CLINICAL, MAMMOGRAPHIC AND ULTRASONOGRAPHIC EVALUATION OF RESIDUAL DISEASE IN WOMEN RECEIVING NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED BREAST CANCER

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ABSTRACT

BACKGROUND

Locally advanced breast cancer (LABC) defined as bulky primary tumour with T3, T4 tumour and N2/N3 disease. Neoadjuvant chemotherapy is the first-line treatment to downgrade these tumours and to make them surgically operable and also better cosmesis. Chemotherapy response is assessed by various methods.

Aim of our study was to assess the residual disease clinically, mammographically and sonographically.

MATERIALS AND METHODS

Residual disease was compared with histopathological response after 4 cycles of chemotherapy followed by classical surgery – Modified Radical Mastectomy.

RESULTS

In our institute, more than 60% of women with breast cancer present with locally advanced disease and are submitted for neoadjuvant chemotherapy. Total 60 cases of LABC were included in this study, 42 patients were of T4bN1M0 stage, 12 were of T3N1M0 stage, 3 were T3N2M0 and 3 were T4bN2M0 stage. Response assessed by RECIST criteria. Pre-chemotherapy mean value of clinical size of tumour was 6.3 cm and post-chemotherapy mean value was 5.2 cm. Mammographically, pre-chemotherapy mean size was 4.23 cm and post-chemotherapy 3.8 cm. In USG pre-chemotherapy mean size was 4.56 cm and post-chemotherapy 3.74 cm. Three patients showed Complete Response (CR) on USG evaluation but none clinically or mammographically. The mean size of tumour was 35% larger on clinical examination as compared to mean size on pathological evaluation. Mammographically tumour size was 8% underestimated and sonographically 4% underestimated than pathological tumour size which is statically significant with p value<0.05.

CONCLUSION

Ultrasonography is superior to clinical and mammographic assessment of residual tumour after neoadjuvant chemotherapy in LABC.

KEYWORDS

Locally Advanced Breast Cancer, Neoadjuvant Chemotherapy, Residual Disease, LABC.

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BACKGROUND

Locally advanced breast cancer (LABC) is defined as bulky primary tumour and or extensive lymphadenopathy. This includes patients of T3 & T4 disease with/or N2/N3 disease. Breast cancer is one of the leading causes of cancer related deaths in women. Its mortality/incidence relationship in developed countries is 29.9% whereas in developing countries it reaches 42.9%.^[1]

The treatment of LABC has considerably changed during last decade and now includes a multidisciplinary approach which is directed both to locoregional control of disease and to destruction of micrometastases.^[2-3] Neoadjuvant chemotherapy may improve the survival rate, enable direct

assessment of response to systemic treatment and causes a reduction in size of primary tumour, allowing a more conservative surgical approach without any increase in locoregional recurrence rate.^[4-5] On the other hand the theoretical disadvantage related to chemotherapy is-

1. Potential delay of surgical treatment particularly where active neoplastic proliferation is detected after four cycles of chemotherapy.
2. Loss of knowledge and information about some prognostic factors such as clinical nodal status and size of tumour which may lead to suboptimal therapy.
3. Modification of biological temporal characteristic as change in cell proliferation.^[6]

Assessment of response to neoadjuvant chemotherapy has slowed down the development of new protocols for breast carcinoma. Clinical, radiological along with pathological evaluation is important to assess proper response.^[7] In our study, total 60 patients of LABC were studied clinically, mammographically and sonographically prior to and after 4 cycles of chemotherapy. We compared the response by these three methods.

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Aim and Objectives

To evaluate the residual disease in LABC after 4 cycles of chemotherapy clinically, mammographically, sonographically and comparing with tumour size pathologically postoperatively.

MATERIALS AND METHODS

Present prospective observational study was conducted in Department of Surgery, Pt. JNM Medical College, Raipur, Chhattisgarh. All female patients diagnosed of LABC undergoing neoadjuvant chemotherapy were included in this study. Total 60 patients were assessed by clinical examination, mammographic evaluation and sonographic evaluation (done before core biopsy was taken), then chemotherapy was started.

Clinical assessment was done by TNM classification and repeated after 4 cycles of neoadjuvant chemotherapy and the response was assessed with RECIST criteria.^[8]

Film screen mammography was done on MAMMAT 3000 Nova machine with standard protocol and response assessed with same criteria.

Sonologic evaluation was done in Department of Radiology under supervision of a qualified sonologist of pre- and post-chemotherapy and response assessed.

RESULTS

The peak incidence of the cases was seen in patients below 35 years of age (41.66%) while mean age was 42.08 years. LABC was found more in left breast that is 36 out of 60 cases (60%) and 42 out of 60 patients were premenopausal females (70%). Clinically, 42 out of 60 patients presented with T4bN1M0. Stage wise distribution of patients shown in Table -1

Stage	No. of Cases	Percentage
T3N1M0	12	20%
T3N2M0	03	5%
T4bN1M0	42	70%
T4bN2M0	03	5%

Table 1. Clinical Stage Wise Distribution

Pre-chemotherapy mean clinical size of lump with standard deviation (SD) was 6.3±1.4 cm. Post-chemotherapy mean clinical size with SD was 5.2±1.9 cm. The difference was statistically significant with p value <0.001. Mean value of mammographic size was 4.2±1.5 cm pre-chemotherapy and 3.6±1.8 cm post-chemotherapy. The difference was statistically significant with p value <0.01.

Ultrasonography mean value of tumour size was 4.5±1.06 cm before chemotherapy and 3.74±1.64 cm post-chemotherapy. The difference was statistically significant with p value <0.01.

Response to chemotherapy is shown in Table 2, 3, with RECIST criteria.

Best Response	RECIST change in sum longest diameter
Complete response (CR)	Disappearance of all target lesions; confirmed at 4 weeks
Partial Response (PR)	At least 30% reduction in the sum of the longest diameter of target lesion, taking as reference the baseline study; confirmed at 4 weeks
Stable Disease (SD)	Neither PR or PD criteria are met, taking as reference the smallest sum of the longest diameter recorded since treatment started
Progressive Disease (PD)	At least 20% increase in the sum of the longest diameter of target lesion, taking as reference, the smallest sum of longest diameter recorded since treatment started or appearance of new lesion.

Table 2. RECIST Criteria of Evaluation of Response to Chemotherapy^[8]

Response	Clinical		Mammography		Sonography	
	No. of Cases	%	No. of Cases	%	No. of Cases	%
CR	0	0%	0	0%	3	5%
PR	24	40%	18	30%	18	30%
SD	33	55%	36	60%	36	60%
PD	3	5%	6	10%	3	5%

Table 3. Response Evaluations on Clinical, Mammography and Sonography Method after Neoadjuvant Chemotherapy

This study showed no complete response as assessed by clinical and mammography methods, but in USG complete response was present in 3 patients. All responses were confirmed by pathological assessment of tumour size. The mean size of tumour was 35% underestimated (Larger) on clinical assessment as compared to mean size on pathological examination. The mean size of tumour was 8% underestimated by mammography and 4% underestimated by sonography than pathological assessment which was statistically significant with p value <0.05.

DISCUSSION

Breast cancers in young women are typically aggressive in part owing to the overexpression of high grade, triple negative disease. Average age of presentation for LABC is 40-45 years in various studies.^[9-10] Our findings are in conformity with the reported range.

In our series, about 60% had left-sided LABC and 40% had right-sided LABC. Possible reasons for left preponderance of carcinoma are highly speculative, sleeping behaviour, handedness, nursing behaviour and asymmetric sun exposure.^[11] Clemmensen (1997) found left breast preponderance in 18% LABC,^[12] Haagensen (1995) in 16.5% and Donegen (1997) in 26% cases of LABC.^[13] Our finding of 20% preponderance in left-sided LABC is in accordance with reports. LABC are aggressive tumour due to ER/PR negativity and HER-2/neu overexpression so commonly seen in premenopausal women.^[14] This study also showed peak incidence in premenopausal women.

Definition of LABC includes palpable axillary lymph nodes. Olivotto IA (2003) defined LABC as patients with T3 or

T4 and N2/N3 disease.^[15] In our study, also all patients were of palpable axillary lymph node with N1 and N2 stage.

All patients received 4 cycles of chemotherapy as per standard protocol and after 4 cycles response was assessed by RECIST criteria.^[8] USG appears superior to clinical examination and mammography in assessment of post-chemotherapy tumour response. Physical examination is often considered unsatisfactory for assessment of response because palpation of fibrotic and necrotic mass may mimic residual tumour mass.^[16-17] Ultrasonography is a superior imaging modality than mammography in evaluating skin thickening and oedema and for evaluating axillary lymphadenopathy. Different researchers reported sensitivity 72-94% and specificity up to 97%^[18] for USG. In our study, also USG assessment of tumour response appears superior compared to clinical and mammographic assessment. In current era, MRI appears to be superior to all for this evaluation in cases of multifocal or multicentric disease. MR data improves accuracy of the second look ultrasound with an increase of ultrasound accuracy from 73 – 84.5%.^[19]

CONCLUSION

LABC is an aggressive form of carcinoma breast; proper response assessment to neoadjuvant chemotherapy is required for better prognostic and cosmetic surgical management of these tumours. USG is a feasible method of noninvasive evaluation of response to chemotherapy in patients with locally advanced breast cancer as compared to physical examination and mammographic evaluation and also where facilities of MRI are not available.

REFERENCES

- [1] Parkin DM, Bray F, Pisani P, et al. Estimating the world cancer burden: Globocan 2000. *Intl J Cancer* 2001;94(2):153-6.
- [2] Fisher B, Brown A, Mamounas E, et al. Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: findings from national surgical adjuvant breast and bowel project B-18. *J Clin Oncol* 1997;15(7):2483-93.
- [3] Abraham DC, Jones RC, Jones SE, et al. Evaluation of neoadjuvant chemotherapeutic response of locally advanced breast cancer by magnetic resonance imaging. *Cancer* 1996;78(1):91-100.
- [4] Dash N, Chafin SH, Johnson RR, et al. Usefulness of tumour marker clip in patient in undergoing neoadjuvant chemotherapy for breast cancer. *Am J Roentgenol* 1999;173(4):911-7.
- [5] Vinicombe SJ, MacVicar AD, Guy RL, et al. Primary breast cancer: mammographic changes after neoadjuvant chemotherapy, with pathologic correlation. *Radiology* 1996;198(2):333-40.
- [6] Fisher B, Mamounas EP. Preoperative chemotherapy: a model for studying the biology and therapy of primary breast cancer. *J Clin Oncol* 1995;13(3):537-40.
- [7] Trecate G, Ceglia E, Stabile F, et al. Tumori della mammella localmente avanzati: ruolo della RMN nella valutazione della risposta alla terapia prechirurgica e del residuo neoplastico prima dell'intervento. *Radiol med* 1998;95:449-55.
- [8] Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumours. *J Natl Cancer Inst* 2004;96(6):487-8.
- [9] Tyagi SP, Khan MS. Carcinoma of breast: its incidence and histomorphological variant in Aligarh. *Indian Jr of surgery* 1990.
- [10] Badwe RA, Mitra S. Clinicopathological features and prognosis of breast cancer in India. *Indian Jr of India* 1990.
- [11] Wilting J, Hagedorn M. Left-right asymmetry in embryonic development and breast cancer: common molecular determinants. *Curr Med Chem* 2011;18(36):5519-27.
- [12] Clemmenson J. Statistical studies in the etiology of neoplasm. Review and results 1997.
- [13] Donegen W. Staging and end results. In: *Cancer of the breast*. Spratt J, Donegen W, (eds). Philadelphia WB, Saunders 1997.
- [14] Smithers DW. Cancer of breast. *Br Jr Radiology* 1952;4(1).
- [15] Olivotto IA, Chua B, Allen SJ, et al. Long-term survival of patients with supraclavicular metastasis at diagnosis of breast cancer. *J Oncol* 2003;21(5):851-4.
- [16] Feldman LD, Hortobagyi GN, Buzdar AU, et al. Pathological assessment response to induction chemotherapy in breast cancer. *Cancer Res* 1986;46(5):2578-81.
- [17] Cocconi G, Di Blasio B, Alberti G, et al. Problems in evaluating response of primary breast cancer to systemic therapy. *Breast cancer Res Treat* 1984;4(4):309-13.
- [18] Walsh R, Kornguth PJ, Soo MS, et al. Axillary lymph node: mammographic, pathological, and clinical correlation. *AJR Am J Roentgenol* 1997;168(1):33-8.
- [19] Londero V, Bazzocchi M, Farte DC, et al. Locally advanced breast cancer: comparison of mammography, sonography, and MR imaging evaluation of residual disease in women receiving neoadjuvant chemotherapy. *Eur Radiology* 2004;14(8):1371-9.