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Original Research Article

Expression of E-Cadherin in Breast Carcinoma and Its Association with Tumor Grade and Nodal Status

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Abstract

Background: E-cadherin is a key cell adhesion molecule involved in maintaining epithelial integrity. Its loss has been implicated in tumor progression, invasion, and metastasis in breast carcinoma. Evaluating its expression may provide important prognostic information.

Aim: To assess the expression of E-cadherin in breast carcinoma and to determine its association with tumor grade and lymph node status.

Materials and Methods: Formalin-fixed paraffin-embedded tissue sections were subjected to immunohistochemistry for E-cadherin. Tumors were graded using the Nottingham grading system. E-cadherin expression was scored based on membranous staining and categorized as preserved or reduced/lost. The association with tumor grade and nodal status was analyzed using the Chi-square test.

Results: Out of 50 cases, 64% showed preserved E-cadherin expression, while 36% showed reduced/lost expression. Reduced expression was significantly associated with higher tumor grade ($p = 0.02$), with most Grade III tumors showing loss of expression. A significant correlation was also observed between reduced E-cadherin expression and lymph node metastasis ($p = 0.03$), with higher loss in node-positive cases.

Conclusion: Reduced E-cadherin expression is associated with higher tumor grade and nodal metastasis, indicating aggressive tumor behavior.

Keywords: E-Cadherin, Breast Carcinoma, Tumor Grade, Nodal Status.

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Introduction

Breast carcinoma remains the most common malignancy among women worldwide and is a leading cause of cancer-related morbidity and mortality. Its heterogeneous nature necessitates the identification of reliable prognostic biomarkers to better predict disease behavior and guide therapeutic strategies. Among various molecular markers, cell adhesion molecules such as E-cadherin have attracted significant attention due to their critical role in tumor progression and metastasis [1].

E-cadherin is a calcium-dependent transmembrane glycoprotein encoded by the CDH1 gene located on chromosome 16q22.1. It is essential for maintaining epithelial cell adhesion, tissue architecture, and polarity. Loss or dysfunction of E-cadherin disrupts intercellular cohesion and promotes epithelial–mesenchymal transition (EMT), a key mechanism facilitating tumor invasion and metastasis [2]. Thus, E-cadherin is widely regarded as a tumor suppressor protein in breast carcinoma. In breast cancer, E-cadherin expression varies across histological subtypes. Invasive lobular carcinoma typically shows complete loss of E-cadherin expression due to CDH1 gene alterations, whereas invasive ductal carcinoma generally retains its expression [3]. This distinction is diagnostically important and reflects underlying molecular differences between tumor types.

Furthermore, the association between E-cadherin expression and lymph node metastasis has been widely studied. Loss of E-cadherin expression facilitates tumor cell detachment and dissemination, thereby increasing metastatic potential. Several studies have demonstrated a significant correlation between reduced E-cadherin expression and positive nodal status, suggesting its

role as a predictive marker for metastasis [4]. Despite these findings, variability in E-cadherin expression across different grades and tumor subtypes necessitates further evaluation to establish its definitive prognostic value. Therefore, the present study aims to assess the expression of E-cadherin in breast carcinoma and to evaluate its association with tumor grade and nodal status. This may provide valuable insights into tumor biology and aid in improving prognostication and management strategies.

Material and Methods

Study Design and Setting: A hospital-based observational, cross-sectional study was conducted at a tertiary care teaching hospital in North India over a period of 12 months from March 2025 to February 2026. The study included 50 patients based on convenient sampling technique method diagnosed with breast carcinoma who underwent surgical resection (modified radical mastectomy/lumpectomy) during the study period. All specimens received in the histopathology laboratory were considered for inclusion.

Inclusion Criteria:

- Histopathologically confirmed cases of primary breast carcinoma
- Patients who underwent definitive surgical treatment
- Availability of adequate formalin-fixed, paraffin-embedded (FFPE) tissue blocks
- Complete clinicopathological data including tumor grade and lymph node status

Exclusion Criteria:

- Patients who received neoadjuvant chemotherapy or radiotherapy
- Recurrent breast carcinoma cases
- Inadequate or poorly preserved tissue samples
- Cases with incomplete clinical or histopathological data

Data Collection: Relevant clinical details including age, tumor size, laterality, and lymph node status were obtained from patient records and pathology requisition forms. Gross and microscopic findings were retrieved from histopathology reports.

Histopathological Examination: Tissue specimens were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Sections of 3–5 µm thickness were cut and stained with hematoxylin and eosin (H&E). Tumors were classified according to the WHO classification of breast tumors. Histological grading was performed using the Modified Bloom–Richardson grading system (Nottingham grading system), categorizing tumors into Grade I, II, and III.

Immunohistochemistry (IHC): Immunohistochemical staining for E-cadherin was performed on FFPE tissue sections using a standard streptavidin-biotin peroxidase method (or polymer-based detection system). Sections of 3–4 µm thickness were mounted on poly-L-lysine-coated slides.

- Antigen Retrieval: Performed using heat-induced epitope retrieval in citrate buffer (pH 6.0)
- Primary Antibody: Anti–E-cadherin monoclonal antibody (specify clone, manufacturer, dilution)
- Incubation: As per manufacturer's protocol
- Detection System: HRP-conjugated secondary antibody with DAB chromogen
- Counterstaining: Hematoxylin

Positive and negative controls were included with each batch of staining.

Evaluation of E-cadherin Expression: E-cadherin expression was assessed by evaluating membranous staining in tumor cells under light microscopy. Cytoplasmic staining, if present, was noted but not considered for scoring. Scoring was done based on the percentage and intensity of membranous staining:

- Score 0: No staining or <10% tumor cells stained (negative)
- Score 1+: Weak membranous staining in ≥10% cells
- Score 2+: Moderate membranous staining
- Score 3+: Strong membranous staining

For statistical analysis, cases were categorized as:

- Preserved expression: Score 2+ and 3+
- Reduced/lost expression: Score 0 and 1+

Assessment of Nodal Status: Axillary lymph nodes obtained from surgical specimens were examined histopathologically. Cases were categorized as node-positive or node-negative based on the presence or absence of metastatic tumor deposits.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using statistical software such as SPSS version 21. Descriptive statistics were used to summarize clinicopathological parameters. The association between E-cadherin expression and tumor grade as well as nodal status was analyzed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

Results

A total of 50 histopathologically confirmed cases of breast carcinoma were analyzed for E-cadherin expression and its association with tumor grade and nodal status.

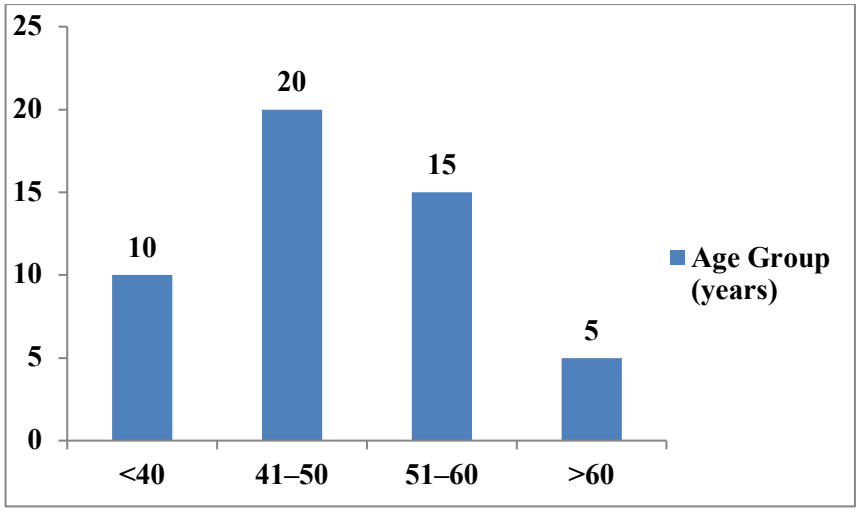

Figure 1: Bar diagram showing age-wise distribution of cases (n=50)

The age of patients ranged from 28 to 75 years, with a mean age of 51.2 ± 10.6 years. The majority of patients were in the 41–50 years age group.

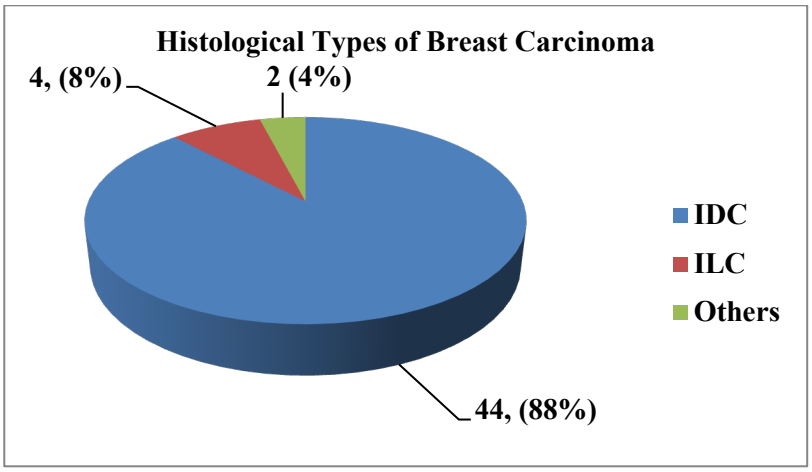

Figure 2: Pie chart showing histological types of breast carcinoma

IDC- Invasive Ductal carcinoma, **ILC-** Invasive Lobular Carcinoma

Others- Includes less common variants:

- Mucinous carcinoma
- Medullary carcinoma
- Tubular carcinoma
- Papillary carcinoma
- Metaplastic carcinoma

Invasive ductal carcinoma (IDC) was the most common histological subtype.

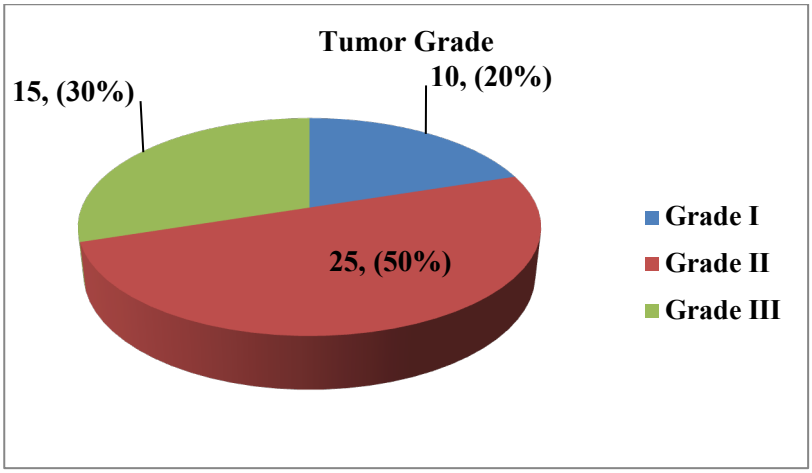

Figure 3: Pie chart showing distribution of tumor grade

Grade II tumors was the most common type of tumor grade.

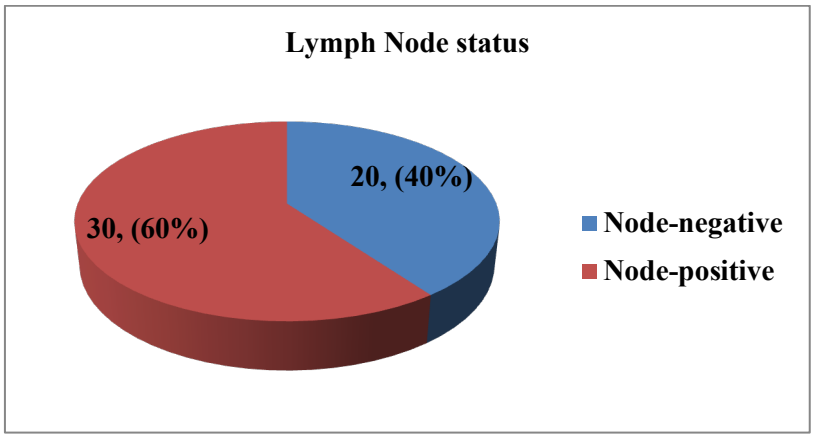

Figure 4: Pie chart showing Lymph node status

Higher proportion of node-positive cases was seen

Table 1: E-Cadherin Expression Pattern

Expression Status	Number of Cases	Percentage (%)
Preserved (2+/3+)	32	64%
Reduced/Lost (0/1+)	18	36%
Total	**50**	**100%**

Table 2: Association of E-Cadherin with Tumor Grade

Tumor Grade	Preserved	Reduced/Lost	Total
Grade I	9	1	10
Grade II	17	8	25
Grade III	6	9	15
Total	**32**	**18**	**50**

- Reduced/lost expression increased with higher tumor grade
- Statistically significant association (Chi-square test, p = 0.02)

Table 3: Association of E-Cadherin with Nodal Status

Nodal Status	Preserved	Reduced/Lost	Total
Node-negative	16	4	20
Node-positive	16	14	30
Total	**32**	**18**	**50**

- Reduced/lost expression was more common in node-positive cases
- Statistically significant association (Chi-square test, p = 0.03)

Table 4: E-Cadherin Expression in Different Histological Types

Histological Type	Preserved	Reduced/Lost	Total
IDC	31	13	44
ILC	1	3	4
Others	0	2	2
Total	**32**	**18**	**50**

- Majority of ILC cases showed loss of E-cadherin expression
- Invasive lobular carcinoma showed marked loss of E-cadherin expression

Summary of Results

- Majority of cases (64%) showed preserved E-cadherin expression
- Loss of E-cadherin was significantly associated with higher tumor grade
- Significant correlation between reduced E-cadherin expression and nodal metastasis

These findings indicate that reduced E-cadherin expression is associated with aggressive tumor behavior and metastatic potential in breast carcinoma.

Discussion

In our study, preserved E-cadherin expression was observed in 64% of cases, while 36% showed reduced or lost expression. This finding is consistent with recent studies demonstrating that E-cadherin expression is retained in a significant proportion of invasive ductal carcinomas but is frequently lost in certain subtypes, particularly invasive lobular carcinoma. Large pooled analyses have shown that reduced E-cadherin expression is strongly associated with lobular histology, supporting its role as a diagnostic and biological marker in breast cancer [3].

The present study demonstrated a statistically significant association between reduced E-cadherin expression and higher tumor grade ($p = 0.02$). A greater proportion of Grade III tumors exhibited loss of E-cadherin compared to Grade I and II tumors. This observation is in agreement with previous studies, which have reported that decreased E-cadherin expression correlates with poor differentiation and aggressive tumor behavior. A meta-analysis has shown that reduced E-cadherin expression is significantly associated with higher histological grade, advanced tumor stage, and increased tumor size [5,6]. These findings reinforce the concept that loss of cell adhesion contributes to tumor progression and dedifferentiation.

In the present study, a significant association was also observed between reduced E-cadherin expression and lymph node metastasis ($p = 0.03$). A higher proportion of node-positive cases demonstrated reduced or lost expression compared to node-negative cases.

This finding supports the role of E-cadherin in maintaining intercellular adhesion, where its loss facilitates tumor cell detachment and dissemination. Similar observations have been reported in recent studies, where reduced E-cadherin expression showed a positive correlation with lymph node involvement and metastatic potential [5,7].

Interestingly, a few recent studies have reported conflicting results, suggesting that increased or aberrant E-cadherin expression may also be associated with poor prognosis in certain contexts. For example, a study by Karsten et al. (2021) reported that higher E-cadherin expression was associated with unfavorable outcomes, indicating the complexity of its role in tumor biology [8]. This paradox may be explained by the dynamic regulation of E-cadherin during tumor progression and the involvement of additional molecular pathways. Furthermore, our study found that the majority of invasive lobular carcinoma cases showed loss of E-cadherin expression, which is in line with well-established literature. E-cadherin loss is considered a hallmark of lobular carcinoma due to CDH1 gene alterations, and it serves as an important diagnostic marker distinguishing it from ductal carcinoma [9].

Recommendations

1. **Incorporation of E-cadherin in Routine IHC Panels:** E-cadherin immuno- histochemistry should be considered as part of routine evaluation in breast carcinoma, especially for differentiating ductal and lobular subtypes and assessing tumor aggressiveness.
2. **Use as a Prognostic Marker:** Given its significant association with higher tumor grade and nodal metastasis, E-cadherin expression can be utilized as an adjunct prognostic marker to identify patients at higher risk of aggressive disease.
3. **Integration with Other Biomarkers:** Future studies and clinical practice should evaluate E-cadherin in combination with other markers such as ER, PR, HER2, and Ki-67 to develop a more comprehensive prognostic profile.

Limitations

1. **Small Sample Size & Single-Center Study:** The study included only 50 cases, which may limit the generalizability of the findings and being conducted at a single tertiary care center, the results may not represent the broader population.
2. **Exclusion of Molecular Correlation:** Molecular studies such as CDH1 gene mutation analysis were not performed, which could have provided deeper insights into E-cadherin alterations.
3. **Observer Variability in IHC Interpretation:** Semi-quantitative scoring of immunohistochemistry may introduce interobserver variability.

Conclusion

E-cadherin expression is significantly associated with tumor grade and nodal status in breast carcinoma. Reduced expression correlates with higher grade tumors and increased lymph node metastasis, indicating aggressive behavior. Thus, E-cadherin can serve as a useful prognostic marker and aid in assessing tumor progression and guiding clinical management strategies.

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