



Original Article

Clinicopathological and Hormone-Receptor Patterns in a Young Breast-Disease Cohort: A Retrospective Analysis of 399 Patients' Records from 2023–2025 in Tripoli, Libya

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Abstract

Background: Breast cancer (BC) is the most globally diagnosed malignancy among women. However, information on clinicopathological patterns in Libyan and North African women remains limited. This study examined age-related differences in histological diagnosis, disease extent, tumor grade, and hormone-receptor status in hospitalized BC women. **Methods:** A retrospective cross-sectional analysis was conducted on 399 patients from 2023–2025. All participants were aged 13–39 years. Age was summarized continuously and categorized as ≤ 29 , 30–34, and 35–39 years. Diagnoses were harmonized into major histological groups. Estrogen receptor (ER), progesterone receptor (PR), and HER2 results were normalized as positive, negative, or unknown. Disease extent was operationally classified from TNM fields as early (T1–T2/N0–N1/M0), locally advanced (T3–T4 or N2–N3/M0), metastatic (M1), or unclassified. Associations were evaluated using Pearson's chi-square tests, with two-sided $P < 0.05$ considered statistically significant. **Results:** showed that the Mean age was 32.9 ± 4.5 years, and the median age was 34 years (IQR 30–37). Invasive ductal carcinoma accounted for 342 records (85.7%), although benign and non-epithelial diagnoses were also present. Grade II and III tumours represented 51.1% and 40.6%, respectively. ER, PR, and HER2 positivity were counted in 44.1%, 37.6%, and 41.6% of cases, respectively. Basal-like, luminal A, luminal B, and HER2-enriched subtypes were recorded for 32.6%, 24.6%, 21.8%, and 20.3%, respectively. Locally advanced disease predominated (61.4%), while 17.0% were metastatic. Histological composition differed across age categories ($P < 0.001$), but age was not significantly associated with grade, ER, PR, HER2, or disease extent. **Conclusion:** This unusually young cohort showed a high burden of grade II–III and locally advanced disease in Libya. However, diagnostic heterogeneity limits generalizability. Registry standardization, pathology verification, and population-based studies are required.

Keywords: breast cancer; young women; HER2; TNM; retrospective study; histology hormone receptors :Libya

Introduction

Breast cancer (BC) is a major global public-health problem and the most frequently diagnosed cancer among females in most countries. GLOBOCAN 2022 estimated approximately 2.3 million new cases of breast cancer in women and about 666,000 deaths worldwide, representing a considerable percentage of the world cancer burden [1,2]. Although breast-cancer mortality has declined in many high-income settings because of earlier diagnosis, organized screening, molecular classification, and improved systemic treatment, major inequalities persist between and within countries [1–4]. Women in resource-constrained settings frequently present with larger tumours, nodal involvement, or metastatic disease, and often face delays in diagnostic confirmation and treatment

initiation [3–6]. In Libya, early-age- BC diagnosed females have dramatically increased [5].

Breast cancer is biologically heterogeneous. Histological type, tumour size, tumour grade, distant metastasis, regional nodal involvement, and expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) are central to prognosis and treatment selection [7–10]. Invasive carcinoma of no special type, historically termed invasive ductal carcinoma, is the most common histological diagnosis, while invasive lobular, metaplastic tubular, mucinous, and other special BC types occur less frequently [7,8]. Histological grade displays nuclear pleomorphism, tubule formation, and mitotic activity; higher-grade tumours generally demonstrate more aggressive biological



behaviour [9]. The TNM classification indicates the anatomical extent of the disease and remains a fundamental pillar for staging, treatment planning, and comparing outcomes. [10].

Immunohistochemical assessment of ER, PR, and HER2 status enables a clinically significant classification of tumors. Hormone-receptor-positive cancers may benefit from endocrine therapy, whereas HER2-positive tumours are candidates for HER2-directed treatment [11–14]. Tumours lacking ER, PR, and HER2 expression are commonly categorized as triple-negative and recurrently interfere with basal-like biological characteristics, although these terms are not completely substitutable [15,16]. Molecular and surrogate immunohistochemical subtypes are associated with differences in age distribution, recurrence patterns, therapeutic options, and survival [11–16]. Consequently, the accuracy of receptor tests has direct clinical implications, particularly in places where advanced genomic testing is unavailable.

Breast cancer in young women is uncommon in absolute terms but is clinically important. Most international screening programs begin at 40 or 50 years of age for women at average risk, which means younger patients commonly present symptomatically [17–19]. Breast cancer diagnosed before 40 years may be associated with hereditary susceptibility, fertility and pregnancy considerations, delayed recognition, and a higher prevalence of aggressive clinicopathological characteristics in some populations [5, 17–22]. Young women also face specific concerns regarding survival and leading a normal life, including the preservation of fertility, premature ovarian insufficiency, pregnancy after treatment, psychosocial distress, employment, sexual health, and the long-term toxicity of treatment. [19–22].

The age distribution of breast cancer differs across regions. African and Middle Eastern series often report a younger median age at diagnosis than registries in Europe and North America. This pattern is partly influenced by population structure, limited screening coverage, referral patterns, and incomplete registration [5, 23–27]. Studies from North Africa have described frequent presentation with stage III disease, high-grade tumours, and substantial proportions of hormone-receptor-negative or HER2-positive disease. Findings vary considerably according to laboratory methods and study setting [23–29]. Therefore,

comparisons must distinguish genuine biological differences from variations arising from case ascertainment, diagnostic practices, and data quality.

In Libya, breast cancer is the leading cancer among women. IARC estimates identify breast cancer as the most common female cancer by both incidence and mortality, and available Libyan studies have reported a predominance of invasive ductal carcinoma with clinically meaningful variation in molecular subtype and receptor expression [2,30–33]. However, national population-based evidence remains limited, and prolonged health-system disruption has affected cancer registration, diagnostic pathways, and continuity of care. Local datasets are valuable for describing patterns of presentation, but careful cleaning and transparent reporting are essential because routine records may contain inconsistent terminology, incomplete staging fields, and diagnoses that do not represent primary epithelial breast cancer.

The present study analysed 399 records dated 2023–2025 to describe age, histological diagnosis, tumour grade, receptor status, surrogate molecular subtype, and TNM-derived disease extent. Because all recorded ages were below 40 years, the study focused on comparisons within a young cohort using three age bands. The objectives were to: (1) summarize the clinicopathological profile of the dataset; (2) compare histology, grade, receptor status, and disease extent across age groups; and (3) identify data-quality limitations relevant to future clinical registries and publication. The analysis was designed as an exploratory study and does not assume that the dataset is population-based.

Materials and Methods

Study design and data source

This retrospective cross-sectional study used records from 399 BC patients in 2023, 2024, and 2025. The workbook included year, age, recorded histopathological diagnosis, grade, ER, PR, HER2, laterality, surrogate subtype, procedure indicators, recurrence, pregnancy/lactation status, metastasis, marital status, family history, and TNM fields. The hospital, laboratory, geographic catchment, and method of case selection were not documented in the workbook and must be added by the investigators before journal submission.



Study population

A total of 339 Tripoli Medical Center patients' recorded data were included in the primary analysis. No duplicate participant identifier was available, so duplicate-person assessment could not be performed. All recorded ages ranged from 13 to 39 years; consequently, the dataset of participants represents a young breast-disease cohort rather than an all-age breast-cancer population. Records containing benign lesions, metastatic non-breast tumours, lymphomas, and sarcomas were retained in descriptive analyses for accurate representing to the recorded dataset.

Data cleaning and variable definitions

Text fields were trimmed, capitalization was standardized, and common spelling variants were harmonized. Histological diagnoses were grouped as invasive ductal carcinoma, invasive lobular carcinoma, fibroadenoma, phyllodes tumour, lymphoma, rhabdomyosarcoma, mucinous/mixed carcinoma, metastatic medulloblastoma, verrucous carcinoma, or other/unspecified. Grade labels were standardized as I, II, III, or unknown. Receptor fields containing "positive" or "strong positive" were classified as positive; those containing "negative" were classified as negative; all other values were classified as unknown. Surrogate subtype labels were harmonized as luminal A, luminal B, HER2-enriched, basal-like, or unknown.

Age and disease-extent categories

Age was analysed as a continuous variable and in three groups selected to preserve clinically interpretable within-cohort comparisons: ≤ 29 , 30–34, and 35–39 years. Since no consolidated stage variable was available, disease extent was derived from the recorded TNM fields. Early disease was defined as T1–T2 with N0–N1 and M0; locally advanced disease was defined as T3–T4 or N2–N3 in the absence of M1; metastatic disease was defined as M1; and

records not meeting these rules because of incomplete or inconsistent values were classified as unclassified. This operational grouping is not a substitute for formal AJCC prognostic staging.

Statistical analysis

Continuous age was summarized using mean, standard deviation, median, interquartile range, minimum, and maximum. Categorical variables were summarized as frequencies and percentages. Pearson's chi-square test was used to examine associations between age group and histological grouping, grade, ER, PR, HER2, and disease extent. Because several detailed histological categories had small expected frequencies, the inferential histology comparison used a binary grouping of invasive ductal carcinoma versus all other recorded diagnoses. Two-sided P values below 0.05 were considered statistically significant. Analyses were conducted in Python using SciPy; charts were generated with Matplotlib. No imputation was performed.

Ethical considerations

The dataset supplied for analysis contained no direct patient identifiers. And had the approval of the Faculty of Medical Technology and Libyan Medical Center committee.

Results

Cohort characteristics

The analysis included 399 records. Mean age was 32.9 ± 4.5 years, median age was 34 years (IQR 30–37), and the range was 13–39 years. The largest age group was 35–39 years (189/399, 47.4%), followed by 30–34 years (139/399, 34.8%) and ≤ 29 years (71/399, 17.8%). Invasive ductal carcinoma was the dominant recorded diagnosis (342/399, 85.7%). Grade II tumours accounted for 204 cases (51.1%) and grade III for 162 (40.6%).

Table 1. Clinicopathological characteristics of the analysed dataset (n=399)

Characteristic	n	%
Age, mean $\pm$ SD	32.9 ± 4.5	—
Age, median (IQR)	34 (30–37)	—
Age ≤ 29 years	71	17.8
Age 30–34 years	139	34.8
Age 35–39 years	189	47.4
Invasive ductal carcinoma	342	85.7
Invasive lobular carcinoma	16	4.0
Other/unspecified diagnosis	20	5.0



Other named diagnoses	21	5.3
Grade I	31	7.8
Grade II	204	51.1
Grade III	162	40.6
ER positive	176	44.1
PR positive	150	37.6
HER2 positive	166	41.6
Luminal A	98	24.6
Luminal B	87	21.8
HER2-enriched	81	20.3
Basal-like	130	32.6
Early disease	79	19.8
Locally advanced disease	245	61.4
Metastatic disease (M1)	68	17.0
Unclassified extent	7	1.8

Hormone receptors, subtype, and disease extent

ER positivity was recorded in 176 cases (44.1%), PR positivity in 150 (37.6%), and HER2 positivity in 166 (41.6%). Basal-like disease was the most frequently recorded surrogate subtype (130/399, 32.6%), followed by luminal A (98/399, 24.6%), luminal B (87/399, 21.8%), and HER2-enriched disease (81/399, 20.3%); three subtype values were missing or unclassifiable. Based on the operational TNM grouping, 245 cases (61.4%) were locally advanced, 79 (19.8%) were early, 68 (17.0%) were metastatic, and seven (1.8%) were unclassified.

Comparisons by age group

The proportion of invasive ductal carcinoma differed significantly across age groups (Pearson $\chi^2=19.86$, $df=2$, $P<0.001$), with a lower proportion among patients aged ≤ 29 years than among those aged 30–34 and 35–39 years. No statistically significant age-group differences were observed for grade ($P=0.941$), ER status ($P=0.929$), PR status ($P=0.232$), HER2 status ($P=0.167$), or disease extent ($P=0.153$). These findings should be interpreted cautiously because the cohort contained no patients aged 40 years or older and included diagnostically heterogeneous records.

Table 2. Clinicopathological characteristics by age group

Characteristic	≤ 29 (n=71)	30–34 (n=139)	35–39 (n=189)	P value
Invasive ductal carcinoma	50 (70.4)	118 (84.9)	174 (92.1)	<0.001
Grade III	29 (40.8)	58 (41.7)	75 (39.7)	0.941
ER positive	31 (43.7)	60 (43.2)	85 (45.0)	0.929
PR positive	27 (38.0)	60 (43.2)	63 (33.3)	0.232
HER2 positive	27 (38.0)	52 (37.4)	87 (46.0)	0.167
Locally advanced disease	39 (54.9)	86 (61.9)	120 (63.5)	0.153
Metastatic disease	18 (25.4)	23 (16.5)	27 (14.3)	0.153

Values are n (% within age group). P values are from Pearson's chi-square tests. The same overall disease-extent test is shown for both extent rows.

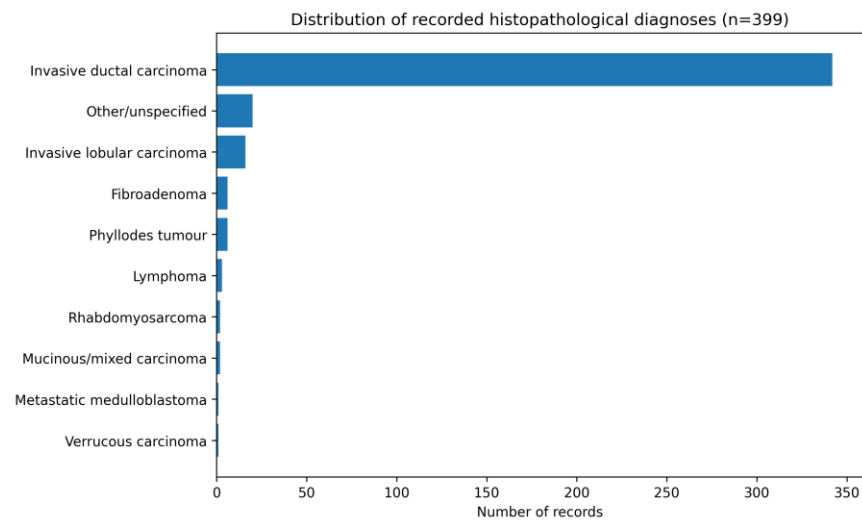


Figure 1. Distribution of recorded histopathological diagnoses. The dataset contains benign and non-epithelial diagnoses in addition to primary breast carcinoma.

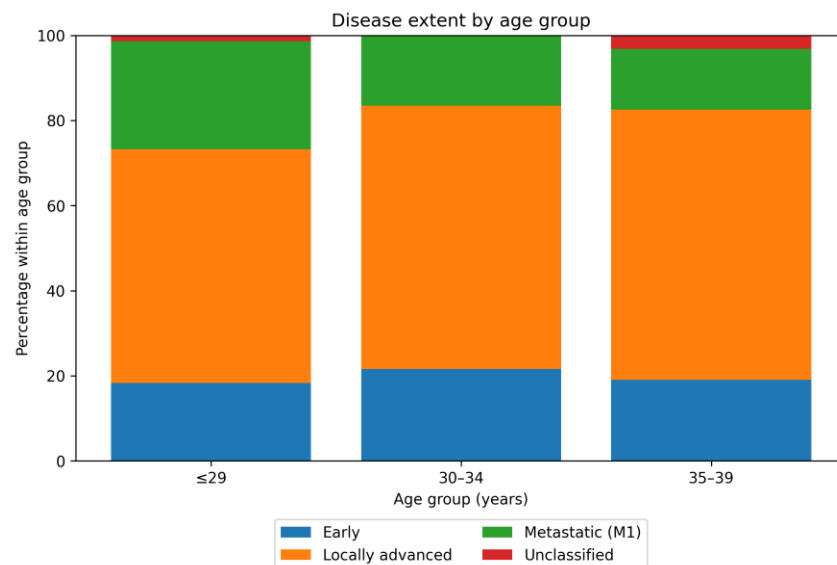


Figure 2. TNM-derived disease extent by age group. Percentages are calculated within each age category.

Discussion

This analysis describes a highly selected cohort of 399 patients younger than 40 years. The principal findings were the predominance of invasive ductal carcinoma, a large proportion of grade II–III tumours, and a high frequency of locally advanced or metastatic disease. Basal-like disease was the most frequently recorded surrogate subtype, while fewer than half of the records were ER positive. These observations may indicate an aggressive

clinicopathological profile, but they must not be interpreted as population prevalence because the sampling frame and referral setting were unavailable.

The mean age of 32.9 years is substantially younger than typical breast-cancer populations and younger than published Libyan cohorts, in which median ages in the forties are more common [30, 33]. However, this study's results agreed with Abuagela's 2026 study, which revealed that younger patients demonstrated more



aggressive tumor biology, whereas older patients showed higher rates of hormone receptor-positive disease.

This disparity is partly attributed to developments in diagnostic methods; consequently, this study—whether by design or due to procedural considerations—was limited to younger patients, a trend observed in Libya in numerous recent studies for reasons that remain unknown. Invasive ductal carcinoma represented 85.7% of records, broadly consistent with its established predominance in breast-cancer series [5,7,8,30,31,32,33,35,36]. However, the file also included fibroadenoma, lymphoma, sarcoma, metastatic medulloblastoma, and other diagnoses. Their presence suggests that data may combine all breast biopsies or breast masses rather than confirmed primary breast carcinomas. The significant difference in histological composition across age groups was driven largely by the greater relative frequency of non-ductal diagnoses in the youngest age group. However, this association should not be interpreted as evidence that breast-cancer histology changes biologically across the narrow age range studied.

The high combined proportion of grade II and III tumours is consistent with reports that young patients may present with less favourable pathological features [17–22]. Similarly, 61.4% of records were operationally categorized as locally advanced and 17.0% as metastatic. Late presentation has been repeatedly documented in low- and middle-income settings and may reflect limited awareness, fragmented referral pathways, constrained pathology capacity, diagnostic delay, and reduced access to screening and specialist care [3,6,23,24,25,27,28,29,34]. Nevertheless, the derived extent variable was based on simplified TNM rules and should be replaced by verified AJCC stage groups when original pathology and imaging records are available.

ER and PR positivity were lower than those reported in many contemporary Western cohorts, whereas HER2 positivity and basal-like classification were relatively high [5,11,18]. Young age, population ancestry, referral bias, and technical variation in immunohistochemistry could all contribute. In addition, the recorded surrogate subtypes were not fully internally validated against receptor combinations; for example, luminal and HER2-enriched labels should be cross-checked against ER, PR, HER2, and Ki-67 results. The absence of Ki-67 and HER2

confirmatory testing information limits formal surrogate molecular classification.

No statistically significant association was found between the three age bands and grade, ER, PR, HER2, or disease extent. The lack of association may be genuine within this young population, but the age range was narrow, and the youngest group was comparatively small. The study was unable to compare young and older women, which is the clinically more informative contrast. Future analyses should include patients aged 40 years and older, preferably with predefined categories such as <40, 40–49, 50–59, and ≥60 years.

The study has strengths. It uses all supplied records, transparently reports cleaning rules, separates descriptive findings from inferential conclusions, and identifies data-quality concerns that might otherwise be overlooked. It also provides a preliminary profile of receptor and TNM patterns in a young cohort during 2023–2025. Its limitations are substantial: the source institution and denominator population were not documented; case selection could not be reconstructed; no unique identifier was available; pathology diagnoses were heterogeneous; potential duplicates could not be assessed; stage was derived rather than directly recorded; survival, treatment, Ki-67, menopausal status, and genetic data were unavailable; and receptor-testing methods were not documented.

Before journal submission, investigators should verify each record against pathology reports, restrict the analytic cohort to primary invasive breast carcinoma where appropriate, remove duplicates, confirm receptor interpretation according to ASCO/CAP guidance, reconstruct AJCC stage, document the study setting and ethics approval, and consider sensitivity analyses excluding benign and non-epithelial diagnoses. A validated registry with standardized coding would greatly strengthen future Libyan breast-cancer research.

Conclusion

Among 399 participants from patients aged 13–39 years, invasive ductal carcinoma predominated, and most tumors were grade II or III. More than three-quarters of cases were categorized as locally advanced or metastatic using TNM-derived rules. Receptor distributions indicated substantial basal-like and HER2-positive disease. Apart from histological composition, clinicopathological features did



not differ significantly across the selected age bands. The findings highlight a potentially severe burden among young patients but also reveal important limitations in case definition and Pathology verification, standardized staging, documented sampling methods, registry quality, and the inclusion of older age groups are essential before drawing population-level conclusions.

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