Original Article

Expression of E-Cadherin and its Association with Histological Prognostic Parameters of Breast Carcinoma

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ABSTRACT

Introduction: *Breast cancer stands as the foremost cause of morbidity and mortality among females globally, including Bangladesh. Metastasis development is a crucial prognostic factor in invasive breast cancer, often requiring systemic treatment. The aberrant expression of adhesion-related antigens on tumor cells strongly indicates the tumor's metastatic potential, leading to a poor prognosis for the patient. This study aimed to assess the expression of E-Cadherin and its association with histological prognostic parameters of breast carcinoma.* ***Methods and materials:*** *This cross-sectional study was conducted at the Department of Pathology, Dhaka Medical College, Dhaka, Bangladesh from March 2020 to February 2022. A total of 41 patients diagnosed with invasive breast carcinoma of no specific type were included in the study using convenient sampling. SPSS Version 23.0 was used for data analysis.* ***Results:*** *In this study, most patients exhibited E-Cadherin negativity, significantly associated with histological grading, increased tumor size (p = 0.024), more metastasized lymph nodes (p = 0.032), and triple-negative breast cancer (p = 0.011). Loss of E-Cadherin expression in both core needle biopsy and mastectomy samples showed a significant association with higher tumor grade (p*

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= 0.009 and 0.028, respectively). ***Conclusion:*** *Assessing E-Cadherin expression may be crucial in evaluating tumor aggressiveness and planning treatment modalities.*

Keywords: *E-Cadherin expression, Histological prognostic parameters, Breast carcinoma, Core biopsy, Mastectomy, Cancer*

INTRODUCTION

Breast cancer is a significant global health concern, constituting 11.6% of new cancer cases and 6.6% of cancer-related deaths worldwide in 2018 [1]. In Bangladesh, 19% of all cancer cases in females were attributed to breast cancer in 2020, with 6.2% of cancer deaths [2]. These figures may be underestimated due to factors such as lack of awareness, misconceptions, low education levels, poor socioeconomic status, limited healthcare access, and a lack of motivation for institutional treatment and management. In developing countries like Bangladesh, a higher proportion of premenopausal breast cancer cases may be attributed to the overall younger population and potential underreporting of cases in older women. Factors such as cultural barriers, reluctance to seek medical help, and lower treatment priority for older individuals could contribute to this pattern [2]. The incidence of breast cancer is on the rise by 0.5% annually in Bangladesh, driven by dietary changes and the adoption of Western lifestyles, including delayed pregnancies, less childbirth, and reduced breastfeeding [3]. Developing countries face a significant increase in breast cancer mortality, with approximately 62% of related deaths occurring in these regions in 2012 [4]. Tumor cell invasion and metastasis involve complex changes in adhesive interactions and intracellular signaling pathways, playing a crucial role in tumor development and progression. The search for effective biological markers for prognosis prediction and improved treatment strategies is ongoing [5]. E-cadherin, with its extracellular, transmembrane, and intracellular domains linked to the actin cytoskeleton, is essential for homotypic cell-cell adhesion, maintaining epithelial cell adhesion, and contributing to cell polarity, glandular differentiation, and cellular layering. E-cadherin plays a pivotal role in preserving the structural and functional integrity of epithelial tissue [6]. Loss of E-cadherin expression, documented in various studies, is linked to aggressive behavior [7,8]. As a recognized tumor suppressor protein, E-cadherin plays a critical role in preventing tumorigenesis; mutations or downregulation impair its function [9]. Reduced E-cadherin expression disrupts intercellular junctions, enabling epithelial cells to migrate and promoting tumorigenesis [10]. The diminished expression facilitates the disaggregation of tumor cells, contributing to local invasion or metastasis, and characterizing the invasive phenotype [11]. Multiple studies have associated the loss of E-cadherin expression with higher tumor grade, advanced stage, increased recurrence rates, and poorer prognosis [12,13]. For preoperative breast carcinoma diagnosis, core biopsy is preferred over fine-needle aspiration (FNA). The objective of this study was to assess the expression of E-Cadherin and its association with histological prognostic parameters of breast carcinoma in core needle biopsy (CNB) and corresponding mastectomy.

METHODS & MATERIALS

This was a cross-sectional study that was conducted at the Department of Pathology, Dhaka Medical College, Dhaka, Bangladesh from March 2020 to February 2022. A total of 41 patients with a histopathological diagnosis of invasive breast carcinoma of NST (no specific type) in core needle biopsy and corresponding mastectomy samples were enrolled, utilizing a convenient sampling technique. The study received approval from the hospital's ethical committee. In this study, written consent was obtained from participants. Exclusions comprised patients with invasive lobular carcinoma, other specific breast carcinoma types, and those subjected to neoadjuvant therapy. Samples were categorized as E-Cadherin positive or negative determined by a semi-quantitative method of scoring based on the percentage of tumor cell staining. 0-50% staining was negative for E- Cadherin expression, >50% staining was considered a positive expression [14]. The E-Cadherin expression in core biopsies and mastectomy tissue samples was compared, and its association with clinicopathological parameters was analyzed. Demographic and clinical data were recorded and analyzed using MS Office and SPSS 23.0, with significance set at $P < 0.05$.

RESULT

In this study, the age distribution revealed that 39.0% of patients were in the 41-50 age group. The mean age was 47.5±10.3 years, ranging from 29 to 70 years **[Table-I]**.

Table I: Age distribution of patients (N=41)

Age (Years)	n	%
≤30	2	4.9
31-40	10	24.4
41-50	16	39
51-60	10	24.4
61-70	3	7.3
Mean ±SD	47.5±10.3	
Age range	29-70	

Upon analyzing the distribution of study patients by sex, it was found that the majority (97.6%) were female, with only 2.4% being male **[Figure-1]**.

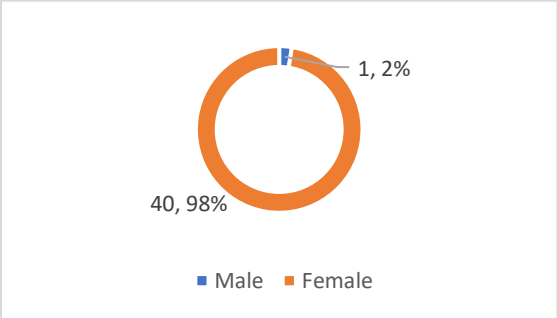

Figure 1: Distribution of participants by sex

According to the distribution of study patients based on E-Cadherin expression in mastectomy specimens, it was observed that more than one-third (36.6%) were E-Cadherin positive, while 63.4% were negative **[Figure 2]**.

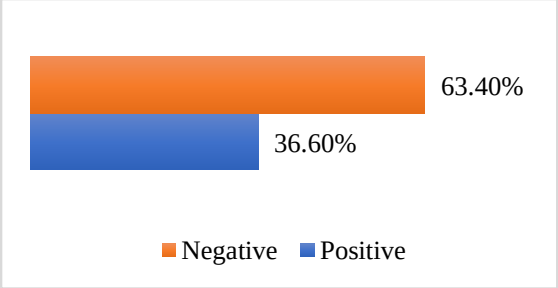

Figure 2: E-cadherin expression status

The study revealed a significant (p-value < 0.05) association between histological grade and E-Cadherin expression. The tendency of E-Cadherin loss or negative expression was higher in grade III, with 91.66% (11/12) showing negative expression. Among Grade II tumors, 46.15% (12/26) were positive, and 53.8% (14/26) were negative **[Table-II]**.

Table II: Association between histological grade and E-cadherin expression in a mastectomy specimen

Grade	Positive (n=15)		Negative (n=26)		p-value
	n	%	n	%	
Grade I	2	66.6	1	33.3	0.028[s]
Grade II	12	46.1	14	53.8	
Grade III	1	8.3	11	91.6	

s = significant, p-value reached from Chi-square test

A significant (p-value < 0.05) association was found between tumor size and E-Cadherin expression. E-Cadherin was mostly positive (66.7%) in tumors smaller than 2 cm. In the 2-5 cm size group, 50% were E-Cadherin positive and 50% were E-Cadherin negative. For tumors larger than 5 cm, E-Cadherin was mostly negative, with 87.5% (14/16) showing negative expression, and this association was significant **[Table-III]**.

Table III: Association between tumor size and E-cadherin expression

Tumor size-cm	Positive (n=15)		Negative (n=26)		p-value
	n	%	n	%	
<2	2	66.7	1	33.3	0.024[s]
2-5	11	50	11	50	
>5	2	12.5	14	87.5	

The association between the number of involved lymph nodes and E-cadherin expression between the number of occurrences (N) and positive/negative outcomes, along with corresponding p-values **[Table-IV]**.

Table IV: Association between the number of involved lymph nodes and E-cadherin expression

Number	Positive (n=15)		Negative (n=26)		p-value
	n	%	n	%	
0 (N0)	3	33.3	6	66.7	0.032[s]
1-3 (N1)	7	63.6	4	27.4	
4-9 (N2)	4	50	4	50	
≥10 (N3)	1	7.7	12	92.3	

The association between molecular subtype and E-cadherin expression revealed that the triple-negative subtype was significantly (p < 0.05) higher in the E-cadherin negative group **[Table-V]**.

Table V: Association between molecular subtype and E-cadherin expression

b t y	Positive	Negative	v a l

	(n=15)		(n=26)		
	n	%	n	%	
Luminal Type					
Present	10	41.7	14	58.3	a0.422ns
Absent	5	29.4	12	70.6	
HER-2-enriched					
Present	4	57.1	3	42.9	b0.158 ns
Absent	11	32.4	23	67.6	
Triple-negative					
Present	1	10	9	90	b0.011 s
Absent	14	45.2	17	54.8	

According to the distribution of the study patients based on E-Cadherin expression in core needle biopsy (CNB), it was observed that more than one-third (34.2%) of patients had E-cadherin positive expression, while 65.8% were negative **[Table-VI]**.

Table VI: Distribution of patients according to E-cadherin expression in CNB expression

Expression	n	%
Positive	14	34.2
Negative	27	65.8

Analyzing the association between histological grade and E-Cadherin expression in core needle biopsy, it was observed that E-Cadherin expression was negative in all Grade-III tumors (100%; 12/12), compared to 33.3% (1/3) in Grade-I and 53.8% (14/26) in Grade-II tumors **[Table-VII]**.

Table VII: Association between histological grade and E-cadherin expression in CNB sample

Grade	Positive (n=14)		Negative (n=27)		p-value
	n	%	n	%	
Grade I	2	66.7	1	33.3	0.009s
Grade II	12	46.2	14	53.8	
Grade III	0	0	12	100	

s = significant, p-value reached from the Chi-square test

Analyzing the association of E-Cadherin expression between core needle biopsy samples and mastectomy specimens, it was observed that among the 15 cases with positive E-Cadherin expression in mastectomy specimens, 14 cases were also positive in core needle biopsy, and 1 case was negative. Additionally, 26 cases with negative E-Cadherin expression in mastectomy specimens were also negative in core needle biopsy. This association was found to be significant **[Table-VIII]**.

Table VII: Association of E-cadherin expression between CNB sample and mastectomy specimen

Expression	Positive (n=15)		Negative (n=26)		p-value
	n	%	N	%	
Positive	14	100	0	0	0.001s
Negative	1	3.7	26	96.3	

DISCUSSION

This study aimed to assess the expression of E-Cadherin and its association with

histological prognostic parameters of breast carcinoma in the CNB sample and mastectomy specimen. In this study, 39.0% of patients were aged 41-50 years, with a mean age of 47.5±10.3 years (range: 29-70 years) [14]. Yang et al. observed a mean age of 49.30±10.48 years in breast cancer patients, ranging from 28 to 75 years, supporting our findings [14]. Nessa et al. reported a mean age of 46.24±7.45 years, with peaks at 41-50 years, consistent with our study [15]. Regarding gender distribution, 97.6% of patients were female, and 2.4% were male in our study, similar to the findings of Karakaya and Yilmaz, where 97.5% were female and 2.5% were male [16]. Suciu et al. also observed a female predominance [6]. In this study, 53.7% of patients had a tumor size of 2-5 cm, with a mean size of 5.54±3.6 cm (range: 1.5-15 cm) [14]. Yang et al. also found that 60.9% of patients had a breast mass size of 2-5 cm [14]. The risk of axillary lymph node metastasis increases with tumor size, making it an important prognostic factor [17]. Regarding tumor grade, our study observed that 63.4% of patients had grade II, followed by 29.3% with grade III and 7.3% with grade I, which is consistent with Yang et al., where 57.3% had grade II [14]. Similarly, Karakaya and Yilmaz found that 50.8% had grade II, followed by 30.8% with grade III and 16.7% with grade I [16]. In this study, 36.6% of patients had lymph vascular invasion, and 31.7% had 10 or more involved lymph nodes, with a mean of 4.58±5.6 [14]. These findings are comparable to Yang et al., who observed that 29.69% of patients had lymph vascular invasion [14]. The molecular subtype, primarily defined by ER and HER2 expression, serves as a significant prognostic factor [17]. In this study, 58.6% of patients were luminal type, 24.3% were triple negative, and 17.1% were HER-2 enriched [14]. These proportions differ from Yang et al.'s study, which found 69.1% luminal, 20.5% triple negative, and 10.4% HER-2 positive [14]. Karakaya and Yilmaz's study reported 85.9% luminal, 3.3% HER-2 overexpression subtype, and 10.8% triple-negative subtype [16]. In this study, 36.6% of patients had E-cadherin positive, and 63.4% had a negative expression, resembling Yang et al.'s findings of a 36.44% positive expression rate [14]. High-grade tumors, especially grade III, tended to E-Cadherin loss, with 91.7% negative expression in grade III, 53.8% negative in grade II, and 46.2% positive in grade II [18]. Yang et al. also reported a highly significant association (p-value < 0.001) between E-cadherin expression and histological grade [14]. Similar observations were also made among the CNB sample. In this study, tumor size >5cm significantly showed negative expression of E-cadherin, with 12.5% positive and 87.5% negative in this group which was similar to another study [19]. A significant (p-value <0.05) association was observed between the number of involved lymph nodes and E-cadherin expression. In this study, E-Cadherin was predominantly positive when the number of metastasized lymph nodes or involved lymph nodes was lower (in Group 1-3). Loss of E-Cadherin expression or negative expression was observed in a higher number of involved lymph nodes, with 92.3% (12/13) in the ≥10 group and 62.5% (5/8) in the 4-9 group. This finding aligns with Younis et al.'s study [20], which reported a significant association between strong E-Cadherin expression and node-negative cases, while node-positive cases predicted negative

expression of E-Cadherin (P = 0.026). In this study, a significant (p-value < 0.05) association was observed between triple-negative breast cancer and E-cadherin loss or negative expression. Margan et al.'s study demonstrated a different association, finding that the loss of E-cadherin was associated with Luminal A-type tumors [21]. In this study, increasing tumor size, a higher number of metastatic lymph nodes, and the presence of triple-negative breast cancers were significantly associated with the loss of E-Cadherin, indicating a poor prognosis. Moreover, there was a significant association between E-Cadherin expression in core needle biopsy and expression in mastectomy specimens.

LIMITATION OF THE STUDY

The study faced constraints due to a limited period. Additionally, being a cross-sectional observational study, it lacked the capacity for patient follow-up, preventing any commentary on long-term outcomes. Future research with an extended timeline and a prospective design could address these limitations, allowing for a more comprehensive understanding of patient outcomes over time.

CONCLUSION & RECOMMENDATION

In this study, loss of E-Cadherin expression was significantly associated with higher histological grade in both core biopsy and mastectomy samples. Factors such as increasing tumor size, a higher number of metastatic lymph nodes, and the presence of triple-negative breast cancers were also significantly associated with the loss of E-Cadherin, all indicating a poor prognosis for the patients. Moreover, E-Cadherin expression in core needle biopsy showed a significant association with E-Cadherin expression in mastectomy specimens. Therefore, evaluating E-Cadherin expression in both core biopsy and mastectomy samples may play a crucial role in planning the treatment modality for breast cancer patients.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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