International Surgery Journal
Shoeb M. Int Surg J. 2017 Aug;4(8):2565-2571
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20173390

Original Research Article

Study of clinico-pathological factors, indications and response to chemotherapy in breast cancer patients in a tertiary care hospital in south India

Mohammad Fazelul Rahman Shoeb*

Department of General Surgery, Gulbarga Institute of Medical Sciences, Gulbarga, Karnataka, India

Received: 28 June 2017
Accepted: 19 July 2017

***Correspondence:**
Dr. Mohammad Fazelul Rahman Shoeb,
E-mail: shoeb11@gmail.com

ABSTRACT

Background: Breast cancer is considered a systemic disease, surgical interventions on most of the patients can reduce the loco regional burden and chemotherapy can reduce systemic burden by reducing chances of metastasis and recurrence and prolong life expectancy. The objective of this study was to assess the clinic-pathological factors of patient presenting with breast cancer and to study the indications and response to chemotherapy for breast cancer.
Methods: A prospective study of fifty patients was carried out at Victoria hospital and Bowring and Lady Curzon Hospital between October 2010 to October 2012 who underwent surgery, chemotherapy, radiotherapy and hormonal therapy.
Results: Most patients presented with palpable axillary lymph nodes (64%) and belonged to stage II disease (50%). Invasive ductal carcinoma was seen in 90% of cases while medullary in 04%, colloid in 2% and Infiltrating lobular was seen in 04% of patients. Totally 64% cases were ER or PR+, and 36% were ER/PR- among the study participants. 70% of the patients operated had positive nodes. All 50 cases received chemotherapy. Chemotherapy was indicated in node positive patients and in patients whose tumour was measuring more than 1 cm. After follow-up of 50 patients for about a period of two years, 3 patients died, 4 patients had metastasis and in the remaining 47 surviving patients none of them had recurrence at the end of second year.
Conclusions: Most cases and belonged to Stage II disease with Invasive ductal carcinoma being most common histological subtype seen in 90% of cases. FNAC is good diagnostic procedure cost effective and reliable as all cases post-operative HPE confirmed malignancy. Patients should be treated by chemotherapy in indicated cases, as carcinoma breast is a systemic disease and chemotherapy can reduce systemic burden by reducing chances of metastasis and recurrence and prolong life expectancy.

Keywords: Axillary clearance, Early and locally advanced breast cancer, Simple mastectomy

INTRODUCTION

Carcinoma breast is the second most common cause of death in Indian women next only to cervical cancer.[1] The incidence appears to be increasing probably due to better screening and diagnostic facilities. Management of carcinoma breast is constantly evolving with new research / studies taking place all over the world.[2] In the last 100 years breast surgery has moved a full circle started with lumpectomy and moved towards radical mastectomy coming back to conservative surgery with neoadjuvant chemotherapy and radiotherapy.[3] In the present study, an attempt has been made to study the various risk factors, natural history of the disease, clinical

signs and symptoms, pathological types, axillary nodal involvement and the management of breast cancer. The objectives of this work were to study the management of patients presenting with breast cancer and to study the indications and response to chemotherapy for breast cancer.

METHODS

A prospective study was designed and carried out on 50 patients of Victoria Hospital and Bowring and Lady Curzon Hospital from October 2010 to October 2012, who were diagnosed to have carcinoma breast and who fulfilled the understated criteria between were included in the study.

Inclusion criteria

- Female patients presenting with breast cancer irrespective of tumour stage and size and location
- Females >18 years.

Exclusion criteria

- Male patients and benign breast disease
- Females <18 years.

A detailed clinical history was elicited from all patients at the time of admission. All the patients who had clinical evidence and FNAC evidence of malignancy were worked up for surgery. The findings and reports obtained were entered in the proforma of all the patients.

- Blood investigations: Hb%, BT, CT, FBS, PPBS, Bl. urea, serum creatinine, LFT
- Chest X-ray
- Ultrasound abdomen for clinical evidence of hepatomegaly, ovarian enlargement or free fluid
- Bone scans if patients had symptoms suggestive of metastasis
- Mammography of opposite breast in selected cases
- Consent of patient for surgery.

After confirmation cases were divided into early breast cancer and locally advanced breast cancer and were treated by multidisciplinary approach with surgery with axillary clearance, chemotherapy, radiotherapy and hormonal therapy depending on stage and histopathology. Biopsy was sent for detailed histological diagnosis including receptor status. All patients were operated under general anesthesia.

Patients were later put on chemotherapy and hormonal therapy. Consent was taken for chemotherapy. FAC regimen was given for chemotherapy. Six cycles of chemotherapy were given with interval of 21 days between two cycles. 5-flurouracil 500 mg/m^2, Doxorubicin 50 mg/m^2, Cyclophosphamide 500 mg/m^2 was given after getting routine investigations like CBC, LFT, ECHO of normal value and cardiology fitness. In neoadjuvant chemotherapy three cycles were given before surgery and three cycles were given after surgery. Post-operative follow-up was done to note the complications both in hospital and after discharge within 2 years. Follow up was done using clinical history, examination, blood investigations, ultrasonography, chest X ray.

Based on hormone receptor status patients were advised tamoxifen therapy. Tamoxifen was advised in dose of 20 mg OD for five years. Follow up of patients was done on OPD basis and clinical evidence of recurrence and metastasis was assessed and any suspected cases underwent investigations to look for recurrent disease or metastasis all of which were recorded in the proforma.

All the data collected from the patients were documented and calculated in MS excel. The data were presented in numbers and percentages.

RESULTS

A prospective study was done and the following data was obtained from the 50 cases studied at Victoria hospital and Bowring and Lady Curzon hospital from October 2010 to October 2012 for a period of 2 years.

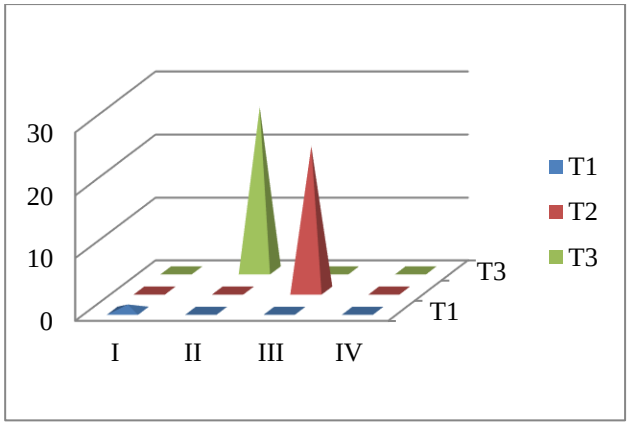
Out of fifty cases majority cases were seen in right side (58%) than left side breast. 58% of total patients were having lump in upper and outer quadrant of breast. 20% of the patients showed fixity to skin was the highest in comparison to other structures. 52% of total patients were more than 5 cm tumor size followed by 2-5 cm (46%).

Clinicopathological factors are given in Table 1. 64% of our patients had palpable axillary nodes on clinical examination. Among the study participants, central group involvement was maximum that is 50% followed by involvement of pectoral or anterior group of lymph nodes that is 42%. Involvement of supraclavicular was clinically not detected in the study group. Internal mammary group of nodes was also not made out. In the present study, none of the patients was involved of opposite breast or axilla. In this series, the study was conducted involving early and locally advanced stage breast cancer. Stage IV breast cancers were not included in the study. 52% of cases belong to stage II and 46% belong to stage III disease (Figure 1). All cases in our series underwent fine needle aspiration cytology and only 2 cases who had inconclusive cytology report underwent excision biopsy. 16% of cases were associated with diabetes mellitus who were controlled with pre-operative insulin. 28% of patients had essential hypertension. Ischemic heart disease was present in 4% of cases, most of them were elderly. Invasive ductal carcinoma was seen in 90% of cases while medullary in 04%, colloid in 2% and Infiltrating lobular was seen in 4% of patients. Totally 64% cases were ER or PR+, and 36% were ER/PR- among the study participants. 70% of the patients operated had positive nodes. 35 cases which had positive

nodes, 26 cases (74.2%) was involved of only level I nodes and 9 cases (25.7%) had involvement upto level II (Figure 2). Out of the 35 cases that had clinically palpable nodes 33 cases (94.2%) were proved to be histologically positive and remaining 2 cases (5%) were not found to have nodal metastasis. Among the remaining 15 cases that had clinically normal axilla, 5 cases (33.3%) still had histologically positive nodes.

Table 1: Clinico-pathological features in breast cancer patients.

	No. of cases	Percentage (%)
Lymph nodes (clinically)		
Absent	18	36
Present	32	64
Group		
Pectoral/Anterior	21	42
Lateral	3	06
Central	25	50
Posterior	3	06
Apical	0	0
Supraclavicular	0	0
Involvement		
Opposite breast	0	0
Opposite axilla	0	0
Procedure		
FNAC	50	100
Excision biopsy	2	4
Associated diseases		
Diabetes	8	16
Hypertension	14	28
DM+HTN	5	10
IHD	2	4
Type of tumor		
Invasive ductal tumor	45	90
Medullary carcinoma	2	04
Paget's disease	0	0
Colloid carcinoma	1	2
Infiltrating lobular carcinoma	2	4
Hormone receptor status		
ER+/PR+	24	48
ER+/PR-	01	2
ER-/PR+	07	14
ER-/PR-	18	36
Axillary node on HPE	35	70
Histopathology of axillary nodes (n=35)		
Clinically palpable nodes which were histologically positive	33	94.2
Clinically palpable nodes but histologically negative. (clinically false positive)	2	5
Clinically normal axilla but positive nodes (clinically false negative)	5	33.3
Tumor size	No of cases operated	% with positive ax nodes in present study (HPE)
T1	1	0
T2	23	52
T3	21	86
T4	05	100



T1: <2 cm, T2: 2-5 cm, T3: >5 cm; Stages: I (T1,N0,M0); II (T0,N1,M0 T1,N1,M0 T2,N0,M0 T2,N1,M0 T3,N0,M0); III (T0,N2,M0 T1,N2,M0 T2,N2,M0 T3,N1,M0 T3,N2,M0 T4,N0,M0 T4,N1,M0 T4,N2,M0 T4,N3,M0); IV (Any T, Any N, M1)

Figure 1: Distribution of patients according to tumor size and stages.

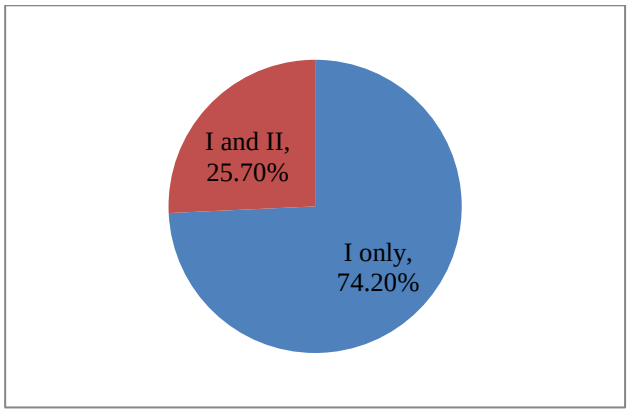


Figure 2: Level of axillary node involvement.

DISCUSSION

A prospective study of fifty cases with early (I, IIa and IIb) and locally advanced cases (IIIa, IIIb and IV) were included in the study. A detailed work up was carried out according to proforma and based on the observations given in the previous tables.

According to the Globocan Project, if we compared breast cancer deaths in India for every 2 women newly diagnosed with breast cancer, one lady is dying of it in year 2012. The diagnosed cases were lesser in comparison to China and US.[4] But the survival rates were lesser, because of lack of awareness and screening.[5]

The upper outer quadrant was the most common site of involvement.[6] The reason for this is that quadrant of breast tissue has the maximum amount of parenchyma. In our series 58% of patients had upper outer quadrant involvement followed by upper inner quadrant in 14%.

In the present study only 2% of patients presented with size <2 cms (T1), 46% of cases had tumor 2-5 cm (T2) and 52% of cases were more than 5 cm (T3). Maximum cases were found having T3. 52% of cases belong to stage II and 46% belong to stage III disease, and only 2% of cases belonged to stage I and none of them belonged to stage IV. Vyas et al, study showed 15.3% of patients with <2 cm size lump and 67.1% of cases of patients with 2-5 cm size and only 17.6% were >5 cm.[7] Bloom et al reported 55% in stage I, 36% in stage II and 6.7% in stage III.[8,9]

In the present study 36% of patients had clinically normal axilla, 64% of patients had axillary lymph nodes. Sen and Das Gupta series showed 56% of cases with palpable nodes and 44% had no nodes on palpation.[6] 50% in the present study group had central group of lymph nodes, 42% central and only 6% had posterior and lateral nodes. This suggests that central group and pectoral group of nodes were most common to be involved. All our cases were subjected to FNAC and in 48 cases provided evidence of malignancy. In 2 patients, the report was inconclusive and underwent lumpectomy later subjected to definitive procedure after HPE. 16% of our patients were diabetics who were managed with pre-and post-operative insulin. 28% of patients were hypertensives and 10% were both diabetics and hypertensive. 4% of patients had history of ischemic heart disease. None of these were associated with any complications in the pre-or post-operative period.

Present study revealed 90% of cases of invasive ductal carcinoma, 4% of medullary carcinoma and 4% of infiltrating lobular carcinoma. This shows that invasive ductal carcinoma is the most common histopathological types.[10] Vyas and coworkers reported 89.5% of cases with invasive ductal carcinoma followed by lower incidence of other types in their study.[7] Fischer et al reported in his observations that 76.6% of patients with invasive ductal carcinoma (Figure 4).[10]

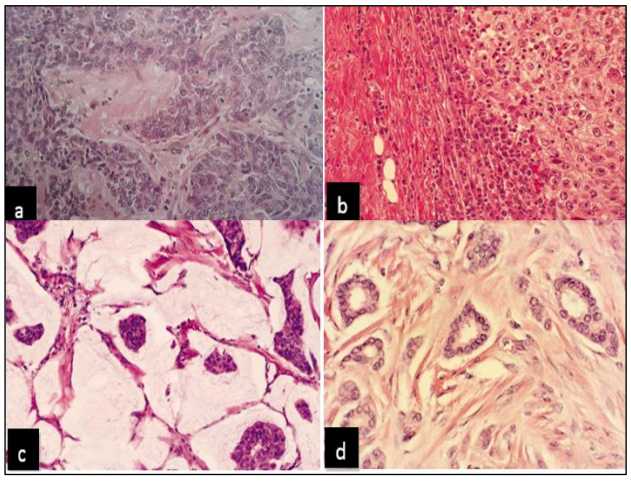


Figure 3: Histological types of tumor. (a) Invasive ductal carcinoma; (b) Medullary carcinoma; (c) Mucinous carcinoma; (d) Tubular carcinoma.

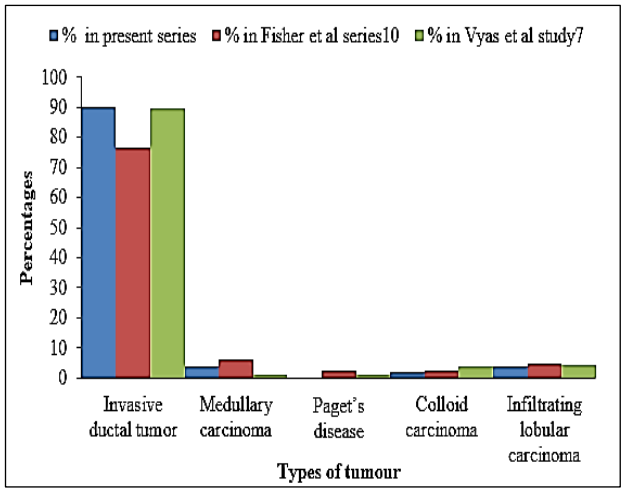


Figure 4: Comparison of different types of tumours with previous studies.

In the present study, totally 64% cases were ER/PR+, and 36% were ER/PR-. This was comparable to Desai et al study in Tata memorial hospital which showed 53.5% cases with ER or PR+, and 56.5% with ER/PR-.[11] All patients with Receptor positive status were given tamoxifen irrespective of age, menopausal status, or involvement of axillary nodes. Benefit of hormone therapy on estrogen receptor negative tumors is very less. 70% of the patients operated had positive nodes in our study. The results were comparable with Sen and Das Gupta study which showed 76.7% of patients with node positive status.[6,12]

Of the 35 cases which had positive nodes in the present study, 26 cases (74.2%) had involvement of only level I nodes, 9 cases (25.7) had involvement upto level II and 5 cases (13.6) had axillary nodes up to level III. Node negative women have 30% risk of recurrence whereas node positive women have 70% risk.

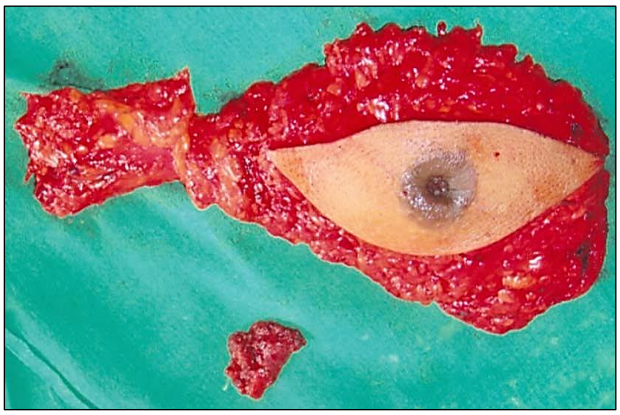


Figure 5: Resected specimen in this study containing breast and axillary node.

Skip metastasis- patient with level III disease usually have many affected nodes in which level II and I are involved, but level I may not show metastasis in some cases. Thus, dissection of level I only will underestimate the degree of spread and will not produce accurate prognostic information.

The NSABP B-04 trial shows that 39% of patients had histologically positive nodes though clinically negative (33.33% in our study), where as in clinically node positive group only 73% of patients were histologically positive (94.2% in our study).[13]

This proves the importance of axillary dissection in all patients, since deposit less than 2 cm in size in the axilla can be detected only by histopathology. The clinical assessment of axillary nodes is unreliable. About 30% of palpable and apparently diseased nodes are found to be histologically free of metastasis.

In the present study, none of patients with T1 tumors had nodal involvement. 52% of T2, 86% of T3 and all 100% of patients with T4 size tumor had nodal involvement. Silverstein et al study showed 16% of patients of T1, 47% of T2, 68% of T3 and 86% of patients with T4 size to have nodal involvement on HPE.[14] When comparing axillary nodal status and tumor size, it was found that the likelihood of axillary LN involvement increases as the size of the primary tumor increases which was comparable to Silverstein et al series (Figure 6).[14]

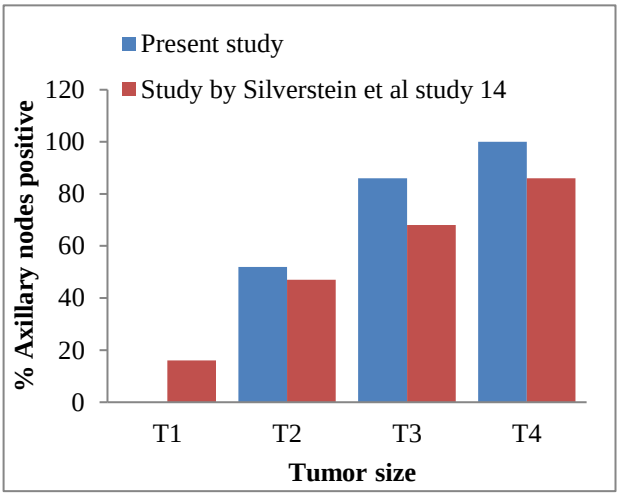


Figure 6: Comparison of axillary node involvement with other studies.

Our study included early stage and locally advanced stage breast cancer. Patients were treated by multidisciplinary approach as breast cancer is considered a systemic disease, surgical interventions on most of the patients can reduce the loco regional burden and chemotherapy can reduce systemic burden by reducing chances of metastasis and recurrence and prolong life expectancy. Surgery was offered to all patients in the form of Modified radical mastectomy or wide local excision which included axillary clearance to look for nodal status even in clinically node negative cases. Axillary clearance

was done till level II lymph nodes. Surgery aimed to provide adequate local clearance.

All patients with axillary node involvement on HPE and tumor size greater than 1 cm were advised chemotherapy that is all of patients in our study were advised chemotherapy. Adjuvant chemotherapy was given in 96% of patients with 6 cycles of FAC chemotherapy regime at 3 weekly intervals. Neoadjuvant chemotherapy was given to 4% of patients with 3 cycles of FAC before surgery and 3 cycles of FAC after surgery at 3 weekly intervals.

Among these 3 patients who died all developed metastasis after completion of chemotherapy, two patients had liver metastasis one had lung metastasis. In the CALGB trial by Henderson IC et al, after median follow up of 5 years for AC, overall survival rates were 77%.[15] The 5-year results of Breast Cancer International Research Group trial 001 by Martin M et al, use of FAC in patients with node-positive breast cancer after following up of five years, the overall survival was 81%.[16] As study duration was two years and few patients were followed up for less than two years the results of our study cannot be compared with results of other studies.

Out of 47 patients who survived none of the patients had recurrence in period of two years. Relapse free survival rate was 100% at the end of second year. As study duration was two years and few patients were followed up for less than two years the results of our study cannot be compared with results of other studies.

CONCLUSION

A study was conducted of 50 cases of carcinoma breast and the following conclusions were drawn. Most cases had tumor size >5 cm (T3), and belonged to Stage II disease. Most patients presented with positive axillary lymph nodes with central group involvement being most common. FNAC is good diagnostic procedure cost effective and reliable as all cases post-operative HPE confirmed malignancy. Invasive ductal carcinoma was most commonly seen pattern on histopathology which was observed in 90 % of cases. As breast cancer is considered a systemic disease, chemotherapy can reduce systemic burden by reducing chances of metastasis and recurrence and prolong life expectancy. Chemotherapy was indicated in patients having positive lymph nodes and in patients whose tumour was measuring more than 1 cm. All patients in our study received chemotherapy. FAC regimen was given for 6 cycles at interval of 3 weeks duration with minimal and minor complications. In neoadjuvant chemotherapy 3 cycles of FAC were given before surgery and 3 cycles were given after surgery.

FAC chemotherapy regimen was used at our hospital as it is economically feasible and effective therapy which can be afforded by a most of the patients. Other drugs like taxanes were not used keeping in mind the economic constraints of general population in Indian set up.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Aswathy S, Reshma J, Avani D. Epidemiology of cervical cancer with special focus on India. Int J Womens Health. 2015;7:405-14.
2. Wood WC, MUSS HB, Solin LJ, Olopade OI. Cancer of the Breast. Devita, Cancer: Principles and Practice of Oncology, 7th edition, Lippincott William and Wilkins, Philadelphia; 2005;33:1400-1487.
3. A guide for women who are considering breast cancer treatment with chemotherapy and/or hormonal therapy before surgery. Available at https://www.bcia.org.au/brochure/neoadjuvant-decision-aid/ANZBCTG%20DOMINO%20AID.pdf. Accessed on 10 May 2017.
4. Statistics of breast cancer in India. Available at: http://www.breastcancerindia.net/statistics/stat_global.html. Accessed on 10 May 2017.
5. Trends of breast cancer in India. Available at: http://www.breastcancerindia.net/statistics/trends.html. Accessed on 10 May 2017.
6. Sen AK, Das Gupta TK. Cancer of breast and its treatment. Ind J Surg. 2009;11:832-47.
7. Vyas JJ, Desai PB, Sarkar S. Operable breast cancer and axillary tumor burden. Indian J Surg. 1989;109-18.
8. Bloom BS, Pouvourville N, Chatre S, Jayadevappa R,Weinberg D. Breast Cancer treatment in clinical practice compared to evidence and practical guidelines, Brit J Canc. 2004;90:26-30.
9. Schaepveld M, Elisabeth GE, Winette TA. The prognostic effect of the number of histologically examined axillary lymph nodes in Breast cancer: Stage migration or age association. Annals of Surgical Oncol. 2006;13:465-74.
10. Lisa A. Newman. "The Breast" F. Charles Brunicardi, Schwatz Principles of Surgery, 9th Edition, Mc graw hill; 2010: 423-474.
11. Desai SB, Moonim MT, Gill AK. Punia RS, Naresh KN, Chinoy RF. Hormone receptor status of Breast cancer in India: A Study of 798 tumors. Department of Pathology, Tata Memorial Hospital, Mumbai. Breast. 2000;9(5):267-70.
12. Chua B, Ung O, Taylor R, Boyages J. Frequency and predictors of Axillary lymph node metastasis in invasive breast cancer. ANZ J Surg. 2002;72(11):786-92.
13. Pritcherd KI. Surgery for breast cancer patients. The 2nd International Breast cancer research group conference. Cancer. 2003;7:98.

14. Silverstein MJ, Skinner KA, Lomes TJ. Predicting axillary nodal positivity in 2282 patients with breast crcinoma. World J Surg. 2001;25(6):767-72.
15. Henderson IC, Berry DA, Demetri GD, Cirrincione CT, Goldstein LJ, Martino S, et al. Improved outcomes from adding sequential Paclitaxel but not from escalating Doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J Clin Oncol. 2003;21:976.
16. Martin M, Pienkowski T, Mackey J, Pawlicki M, Guastalla JP, Weaver C, et al. Adjuvant docetaxel for node-positive breast cancer. N Engl J Med. 2005;352(22):2302-13.

Cite this article as: Shoeb M. Study of clinico-pathological factors, indications and response to chemotherapy in breast cancer patients in a tertiary care hospital in south India. Int Surg J 2017;4:2565-71.