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AXILLARY NODAL RESPONSE TO NEOADJUVANT ANTHRACYCLINE BASED CHEMOTHERAPY IN BREAST CANCER PATIENTS

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Abstract: **Introduction: Historically, the standard approach to clinically node-positive breast cancer is with axillary lymph node dissection. However, this has been associated with higher surgical complications and long-term symptomatic risks of lymphedema, seroma, limited mobility in that extremity, and neuropathy which can greatly lessen quality of life. Currently, randomized controlled trials examining the question of whether neoadjuvant therapy can decrease the need for axillary lymph node dissection are ongoing. However, guidelines still recommend upfront systemic therapy for clinically node-positive disease to permit for less extensive surgery on the axilla based on data from other trials.**

Objective: This study was aimed at assessing the nodal response to anthracycline based neoadjuvant chemotherapy (cyclophosphamide, doxorubicin/adriamycin and 5-flourouracil (CAF) regimen).

Methodology: This is a 3 year prospective study carried out at the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Amaku-Awka. The study span from January, 2021 to December, 2023. All the premenopausal patients with confirmed node positive breast carcinoma who gave their consent were recruited for the study. They were given 4 courses of CAF at 3 weekly interval. The regimen consisted of: cyclophosphamide 500 mg/m^2, Doxorubucin 50 mg/m^2, and 5-Fluorouracil 500 mg/m^2 all were given on day one. The axillary nodes were assessed before and after the 4th course of chemotherapy.

Results: A total of 147 female patients were recruited. The age of the study population ranged from 24 to 54 years with a mean of 40.92±7.98 years. The pre-chemotherapy nodal stages were: 60(40.8%) of the patients, N_1 according to AJCC (TNM) staging, 78(53.1%) were classified as N_2 and 9(6.1%) were N_3. After 4th course of neoadjuvant chemotherapy, the nodal status of majority of the patients was down staged to N_0 51(34.7%), N_1 66(44.9%), N_2 27(18.4%) and 3(2.0%) was N_3. The clinical complete response rate cCR in this study in relation to nodal status was 34.7%.

Conclusion: The above findings demonstrated the ability of neoadjuvant chemotherapy to transform clinically node-positive breast cancers to node-negative stage.

Keywords: **Breast cancer, Response, Axillary node, Chemotherapy, Neoadjuvant.**

1. INTRODUCTION

Breast diseases vary widely, ranging from benign to malignant variety.[1-6] Benign breast diseases are commoner however the malignant breast disease is on the increase especially in the developing countries.[3-6] Breast carcinoma is the commonest diagnosed cancer among women and the leading cause of cancer death.[6-8] Breast cancer in Nigeria and other developing countries is characterized by the late presentation and poor outcome primarily due to ignorance, superstition, self-denial,

fear of mastectomy and unavailability of treatment facilities.[3,5,6,9] Breast cancer presents a decade earlier in Nigerian women and other black women with worse biological behaviour and poor prognosis.[3-6,8] Studies have shown that locally advanced and metastatic breast cancers are the most familiar presentation mode in most middle and low-income countries.[3-6,8]

Historically, the standard approach to clinically node-positive breast cancer is axillary lymph node dissection. However, this has been associated with higher surgical complications and long-term symptomatic risks of lymphedema, seroma, restrained mobility in that extremity, and neuropathy, significantly reducing life quality.[10] Currently, randomized controlled trials examining whether neoadjuvant therapy can decrease the need for axillary lymph node dissection are continuous. However, guidelines still suggest upfront systemic therapy for clinically node-positive disease to allow for more minor far-reaching surgery on the axilla based on data from other trials.[10] This study was aimed at assessing the nodal response to anthracycline based neoadjuvant chemotherapy with cyclophosphamide, doxorubicin/adriamycin and 5-flourouracil (CAF) regimen.

2. METHODOLOGY

This is a 3 year prospective study carried out at the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Amaku-Awka. The study span from January, 2021 to December, 2023. All premenopausal patients with confirmed node positive breast carcinoma who gave their consent were recruited for the study. The clinical regional lymph node assessment was done before each course of chemotherapy and three weeks after the 4th course of NAC. The regional lymph nodes were graded according to the AJCC (TNM) system of staging of breast cancer.[11] A Doxorubicin containing regimen was used. The regimen: cyclophosphamide, doxorubicin and 5-fluorouracil (CAF) consisted of cyclophosphamide 500 mg/m^2, Doxorubicin 50 mg/m^2, and 5-Fluorouracil 500 mg/m^2 all were given on day one. The Cyclophosphamide and Fluorouracil were given as bolus injection in a free-flowing intravenous line, and the doxorubicin was given as an infusion. The cycles of the CAF were repeated at 3 weekly intervals. However, all eligible women who complied (by signing the consent form) were given four courses of CAF.

Ethical approval was sort and obtained from the Ethical committee of the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka. The data collected were recorded initially in the proforma used for the study. The data were analyzed using the SPSS statistical software version 23.0. (Statistical Package for Social Sciences SPSS Inc.). The results were presented in simple frequency and graphic statistics.

3. RESULTS

A total of 147 female patients were recruited. The age of the study population ranged from 24 to 54 years with a mean of 40.92±7.98 years.

A. Lymph nodal status pre-chemotherapy:

At pre-chemotherapy stage, 60(40.8%) of the patients have a nodal status of N_1 according to AJCC (TNM) staging and 78(53.1%) were classified as N_2 (Table 1).

B. Lymph nodal status after 4th course:

After 4th course of neoadjuvant chemotherapy, the nodal status of majority of the patients down staged to N_0 51(34.7%), N_1 66(44.9%) and N_2 27(18.4%) (Table 1).

Table 1: Frequency distribution of nodal status pre- and post-chemotherapy.

Nodal status	Frequency(percent) pre-chemotherapy	Frequency(percent) after 4th course chemotherapy
N_0	0(0%)	51(34.7%)
N_1	60(40.8%)	66(44.9%)
N_2	78(53.1%)	27(18.4%)
N_3	9(6.1%)	3(2.0%)
Total	147(100%)	147(100%)

4. DISCUSSION

Neoadjuvant chemotherapy (NAC) relates to systemic treatment before definite surgery. In the past, NAC was reserved for patients with locally advanced or inoperable breast carcinoma with the primary purpose to reduce the tumour size/down-staging to allow for breast-conservation surgery and possibly omit axillary dissection in patients who refuse to have an extensive operation.

In the current research, the lymph node status before the commencement of neoadjuvant chemotherapy was as follows: N_1 (40.8%); N_2 (53.1%) and N_3 (6.1%). The nodal status after the 4th course of neoadjuvant chemotherapy showed marked down-staging as follows: N_0 (34.7%); N_1 (44.9%); N_2 (18.4%) and N_3 (2.0%) (Table 1). The above findings demonstrated the ability of neoadjuvant chemotherapy to transform clinically node-positive breast cancers to the node-negative stage. The clinical complete response rate (cCR) in this study concerning nodal status was 34.7%. This finding correlates with a clinical response rate of 46.1% for axillary nodes (cCR, 34.6%; PR, 11.5%) and 20% for supraclavicular nodes (cCR, 20%) as documented by Egwuonwu.[14]

In a prospective study by Mamtani et al.[15], of 288 node-positive stage II–III breast cancer patients receiving neoadjuvant therapy, clinically node-negative patients after treatment were candidates for sentinel lymph node biopsy. 68% of those who had surgery became clinically node-negative after NAC and were able to experience a sentinel node biopsy as opposed to axillary lymph node analysis. Of the 128 sentinel lymph node biopsy cases, 48% avoided a subsequent axillary lymph node dissection, which supports the role of neoadjuvant therapy in reducing the need for axillary lymph node dissection among patients with metastases. One vital concern with neoadjuvant therapy supported by sentinel lymph node biopsy instead of axillary lymph node dissection in patients who were baseline clinically node-positive is the potential false-negative rate of sentinel lymph node biopsy. By this, no evidence of nodal metastases on sufficient sentinel lymph node biopsy, but later found to have nodal metastases on an axillary lymph node dissection. The ACOSOG Z1071 trial explicitly addressed this concern. The first multi-institutional trial confirmed that the false-negative rate of sentinel lymph node biopsy after NAC was 12.6%.[16] However, a secondary analysis of the research showed that in patients who had a clip set in the positive node at the initial biopsy and had a sentinel lymph node biopsy of at least two nodes, that the clip was recovered within the sentinel lymph node specimen 83.7% of the time.[17] Another study showed that in 118 patients undergoing sentinel lymph node biopsy followed by axillary lymph node dissection, if the clipped node was included in the sentinel lymph node biopsy, the false-negative rate decreased significantly, from 10.1% to 1.4%.[18] Thus, a reasonable approach to clinically node-positive disease is to place a clip during the biopsy, pursue neoadjuvant therapy, and then if then down-staged to clinically node-negative condition, move forward with a sentinel lymph node biopsy. Sentinel lymph node biopsy should include the clip to decrease the false-negative rate. If sentinel lymph node biopsy is positive for nodal metastasis, then axillary lymph node dissection can be performed. If sentinel lymph node biopsy is negative, potential complications and sequelae of axillary lymph node dissection can be avoided.

5. CONCLUSION

The above findings demonstrated the ability of neoadjuvant chemotherapy to transform clinically node-positive breast cancers to node-negative stage. This can potentially reduce the extent of axillary dissection in patients that were initially node positive.

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