Correlation between Expression of E-cadherin and over-expression of Her2/neu in Breast Cancer in Sudanese Patients

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Abstract

Background: Breast cancer mortality is high in Sudan and most patients are detected at later stages of the disease due to the lack of awareness and absence of screening programs.

Objectives: The aim of this study is to assess the correlation between E-cadherin expression and over expression of her2/neu in breast cancer in Sudanese patients.

Materials and Methods: The study comprised 37 breast cancer patients admitted to histopathology department at Radiation and Isotope Center of Khartoum during the period 2013–2014. All patients were female Breast cancer patients ranged in age from 29 to 75 years with mean age of 42 years, thirty three cases (3) were invasive ductal carcinoma89.2%, two(2) cases were invasive lobular carcinomas5.4% , one case was medullary carcinoma2.7% and one case was metaplastic carcinoma 2.7%.

Representative sections from formalin-fixed paraffin embedded tissue blocks were taken from the 37 cases of breast cancer, and were stained for E-cadherin and her2/neu expression by

immunohistochemical technique. Stained sections were classified according to the intensity of staining and the percentage of cells showing E-cadherin and her2/neu staining.

Results: Immunohistochemical staining performed in the total number of 37 cases the result showed that positive staining of her2/neu in 2 cases 5.4% and negative staining in 35 cases 94.6% of the breast cancer cases and positive staining of E.cadherin in 32 cases 86.5% and negative staining in 5 cases 13.5%.

Conclusion: We found that E-cadherin expression has no correlation with expression of her2/neu status breast cancer.

Key words: E.cadherin, Breast Cancer, her2/neu, Sudan

Introduction

Breast cancer mortality is high in Sudan and most patients are detected at later stages of the disease due to the lack of awareness and absence of screening programs. [1] One of the main problems concerning breast cancer relates to the lack of patients awareness about the disease. Limitations in implementing breast self-examination and mammography screening programs are the other important issues. Overall survival and mortality due to this disease are influenced strongly by the stage of the disease at diagnosis. About 54% of the women are diagnosed in stage II, while only 16% are diagnosed in stage I. [2]

Her2 /neu is member of epidermal growth factor.[3] it is oncoprotein located in human chromosomes17 encoded a 185-kda transmembrane receptor with tyrosine kinase activity[4,5]over expression or amplification in breast cancer has become important factors in guiding management of patient with breast cancer and correlate with poor prognosis for patient with breast cancer[6].

E-cadherin is transmembrane glycoprotein[7] located in chromosome 16q22[8-9-10] that mediate epithelial cell to cell adhesion.[7-9])and help in glands formation an stratification and epithelial polarization [8-11] because loss of E-cadherin expression result in disruption of cellular clusters lead to metastases an invasiveness hence E-cadherin play important role in the suppression of invasion and metastasis[8-10-12].

The expression levels of E-cadherin and her2/neu play important role in Varity of physiological and pathological process in breast cancer.

In the present article we set out to correlate the expression of E-cadherin and over expression of her2/neu in Sudanese breast cancer patients.

Materials and Methods

The study comprised 37breast cancer cases registered in the histopathology department of Radiation and Isotope Center of Khartoum [RICK], during the period 2013–2014.

Haematoxylin and eosin stained sections from all the cases were reviewed by the authors to confirm the diagnosis and the different histopathological prognostic parameters as histological type, tumor grade, lymphatic vascular invasion, lymph nodes involvement, and extranodal extension. Pathology reports of the patients were reviewed to collect the data needed as tumor size, number of lymph nodes involved, and whether resection margins were involved by the tumor or not.

Representative sections from formalin-fixed paraffin embedded tissue were taken from the 37cases of breast cancer, and immunohistochemical stain of E-cadherin and her2/neu was performed.

IHC stain of E-cadherin and her2/neu:

The procedure was done as follows: two section [3mm]from formalin fixed paraffin embedded tissues were cut and mounted into salinized slides [fisher-band] following deparaffanization in xylene ,slide rehydration through graded series of alcohol and steamed for antigen retrieval for E-cadherin and Her2/neu using pt link slide . slides placed in coplin jars containing sodium citrate buffer[PH 9.0],then boiled at high temp for 10 minutes, then cool at RT.endogenouse peroxidase activity blocked with 3%hydrogen peroxidase and methanol for 10 minutes for two slides, then slides incubated with 100-200ml of primary antibodies for 10 minutes at room temperature for primary antibodies [E-cadherin in one slide and Her2/neu in second slides],and then rinsed in phosphate buffer saline for 3 minutes ,binding of antibodies detected by incubating for 20minutes with dextran labeled polymer[Dako-E.n vision TM Flex Kit],finally two sections washed in three change of PBS, followed by adding 3.3diaminobenzidine tetra hydro chloride [DAB][DAKO]as chromogen to product the characteristic brown stain for the visualization of antibodies enzyme complex for up to 5minutes ,slides counterstained with hematoxylin ,for each run of staining ,positive and negative control slides prepared "the positive control slides contain the under investigation and the negative of primary antibodies –each slides evaluated with investigators then the result confirmed by two consultant Histopathologists.

Statistical analysis

Gross tabulation was used during the statistical analysis and chi-square test was assessed to correlate between expression of E-cadherin and tumor grade, and her2/neu over expression.

Ethical clearance

Permission was taken from the ethical committee of the faculty of medical laboratory science- AL-Neelain University, Sudan to perform this work.

Results

The study was retrospective study performed at Histopathology department of radiation an isotope center of Khartoum [RICK] during the period from 2013 to 2014. 37 cases of breast cancer were

included in this study with mean age of 41 years old. Thirty three (33) cases were invasive ductal carcinoma 89.2%, 2 cases were invasive lobular carcinoma 5.4%, one case was medullary carcinoma2.7% and one case were metaplastic carcinoma 2.7%.Figure(1)

Immuostaining was performed on total number of 37 cases and the result showed that positive staining of her2/neu in 2cases 5.4%, and negative staining in 35 cases 94.6%. Also immuostaining was performed on total number of 37 cases for E-Cadherin and the result showed that positive staining of E-cadherin in 32 cases 86.5%, and negative staining in 5 cases 13.5%.

Relation between tumor type and E-cadherin expression had been done and the result showed P value of 0.701 which statistically not significant and there is no relationship between tumor type and E-cadherin expression (table1). Also relation between tumor type and her2/neu overexpression is done with P value is 0.256 which means no statistically significance is found and there is no relationship between tumor type and her2/neu expression (table 2).

Relation between E-cadherin expression and her2/neu overexpression is done and the result showed P value is 0.330 which is statistically not significant and there is no relation between E-cadherin expressions and her2/neu overexpression (Figure 2).
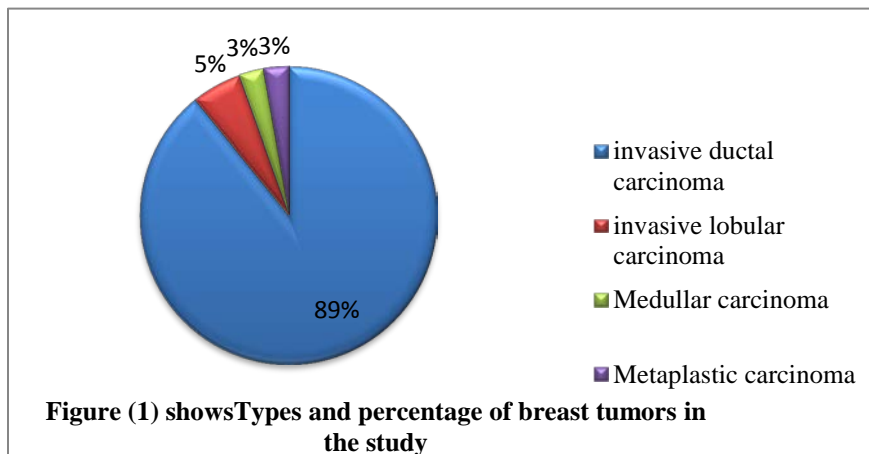

Figure (1) showsTypes and percentage of breast tumors in the study

Table 1: show the relation between tumor type an E-cadherin expression

Tumor type	E-Cadherin		
	+ve	-ve	Total
Metaplastic carcinoma	1 2.7%	0 .0%	1 2.7%
Invasive ductal carcinoma	28 75.7%	5 13.5%	33 89.2%
Invasive lobular carcinoma	2 5.4%	0 .0%	2 5.4%
Medullary carcinoma	1 2.7%	0 .0%	1 2.7%
Total	32 86.5%	5 13.5%	37 100.0%

Table [2] show the relation between her2/neu overexpression and

tumor type

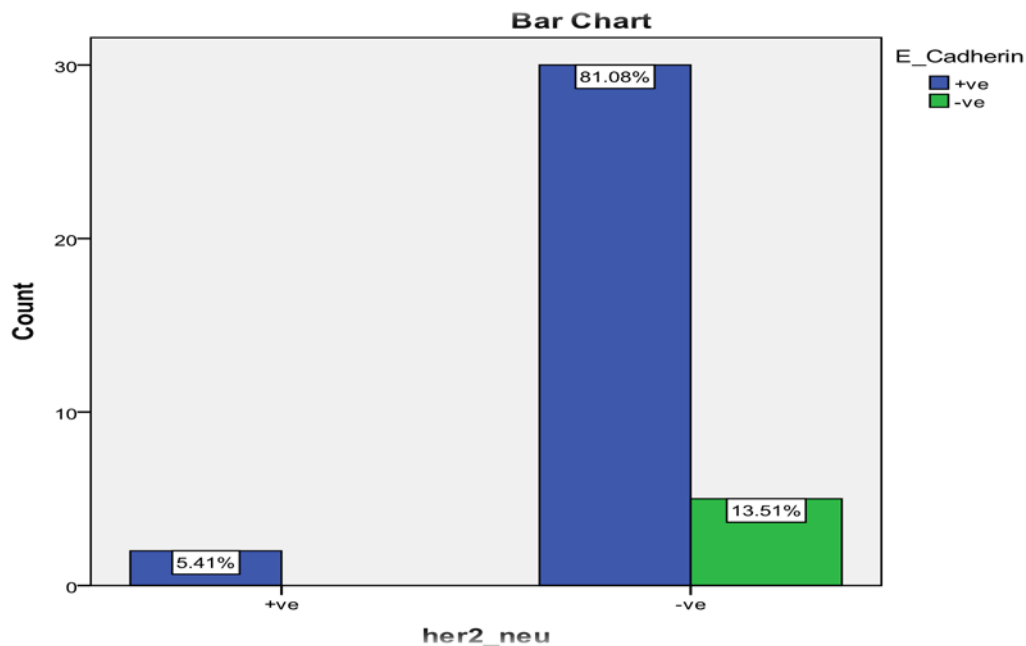| Tumor type	her2_neu		
	+ve	-ve	Total
Metaplastic carcinoma	0 .0%	1 2.7%	1 2.7%
Invasive ductal carcinoma	2 5.4%	31 83.8%	33 89.2%
Invasive lobular carcinoma	0 .0%	2 5.4%	2 5.4%
Medullary carcinoma	0 .0%	1 2.7%	1 2.7%
Total	2 5.4%	35 94.6%	37 100.0%

Figure 2: The relation between E-cadherin expressions and her2/neu overexpression.

Discussion

The human epithelial growth factor receptor 2 (HER2) is one of the main mediators of key pathways involved in breast carcinogenesis, invasive behavior and cell growth. Many important signal pathways such as the PI3K pathway, AKT and Rac1/ERK pathway, and RAF (RAF)/ MEK/ERK-signaling all consists of major effectors of the HER2 activity[13]. E-cadherin has a critical role in epithelial cell adhesion, in invasive breast cancer, reduction or loss of E-cadherin expression might correlate with lymph node metastases. It has lower expression in lymph node metastasis in diverse tumors, particularly in invasive breast cancer tissue specimens [14]. Dissimilarities in E-cadherin expressions in ductal and lobular breast carcinomas have been reported by Berx et al. and Acs et al [15, 16]. However, some studies reported that E-cadherin expression was not correlated with lymph node involvement and tumor grad in breast cancer patients (17, 18).

In the current study Our results showed that there is no significant correlation between E-cadherin expressions and her2/neu over expression ,which is consistent with the finding by Mohammadizadeh F1 et al[19] , which their study indicated that There is no association between co-expression of E-cadherin/ER, E-cadherin/PR, E-cadherin/Her-2neu, and E-cadherin/p53 and Her-2neu/p53 on one hand and Ki67 status and tumor grade. And interestingly this finding also support the previous reported finding by Abdalrhman, *et al* [18] which they reported no correlation between E-Cadherin and other markers and grade in Sudanese breast cancer.

To our knowledge this is the first study to be done in Sudanese patients to correlate E-cadherin and her2/neu over expression, and as Sudanese population are diverse and heterogeneous genetically and cultural, and cancer research in Sudan still in its infancy, and due to lack of cancer registry all these factors mad this findings is still limited and need for further studies and confirmations.

Conclusion

According to these finding we conclude that there is no correlation between expressions of E-cadherin and her2/neu in Sudanese breast cancer.

Acknowledgements

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