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## *Full Length Research Article*

# CORRELATION BETWEEN HER2\neu, ER&PR STATUS AND HISTOLOGICAL STAGE IN BREAST CANCER

**[1*]Riyadh Hamed, [2]Ahmed Abdelbadie, [3]Ihsan Osman and [4]HusamEldein Omer**

[1]Buraydah Private College, KSA
[2]Alribat National University, Sudan
[3]Alzaiem Alazhari University, Sudan
[4]Jazan University, KSA

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**ABSTRACT**

**Background:** The aim of this study is to understand the HERR-2/neu over expression and its correlation with ER&PR status and histological stage in breast cancer.
A total of 328 women were selected retrospectively from this group the tissue samples of breast cancer had been analyzed using immunohistochemical techniques for HERR-2/neu over expression and ER&PR status**.**
**Objective:** To evaluate the expression of tumor markers (HER2/neu) with ER&PR status and histological stage in breast cancer**.**
**Results:** The correlation between HER-2/neu overexpression and ER&PR status in stage I – III B breast cancer. HER-2/neu–ve and ER +ve cases are (81%), whereas HER-2/neu+ve and ER +ve cases are (19%). While HER-2/neu–ve and ER –ve cases are (72%), compared to HER-2/neu+ve and ER –ve which are (28%). HER-2/neu–ve and PR +ve cases are 87 (84%), whereas HER-2/neu+ve and PR +ve cases are 17 (16%). Whereas HER-2/neu–ve and PR –ve cases are 132 (62%), and HER-2/neu+ve and PR –ve are 42 (38%). The correlation between HER-2/neu overexpression and ER&PR status in stage IV breast cancer. HER-2/neu–ve and ER +ve cases are (100%), whereas HER-2/neu+ve and ER +ve cases are (0%). Whereas, HER-2/neu–ve and ER –ve cases are (50%), and HER-2/neu+ve and ER –ve which are (50%). HER-2/neu–ve and PR +ve cases are (0%), whiles HER-2/neu+ve and PR+ve cases are (100%). Whereas HER-2/neu–ve and PR –ve cases are (60%), and HER-2/neu+ve and PR –ve are (40%). The correlation between HER-2/neu overexpression and ER&PR status in stage I – IV breast cancer. HER-2/neu–ve and ER+ve cases are (82%), while HER-2/neu+ve and ER +ve cases are (18%). Whereas, HER-2/neu–ve and ER–ve cases are (69%), and HER-2/neu+ve and ER–ve which are (31%). HER-2/neu–ve and PR +ve cases are (82%) and HER-2/neu+ve and PR +ve cases are (18%). Whereas, HER-2/neu–ve and PR –ve cases are (74%), and HER-2/neu+ve and PR –ve are (26%).
**Conclusion:** In this study population, the HER-2/neu expression its relation with ER&PR status and histological stage in breast cancer determined.



## INTRODUCTION

The American cancer society estimates that about 30% of Americans will get cancer at some point during their lives and about 40% of those in whom cancer is diagnosed will be alive five year later. Currently in the United States, one death in five is from cancer.

***Corresponding author: Riyadh Hamed***
*Buraydah Private College, KSA*

Breast cancer is the most frequently diagnosed cancer among women in the United States and is the second leading cause of cancer deaths among women today (American Cancer Society). Although breast cancer continues to be a leading cause of cancer morbidity and mortality today, the death rates have drastically decreased due to earlier detection and more effective treatment methods (Connor *et al*., 2002). Breast cancer is the commonest cancer in women in the world; it is rising at, a rate of approximately 2% per year in all population (Parkin *et al*., 1992). The number of annual deaths from breast

cancer has remained about the same for the past 50 years, although the number of cases is increasing. This shows the benefits of early detection, which impacts survival. Also, effective treatment is increasing survival in all breast cancer patients. One in nine women will get breast cancer in the U.S.A. during their lifetimes. In the U.K, cancer accounts for about 25% of all deaths. Only ischemic heart disease exerts a greater tool (MacSween and Whaley, 1992). The cancers have types; the most common one is a carcinoma which constitutes about 85% of cancer. According to data from UK at 2001 the breast cancer is most common (29% of all cancers) (Souhami *et al*., 2001). Estrogen Receptor (ER), Progesterone Receptor (PR) and human epidermal growth factor receptor 2 (Her-2\neu) expressions are crucially important in the biology of breast carcinoma, and yet the expression of these have not been studied in breast carcinoma in Jordan (Abalkhail *et al*., 2003). It is known that ER and PR expression are the only predictive factors with proven usefulness in selecting patients who are likely to respond to adjuvant endocrine therapy. Patients lacking these receptors tend to have shorter disease free survival and earlier recurrences than those expressing these receptors (Allred *et al*., 1998).

Clinical diagnosis for breast cancer means the variety of symptoms that can be detected. Unfortunately, the early stages of breast cancer may not have any symptoms (Kufe *et al*., 2003). Depending on the results of the mammograms and/or ultrasounds, doctor may recommend that a biopsy has to be taken. Biopsy allows cells to be examined under a microscope and it the only way to confirm cancer (Chaney *et al*., 2000). Physicians often examine hormone receptors in breast cancer cells at the time of biopsy or breast surgery to determine whether Estrogen Receptors (ER) or Progesterone Receptors (PR) is present. Patients whose cancers have ER or PR tend to have a better prognosis than patients whose cancers do not have these receptors. Cancers with ER or PR positive are also much more likely to respond to chemotherapy or hormone treatment (Devita *et al*., 2001). Breast cancer cell that express ER in their nuclei also tend to respond better to hormonal manipulation. For example, the drug tamoxifen is used to block the female hormone estrogen from estrogen receptors, thus slowing the growth and reproduction of cancerous cells. Researchers know less about PR-positive but have noticed that cells that contain ER-positive receptors often contain PR-positive receptors too. If a cell contains a PR positive receptors but no ER positive receptors a patient's prognosis may be worsens (Hartmann *et al*., 1994). Since breast cancer is one of the hormone dependent tumors much attention has been paid to the relationship between ER and PR and breast cancer (sugano *et al*., 1994).

## MATERIALS AND METHODS

This is a descriptive study to evaluate the tumor marker (ER-PR- and HER-2/neu) expression in malignant breast palpable lumps. 328 females, were eligible for analysis.

### Sample collection

428 sections (328 cancer patients and 100 patients used as control), taken from patients with breast palpable lumps. For histopathology and immunohistochemistry biopsies collected from patients.

### Sample Processing

### For Histopathology

Biopsies will be collected form tissues, and stained in hematoxylin and eosin.

### For immunohischemistry

Sections were cut at 3-5 µm thicknesses, mounted onto silanized slides and left to dry overnight at 37°C. Sections were then deparaffinized and rehydrated. Antigen retrieval was achieved by heat retrieval using a bench autoclave. Briefly, slides were placed in Coplin jars containing enough 0.01 M sodium citrate solution (pH 6.0) to cover the sections, then autoclaved at 121°C for 10 minutes for Her-2 (water path 95°C for 30 min). Slides were incubated with Peroxidase blocking reagent for 10min followed by protein blocking reagent for 10min, then rinsed in PBS Slides were incubated with 100-200 µl of primary antibodies for 30 minutes at room temperature in a moisture chamber, then rinsed in PBS. The dilution of the primary antibodies against Her-2/neu (Dako, Carpintera, Ca, USA) 1:50. After washing, binding of antibodies was detected by incubation for 10 minutes with biotinylated goat anti-mouse antibody ready to use (LSAB2) from Dako; the slides were then rinsed with PBS. Sections were then incubated with streptavidin-horse radish peroxidase for 10 minutes. Finally, the sections were washed in 4 times in 4 minute changes of PBS, followed by adding 3, 3 diaminobenzidine tetra hydrochloride (Biogenex) as a chromogen to produce the characteristic brown stain.

For each run of staining, a positive and negative control slide were also Prepared. The positive control slides were prepared from breast carcinoma known to be positive for the antigen under study. The negative control slides were prepared from the same tissue block, but incubated with PBS instead of the primary antibody. Her-2/neu was scored on a 0 to 3 scale according to the criteria set by Dako. The staining was scored as: negative (0) when no membrane staining was observed, or when membranous staining was observed in less than 10% of the tumor cells; weak positive (1+) if weak focal membrane staining was seen in more than 10% of the tumor cells; intermediate (2+) if weak to moderate, complete membrane staining was seen in more than 10% of the tumor cells; and strongly positive (3+) if intense membrane staining with weak to moderate cytoplasmic reactivity was seen in more than 10% of the tumor cells. In the final analysis, however, scores 0 and 1 were considered negative; score 2 was considered weakly positive; and score 3 was considered strongly positive. Only score 3 cases were considered as Her-2 overexpressing cases.

## RESULTS

The correlation between HER-2/neu overexpression and ER&PR status in stage I – III B breast cancer. HER-2/neu–ve and ER +ve cases are 145 (81%), whereas HER-2/neu+ve and ER+ve cases are 33 (19%). While HER-2/neu–ve and ER –ve cases are 72 (72%), compared to HER-2/neu+ve and ER –ve which are 28 (28%). There is no statistically significant difference between these groups (chi square equal to 3.38).HER-2/neu–ve and PR +ve cases are 87 (84%), whereas HER-2/neu+ve and PR +ve cases are 17 (16%). Whereas

HER-2/neu negative and PR –ve cases are 132 (62%), and HER-2/neu+ve and PR –ve are 42 (38%). There is no statistically significant difference between these groups (chi square equal to 2.65). The correlation between HER-2/neu overexpression and ER&PR status in stage IV breast cancer. HER-2/neu–ve and ER +ve cases are 8 (100%), whereas HER-2/neu+ve and ER +ve cases are 0 (0%). Whereas, HER-2/neu–ve and ER –ve cases are 8 (50%), and HER-2/neu+ve and ER –ve which are 8 (50%). There is statistically significant difference between these groups (chi square equal to 6.02).HER-2/neu–ve and PR +ve cases are 0 (0%), whiles HER-2/neu+ve and PR +ve cases are 2 (100%). Whereas HER-2/neu–ve and PR –ve cases are 13 (60%), and HER-2/neu+ve and PR –ve are 9 (40%). There is no statistically significant difference between these groups (chi square equal to 2.65).

The correlation between HER-2/neu overexpression and ER&PR status in stage I – IV breast cancer. HER-2/neu–ve and ER +ve cases are 153 (82%), while HER-2/neu+ve and ER +ve cases are 33 (18%). Whereas, HER-2/neu–ve and ER –ve cases are 80 (69%), and HER-2/neu+ve and ER –ve which are 36 (31%). There is statistically significant difference between these groups (chi square equal to 8.75). HER-2/neu–ve and PR +ve cases are 87 (82%) and HER-2/neu+ve and PR +ve cases are 19 (18%). Whereas, HER-2/neu–ve and PR –ve cases are 145 (74%), and HER-2/neu+ve and PR –ve are 51 (26%). There is statistically significant difference between these groups (chi square equal to 4.04).

## DISCUSSION

This study confirmed correlation between the HER2/neu expression, ER and PR status and histological stage in breast cancer. Their findings will provide us with greater insight into breast cancer an etiology and will help us identify any association that would help discriminate subgroups of HER2/neu expression, ER&PR status and histological stage in breast cancer.

### Conclusion and Recommendation

Their findings will provide us with greater insight into breast cancer an etiology and will help us identify any association that would help discriminate subgroups of HER-2/neu over expression, ER&PR status and histological stage in breast cancer. Further innovative studies with larger sample sizes are needed to examine how the status of this potentially modifiable HER-2/neu over expression, ER and PR status and histological stage in breast cancer. Lastly, we recommend further studies in this field with wider scope.

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