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RESEARCH ARTICLE

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CORRELATION OF CLINICAL EXAMINATION, MAMMOGRAPHY AND COLOR DOPPLER ULTRASONOGRAPHY WITH HISTOPATHOLOGICAL FINDINGS IN PATIENTS OF CARCINOMA BREAST UNDERGOING NEO-ADJUVANT CHEMOTHERAPY

ABSTRACT

Background

Neoadjuvant chemotherapy has become an accepted component of the multidisciplinary treatment of clinical stage II and III breast cancer. The response to the neoadjuvant chemotherapy is important indicators of survival. Patients who achieve pathologic complete response (pCR) may not require surgery for optimum local control. However, at present, surgical excision and histological examination of the resected specimen is the only way to reliably identify this small subgroup of patients. More effective imaging strategies that can non-invasively identify complete pathological responders could potentially distinguish a subgroup of patients who need not undergo surgery at all. Aim of the present study was (1) assess the chemotherapeutic response for neoadjuvant chemotherapy by clinical examination, color doppler ultrasonography and mammographic examination. (2) To correlate clinical examination, color doppler ultrasonography and mammographic measurements of breast tumor and regional lymph nodes with that of histopathological findings.

Material and methods

The present prospective clinical study conducted during December 2009 to May 2011 includes 30 patients of breast cancer. All patients received 3-4 cycles of neoadjuvant chemotherapy CAF (Cyclophosphamide 500mg/m^2, Doxorubicin 50mg/m^2 and 5-FU 500mg/m^2). Above patients underwent modified radical mastectomy after 10-15 days from last cycle of chemotherapy. The assessment of the chemotherapeutic response in the breast tumor was done by all three methods (Clinical examination, Color Doppler Sonography and Mammography) with respect to the reduction in the calculated volume. Response of the lymph nodes to chemotherapy was determined by Clinical examination and Color Doppler Sonography from the reduction in the largest dimension.

Results

The correlation between histopathological response with response of the tumor assessed by clinical examination, mammogram and ultrasonography were k=0.219, p=0.017; r=0.570, p=0.009 Vs k=0.077, p=0.628; r=0.449; p=0.047 Vs k=0.538; p=0.000; r=0.714; p=0.001 respectively. The correlation between the chemotherapeutic response assessed by Doppler parameters and histopathological parameters were k=0.339; p=0.04; r=0.075; p=0.77 Vs k=0.440; p=0.765; r=0.297; p=0.207 Vs k=0.44; p=0.767; r=0.114, p=0.633 for RI, PI and Vmax respectively. The percentages of overestimation and underestimation of the tumor in 20 patients compared with the histopathological examination by clinical examination, sonography and mammogram were 75% and 25% Vs 25% and 75% Vs 50% and 50% respectively. The mean of overestimation and underestimation by three methods were 1.22±0.77; 0.75±0.288 Vs 0.957±1.59; 1.07±1.32 Vs 0.538±0.255; 0.943±0.609 respectively. The correlation between clinical examination, sonography and mammogram with that of histopathologial examination as the gold standard on estimation of the tumor size were t=-0.257, p=0.801; r=0.797, p=0.00 Vs t=2.87, p=0.009; r=0.693, p=0.00 Vs t=0.718, p=0.04; r=0.911; p=0.00 respectively

Conclusion

Mammogram is the best non invasive modality in both assessing the chemotherapeutic response and estimation of size of the residual breast tumor than Clinical examination and Color Doppler Ultrasonography while considering histopathological examination as gold standard. In assessing the chemotherapeutic response of axillary lymph nodes, Clinical examination is a better modality than Color Doppler Ultrasonography.

Key words: breast cancer, Neoadjuvant chemotherapy, mammogram, Color Doppler ultrasonography

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INTRODUCTION

Breast cancer significantly influences the women's health and is assuming greater importance in the developing countries due to the rising incidence, delay in presentation and dismal outcome[12]. In patients of breast cancer, tumor size and lymph nodes status are important prognostic factors. The initial assessment of tumor size is used to select those patients who may benefit from neoadjuvant chemotherapy. Tumor size continues to be monitored to ensure that the selected drug regimen is having the desired effect[6].

Neoadjuvant chemotherapy has become an accepted component of the multidisciplinary treatment of clinical Stage II and III breast cancer[11,14]. The advantage of the NACT approach is that, it provides an in vivo test of the tumor's response to a particular chemotherapeutic regimen[1,14,18] .Other advantages of chemotherapy include down staging of the tumor, allowing less extensive surgery, and control of local and distant recurrence, thereby improving the patient's quality of life, long term disease free survival and overall survival [7-9,11].

Accurate prediction of residual pathologic tumor size after neoadjuvant chemotherapy is critical in guiding surgical therapy. Although clinical examination, ultrasonography, and mammography have all been used to predict residual tumor size, there have been conflicting reports about the accuracy of these methods in the neoadjuvant setting[2]. Combined mammography, clinical examination, and ultrasonography were more sensitive than any other individual test and they are complementary to each other, in order to obtain a more accurate measurement of the breast cancer[2,6] . In this study, we sought to assess the accuracy of residual tumor size and to correlate the chemotherapeutic response assessed by clinical examination, color doppler ultrasonography and mammogram with that of histopathological findings.

Materials and methods

The present prospective clinical study conducted during December 2009 to May 2011 includes 30 patients of breast cancer. The departmental research committee and the Institute postgraduate research board have approved the study and the informed written consent of the subjects has been recorded individually. Patients selection criteria includes (1) histopathologically proven cases of invasive breast carcinoma (2) Age more than 18 years and less than 70 years (3) Karnofsky performance score of 70 or more. Other selection criteria were patients with normal liver function test, renal function test, hematological parameters and echocardiogram, patients with negative pregnancy test, non metastatic disease and without the previous history of cancer. All patients received 3-4 cycles of neoadjuvant chemotherapy CAF (Cyclophosphamide 500mg/m^2, Doxorubicin 50mg/m^2 and 5-FU 500mg/m^2). Above patients underwent modified radical mastectomy after 10-15 days from last cycle of chemotherapy.

Clinical Evaluation

A detailed history and clinical evaluation was done in all the patients. Examination of both breasts and axilla and evaluation for probable metastasis was done. Breast lump was measured along two perpendicular diameters using Vernier calipers and mean diameter and Volume (Volume= π /6x$d^{3,}$ where d=mean diameter in centimeters) were calculated. Staging of the disease was done using AJCC staging system 2002

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Color Doppler Ultrasonography

Color Doppler examination of the tumor aws done with LOGIQ 400 CL System (GE Medical System) using a high frequency (11 MHz) linear electronic array probe. The diameters of the tumor were measured as largest diameter and another is perpendicular to it and the thickness of the lesion was recorded using the electronic calipers. The sonographic tumor volume (Vs) was calculated as Vs = π /6xd1xd2xD; Where d1, d2 are diameters and D is depth of the tumor in centimeters.

The Doppler parameters were recorded by standardized machine setting were used to optimize sensitivity to low velocity and low volume blood flow (wall filter-low frequency; dynamic range 60DB; persistent shift; color threshold- 50). Resistivity index (RI),Pulsatility index (PI), Maximum flow velocity (Vmax) of intratumoral vessels were recorded. Peritumoral flow was not taken into account for assessment. The RI and PI are calculated as RI = Peak systolic velocity - End diastolic velocity/ Peak systolic velocity and PI = Peak systolic velocity - End diastolic velocity /Average velocity.

Mammogram

Bilateral mammogram was performed with dedicated mammographic equipment (GE Senographe DMR Plus Mammography Machine), using standard craniocaudal (CC) and mediolateral oblique (MLO) with 30º projections after adequate breast compression. All examinations were performed by radiographictechnicians under direct supervision of a radiologist experienced in mammography. Depending upon the texture of breast, adjustments were made between 22-30 kV and 40-160 mAs.

Size of the tumor by mammogram was measured as the largest diameter of the whole tumor in any direction with a ruler and another dimension perpendicular to that and the volume was calculated as Vm= π /6xd³; d= mean diameter in centimeters..

Response evolution

The assessment of the chemotherapeutic response grade in the breast tumor was done by all three methods (Clinical examination, Color Doppler Sonography and Mammography) with respect to the reduction in the calculated volume. Percentage change in vascular indices (RI, PI, Vmax) was assessed both in breast tumor. Finally, these were correlated with the grades of response observed on histopathological examination. Accuracy of clinical, sonological examination and mammogram in determining the size of breast tumor and axillary lymph nodes were assessed, considering histopathological examination as the gold standard. Grades of response were measured as per table-1

Statistical analysis

At the end of the study, the results were tabulated and analyzed using statistical software package SPSS version 16. Relevant statistical tests such as Karl Pearson's Correlation Co-efficient, Weighted Kappa statistics, Spearman correlation coefficient and Paired t-tests were used.

RESULT

Out of 30 patients, 20/30 (66.6%) patients had received 3 cycles of neoadjuvant chemotherapy followed by surgery (modified radical mastectomy). Five out of 30 patients (16.6%) who had undergone a few cycles of chemotherapy and then defaulted and remaining 5/30 (16.6%) patients who developed metastatic lesion and patients with locally inoperable progressive disease during neoadjuvant

chemotherapy (2 patients developed lung metastasis, 1 patient developed brain metastasis and 2 patients developed locally advanced inoperable progressive disease). Patients characterization were tabulated in table-2

After the complete history and clinical examination all patients underwent color Doppler ultrasonography and mammogram. The tumor and lymph nodes measurements by clinical examination, mammogram and color Doppler ultra sonography at the time of presentation were as shown in table-3.

The mean diameter and volume of the tumor assessed after chemotherapy by clinical examination, ultrasonography and mammogram were 4.38±1.98cc, 68.42±91.32cc ; 3.54±2.01cm,37.55 ± 98.21 cc and 4.17±1.40cm; 39.25 ± 44.8cc respectively. After the surgery the histopathological examination findings were tabulated as in table-4.

The correlation between histopathological response with response of the tumor assessed by clinical examination, mammogram and ultrasonography were k=0.219, p=0.017; r=0.570, p=0.009 Vs k=0.077, p=0.628; r=0.449; p=0.047 Vs k=0.538; p=0.000; r=0.714; p=0.001 respectively. The correlation between the chemotherapeutic response assessed by Doppler parameters and histopathological parameters were k=0.339; p=<0.04; r=0.075; p=0.77 Vs k=0.440; p=0.765;r=0.297; p=0.207 Vs k=0.44; p=0.767;r=0.114, p=0.633 for RI, PI and Vmax respectively.

The clinical response to chemotherapy was observed to be grade 3 in 10/20 (50%) patients, grade 2 in 6/20 (30%) patients and grade 1 in 4/20 (20%) patients. No patient had grade 4 response (fig-1). The sonologically assessed grade of response of the tumor following chemotherapy was grade 3 in 9/20 (45%) patients, grade 2 in 6/20 (30 %) patients and 5/20 (25%) patients showed grade 1 response (fig-2). The mammographically assessed grade of response of the volume of the tumor following neoadjuvant chemotherapy was grade 2 in 12/20 (60%) patients, grade 1 in 35% patients and grade 3 in 5% patients (fig-3).

The grade of response assessed by RI of the tumor, following chemotherapy, was grade 2 in 55% patients and grade 1 in 45% patients. No patient had grade 3 or grade 4 response. The grade of response assessed by PI of the tumor following chemotherapy was grade 1 in 40% patients, grade 2 in 35% patients and grade 3 in 25% patients. No patient was found with grade 4 response. With regard to the grade of response of Vmax of the tumor following chemotherapy, 40% of the patients had grade 1 response, 35% patients had grade 3 and 25% patients had grade 2 response. No patient was found with grade 4 response (fig-4). The histopathological response to chemotherapy of the breast tumor assessed after surgery was in the range of 25%-50% (Grade-2) and ≥ 50% (Grade-3) in 8/20 (40%) patient each . In 4/20 (20%) patients, response to chemotherapy was ≤ 25% (Grade-1). No patients had complete histopathological response (fig-5).

The mean value of the difference in size of 20 patients estimated by histopathological examination with clinical examination, mammogram and ultrasonography in breast tumor were 1.94 ± 0.074 cms, 0.541±0.12 cms and 1.19 ± 1.06 cms respectively. The minimum and maximum difference in size was 0.5cm & 3.0cms respectively.

The percentages of overestimation and underestimation of the tumor in 20 patients compared with the histopathological examination by clinical examination, sonography and mammogram were 75% and 25% Vs 25% and 75% Vs 50% and 50% respectively. The mean of overestimation and underestimation by three methods were 1.22±0.77; 0.75±0.288 Vs 0.957±1.59; 1.07±1.32 Vs 0.538±0.255; 0.943±0.609 respectively.

The correlation between clinical examination, sonography and mammogram with that of histopathologial examination as the gold standard on estimation of the tumor size were t=-0.257, p=0.801; r=0.797, p=0.00 Vs t=2.87, p=.009;r=0.693,p=0.00 Vs t=0.718, p=0.04;r=0.911; p=<0.00 respectively.

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DISCUSSION

Neoadjuvant chemotherapy (NACT) is the use of chemotherapy as the initial treatment modality before definitive locoregional therapy is applied. Breast conservation surgery was offered to responding patients, who were otherwise considered to require mastectomy[1] (Mieog JSD et al. 2007). Unlike orthodox adjuvant chemotherapy where all assessable tumors have been removed, a clinical response of the primary tumor to NACT confirms that tumor's sensitivity to those specific drugs. If no response is observed, the ineffective chemotherapy regimen is discontinued, which avoids unnecessary toxicity and an alternative form of systemic therapy or surgical intervention may be instituted[1,14,18]. Response to NACT is also a prognostic indicator as response is predictive of long term disease free survival and overall survival[7-9] .

In our study, clinically grade-3 response to chemotherapy in tumor volume was observed in 10/20 (50%) patients. 30% patients had grade-2 and 20% patients had grade-1 response. No patient was observed with grade-4 response. One patient showed increase in tumor volume after neoadjuvant chemotherapy.

In a study by Singh S. et al. (2009), twenty-four of 25 patients showed a clinical regression in tumor volume following chemotherapy. Five cases (20%) had complete disappearance of the lesion. Clinical response grade of 1, 2, 3 and 4 in breast tumor was observed in 18.75%, 25.0%, 45.83% and 10.4% patients respectively.

Roubidoux et al. (2005), prospectively evaluated low-stage breast cancers with a mean maximum size of 24 mm in 34 patients before and after neoadjuvant chemotherapy by using US. The sensitivity was high for residual tumors of 7 mm or larger; four false-negative results occurred with residual tumors less than 6 mm in size. Three false-positive results were caused by fibrosis or biopsy-related changes.

The mean of largest diameter of the tumor before and after chemotherapy was found to be 5.02± 2.34 cms (range 2.84-13.7 cms) and 3.54 ± 2.08 (range 1.46-11.8 cms). In a study by Singh et al. (2005), sonographically the breast tumor diameter ranged from 1.08-5.6 cms with a mean of 3.62 ±1.33 cms.

In the study by Lonedro et al. (2004), the mean diameter of the tumor, which was calculated based on the sonographic measurements, was 32.4 mm before chemotherapy, 27.4 mm after two courses of chemotherapy and 17.3 mm after the end of chemotherapy.

In this study, the mean volume of the tumor was found to be 76.35 ± 143.1cc (range 8.7-666 cc) and 37.55 ± 98.21 cc (range 1.31-451.97cc) in pre and post chemotherapy patients respectively. No patient was observed to have an increase in size or complete response following chemotherapy.

In the study by Lonedro et al. (2004), breast tumors had a mean volume of 91.4 cc (range 1.4–523.3 cc) on sonologic examination before chemotherapy and 46.5 cc (range 0.3–267.9 cc) after two courses of chemotherapy and 14.2 cc (range 0–95.2 cc) at the end of chemotherapy.

In the present study, with regard to the sonologically assessed grade of response in volume of the tumor following chemotherapy, 9/20 (45%) patients had grade-3 response, 6/20 (30 %) patients had grade-2 response and 5/20 (25%) patients shows grade-1 response.

In the study by Singh et al. (2005), twentythree of 25 patients showed a sonographic regression in tumor volume following chemotherapy. Nine patients (36%) showed histological complete response to chemotherapy referred to as total annihilation while 8 patients each showed minimal and moderate changes in the form of stromal fibrosis, lymphocytic infiltrates and tumor necrosis.

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However, in the present study, the histopathological response of the breast tumor assessed after surgery in the patient who received neoadjuvant chemotherapy (Group I) was found to be in the range of 25%-50% (Grade-2) and ≥ 50% (Grade-3) in 8/20 (40%) patients each and ≤ 25% (Grade-1) in 4/20 (20%) patients. No patient had complete histopathological response.

Huber et al, (2000), evaluated color Doppler US in 17 patients before and after neoadjuvant chemotherapy. Concordance between histopathologic results and color Doppler US was 0.87 vs. 0.474 for histopathological results and clinical examination, using Kappa statistics.

Singh G et al. (2009), in a study of 50 patients, found that the mean value of RI at the time of presentation was 0.89±0.13.27. 27(54%) patients showed regression in RI while 23 (46%) patients had increase in RI following chemotherapy. Kumar A et al. (2007), in a study of 50 patients, found the mean measured value of RI, at the time of presentation was 0.756 ± 0.246. 4/50 (8%) patients showed increase in RI following chemotherapy.

In this study, the mean RI value of the tumor before and after chemotherapy were 0.82±0.28 and 0.83±0.24 respectively. Three patients (15%) were observed to have an increase in RI value after chemotherapy. No patient had complete response to chemotherapy. With regard to the grade of response assessed by RI of the tumor following chemotherapy, 55% patients had grade-2 response and 45% patients had grade-1 response. No patient had grade-3 or grade-4 response. Kumar A et al. (2007), in a study of 50 patients observed Grade-1, 2, 3 and 4 RI response in breast tumor in 22(44.0%), 4(8.0%), 0(0%), and 24(48.0%) patients, respectively. Singh G et al. (2009), in a study of 50 patients observed Grade-1, 2, 3 and 4 RI response in the breast tumor in 43(86.0%), 4(8.0%), 1(2.0%) and 2(4.0%) patients, respectively.

In our study, fair agreement and slight correlation (k=0.339; p=< 0.04; r=0.075; p=0.775) has been found between RI and histopathological response in breast tumor. In the study by Singh S et al. (2005), in 25 patients, the Color Doppler US showed a sensitivity of 88.8% for predicting complete histological response with a negative predictive value of 92.3%. A significant correlation was obtained between Color Doppler US and histological response(r=0.688, p=≤0.001; k=0.251, p=≤0.0002).

Oksuzoglu B et al. (2006), found that the greater the shrinkage of the tumor with chemotherapy, the lower the RI (r = 0.70, p = 0.078). The authors concluded that the decrease in RI with chemotherapy, which means increased blood flow at diastole of the cardiac cycle into the tumoral tissue, may be related to decreasedintratumoral pressure secondary to tumor shrinkage and may reflect a new type of response, that is vascular response. However, in the present study this correlation was not observed (r = 0.273, p=0.208) in breast tumor.

Singh G et al. (2009), in a study of 50 patients found the mean values of PI at the time of presentation was 10.65±5.75. 20 (40%) patients showed regression in PI while 30 (60%) patients had increase in PI following chemotherapy. Kumar A et al. (2007), in a study of 50 patients found the mean measured value of PI at the time of presentation was 1.358 ± 0.546. 8/50 (16%) patients showed increase in PI following chemotherapy.

In the present study, the mean PI value was 1.96±0.21 and 1.91±0.94 in pre and post chemotherapy assessment respectively. Three patients (15%) were observed with increase in PI value after chemotherapy. No patient had complete response to chemotherapy.The grade of response assessed by PI of the tumor following chemotherapy was grade-1 in 40%, grade-2 in 35% patients and grade-3 in 25% patients. No patient was found to have a grade-4 response.

Kumar A et al. (2007), observed Grade-1, 2, 3 and 4 response in breast tumor PI in 18(36.0%), 6(12.0%), 2(4.0%) and 24(48.0%)

patients respectively. Singh G et al. (2009), in a study of 50 patients observed Grade 1, 2, 3 and 4 response in breast tumor PI in 30(60.0%), 8(16.0%), 10(18.0%) and 2(4.0%) patients respectively. Singh S et al. (2005), found a significant correlation between color Doppler US (PI response) and histological response(r=0.751, p=≤0.001; k=0.123, p=≤0.716). In our study, fair agreement and slight correlation (k=0.440, p=0.765; r=0.297, p=0.207) has been found between PI and histopathological response in breast tumor.

Singh G et al. (2009), in a study of 50 patients, found the mean values of peak systolic velocity (PSV) at the time of presentation to be 22.15±16.02 cm/s. 30 (60%) patients showed regression in PSV while 20 (40%) patients had increase in PSV following chemotherapy. Patients with an intratumoral blood flow velocity increase after chemotherapy had a greater likelihood of local recurrence and metastasis compared with patients in whom flow velocity decreased after chemotherapy. Kumar A et al. (2007), in a study of 50 patients found the mean measured value of Vmax, at the time of presentation as 0.396 ± 0.294 m/s. No patient showed increase in Vmax following chemotherapy.

In the present study, the mean Vmax value of the tumor was found to be 25.1±15.1cm/s and 20.25.43±11 cm/s in pre and post chemotherapy patients, respectively. Three patients (15%) showed an increase in Vmax value after chemotherapy. No patient had complete response to chemotherapy. With regard to the Vmax grade of response of the tumor following chemotherapy, 40% of the patients had grade-1 response, 35% patients had grade-3 and 25% patients had grade-2 response. No patient showed a grade-4 response.

In our study, moderate agreement and slight correlation (k=0.44; p=0.767;r=0.114, p=0.633) has been found between Vmax and histopathological response in breast tumor.

Singh G et al. (2007), concluded that tumor blood flow velocity (Vmax) measured by ultrasound may predict disease-free survival of breast cancer. The log rank p value was significant (<0.05) between change in PSV at presentation and survival (median follow was 24months and survival was 13 months). A change of PSV on color Doppler US in pre- and post-chemotherapy may predict a good correlation between clinical grading and change in blood flow velocity in breast tumors. The log rank p value was 0.002 ($p < 0.05$). However, neither RI nor PI was found to correlate with the clinical response.

The mean number of nodes before and after chemotherapy was 2.8 ± 1.2 and 2.5 ±1.2. 0ne patient (5%) was observed with increased total number of lymph node after chemotherapy. 3/20(15%) patients had complete response of lymph nodes to chemotherapy. The mean diameter of the axillary lymph nodes before and after chemotherapy was 1.91 ±0.81 and 1.26 ±0.75. The grade of response assessed by largest diameter of the axillary lymph node following chemotherapy, by sonography, was grade-2 in 45 % of the patients, grade-1 in 35% patients and grade-3 in 15% patients.

In our study, mild agreement and weak correlation (k=0.085; p=<0.454; r=0.095; p=0.691) has been found between clinical and histopathological response in axillary lymph nodes.

In our study, the mean diameter of the tumor before and after chemotherapy was 5.37 ± 1.37 cmsand 4.17 ± 1.4 cms. One patient showed increase in the size of the diameter and no patient had complete response. In the present study, the volume of the tumor assessed by mammogram before chemotherapy was <100 cc in 15/20 (75%) patients and after chemotherapy, the volume of the tumor in the same range was seen in 18/20 (90%) patients. The mean volume of the tumor before and after chemotherapy was 90.03 ±82.90 cc and 39.25 ± 44.8 cc respectively. Tumor volume was in the range of 19.66-381.26cc and 2.80-179.3cc,before and after chemotherapy, respectively.

In the study of Londero et al. (2004), the assessment of the size of the tumor was performed in 13/15 cases. The volume of the tumor, which was calculated based on the mammograms' measurements, had a mean value of 192.8 cm3 (range24.3–761.8 cm3) before

chemotherapy, of 163.4 cm3 after two courses of chemotherapy and of 164.2 cm3 after the end of chemotherapy. In detail, the Responders presented a mean volume of 65 cm3 (range 0–329.8 cm3) after the end of chemotherapy. The mean diameter of the tumor, which was calculated based on the mammograms' measurements, was 37.5 mm before chemotherapy, 32.6 mm after two courses of chemotherapy and 29.4 mm at the end of chemotherapy. The mean diameter of the tumor measured in the pathologic specimen was 23 mm.

Londero et al. (2004) using the RECIST criteria, based on the measurements performed on mammograms, demonstrated CR in one case (6.5%), PR in eight cases (53.5%), SD in four cases (27%) and PD in none. Therefore, 9/15 patients (60%) were classified as responders, and 4/15 patients (27%) as non-responders.

In the study by Carla et al. (2001), one hundred forty-one patients had clinical examination, adequate mammography and echography assessment before and after chemotherapy. A disease response to treatment was more frequently observed with clinical palpation than either echography or mammography. Comparisons of clinical and mammographic response to treatment showed some agreement in 40 cases (28.4%) and disagreement in 101 cases (71.6%). This was comparable with clinical versus echographic responses: 41 cases (29.1%) and 100 cases (70.9%), respectively. The mammographic assessments in patients attaining a complete clinical response to primary chemotherapy revealed 2 CR, 11 PR and 19 SD while the corresponding echographic results were 3 CR, 12 PR and 17 SD.

In our study, moderate agreement and substantial correlation was found between mammogram and histopathological response in breast tumor (k=0.538, p=0.000; r=0.714, p=0.001).

In conclusion, mammogram is the best non invasive modality of assessing the chemotherapeutic response in breast tumor than Clinical examination and Color Doppler Ultrasonography. In assessing the chemotherapeutic response of axillary lymph nodes, Clinical examination is a better modality than Color Doppler Ultrasonography while considering histopathological examination as gold standard. In estimation of size of the breast tumor, mammogram is better than Clinical examination and Ultrasonography. In assessing size of axillary lymph node, Clinical examination is better than Ultrasonography while considering histopathological examination as gold standard.

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	Grades	Criteria
Tumor size, RI, PI, Vmax	1	Increase/No change/<25% decrease
	2	25-50% decrease
	3	>50% decrease
	4	Complete disappearance of mass (tumor volume) Complete disappearance of flow signals.
Post-mastectomy histology	1	No chemotherapeutic change
	2	Minimal chemotherapeutic changes
	3	Moderate chemotherapeutic changes
	4	Total annihilation of tumor tissue (100% disappearance)

Table-1; Grades Of Response (Singh et al. 2005), (Kumar A et al. 2007)

Characteristics	Total no. of patients (30)
Age (years)	Mean -52.20±10.64
Menopausal status	

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pre	7(23.3%)
peri	4(13.3%)
menopausal	19(63.3%)
Laterality	
Right	15(50%)
Left	14(46.6%)
Bilateral	1(3.3%)
Duration (mean in months)	12.85±8.74
Quadrant	
Upper outer	19(60.3%)
Upper inner	4(10.3%)
Lower outer	1(3.3)
Lower inner	0
Central	6(20%)
T status	
T2	1(3.3%)
T3	9(30%)
T4a	2(6.6%)
T4b	12(40%)
T4c	6(20%)
N status	
N1	22(73.3%)
N2	7(23.3%)
N3	1(3.3%)

Table-2: Patients characteristics

Characteristics	Clinical examination: range(mean)	Mammogram: range(mean)	Color Doppler ultra sonography: range(mean)
Tumor :			
Largest diameter(cms)	3.5-15 (7.25±2.53)	3.5-9.6 (5.54 ± 1.56)	2.84-13.7 (5.04± 2.14)
Volume (cc)	14.12-1765(263.4±243.5)	19.6-381.26 (90.45±105.63)	8.5-666.05 (70.75± 105.1)
Doppler parameters			
RI			1.31-0.53(0.85±0.19)
PI	-	-	0.87-4.75 (2.18±0.868)
V max (cm/s)	-	-	6.4-62.9 (23.88±13.49)
	-	-	

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Lymph nodes: range(mean)	1-5 (2.31±0.94)	-	2-8(2.70±1.94)
Total number	1-4(2.39±1.26)	-	0.8-4.1 (1.84±0.92)
Largest diameter (cms)	-	-	
Doppler parameters	-	-	0.57-1.31(0.982±0.46)
RI	-	-	1-3.24(1.89±0.54)
PI	-	-	9.6-58.2 (24.6±12.5)
V max (cm/s)			

Table-3: Tumor and lymph nodes characteristics at the time of presentation

Characteristics	Histopathologiocal findings
Tumor	
Largest Diameter(cms) [Range (mean)]	2-8(4.3 ± 1.68
Volume (cc) [Range (mean)]	1.7-235.8 (31.07 ± 27.53)
Grade of the tumor [no. (%)]	
Grade 1	1 (5%)
Grade 2	7 (35%)
Grade 3	12(60%)
Grade 4	0
Lymphovascular invasion [no. (%)]	
Absent	6(30%)
Present	10 (50%)
Not known	4(20%)
Estrogen receptor [no. (%)]	
Positive	11(55%)
Negative	8(45%)
Not Known	1(5%)
Progesterone receptor [no. (%)]	
Positive	12(60%)
Negative	7 (35%)
Not Known	1(5%)
Her-2 neu receptor [no. (%)]	
Positive	8(40%)
Negative	11(55%)
Not Known	1(5%)
Lymph nodes	
No dissected [Range (mean)]	7-27 (15.4±6.35)
Positive [Range (mean)]	1-17 (9.6±3.7)
Largest Diameter (cms)[Range (mean)]	1-4(2.46±0.54)

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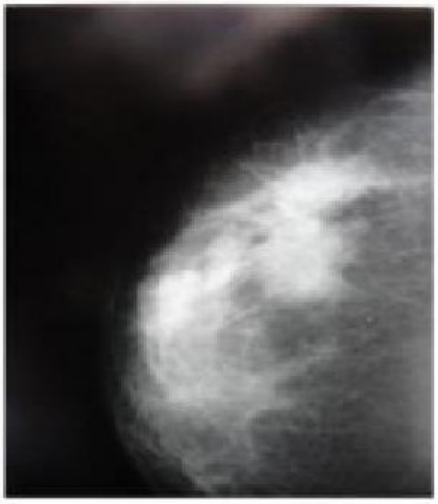
Table-4: Histopathological tumor characteristics.

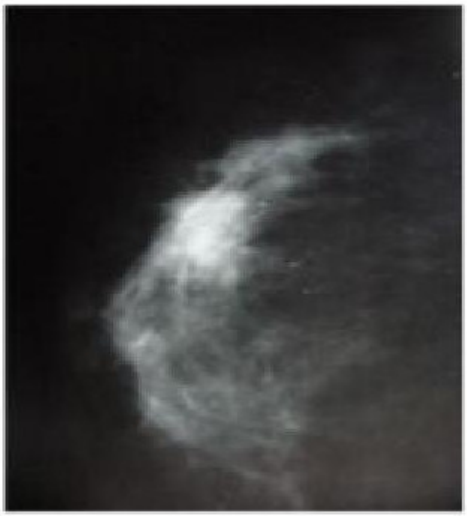
Pre-chemotherapy clinical photograph

Post-chemotherapy clinical photograph

Fig-1: chemotherapeutic response by Clinical Examination



Mammographic photograph (pre-chemotherapy)



Mammographic photograph (post-chemotherapy)

Fig-2: chemotherapeutic response by Mammogram

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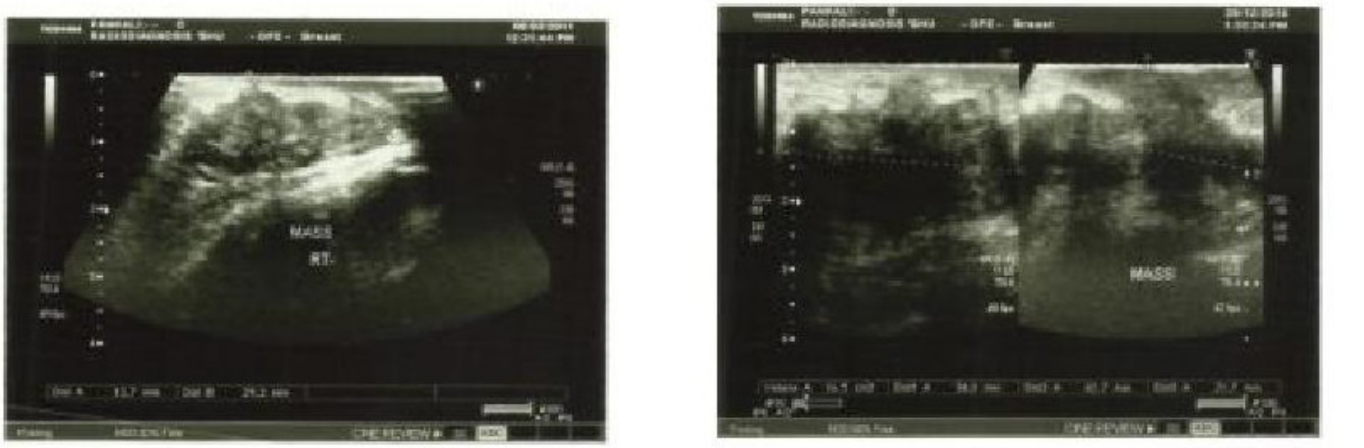
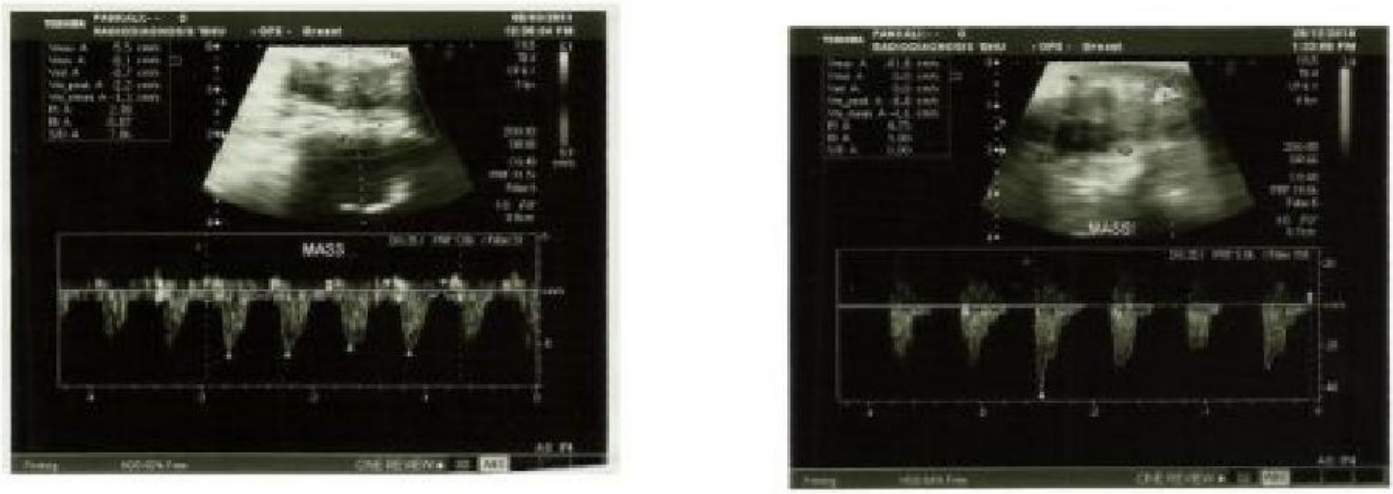


Ultrasonography of the breast (Post-chemotherapy) *Ultrasonography of the breast (Pre-chemotherapy)*

Fig-3: chemotherapeutic response by Ultrasonography



Doppler Parameters (Post-chemotherapy) *Doppler Parameters (Pre-chemotherapy)*

Fig-4: chemotherapeutic response by color Doppler examination

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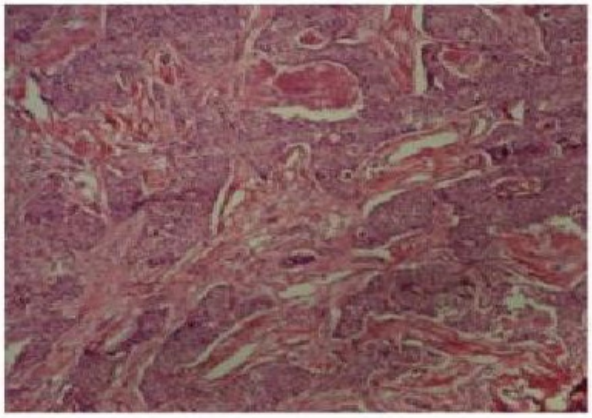
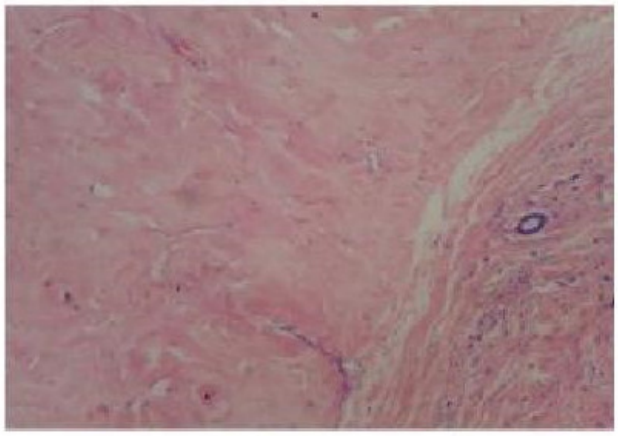


Histopathological photograph (pre-chemotherapy)

Fig-5: chemotherapeutic response by Histopathological examination.



Histopathological photograph (post-chemotherapy)

Fig -5: histopathological chemotherapeutic response

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