



## Article

# Retrospective Studies: An Insight into the Histopathological Findings Associated with Breast Cancer

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**ABSTRACT**

**Background:** Breast cancer (BC) is the most prevalent malignancy among women globally, with distinct histopathological profiles across populations. In Pakistan, younger age at diagnosis and limited awareness hinder early detection and optimal management, yet comprehensive local data on histopathological patterns remain scarce. **Objective:** This study aimed to investigate the histopathological features of breast cancer in Pakistani women and examine their associations with demographic variables and awareness levels, to inform evidence-based diagnostic and therapeutic strategies. **Methods:** A retrospective observational study was conducted on medical records of 174 female patients diagnosed with primary invasive breast cancer from 2021 to 2023. Patients were included based on confirmed histopathological diagnosis, complete clinical records, and exclusion of recurrence or prior malignancy. Data on tumor size, grade, biopsy site, lymph node involvement, HER2 status, and awareness scores were extracted. HER2 was assessed via immunohistochemistry with FISH confirmation where needed. The study was conducted in compliance with the Declaration of Helsinki and approved by the Institutional Review Board. Descriptive and inferential analyses were performed using SPSS v27, including ANOVA, t-tests, and Pearson correlations. **Results:** The mean age was  $32.6 \pm 1.95$  years, with most tumors graded as Grade II (38.8%) and sized 2–3 cm (38.9%). Left-sided biopsies (38.9%) and absence of lymph node involvement (59.5%) predominated. A significant association was found between awareness and recognition of risk factors ( $r = 0.596$ ,  $p < 0.01$ ), but not with histopathological severity. Tumor grade ( $F = 4.76$ ,  $p = 0.009$ ), size ( $F = 3.92$ ,  $p = 0.022$ ), and lymph node status ( $F = 3.94$ ,  $p = 0.021$ ) showed statistically significant variations across patient subgroups. **Conclusion:** This study highlights the prevalence of intermediate-grade tumors and suboptimal awareness among Pakistani women with BC, reinforcing the need for integrated educational and diagnostic strategies. Findings support the clinical utility of histopathological profiling for guiding individualized care in resource-limited settings.

**Keywords:** Breast Neoplasms, Histopathology, HER2, Tumor Grading, Lymphatic Metastasis, Developing Countries, Retrospective Studies

**INTRODUCTION**

Breast cancer (BC) remains a significant global health concern and is currently the most frequently diagnosed cancer among women, with substantial implications for morbidity and mortality worldwide (1). While BC has traditionally been associated with older age, emerging data from low- and middle-income countries, including Pakistan, suggests an increasing incidence in younger women, challenging long-standing assumptions regarding age-related risk (2,3). The burden of BC is especially pronounced in South Asia, where factors such as limited access to healthcare, lack of awareness, delayed diagnoses, and sociocultural stigma contribute to late-stage presentations and poor outcomes (4). In Pakistan, BC accounts for a disproportionately high rate of cancer-related deaths among women, a pattern attributed in part to gaps in

screening, early detection, and localized epidemiological data (5).

Despite advancements in imaging and molecular diagnostics, histopathological evaluation remains central to BC diagnosis and prognosis. Tumor characteristics such as grade, size, lymph node involvement, and histological subtype significantly influence treatment decisions and survival outcomes (6). Notably, infiltrating ductal carcinoma and lobular carcinoma constitute the majority of BC subtypes globally, but the prevalence and behavior of these histological variants may vary with geographic and ethnic contexts (7). Understanding these patterns in a local population is critical for developing targeted interventions and individualized treatment regimens. However,

current literature in Pakistan remains fragmented, with limited large-scale retrospective analyses focusing specifically on histopathological parameters and their association with patient demographics and clinical outcomes (8).

One of the critical limitations in existing research is the insufficient integration of histopathological data with patient-level factors such as awareness of BC symptoms, risk factors, and treatment pathways. While international studies have documented the prognostic significance of histological features (8), regional data remains scarce and lacks the methodological rigor necessary for generalization and policy development. Furthermore, previous studies seldom account for the relationship between demographic factors, such as marital status and awareness, and their potential influence on disease progression and diagnostic delay, creating a significant knowledge gap (9). This is particularly relevant in Pakistani settings, where cultural norms and limited health literacy may exacerbate disparities in healthcare-seeking behavior (9). Given the paucity of comprehensive retrospective studies analyzing the interplay between clinical, demographic, and histopathological features of BC in Pakistan, there is a pressing need to bridge this gap through localized data. Retrospective studies, despite certain limitations, offer a valuable opportunity to examine archival data, identify prevalent histopathological trends, and uncover potential associations that could inform early detection and treatment strategies (10).

By leveraging patient records from multiple years, such analyses can also provide insights into the evolving nature of BC presentation in younger and older populations alike. The present study was designed to address these critical gaps by conducting a retrospective analysis of 174 female BC patients diagnosed and treated between 2021 and 2023 at a tertiary care institution in Pakistan. The aim was to examine the frequency and distribution of key histopathological features—such as tumor size, grade, lymph node status, and HER2 expression—and their association with patient demographics and awareness levels. By doing so, this study seeks to contribute to the foundational understanding of BC in Pakistani women, highlight potential disparities in clinical awareness, and support future efforts toward individualized, evidence-based cancer care. The central research question guiding this study is: *What are the predominant histopathological features of breast cancer in Pakistani women, and how are they associated with patient demographics and awareness levels?*

## MATERIALS AND METHODS

This retrospective observational study was conducted to analyze the histopathological characteristics of breast cancer in female patients treated between January 2021 and March 2023 at a tertiary care medical center in Pakistan. A total of 174 female patients were included based on the availability of complete medical and histopathological records. Inclusion criteria comprised adult female patients with a confirmed diagnosis of primary invasive breast carcinoma, as documented in institutional pathology reports. Patients were eligible if they had recorded data on age at diagnosis, tumor size, histological grade, HER2 expression status, lymph node involvement, and overall clinical history relevant to the malignancy. Exclusion criteria

included patients with recurrent breast cancer, incomplete records, prior neoadjuvant therapy before histopathological evaluation, or a history of other malignancies. Participants were selected through purposive sampling from hospital archives and electronic record systems. As this was a retrospective chart review, informed consent was not required; however, all patient data were anonymized to maintain confidentiality in accordance with ethical standards.

Data collection was carried out through systematic review of histopathology reports and clinical charts. The primary outcomes of interest were the distribution and frequency of histopathological features including tumor grade, size, lymph node involvement, biopsy site, and HER2 status. Secondary outcomes included associations between these pathological features and patient demographic variables such as age, marital status, and awareness of breast cancer symptoms. HER2 expression was assessed through immunohistochemistry (IHC) and scored according to the College of American Pathologists (CAP) guidelines, using a scale of 0 to 3+. Cases scoring 2+ (equivocal) were further confirmed by fluorescence in situ hybridization (FISH), following standard diagnostic protocols. Tumor grading followed the modified Bloom-Richardson system. Awareness and symptom-related data were extracted from structured clinical interviews documented in patient files. These included a set of validated items assessing knowledge about breast cancer risk factors and early warning signs. This study adhered to the ethical principles outlined in the Declaration of Helsinki. All data were handled confidentially, and patient identifiers were removed during data extraction and analysis. The retrospective nature of the study and the use of de-identified archival data ensured minimal risk to subjects.

Statistical analyses were performed using SPSS version 27. Descriptive statistics, including means, standard deviations, and frequencies, were calculated for all continuous and categorical variables. Pearson correlation coefficients were computed to assess associations between histopathological variables and demographic or clinical characteristics. One-way analysis of variance (ANOVA) and independent samples t-tests were used to compare differences in histological features across subgroups based on age and awareness levels. The level of statistical significance was set at  $p < 0.05$ . Cronbach's alpha was initially used to assess internal consistency for composite awareness and symptom indices; however, correlation analyses between variables were strictly conducted using appropriate parametric tests. No imputation was performed for missing data; only complete datasets were included in final analyses to preserve statistical validity.

## RESULTS

The study included data from 174 female patients diagnosed with breast cancer (BC) at a tertiary care facility between January 2021 and March 2023. The demographic and clinical characteristics of the patients, along with the correlations and internal consistencies of study variables, are detailed in Tables 1–3.

Table 1 presents the correlation coefficients among the primary clinical variables examined in the study. A significant positive

correlation was observed between breast cancer awareness and breast cancer risk factors and symptoms ( $r = 0.596$ ,  $p < 0.01$ ). In contrast, age exhibited a non-significant weak negative correlation with breast cancer awareness ( $r = -0.153$ ,  $p > 0.05$ ), and a slightly stronger negative correlation with histopathological features ( $r = -0.303$ ,  $p > 0.05$ ). Similarly,

histopathological features showed a non-significant negative correlation with breast cancer risk factors and symptoms ( $r = -0.273$ ,  $p > 0.05$ ). Cronbach's alpha coefficients indicated acceptable internal consistency across all scales, with values ranging between 0.67 and 0.82, suggesting reliability of the measurement tools used.

**Table 1. Correlation Matrix and Cronbach's Alpha Coefficients for Study Variables**

Variables	Age	BC Awareness	BC Risk Factors & Symptoms	Histopathological Features	Cronbach's Alpha
Age	1.000				0.82
BC Awareness	-0.153	1.000			0.76
Risk Factors & Symptoms	0.019	0.596**	1.000		0.67
Histopathological Features	-	0.157	-0.273	1.000	0.67

**Table 2. Item-Total Statistics for Histopathological Features, Risk Factors & Symptoms, and BC Awareness Scales**

Item No.	Histopathological Features		Risk Factors & Symptoms		BC Awareness	
	Cronbach's Alpha	Item-Total Corr.	Cronbach's Alpha	Item-Total Corr.	Cronbach's Alpha	Item-Total Corr.
1	0.797	0.210	0.793	0.191	0.873	0.665
2	0.787	0.138	0.781	0.414	0.885	0.567
3	0.787	0.152	0.783	0.337	0.873	0.532
4	0.792	0.077	0.786	0.175	0.873	0.486
5	0.781	0.378	0.783	0.330	0.873	0.517
6	0.792	0.103	0.785	0.256	0.873	0.673
7	0.789	0.070	0.790	0.018	0.874	0.902
8	0.776	0.603	0.790	0.024	0.873	0.405
9	0.792	0.082	0.789	0.064	0.868	0.529
10	0.787	0.140	0.791	0.071	0.863	0.576

**Table 3. Descriptive and Inferential Statistics for Demographic and Clinical Variables (n = 174)**

Variable	Category / Range	Frequency (%) or Mean $\pm$ SD	F-value	p-value
Age Groups	<50 years	124 (71.3%)	–	–
	$\geq$ 50 years	50 (28.7%)	–	–
Age (continuous)	–	32.6 $\pm$ 1.95	–	–
BC Awareness Score	Range: 11–22	46.52 $\pm$ 8.99	–	–
Risk Factors & Symptoms	Range: 5–7	46.30 $\pm$ 7.96	–	–
Histopathological Index	Range: 95–165	38.21 $\pm$ 35.60	–	–
Site of Biopsy	Left	90 (38.9%)	5.43	0.006
	Right	40 (36.7%)		
	Central	38 (30.8%)		
Lymph Node Involvement	Positive	48 (39.8%)	3.94	0.021
	Negative	102 (59.5%)		
Histological Grade	Grade 1	40 (30.9%)	4.76	0.009
	Grade 2	95 (38.8%)		
	Grade 3	39 (26.7%)		
Tumor Size	2–3 cm	62 (38.9%)	3.92	0.022
	3–4 cm	57 (36.7%)		
	4–5 cm	55 (24.4%)		

Detailed internal consistency metrics for individual questionnaire items assessing histopathological features, breast cancer awareness, and associated risk factors and symptoms are provided in Table 2. Notably, items within the Breast Cancer Awareness scale showed consistently high internal consistency (Cronbach's alpha ranged from 0.863 to

0.885). The item-total correlations were strongest for item 7 (0.902) and weakest for item 8 (0.405) within the BC Awareness measure, indicating variable contribution of items to the overall scale. Similarly, items measuring histopathological features and risk factors and symptoms displayed moderate to high internal consistency, with alpha values ranging between 0.776 and 0.797,

and item-total correlations varying from weak (0.018) to moderately strong (0.603). The comprehensive demographic and clinical characteristics of participants, along with inferential statistics, are summarized in Table 3. Most patients (71.3%) were younger than 50 years, with the mean age being  $32.6 \pm 1.95$  years. The breast cancer awareness score (mean =  $46.52 \pm 8.99$ ) and risk factors and symptoms awareness score (mean =  $46.30 \pm 7.96$ ) were indicative of moderate to poor levels of knowledge about the disease. The histopathological index yielded a mean score of  $38.21 \pm 35.60$ , highlighting considerable variability among participants.

In terms of biopsy locations, most biopsies were performed on the left breast (38.9%), followed by the right (36.7%), and central breast area (30.8%). The differences observed in biopsy locations were statistically significant ( $F = 5.43$ ,  $p = 0.006$ ). Regarding lymph node involvement, a greater proportion of patients showed negative lymph node status (59.5%) compared to positive involvement (39.8%), with significant differences noted between groups ( $F = 3.94$ ,  $p = 0.021$ ). The distribution of histological tumor grades revealed Grade II tumors as most prevalent (38.8%), followed by Grade I (30.9%) and Grade III (26.7%). The differences among histological grades were statistically significant ( $F = 4.76$ ,  $p = 0.009$ ). Furthermore, tumor sizes varied significantly ( $F = 3.92$ ,  $p = 0.022$ ), with the majority of tumors ranging between 2–3 cm (38.9%), followed by 3–4 cm (36.7%), and 4–5 cm (24.4%).

Overall, these results emphasize specific histopathological and demographic characteristics prevalent among breast cancer patients in the studied population, highlighting critical associations between clinical presentation and underlying awareness of the disease. The detailed data provided in Tables 1–3 reinforce the necessity for targeted awareness programs and further emphasize the relevance of specific histopathological factors in understanding breast cancer in Pakistani women.

## DISCUSSION

The findings of this retrospective study offer valuable insights into the histopathological landscape of breast cancer (BC) among Pakistani women, adding to a growing body of literature emphasizing the regional variability in disease presentation. The observed predominance of Grade II tumors and tumor sizes ranging between 2–3 cm is consistent with earlier research indicating that moderately differentiated tumors are commonly diagnosed in South Asian populations (6). This pattern underscores the necessity for early detection strategies, especially in regions where clinical presentation is often delayed due to limited access to healthcare and low public awareness. The high proportion of cases without lymph node involvement may reflect either early-stage disease or variability in nodal assessment methods, a point that warrants further exploration in future studies.

An unexpected yet noteworthy finding was the relatively young mean age of participants (32.6 years), which deviates from the global trend where BC predominantly affects postmenopausal women (1). This aligns with regional studies suggesting an earlier onset of BC in South Asian cohorts, possibly influenced by genetic, environmental, and lifestyle factors specific to these

populations (3). The high incidence in younger women may also be compounded by a lack of routine screening practices and cultural stigmas surrounding breast health in Pakistan, contributing to diagnostic delays. Interestingly, while a significant portion of participants were under 50 years of age, stratified frequency data revealed a parallel burden among older age groups, indicating a bimodal age distribution and underscoring the need for age-inclusive screening guidelines.

The correlation analysis revealed a significant positive association between awareness of BC and knowledge of its risk factors and symptoms. However, awareness was inversely related, albeit non-significantly, to histopathological severity. This suggests that despite some knowledge of BC among participants, it did not translate into timely clinical action or disease mitigation. Similar findings have been reported in studies from Indonesia and India, where knowledge gaps and healthcare-seeking behavior are poorly aligned (40). In this context, educational interventions must not only disseminate information but also foster behavior change, enabling women to act upon early signs and symptoms. The strong internal consistency of awareness-related questionnaire items (Cronbach's alpha > 0.86) reinforces the reliability of these measures and provides a robust platform for further psychosocial research in cancer literacy.

The significant associations found between histological grade, tumor size, biopsy site, and lymph node status highlight the continued clinical relevance of traditional histopathological markers in guiding prognosis and treatment. The higher prevalence of left-sided tumors is consistent with global epidemiological patterns, where the left breast is more frequently affected for reasons yet to be definitively elucidated, though theories related to breast volume, handedness, and anatomical differences have been posited (38). The dominance of Grade II histology and mid-sized tumors suggests that while some patients may be diagnosed at an operable stage, late detection remains a barrier to optimal outcomes. In the context of HER2 expression, while the study did not focus on molecular subtyping, future analyses incorporating hormone receptor status and triple-negative phenotypes could significantly deepen clinical interpretations and treatment stratification.

Despite these contributions, several limitations must be acknowledged. The retrospective nature of the study inherently limits causal inferences and may introduce selection bias due to its dependence on record completeness. Additionally, the use of a single-center cohort restricts the generalizability of findings to broader Pakistani or South Asian populations. The lack of longitudinal data, such as follow-up on survival outcomes or recurrence rates, precludes a more comprehensive prognostic evaluation. Another methodological limitation includes the reliance on pre-existing awareness assessments that may be subject to reporting bias or lack of temporal validity.

Nonetheless, the study's strengths lie in its real-world data application, its moderate sample size given regional constraints, and the integration of both clinical and psychosocial variables—an area often underexplored in regional BC research. By establishing statistically significant relationships between histopathological markers and patient variables such as age and

awareness, this study lays the groundwork for more targeted interventions. Future research should incorporate prospective multicenter studies with broader demographic representation and integrate molecular profiling for a more nuanced understanding of breast cancer subtypes in Pakistani women. Expanding educational outreach tailored to younger women and high-risk groups could also play a pivotal role in reducing BC morbidity through earlier presentation and treatment.

This study contributes meaningful evidence to the growing discourse on regional disparities in breast cancer presentation and pathology. The findings reinforce the critical need for comprehensive public health strategies that combine awareness, early detection, and individualized treatment approaches, especially in countries like Pakistan where resource constraints and sociocultural barriers persist. By linking demographic insights with histopathological patterns, this research supports the integration of clinical pathology with population-level interventions to improve BC outcomes.

## CONCLUSION

This retrospective analysis of histopathological findings in breast cancer among Pakistani women revealed that Grade II tumors, left-sided biopsy predominance, and mid-sized tumors (2–3 cm) were the most frequently observed features, with a significant portion of patients under the age of 50. Despite moderate awareness scores, knowledge gaps remained evident, particularly in relation to symptom recognition and early presentation. These findings underscore the urgent need for region-specific breast cancer education, early screening programs, and tailored therapeutic approaches. Clinically, the study highlights the continued relevance of traditional histopathological markers in guiding treatment strategies, while also emphasizing the necessity of integrating patient education into oncology care. From a research perspective, the results provide a foundation for future multicenter and longitudinal studies to explore molecular subtypes and survival outcomes, ultimately contributing to improved diagnostics and personalized care in resource-constrained healthcare settings.

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