

## Prevalence of hormonal receptors ER, PR and HER-2 NEW in breast cancer cases in Palestine

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### Abstract

Although, breast cancer is the most common malignancy affecting Palestinian women, little is known about their biological characteristics. The treatment of breast cancer requires the evaluation of ER, PR and Her 2/neu receptor status that were correlated with disease free survival and overall survival. An ethnic variation of these receptors is well documented.

**Purpose:** The aim of this study is to determine the prevalence of ER, PR and Her 2/neu receptor among Palestinian women with breast cancer at Augusta-Victoria Hospital Cancer Care Center.

**Patients and Methods:** A retrospective analysis was performed on 167 cases of breast cancer diagnosed or referred for treatment at Augusta-Victoria Hospital Cancer Care Center in the period between January, 2003 and January 2008. Standard immunohistochemical stains were used for evaluation of ER, PR and Her 2/neu receptor and FISH testing for Her 2/neu receptor in patients with plus 2 on immunohistochemistry.

**Results:** Of these 167 cases, 106(63%) ductal carcinoma of variable histologic grades, 78(52.7%) of which were ER positive, 70(47.2%) were PR positive and 27(16.1%) were Her 2/neu receptor positive. Seven (4.19%) of all cases were lobular carcinomas, four of which were ER positive and four were PR positive and 6 were Her 2/neu receptor negative. 27(16.1%) of all study population were Her 2/neu receptor positive and 21(12.5%) of all cases were triple negative.

**Conclusion:** The prevalence of hormonal receptors positivity in Palestinian women is lower than the western countries and close to the Jordanian and Egyptian women. The Her-2/neu receptor positivity and triple negativity in our study sample are similar to other populations.

### Introduction

Breast cancer is the most common cancer in women in Palestine. Axillary lymph node status, hormonal receptors (HR) and HER-2/neu receptor expression are significant prognostic factors for early breast cancer. The tumor is highly heterogeneous with a wide range of biological, pathological and clinical characteristics, which have a large influence on outcome. It has been well documented that estrogen has a crucial role in the development of breast cancer and ER are the most important therapeutic target (1). Beatson (1896) discovered this over a 100 year ago, when he demonstrated response in premenopausal lady after an oophorectomy. The

role of hormonal receptors as prognostic and therapeutic tools has a widespread acceptance in the management of breast cancer. ER expression is thought to be of great importance, predicting a response to hormonal therapy in a 50-70% of patients (3, 4). Her-2/neu gene amplification associated with a poor prognosis and this is firstly determined in 1987 by Salmon et al paper (5) that showed the correlation between gene amplification and disease free survival and overall survival. Also it can be a very important therapeutic target to Herceptin therapy in metastatic and adjuvant settings.(6,7) The aim of this study is to determine the prevalence of ER, PR, Her-2/neu receptor among Palestinian women with breast cancer and to compare them with those in the literature in other population.

### Materials and methods

The medical records of the patients diagnosed and managed at Augusta-Victoria Hospital Cancer Care Center or referred to our cancer center from all over the country for radiotherapy treatment, as we are the only center having this facility, between 2003-2008 were retrospectively reviewed. Numbers of patients with primary or recurrent breast infiltrative ductal and lobular carcinoma were studied. The pathology reports were reviewed for patient age, histologic type, nuclear grade, hormonal receptor and Her-2 neu receptor status. The studied cases were received either fresh as surgical specimens or paraffin embedded blocks. Surgical specimens were mastectomies, lumpectomies, trucut biopsies, excisional biopsies and chest wall skin biopsies. The surgical specimens were processed for routine hematoxyline and eosin staining. Breast carcinomas were classified according to WHO classification of breast tumors and graded using modified Bloom Richardson grading system.(8) There were 106(63%) ductal, 7 (4.19%)lobular, 6 (3.59%) mixed and 7 (4.19%) isolated DCIS, 21 (12%) were either ductal or lobular with DCIS component and 27 (16.1%) cases were unknown. 27 (16.1%)were grade I-II and 54 (32.3%) were grade III and IV, while 92 (55%) were with unknown nuclear grade. Hormonal receptors and Her-2/ neu receptor status were determined using immunohistochemistry for ER, PR, Her-2/neu receptor and FISH for unequivocal her-2 neu receptor (+2).All procedures were performed manually and according to manufacture's guidelines. The primary antibodies used were obtained from Zymed Company, all and appropriate positive controls were included for each immunohistochemical staining. Immunoreactivity was assessed by one pathologist by estimating the percentage of positively stained nuclei for ER and PR and the membranous staining for Her-2/ neu receptor. Cases with complete membranous

staining in more than 10% of the cells were considered +3, those with moderate focal staining in more than 10% of the cells were considered +2 and those with no or faint incomplete membranous staining were considered negative (0 or +1). Evaluation of Her-2/ neu receptor by FISH was undertaken in equivocal cases with +2 staining, using commercially available tests. (monoclonal antibody TAB 250,Zymed company).

## Results

A total of 167 cases were studied. Of those 106 (63%) were ductal, 7 (4.19%) were lobular, 6 (3.59%) were mixed and 7(4.19%) were isolated DCIS, 21(12%) were ductal or lobular with DCIS component and 27 (16.7%) cases were unknown. Figure 1. Patients age ranged between 22 and 71years. 71 patients were 50 years or below. The ductal carcinomas were of variable grade. 2 (1.88%) were grade I, 24 (22.6%) were grade II and 51(48%) were grade III. 78(52.7%) patients were ER positive, 70(47.2%) were PR positive and 27(16.1%) of the total patients studied were Her-2 /neu receptor positive and 14 were +2 and not obtained on them FISH testing, 5 of which were negative for both ER,PR, 17 were unknown, two of which were negative for both ER,PR, all of them were in 2003, in which time Her-2/neu receptor testing were unavailable, that might affect the prevalence of triple negative breast cancers.31(43.6%) patients 50 years or below were ER positive and 31(43.6%) were PR positive. Patients more than 50 years, 48(61.5%) of them ER positive and 39(48.7%) were PR positive. 148 (88.6%) were positive for both ER and PR, 17 (1.0%) were ER+PR-, 9 (0.48%) were ER-PR+, 25(1.5%) were negative for ER, PR receptors and 21(12.5%) were triple negative. There were two ductal carcinoma grade I, one of them with unknown receptor status and the other one was positive for both ER and PR and the other was positive for Her-2/ neu. 18 of the grade II were positive for either ER or PR and none of them was positive for Her-2/ neu and all 3 cases of grade II were negative for both ER and PR. 31 of grade III were positive for either ER or PR, three of them were Her-2/ neu receptor positive+3 and four were +2 by immunohistochemistry.

## Discussion

The survival of women with breast cancer varies with racial background and geographical location. Hormonal receptor status and tumor responsiveness to hormonal therapy is of paramount in the patient's survival. Most of the studies evaluating hormonal receptor status were conducted in the west. (9, 10, 11, 12). The aim of this study is to evaluate hormonal receptor status and Her-2/ neu receptor status in patients with primary or recurrent breast carcinoma in Palestine, who were referred to Augusta-Victoria Hospital Cancer Care Center between January 2003 and January 2008. Numerous studies have demonstrated differences in hormonal receptor status and histology by race and ethnicity among women in the western countries. In a study done in the US in women with breast cancer 63.9% of white Americans were ER+PR+, 19.8% were ER-,PR-,12.8% were ER+,PR- and 3.6% were ER-,PR+, while among black women 48.3% were ER+PR+,34.8% were ER-PR-,11.8% were ER+PR- and 5% were ER-PR+.(14) In Austria ER+ positive in 80.6% and PR+ in 61.3% of primary breast cancer patients.(15) In a study done in Nigerian women with primary breast carcinoma, 24% were positive for ER and 13.9% were positive for PR.(18) Limited data are available in Arab countries. In a study done in Jordan by Almasri et al, which included 91 cases of breast cancer patients showed a 53% ER positive tumors, which is strongly correlated with the patient's age (30) and in another study done also in Jordan by Maher A Sughayer et al from King Hussien Cancer Center ,which included 267

patients, showed 50.8% ER positive and 57.5% PR positive tumors. Both studies showed lower prevalence of hormonal receptors in Jordanian women than that of western population.(31) In a study done on 88 Iraqi women with locally advanced or metastatic breast carcinoma, 34.2% were ER+PR+ and 43.8% were ER-PR-.(19) In a study done in Lebanon, 43% of cases showed positivity for ER and PR.(20) In Saudi females, one study showed 33.3% positivity and 52.4% negativity for both hormonal receptors.(21) Regarding lobular carcinomas, a study done on American females showed 92.7% of the tumors were positive for ER and 67.4% were positive for PR. In this study, 7 of the tumors were positive for either ER or PR and 4 of them were negative for ER, PR and Her-2/neu receptor was negative in 9 tumor specimens. (23) In different studies done in several Arab countries, Her-2/ neu gene was found to be amplified in 20-25% of primary breast carcinoma cases, 25% in Tunisia (6) 40% in Egypt (27) and 65% in Lebanon(20). In this study, Her-2/neu gene was amplified in 27 (16.1%) and there were 21(12.5%) tumors triple negative. Although our sample is small, our results reveal, that in comparison with white Americans females the Palestinian women have a lower hormonal receptors ER, PR expression rates. Our results are close to American black females. This could be partially explained by the age at diagnosis of breast cancer in Palestinian women. About 77% of American females diagnosed with breast cancer and 46% of Palestinian women were above the age of 50 years at the time of diagnosis. In our study 57.4% negative ER breast cancer case was below the age of 50 year. Biological and lifestyle factors are likely to contribute to these findings. A detailed study of hormonal receptor status and other important factors and the recently described gene expression profiling is recommended to understand the reasons for these differences.

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## Tables

Table 1: Ductal carcinoma cases

|              | <b>Age</b> | <b>&lt; 50 years</b> | <b>Age &gt;</b> | <b>50 years</b> | <b>Total</b> |
|--------------|------------|----------------------|-----------------|-----------------|--------------|
|              | N          | %                    | N               | %               |              |
| <b>ER</b>    | 31         | 43.6%                | 48              | 61.5%           | 78           |
| <b>PR</b>    | 31         | 43.6%                | 39              | 48.7%           | 70           |
| <b>Total</b> | 71         |                      | 78              |                 | 148          |