

## Case Series of Locally Advanced Breast Cancer: A Study in a Tertiary Care Hospital, Rangpur, Bangladesh

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## Abstract

## Original Research Article

**Introduction:** Breast cancer is the most common cancer in Bangladeshi women. Locally advanced breast cancer is a clinical challenge which represents a wide range of clinical scenario. Including large primary tumor (Stage T4). Advanced nodal disease (Fixed axillary lymph nodes; or involvement of ipsilateral supraclavicular, infraclavicular or internal mammary nodes) and inflammatory carcinoma. Women with LABC require multimodal therapy and coordinated treatment approach to optimize patient care. **Aim:** The aim of our study was to determine various mode of presentation of patients in clinical practice, to justify various methods of treatments given, response of patients to neoadjuvant chemotherapy and along with possible outcome of our treated patients. **Materials & Methods:** Total 36 patients were selected based on histopathological diagnosis of LABC, who came to our private clinic in the time span of 2011-2016. Cases are reviewed on basis of their clinical presentation, re-investigation findings to exclude metastases; histopathological reports reviewed & TNM status determined for individual patients. Including receptor status assessment. We assess the response of patients to preoperative chemotherapy & review the treatment & follow-up records. **Results:** Among 36 patients 29.5% were in 31-40 years age group. 11 patients (25%) were in 41-50 years age group. Seven (16%) patients were (51-60) years age groups. 5 (11.3%) patients were 61-70 years age group. 100% patients presents with breast lump which are self-detected due to large size. 27 (75%) patients present with nipple retraction skin ulceration in 7 (19.4%) patients satellite nodules 3 (8.33%) patients. Skin oedema 3 (8.33%) patients. Mobile ipsilateral axillary lymph node in 17 (47.2%) fixed ipsilateral axillary lymph node 14 (38.7%) patients. No patient has distant metastasis at presentation. 29 (80.5%) patients sent for preoperative chemotherapy 7 (19.4%). Patients underwent operative treatment as their initial modality of management. 20 patient (55.5%) were ER & PR positive 19 (52.7%) patient were triple negative. Her 2 positive were 2 (5.5%) patients. Partial clinical response obtained in 19 (52.71%) patients. Pathological complete response in 2 (5.5%) patients. Disease recurrence in median time of 10 months period was 11 (30.5%) patients. 7 (19.4) patients develop distant metastases in a median time of 18 months. 9 (25%) patients lost from follow up. 5 (13.9%) patients died within the follow up period of 2 years. **Conclusion:** Challenging situation like locally advanced breast cancer is a difficult clinical problem due to high rate of relapse & low rate of survival but this scenario can be improved by increased utilization of screening by self-breast examination, along with increase awareness of general people with proper utilization of available resources judicious use of neoadjuvant chemotherapy with proper local control by surgery & radiotherapy.

**Keywords:** Locally Advanced, Breast cancer.

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## INTRODUCTION

Commonest cancer in Bangladeshi women is breast cancer with an incidence of 22.5/million. In case of Bangladeshi women in 15-44 years age range breast cancer is at the highest prevalence 19.3/100,000 compared to any other cancer [1]. Locally advanced breast cancer in our country is a challenging clinical

problem with a poor prognosis. Locally advanced breast cancer is characterized by large primary tumor >5cm (T3) associated with or without skin or chest wall involvement or with fixed matted axillary lymph nodes or disease spread to ipsilateral internal mammary or supraclavicular lymph nodes in the absence of any evidence of distant metastasis [2]. Inflammatory breast cancer also included in the definition which has distinct

biological feature & clinical behavior and this type of patient is not included in our series [3]. Locally advanced breast cancer is staged as stage II B (T3 No) & III a & IIIb according to American joint committee on Cancer staging and end result report. In population having screening mammography <5% patients presents with locally advanced breast cancer [4]. Three (3) years survival in stage III cancer 70% and 5 years survival 55% [5]. Median survival for women with stage III disease is 4.9 years. There is no published report of the locally advanced breast cancer prevalence in our country. The ideal methods of treating these patients using multimodal approach. Comprising neoadjuvant chemotherapy. Surgical treatment in form of modified radical mastectomy adjuvant chemotherapy: adjuvant radiotherapy & hormone therapy given according to the merit of the patients. We reviewed our patients retrospectively to determine the various mode of clinical presentation reasons for referral of patients to neoadjuvant chemotherapy and response achieved, evaluations of the patients in relation to different modalities of treatment given & possible outcome following treatment including surgery chemotherapy and radiotherapy.

## OBJECTIVES

### General Objective

- To observe 36 cases of personal series of locally advanced breast cancer in relation to clinical presentation and final.

### Specific Objectives

- Asses various mode of presentation of patients in clinical practice
- To justify various methods of treatments given
- Measure response of patients to neoadjuvant chemotherapy
- Along with possible outcome of our treated patients

## MATERIAL AND METHODS

These 36 patients are attained our hospital outdoor from a time span of 2011-2016. Patients are reviewed in relation to their different clinical presentation including palpable breast lump, nipple retraction skin ulceration satellite nodules, and skin oedema, mobile or fixed ipsilateral axillary lymph nodes without any evidence of distant metastasis. All of the patients were histopathologically confirmed by core cut biopsy to have breast cancer. Investigations are reviewed like CBC, CXR, USG both breast, bilateral mammograms, USG WA; liver enzyme & bone scan & metastasis excluded. Immunohistochemistry reports reviewed to determine ER, PR & HER2 status post-operative histopathological reports assessed and final TNM status determined, along with assessment of pathological response & clinical response following neoadjuvant chemotherapy. Finally overall response of multimodality treatment assessed in relation to disease

recurrence & development of distant metastases & patient death.

### Inclusion Criteria

- Patients aged  $\geq 30$  years.

### Exclusion Criteria

- Age < 30 years.

## RESULTS

Among 36 patients 29.5% were in 31-40 years age group. 11 patients (25%) were in 41-50 years age group. 7 (16%) patients were (51-60) years age groups. 5 (11.3%) patients were 61-70 years age group. 100% patients presents with breast lump which are self-detected due to large size. 27 (75%) patients present with nipple retraction skin ulceration in 7 (19.4%) patients satellite nodules 3 (8.33%) patients. Skin oedema in 3 (8.33%) patients. Mobile ipsilateral axillary lymph node 17 (47.2%) fixed ipsilateral axillary lymph node 14 (38.7%) patients. No patients has distant metastasis at presentation. 29 (80.5%) patients sent for preoperative chemotherapy. Seven (7) (19.4%). Seven (7) 19.4% patients underwent operative treatment as their initial modality of management. 20 patient (55.5%) were ER & PR positive 19 (52.7%) patient were triple negative. Her 2 positive were 2 (5.5%) patients. Partial clinical response obtained in 19 (52.71%) patients. Pathological complete response in 2 (5.5%) patients. Disease recurrence in median time of 10 months period was 11 (30.5%) patients. 7 (19.4) patients develop distant metastases in a median time of 18 months. 9 (25%) patients lost from follow up. 5 (13.9%) patients died within the follow up period of 2 years.

**Table-1: clinical feature at presentation are summarized in table. (n=36)**

Disease Name	n	%
Breast Lump	36	100%
Nipple Retraction	27	75%
Skin Ulceration	2	5.5%
Satellite Nodules	3	8.33%
Skin Oedema	3	8.33%
Mobile Ipsilateral Axillary LNS	17	47.2%
Fixed Ipsilateral Axillary LNS	14	38.9%

All of the 36 patients presented with breast lump or majority of them are self-detected abnormality due to presence of large lump. 27 (75%) patients presents with nipple retraction. Skin ulceration with fungating mass present in 2 (5.6%) patients.

Satellite nodules were found in 3 (8.33%) patients' mobile ipsilateral lymph nodes present in 17 (47.2%) patients. Fixed ipsilateral axillary lymph nodes in 14 (38.9%) patients. No evidence of distant metastases present at presentation among these 36 patients.

**Table-2: Clinical Staging of the study participants. (n=36)**

Age	n	n	T	N	M	TNM staging
31-40 Years	13 (29.5%)	6	T2	N2	M0	III A
		3	T3	N1	M0	III A
		4	T4	N0	M0	III B
41-50 Years	11 (25%)	5	T2	N2	M0	III A
		3	T3	N2	M0	III A
		3	T4	N1	Mo	III B
51-60 Years	7 (16%)	4	T2	N2	M0	III A
		2	T3	N1	M0	III A
		1	T4	N0	M0	III B
61-70 Years	5 (11.3%)	3	T2	N2	M0	III A
		2	T3	N1	M0	III A

Among 36 patient 26 patients (72.2%) were TNM stage III A, 10 (27.8%) patients were TNM stage III B. Maximum number of patient 13 (29.5%) was in 3<sup>rd</sup> of decade of life among them 9 patients were III A & 4 patients were stage III B. In 4<sup>th</sup> decade of life there were 11 patients (25%) & 8 patients were III A. Three Patients were III B. In 5<sup>th</sup> decade there were 7 (16%) patients 6 of them were in stage III A & One patient

belongs to stage III B. In 6<sup>th</sup> decade of life we have 5(11.3%) patients all of them belong to stage III A. In relation to clinical & pathological response of patients receiving pre-operative chemotherapy. Among (29) patients sent for pre-operative chemotherapy partial clinical response achieved in 18 (62%) patients with reduction in tumour size & axillary lymph node. 6 patients (20.6%) had complete clinical response. (No evidence of cancer on any imaging, do not mean cancer gone) pathological complete response with no evidence of any viable tumour observed in 2 (6.9%) patients. Stable disease after neoadjuvant chemotherapy (Tumour neither growing nor shrinking, means cancer has not increased in size by >50% or decreased in size by >30% also means that tumour has not developed any metastases. Progressive disease means tumour has increased in size by at least 20% and a little worse than partial response. Partial response means tumour decreased in size by at least 50% were found in 3 (8.33%) patient's one patient (2.8%) had progressive disease.

**Table-3: Response criteria of the study participants. (n=36)**

Response criteria	n	%
<b>i)</b> Reduction in tumours size or nodes (Partial clinical response)	17	58.62%
<b>ii)</b> Complete clinical response (CCR)	6	20.6%
<b>iii)</b> Pathological complete response with no evidence of viable tumour.	2	6.9%
<b>iv)</b> Stable disease after neoadjuvant chemotherapy	3	8.33%
<b>v)</b> Progressive disease after neoadjuvant chemotherapy	1	2.8%

**Table-4: Receptor status in 36 patients. (n=36)**

	n	%
ER (+ve)	11	30.55%
PR (+ve)	9	2.5%
ER & PR Both (+ve)	12	33.3%
ER& PR Status Both (-ve)	8	22.2%
Her 2 (+ve)	1	2.8%
triple (-ve)	7	19.4%

ER (+ve) in 11 patients (30.55%), ER & PR Both (+ve) in 12 (33.3%), ER & PR (-ve) in 8 patients

(22.2%), Her 2 (+ev) in 1 patient (2.8%), 7 patients (19.4%) are triple negative

**Table-5: Patient's criteria for referral to neoadjuvant chemotherapy.(n=29)**

Patients Criteria		n	%
TNM Stage	Stage III A	21	58.3%
	Stage III B	8	22.2%
Chemotherapy recommendation	(Doxorubicin & cyclophosphamide) AC/FAC	20	69%
	AC & Taxane	9	31%

## DISCUSSION

In our country many newly diagnosed patients present with locally advanced breast cancer (of which no exact percentage is known due to lack of clinical trials in our country) in comparison to western word. Where population receiving regular screening mammography LABC is 4.6% [6]. In our country late presentation due to lack of social awareness. Low level of education; lack of screening protocol; fear of attaining medical management all contribute together. In our personal series all of our patients presented with

self-detected breast lump because lumps were big enough to (3-5 cm) to be detected as an abnormality none of them received any screening mammogram prior to attain our clinic. As chance of distant metastases are bigger in LABC [7] all of our patients underwent core cut biopsy followed by staging investigations and distant metastases excluded, 29 patients (80.5%) referred for neoadjuvant Systemic Therapy (NST) among them 26 patients (89.6%) showed response to it in the form of partial clinical response in 58.6% patients; complete clinical response in 20.6%, patients with pathological complete response in 6.9% patients. 4

(13.79%) Patients did not respond to chemotherapy, who further submitted to neoadjuvant radiotherapy followed by surgery. All patients undergone surgical treatment in the form of modified radical mastectomy followed by adjuvant radiotherapy as part of loco regional control of disease & minimize local recurrence 7 patients (24%) patients considered operable at presentation underwent modified radical mastectomy followed by adjuvant chemotherapy and radiotherapy [8]. Studies of LABC shows that more advanced breast cancer are more ER & PR (-ve) Bird PA, Hill AG, Houssain N 2008- Poor hormone receptor expression in East African breast cancer Ann & surg oncol.15 1983-8. We found that 33.3% patients are both ER & PR (+ev) 22.2% patients are both ER & PR (-ve). Triple (-ev) were 19.4%. Triple (-ev) breast cancer has worse prognosis with earlier recurrences Dent R, Pritchard KI *et al.*, 2007, Triple (-ev) breast cancer feature and pattern of recurrence clin cancer Res 13, 4429-34) Further studies in our country required to assess the prevalence of triple (-ev) disease in LABC population to improve our knowledge on tumour biology and prognosis. Of our patients who were ER & or PR (+ev) prescribed hormonal therapy for 5 years post operatively. Pathological complete response which was assessed on basis of post-operative histopathological assessment was found in 2 (6.2%) of patients. Pathological Complete Response (PCR) to neoadjuvant systemic therapy has been shown to be the best predictor of disease free survival patients with Pathological Complete Response (PCR). In our study have no disease recurrence in our follow up period but this small number of patient makes its significance difficult to interpret. 12 patients (23.3%) patients develop local recurrence within a median time frame of 11 months. 9 patients (25%) patients develop distant metastases within a median time frame of 18 months. 4(11.11%) patients died due to complication of distant metastases within our follow up period of 2 years. Optimal management of locally advanced breast cancer encompasses combined modality treatment with neoadjuvant chemotherapy followed by low regional therapy in the form of surgery and radiation involvement of multidisciplinary team from the on set of patient management is very vital. Neoadjuvant chemotherapy can down stage the tumour to make it operable. Even with aggressive management LABC remains a difficult clinical problem, due to high rate of recurrence & low rate of survival. It is particularly important to address this disease in a developing nation. Like ours in which 70% of all cancer cases will occur by 2020. So systemic studies & research needed in these setting which will guide judicious use of available financial & human resources [9].

#### Limitations of the Study

Limitation of this studies is it retrospective methodology; treatment and clinical response were not

meticulously documented in the clinical chart. Making their assessment difficult and also small sample size

#### CONCLUSION AND RECOMMENDATIONS

In conclusion it can be said that to help the patients of LABC in our country we should design cost effective multimodal treatment approach. Public awareness campaigns training of community health workers educate the patient to perform clinical breast examination along with national guideline for effective judicious pre-operative chemotherapy regimen so that few but effective chemotherapy public regimen can be Use at & arrangement for facilities for delivering radiation therapy in cost effective radiation methods like shorter regimens.

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