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ORIGINAL ARTICLE

The Value of E-Cadherin and Hormonal Receptors in Histological Assessment of Ductal and Lobular Carcinoma

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ABSTRACT

Background: *E -cadherin is a key component of the adherens junctions that are integral in cell adhesion and maintaining epithelial phenotype of cells. Homophilic E-cadherin binding between cells is important in mediating contact inhibition of proliferation when cells reach confluence.*

Objective: *The object of this study is to asses the role of E- cadherin in differentiation of ductal and lobular breast carcinoma in tru' cut biopsy as diagnostic biomarker.*

Material and Method: *50 cases were in this study, who previously diagnosed with primary breast cancer by histopathological examination, collected from AL-Sadder Teaching Hospital (AL-Kufa Training Center) , from 1st of October 2022 to 1st of September 2023. The pathological specimens stained with monoclonal antibody of E-cadherin*

Result: *the percentage of total cases(50) were (90%) for invasive ductal carcinoma and (10%) for invasive lobular carcinoma, all ductal type express E-cadherin and nearly all lobular type were negative except one case. there were significant correlation with histopathological grade(p=0.01) and Histopathological subtype(p=0.001). no significant association with age(p=0.6) and Molecular subtype(p=0.8).*

Conclusion: *Loss of E-cadherin is a sensitive and relatively specific biomarker to confirm a diagnosis of ILC and its variants. A positive stain may not completely exclude the diagnosis ILC because E-cadherin expression may be retained in a minority of cases with characteristic ILC morphologic features. E-cadherin positivity obviously favors ductal differentiation in questionable cases.*

Keywords: *Breast cancer, core needle biopsy, E-cadherin, invasive ductal carcinoma(NST), invasive lobular carcinoma .*

1. INTRODUCTION

Epithelial cadherin (E-cadherin) is Cell adhesion molecules are a type of glycoprotein mediating cell-cell and cell-extracellular matrix adhesion, and they serve an important role in the genesis, development, invasion and metastasis of tumors (1). E-cadherin interacts with p120 catenin and beta-catenin through its cytoplasmic domain forming a core complex that connects the adherens junctions to the actin cytoskeleton and preserves junctional maintenance and dynamics (2). E-cadherin adhesions inhibit growth signals, which initiates a kinase cascade that excludes the transcription factor YAP from the nucleus (3). E-cadherin has been found to have a role in epithelial morphogenesis and branching, such as during the formation of epithelial buds. Physiologically, branching is an important feature that allows tissues, such as salivary glands and pancreatic buds, to maximize functional surface areas (4).

The heterogeneous expression of E-cadherin is observed either as wild type (strong membranous) expression or aberrant expression (cytoplasmic expression) (5). Catenins provide structural support as part of the adaptor complex that attaches the actin cytoskeleton to E-cadherin. With the presence of E-cadherin, structural β-catenin is prevented from participating in WNT ligand–mediated signaling (6). E-cadherin levels do not seem to be promising in terms of patients' survival rates assessment, however, there are some reports indicating that higher levels of E-cadherin were associated with shorter survival rates in patients with invasive breast carcinoma (6,7). Lowered E-cadherin expression is positively associated with lymph node metastasis (8).

2. METHODOLOGY

50 cases were in this study, who previously diagnosed with primary breast cancer by histopathological examination, collected from AL-Sadder Teaching Hospital (AL-Kufa Training Center) , from 1st of October 2022 to 1st of September 2023. For each case, was reviewed concerning on the immunohistochemical analysis including (estrogen receptor (ER), progesterone receptor (PR), Her2) already done and evaluate immunohistochemical staining of E- cadherin in these cases, age distribution, histological type, histological grade

Immunohistochemical staining evaluation:

The immunohistochemical evaluation was performed by using a light microscope under the 10X and 40X magnification power, And was performed for 50 patients with breast cancer to determine the expression levels of E-cadherin,E-cadherin scoring used a 4-point scale adapted from: negative = 0; weak and heterogeneous = 1+; mild or weak and homogeneous = 2+; moderate or strong and heterogeneous = 3+; intense or strong and homogeneous = 4+. The intensity of staining was scored from 0 – 3, where 0 = complete absence or negative; 1 = < 10% bright membrane expression; 2 = >10% but ≤ 50% membrane expression; and 3 = > 50% membrane expression (9). then divided into two group according to the expression: 1- Positive staining 46 cases 2- Negative staining 4 cases

Statistical analysis:

Data entry was done using Microsoft Excel 2019. Data was recorded into different quantitative and qualitative variables for the purpose of analysis. Statistical Package of Social Science software (SPSS, version 26) used to calculate Fisher's exact probability. Data was summarized using measures of frequency (mean), and graphs. The Fisher's exact and Chi square probability are considered statistically significant at P-value ≤ 0.05.

3. RESULTS

A total of 50 cases underwent IHC staining for E-cadherin. Out of 50 cases 46 cases (92%) were showing positive immunohistochemical staining for E-cadherin, while the remaining 4 cases(8%) showed negative staining, one of the lobular type expressed E-cadherin. The other confirmatory test is P120 cytoplasmic expression in lobular type. There is significant correlation between histopathological type and e cadherin expression(p=0.001) according to the proposed study in which 45(90%) cases of invasive ductal type and 5(10%) of invasive lobular type as illustrated in (**Table 1**). There is no significant association between E-cadherin and molecular subtype (P =0.8) (**Table 2**). According to the current study there is significant association between the grade and E cadherin expression(p=0.01) in which 47(94%) cases of grade II and 3(6%) cases of grade III as illustrated in (**Table 3**). In the proposed study there is no significant correlation between age and E-cadherin expression (p- value=0.609) in which 25(50%) cases less than 55years and 25(50%) cases equal or more than 55years old as illustrated in (**Table 4**).

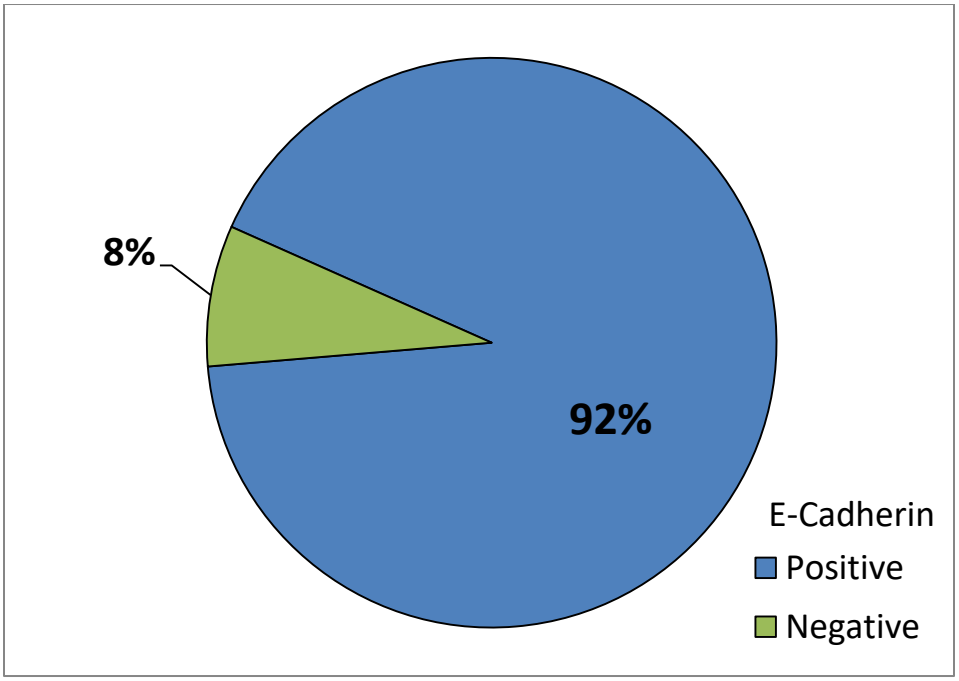

Figure 1. Patterns of immunohistochemical staining for E-cadherin of cases with breast carcinoma N=(50)

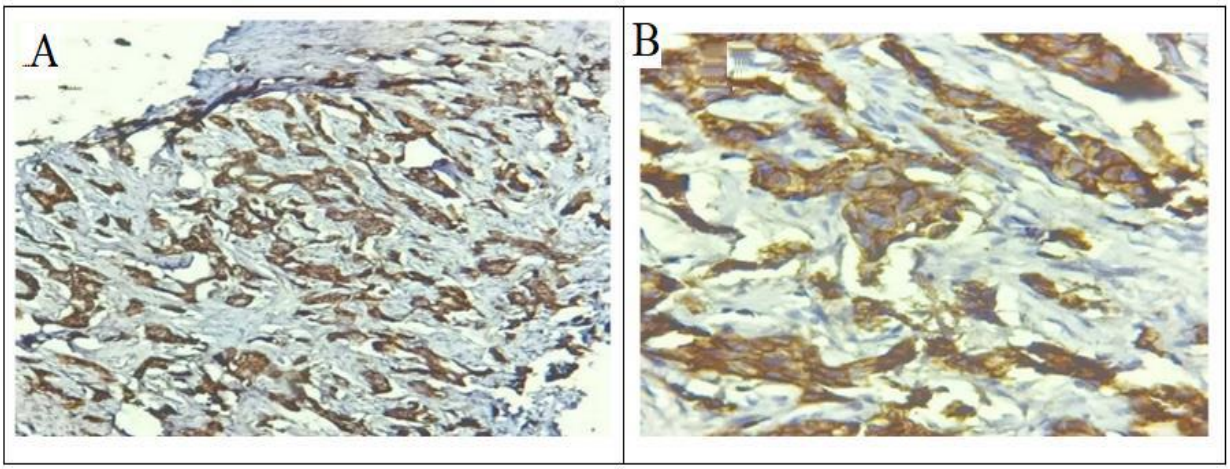

Figure 2. A- Low (10X) & B- High power view(40X) of E-cadherin show diffuse positive membranous staining of invasive ductal carcinoma

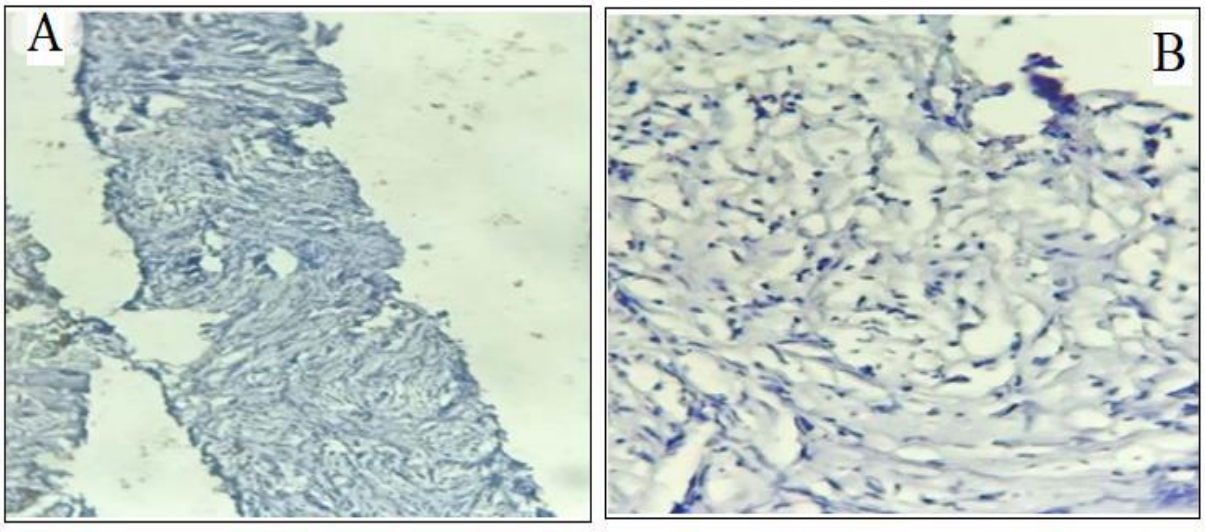

Figure 3. A- Low (10X) B- High power view (40X) of E-cadherin show negative staining of invasive lobular carcinoma.

Table 1. The correlation of E-cadherin and Histological type

Histological type	E-cadherin				Total
	Negative		Positive		
	No.	%	No.	%	
Invasive ductal carcinoma	0	0.0	45	100.0	45
Invasive lobular carcinoma	4	80.0	1	20.0	5
Total	4	8.0	46	92.0	50

P. value = 0.001

Table 2. The correlation of E-cadherin and molecular subtype

Molecular subtype	E-cadherin				Total
	Positive		Negative		
	No.	%	No.	%	
ER & PR (+), Her2 (–)	25	92.6	2	7.4	27
ER & PR (+), Her2 (+)	12	92.3	1	7.7	13
ER & PR (–), Her2 (+)	3	100.0	0	0.0	3
Triple negative	6	85.7	1	14.3	7
Total	46	92.0	3	8.0	50

P. value = 0.800

Table 3 The correlation of E-cadherin and histological grade

Grade	E-cadherin				Total
	Positive		Negative		
	No.	%	No.	%	
II	2	4.3	45	95.7	47
III	2	66.7	1	33.3	3
Total	4	8.0	46	92.0	50

P. value = 0.010

Table 4. The correlation of E-cadherin and age

Age (year)	E-cadherin				Total
	Positive		Negative		
	No.	%	No.	%	
< 55	24	96.0	1	4.0	25
≥ 55	22	88.0	3	12.0	25
Total	46	92.0	4	8.0	50

P. value = 0.609

4. DISCUSSION

In the current study, IDC comprising 45 cases from 50 cases (90%), While ILC composed 5 cases (10%), this agree with many researches. Gaber et al, (190) Found that the most common histological type determined microscopically was invasive ductal carcinoma (78.5%), followed by lobular carcinoma (19.6%) and mixed IDC and lobular carcinoma (1.9%). Alaa Edin et al,(10) found that E-cadherin was positive in 46/60 (76.7%) of IDC; 15/60 (25%) showed strong membranous staining. Dabbs et al,(11) found that Of 49 ILC specimens with the classic histopathologic pattern, 44 (90%) showed complete loss of E-cadherin, 5 (10%) of typical histopathological ILC specimens showed complete membrane staining in 100% of tumor cells . Dabbs et al,(11) found that Among breast cancers, nearly 90% of invasive lobular carcinomas display complete or partial loss of E-cad immunohistochemical expression that is considered an important (but not necessary) diagnostic feature for this histological subtype (12) .

Fulga et al,(13) found that Invasive lobular carcinomas have a different pattern of E-cadherin expression at primary and metastatic sites, which suggests a different role of E-cadherin in this form of cancer. Positive staining may not completely exclude the presence of lobular carcinoma because E-cadherin expression may be retained in a minority of cases with characteristic morphological features of lobular carcinoma. We consider that E-cadherin positivity favors ductal differentiation in ambiguous cases. In contrast, partial loss of E-cadherin expression in some poorly differentiated ductal carcinomas is not of diagnostic significance. Younis et al(14) show that there was no correlation between the E-cadherin and the parameters as ER-PR-Her2 (P=0.42),(P=0.1),(P=0.6) respectively, Ali et al.(15) found that There is statistically significant association was also found between E-cadherin and grade ($p < 0.05$). Mohammed et al (16). found there is no significant relation with the age ($P = 0.72$).

5. CONCLUSIONS

E-Cadherin is a useful bio marker to differentiate between IDC and ILC since all Lobular carcinomas were negative for E-Cadherin expression. However, since there was only one case of ILC express E- cadherin. Loss of E-cadherin is a sensitive and relatively specific biomarker to confirm a diagnosis of ILC and its variants. A positive stain may not completely exclude the diagnosis ILC because E-cadherin expression may be retained in a minority of cases with characteristic ILC morphologic features. E-cadherin positivity obviously favors ductal differentiation in questionable cases. The presented study showed that there is no significant association with age, molecular subtype except with histopathological grade, histopathological subtype there is significant association.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association , 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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