several factors, including genetic predisposition (e.g., BRCA1 and BRCA2 mutations), lifestyle factors (e.g., alcohol consumption & obesity), hormonal influences, and environmental exposures [6].

IBC is classified based on histological features, including cell morphology, architectural patterns, and degree of differentiation. Accurate classification and grading are essential for determining prognosis and guiding therapy [7].

Beyond traditional histopathological classification, IBC is further stratified into molecular subtypes based on immunohistochemical surrogates reflecting gene expression profiles [8]. These molecular classifications are critical in guiding prognosis and treatment. Luminal A tumors are characterized by positive expression of estrogen receptor (ER) and/or progesterone receptor (PR), negative HER2 status, and a low Ki-67 proliferation index. This subtype is typically associated with a favorable prognosis and demonstrates strong responsiveness to hormonal therapy. Luminal B tumors also express ER and/or PR but have either a positive or negative HER2 status and a high Ki-67 index, correlating with a more aggressive clinical behavior and relatively poorer outcomes compared to Luminal A tumors [9].

HER2-Enriched tumors lack ER and PR expression but are Human epidermal growth factor receptor 2 (HER2) positive. These cancers are biologically aggressive; however, they often respond well to HER2-targeted therapies such as trastuzumab [10]. Triple-Negative Breast Cancer (TNBC) is defined by absence of ER, PR, and HER2 expression. This subtype is associated with a high metastatic potential, limited targeted treatment options, and an overall poor prognosis [11].

The objective of our study was to characterize key pathological features of IBC in an Egyptian cohort, focusing on immunohistochemical evaluation of ER, PR, HER2, and Ki-67 expression, and to investigate their associations with clinicopathological parameters and potential implications for treatment planning and patient outcomes.

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MATERIALS AND METHODS

Patient selection: A cohort of 373 patients diagnosed with invasive breast carcinoma was selected for this retrospective study. The clinico-pathological data of cases were gathered from their files in archives of Pathology Department, Faculty of Medicine, Benha University through the period from March 2019 to July 2024. Pathology code numbers were used instead of patients' names to ensure confidentiality and anonymity.

Inclusion criteria: Any patient's age is included. Other inclusion criteria included patients who had undergone surgical resection (273 cases were modified radical mastectomies & 100 cases were wide local excision with axillary clearance), and sufficient tissue samples for histopathological and immunohistochemical analysis.

Exclusion criteria: No full clinicopathological data, cases with duct carcinoma insitu (DCIS) only and no complete biological profiles.

Sample collection and processing: Breast tissue samples were collected through surgical excision. The samples were fixed in 10% neutral buffered formalin and embedded in paraffin.

Cases were studied as follows: 1- Clinicopathological data regarding each studied case including age at diagnosis, laterality, histopathologic types, pathologic grade, AJCC stage, lymphovascular invasion, carcinoma insitu and biological subtypes.

2- Serial sections from paraffin embedded sections for each case were subjected to:

A- Routine haematoxylin and eosin (H & E) staining to revise diagnosis and for classification according to WHO [12], grading [13] and staging according to AJCC [14].

B- Immunohistochemical study of estrogen receptor, progesterone receptor, HER2 and Ki-67.

Immunohistochemistry (IHC):

IHC was performed to evaluate expression of key prognostic markers:

ER: Positive if ≥1% of tumor cell nuclei stained [15]. **PR:** Positive if ≥1% of tumor cell nuclei stained [15]. **HER2:** Scored as 0, 1+, 2+, or 3+; 3+ considered positive for HER2 overexpression [15]. **Ki-67:** High proliferation index defined as >20% of tumor cell nuclei stained [16].

Molecular subtypes (luminal A, luminal B, HER2-enriched and triple-negative) were determined based upon immunohistochemical analysis of ER, PR, HER2, Ki-67, and SISH for equivocal HER2 (HER2 score 2) [16].

Ethical considerations: The study was done after being accepted by Research Ethics Committee, Benha University (Approval number: RC 8-5-2025). This work has been carried out in accordance with Code of Ethics of World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were reviewed, coded, and analyzed using SPSS software (Statistical Package for Social Sciences), version 23.0 for Windows. Descriptive statistics included means, frequency distributions, and cross-tabulations. Inferential tests comprised Chi-square test for categorical variables and Spearman's correlation for continuous data. A p-value ≤ 0.05 was considered statistically significant. Results were organized, interpreted, and presented accordingly.

RESULTS

The age of the studied 373 malignant cases patients presenting by breast lump ranged from 29 to 70 years old, 12.6% of cases were before 40, 36.7% between 40-49, 32.4% between 50-59 and 18.3% after 60 years old. Tumor size ranged from 0.7 cm to 16 cm in its largest dimension with mean diameter was 3.5 cm. According to WHO classification, invasive ductal carcinoma was predominant histologic type (294 cases, 78.8%), followed by invasive lobular carcinoma (38 cases, 10.2%), mixed ductal and lobular carcinoma (30 cases, 8%), metaplastic carcinoma (9 cases, 2.4%), and mucinous carcinoma (1 case, 0.3%) as presented in **table (1) and figure (1)**.

Invasive breast cancer was slightly more common in left breast (51.5%). At diagnosis, 62.7% of tumors were grades II, while 36.7% were grade III. Ductal carcinoma in situ (DCIS) was found in 18.2% of cases, and lymphovascular invasion was present in 29.0%. Negative surgical margins were observed in 76.7% of cases, as detailed in **table (1)**.

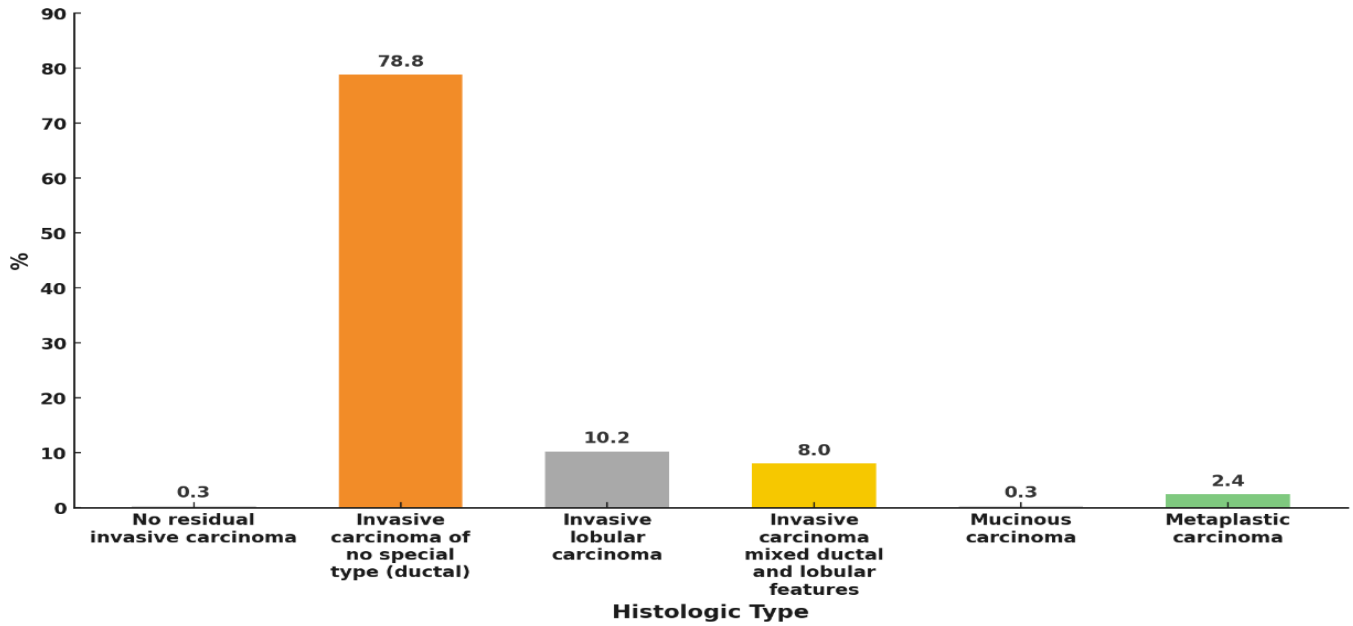

Figure (1): Charcteristics of histopathological types of invasive breast carcinoma.

Table (1): Clinic- pathological characteristics of studied tumor

	Histopathological parameters	N=373	%
Age group	<40	47	12.6
	40-49	137	36.7
	50-59	121	32.4
	≥60	68	18.3
Histologic Type	Invasive carcinoma of no special type (ductal)	294	78.8
	Invasive lobular carcinoma	38	10.2
	Invasive carcinoma with mixed ductal and lobular features	31	8.3
	Mucinous carcinoma	1	0.3
	Metaplastic carcinoma	9	2.4
Histologic Grade	Grade I	1	0.3
	Grade II	234	62.7
	Grade III	138	37
pT	pT1a	62	16.6
	pT1b	70	18.8
	pT2	172	46.1
	pT3	65	17.4
	pT4a	3	0.8
	pT4b	1	0.3
pN	pN not assigned	18	4.8
	pN0	53	14.2
	pN1a	132	35.4
	pN2a	72	19.3
	pN3a	98	26.3
Tumor size	≤3.5 cm	264	70.8
	>3.5	109	29.2
laterality	Right	181	48.5
	left	192	51.5
Focality	Single focus	251	67.3
	Multiple foci	122	32.7
DCIS	Absent	305	81.8
	present	68	18.2
LVI	Absent	265	71.
	present	108	29.0
Margin Status	Not applicable	28	7.5
	All margins negative for invasive carcinoma	286	76.7
	Invasive carcinoma involving a margin	59	15.8

n: number, pT: pathological tumor stage, pN: pathological nodal stage, DCIS: ductal carcinoma in situ, LVI: lymphovascular invasion.

Out of 373 cases of invasive breast carcinomas, 47.7% was luminal A, 5% of cases was luminal B "HER2 negative ", 34.0% was luminal B "HER2 positive", 11.5% was Triple negative & least number of cases (1.6%) was HER2 positive as detailed in **table (2) & figure (2).**

Table (2): Hormonal expression, HER2 neu & Molecular subtyping among studied cases

	N=373	%
ER		
-ve	56	15.0
+ve	317	85.0
PR		
-ve	80	21.4
+ve	293	78.6
HER2score		
score 0	203	54.4
1+	22	5.9
2+	15	4.0
3+	133	35.7
Ki67		
Low (<20%)	277	74.3
High (more than20%)	96	25.7
ER-/PR-	53	14.2
ER-/PR+	3	.8
ER+/PR-	27	7.2
ER+/PR+	290	77.7
Molecular subtypes		
luminal A	178	47.7
luminal B "her2 negative "	19	5.1
luminal B"her2 positive"	127	34.0
HER2 positive	6	1.6
Triple negative	43	11.5

n: number, **ER:** estrogen receptor, **PR:** progesterone receptor, **HER2:** human epidermal growth factor receptor 2, **Ki67:** Ki-67 proliferation index.

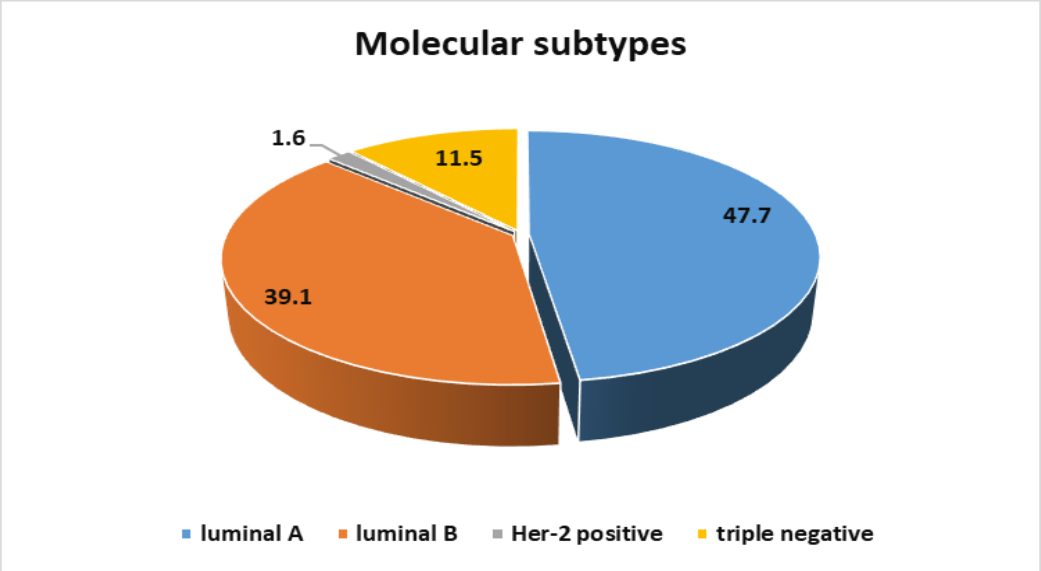

Figure (2): Molecular subtypes among the studied cases.

Relations between molecular subtypes and clinicopathological parameters: A statistically significant association was observed between molecular subtypes and age group (p = 0.037), lymphovascular invasion (p = 0.001), and pT stage (p = 0.029). However, no significant correlations were found with histological type, tumor grade, or tumor size (p > 0.05) (Table 3).

Table (3): Relations between molecular subtypes and clinicopathological parameters

Clinicopathological parameters	Luminal A N=178	Luminal B N=146	Her2 positive N=6	Triple negative N=43	*p value*
<50	81(45.5)	84(57.5)	1(16.7)	18(41.9)	0.037*
≥50	97(54.5)	62(42.5)	5(83.3)	25(58.1)	
Procedure					
Excision	50(28.1)	45(30.8)	2(33.3)	17(39.5)	0.538
Total mastectomy	128(71.9)	101(69.2)	4(66.7)	26(60.5)	
laterality					
Right	78(43.8)	72(49.3)	3(50)	28(65.1)	0.095
left	100(56.2)	74(50.7)	3(50)	15(34.9)	
Histologic Type					
Invasive carcinoma of no special type (ductal)	132(74.2)	121(82.9)	5(83.3)	36(83.7)	0.318
Invasive lobular carcinoma	24(13.5)	10(6.8)	1(16.7)	3(7)	
Invasive carcinoma with mixed ductal and lobular features	17(9.6)	10(6.8)	0	4(9.3)	
Mucinous carcinoma	1(0.6)	0	0	0	
Metaplastic carcinoma	4(2.2)	5(3.4)	0	0	
Histologic Grade					
Grade I	0	1(0.7)	0	0	0.953
Grade II	115(64.6)	89(61)	4(66.7)	26(60.5)	
Grade III	63(35.4)	56(38.4)	2(33.3)	17(39.5)	
Tumor size					
≤3.5 cm	132(74.2)	97(66.4)	2(33.3)	33(76.7)	0.07
>3.5	46(25.8)	49(33.6)	4(66.7)	10(23.3)	
Focality					
Single focus	104(58.4)	121(82.9)	5(83.3)	21(48.8)	0.001*
Multiple foci	74(41.6)	25(17.1)	1(16.7)	22(51.2)	
DCIS					
Absent	146(82)	119(81.5)	5(83.3)	35(81.4)	0.999
present	32(18)	27(18.5)	1(16.7)	8(18.6)	
LVI					
-ve	98 (55)	112 (76.7)	4 (66.7)	34 (79.1)	0.001*
+ve	80 (45)	34 (23.3)	2 (33.3)	9 (20.9)	
Margin Status					
Not applicable	13(7.3)	11(7.5)	1(16.7)	3(7)	0.276
All margins negative for invasive carcinoma	142(79.8)	105(71.9)	3(50)	36(83.7)	
Invasive carcinoma involving a margin	23(12.9)	30(20.5)	2(33.3)	4(9.3)	
pT					
T1	70(39.5)	50(34.5)	1(16.7)	8(19)	0.029*
T2	76(42.9)	68(46.9)	2(33.3)	26(61.9)	
T3	29(16.4)	27(18.6)	3(50)	6(14.3)	
T4	2(1.1)	0	0	2(4.8)	
pN					
N0	19(11.4)	26(17.9)	1(25)	7(17.5)	0.005*
N1	73(44)	37(25.5)	2(50)	20(50)	
N2	38(22.9)	27(18.6)	1(25)	6(15)	
N3	36(21.7)	55(37.9)	0(0)	7(17.5)	

n: number, DCIS: ductal carcinoma in situ, **LVI:** lymphovascular invasion, **pT:** pathological tumor stage, **pN:** pathological nodal stage, *****: significant p-value.

DISCUSSION

BC is the most commonly diagnosed malignancy and leading cause of cancer-related mortality among women worldwide, affecting both developed and developing nations [17]. In Egypt, it ranks as most frequent female cancer, accounting for 38.85% of all cases, and is second leading cause of cancer-related death after hepatocellular carcinoma [18]. Its primary risk factors are genetic and hormonal, encompassing hereditary mutations and sporadic cases driven by hormonal influences [19].

In our cohort, 36.7% of the studied cases aged between 40-49 and 32.4% between 50-59 at diagnosis. This observation aligns with findings reported by **Dey *et al*.** [20] who analyzed data from Gharbiah population-based cancer registry in Egypt. They found that highest prevalence occurred in women aged 40–49 (32.27%), with 50–59 age group following at 28.8%. Also **Najjar and Easson** [21] who conducted an extensive review of breast cancer literature across Arab countries, encompassing 28 studies with a cumulative sample of 7,455 patients. Their analysis revealed that nearly half of Lebanese breast cancer cases were also diagnosed before age of 50. In contrast, a study by **Mostafa *et al*.** [22] showed that highest incidence occurred in 50–59 age group (28.8%), followed by those aged 40–49 years (28%), and then 29–39 years (20.6%).

WHO has estimated that nearly half of all cancer cases in Eastern Mediterranean Region (EMR) occur before age of 55, and cancer incidence rates in this region are projected to double with increased exposure to risk factors. This age distribution differs markedly from that observed in Western nations, where peak incidence generally occurs later in life [23]. In this study, the most frequently encountered malignant breast tumor was invasive carcinoma of no special type (NST), accounting for 78.8% of cases. This was followed by invasive lobular carcinoma (10.2%) and mixed ductal-lobular carcinoma (8%). These proportions are consistent with findings from other regional cancer registries. For example, **Nikhoo *et al*.** [17] reported NST in 82.7% of cases and lobular carcinoma in 8.2%.

Concerning pathological staging in present cohort, 46% of patients were classified as pT2 and 26.3% as pN3 at time of diagnosis. This indicates that more than half of studied population presented with stage II or III disease. The high proportion of advanced-stage cases may be attributed to limited access to screening services and insufficient public awareness regarding early detection methods, such as routine clinical and self-breast examinations.

Comparable findings were reported by **Mostafa *et al*.** [21], where over one-third (37%) of female patients were diagnosed as stage III, and 21% had distant metastases. Similarly, **Mutar *et al*.** [24], investigating breast cancer presentation patterns in Iraq, found that 42.9% of patients were diagnosed at stage III and 25% at stage IV. **Thangjam *et al*.** [25], studying women under 40 years in Manipur, also noted stage III as most common presentation among younger patients (47%), in contrast to 18% in older age groups.

Concerning positivity of hormone –receptors in our study, 85%, 78.6% & 77.7% of studied cases were positive for estrogen, progesterone and both of them respectively. This finding is in parallel to that reported by **Farouk *et al*.** [26] and **Mahfouz *et al*.** [27].

In our cohort, the most frequently observed molecular subtype was luminal A, defined by concurrent estrogen and progesterone receptor positivity, accounting for 47.7% of all cases. This finding aligns with prior studies, including **Abiltayeva *et al*.** [28] and **Al-Thoubaity** [29] at King Abdul-Aziz University Hospital in Saudi Arabia, who reported a luminal A frequency of 58.5%.

In the present study, molecular subtypes showed significant associations with hormone receptor status, age above 50, lymphovascular invasion and pT & pN stage. Findings are consistent with those of **ElKablawy *et al*.** [30]. However, no significant correlations were observed between molecular subtypes and either tumor grade or histopathological type. Interestingly, **Gaber *et al*.** [31] found a significant link between tumor grade and hormone receptor expression, which may differ from our results due to relatively low proportion of grade III tumors in our sample.

CONCLUSION

The high incidence and increasing burden of BC among Egyptian women underscores urgent need for comprehensive national cancer control programs focused on early detection. Enhancing public awareness about the value of clinical breast examinations, self-examination, and timely medical evaluation represents a critical strategy in improving early diagnosis, reducing disease progression, and ultimately improving outcomes for affected women in Egypt.

RECOMMENDATIONS

Improving BC survival rates in Egypt depends largely on early detection of cases, particularly in underserved rural areas. Establishing nationwide screening programs, enhancing public awareness about importance of breast self-examination, and encouraging prompt medical consultation are essential steps. Furthermore, improving access to modern therapeutic modalities and ensuring availability of personalized treatment options could lead to significantly better prognoses and outcomes for Egyptian women with BC.

LIMITATIONS

This study has several limitations. It was conducted in a single medical center, which may limit generalizability of results to broader Egyptian population. Additionally, improper filing and inconsistent registration systems resulted in incomplete clinical data for some cases. A further limitation was lack of adequate follow-up and documentation, which hindered evaluation of long-term survival outcomes and prevented comprehensive assessment of patients' medical and family histories.

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