

Spectrum of Histomorphological Prognostic Factors in Invasive Breast carcinoma-NST

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ABSTRACT

Introduction: Breast carcinoma is one of the leading causes of mortality and morbidity in females. This study was undertaken with the aims and objectives to look into the spectrum of various gross and microscopic histomorphological factors of invasive breast carcinoma.

Material and methods: This is a retrospective study, only patients diagnosed with Invasive breast carcinoma-NST from 2007-2015 (8years) were included. MRM specimen's gross and microscopic finding were collected and studied.

Results: Total 257 cases were studied; maximum patients were in fifth decade, multiparous and from middle socio-economic status. Left sided carcinoma was seen in 59% cases and 41% were in UOQ. Nipple-areola was found normal in 63.2% cases and retracted in 37.6% patients. Similarly overlying skin was normal in 67.3% cases, dimpling and peau-d-orange was present in 11.3% and 9.5% respectively. ER/PR positive was found in 44.7% and negative in 49.8% while HER2 was found negative in 70.8% cases.

Conclusion: in developing countries patients invariably presents with advance stages of breast carcinoma with dimpling, peau-d-orange of skin, nipple retraction and ulceration. In majority of patients tumour sizes is invariably more than 2 cm and already have positive axillary lymph nodes, tumour emboli and majority have negative ER/PR.

Keywords: Breast Carcinoma, Prognostic Factors, Histomorphological

patients with similar pathological characteristics treated with identical regimens have highly variable clinical outcomes⁵, suggesting that identification of additional prognostic factors may improve patient stratification. As the range of options for the treatment of patients with breast carcinoma widens, it becomes increasingly important that the clinician is provided with accurate prognostic information on which therapeutic decisions are based. Therefore accurate and complete pathological examination is crucial to decisions regarding appropriate management of the breast cancer patients. Pathology report plays an important part in therapeutic decisions.

MATERIAL AND METHODS

The present study is a combination of both retrospective as well as prospective study on breast carcinoma, and was carried out in department of Pathology, at a tertiary care hospital during a period from June 2013 to September 2015 (cases included from May2007 to September 2015). All the MRM specimens with axillary node dissection which were diagnosed to be Invasive breast carcinoma-NST on microscopy were included in the study, retrospectively from May2007-June 2013 and prospectively from July2013-September2015. Demographic data was noted from chart: age, sex, parity, socio-economic status according to BG Prasad Socio-economic classification 2014.⁶

Gross of specimen: Gross morphological features were noted: tumour size, changes in overlying skin, nipple-areola complex changes, tumour fixity to overlying and underlying tissue and any other gross finding

INTRODUCTION

Worldwide breast cancer is the most frequent cancer in women and represents the second leading cause of cancer death among women.¹ Breast carcinoma is on the rise in developing countries. Due to poor socio-economic status, illiteracy, painless lump, lack of screening mammography facility/awareness and other social taboo it is often neglected too long only to get diagnosed at an advanced stage. Locally advanced breast cancer constitutes more than 50-70% of the patients presenting for treatment in India.² Over 100,000 new breast cancer patients are estimated to be diagnosed in India with premenopausal patients constituting about 50% of all patients.³ Management of breast cancer is immunologically and histologically heterogeneous in character and requires multidisciplinary treatment. A number of pathological characteristics have been identified, which can be used as prognostic factors, including tumour size and grade, hormone receptor, HER2, and lymph node status⁴ which are all considered when predicting prognosis and determining the most effective treatment options. Despite these factors and tests, predicting patient outcome is imprecise, as

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Microscopy: Histologic sections of specimen and axillary lymph nodes were retrieved and reviewed to confirm the findings of histopathology which were in the report given by Pathology department. In addition all the slides were reviewed for additional prognostic factors if anything missing in original report. Histological type of carcinoma: Classification is done according to WHO 2012. Only invasive breast carcinoma-NST was taken into account and was confirmed (according to inclusion criteria). Histological grading was done according to modified Bloom Richardson by Elston and Ellis method. Following aspects of tumour were also recorded: Skin Invasion by tumour, In-situ component, Paget's disease, Lymph node involvement, Tumour margins, Tumour emboli, Surgical margins and Tumour Necrosis

RESULTS

Out of total 291 cases, 257 (88.4%) were of Invasive breast carcinoma-NST and 34 (11.6%) were other types of breast carcinomas.

Demographics: Maximum number of patients were from age group of 41-50 years (34.5%) followed by 51-60 years (26.7%) with mean age of 50.2 years. Majority of the patients

Size	Frequency	Percent
Up to 2 cm	21	8.2
2.1 to 5 cm	153	59.5
to 10 cm	72	28
>10 cm	11	4.3
Total	257	100

Table-1: Showing tumour size distribution

Tumour Grade	Frequency	Percent
Grade I	24	9.3
Grade II	111	43.2
Grade III	122	47.5
Total	257	100

Table-2: Showing tumour grade according to modified RB score

No. of lymph nodes involved	Frequency	Percent
0	121	47
1-3	47	18.3
4-7	36	14
8-10	29	11.3
>10	24	9.4
Total	257	100

Table-3: Showing the frequency and number of of lymph node involvement

ER/PR	Frequency	Percent
P/P	115	44.7
N/N	128	49.8
P/N	10	3.9
N/P	4	1.6
Total	257	100

Table-4: Showing distribution of cases according to ER/PR status

HER2	Frequency	Percent
Positive	75	29.2
Negative	182	70.8
Total	257	100

Table-5: Showing distribution of cases according to HER2 status

(83.5%) patients were multiparous, 9% were primiparous and 7.5% were nulliparous. Maximum number of patients were from low socio-economic status (72.6%), followed by 24.5% which were of middle socio-economic status and only 2.9% were from high socio-economic status.

Histomorphological factors: Left sided breast carcinoma was seen in 59% cases and 41% patients had breast carcinoma on right side. According to quadrant involved, upper outer quadrant was seen in 42.7% cases followed by upper inner quadrant in 33.4% cases.

Maximum number of patients had felt lump from 2-6 months duration (34%), followed by 21.2% who felt lump for less than 2 months duration. Lump was felt from 6-12 months in 18.5% of patients. Fixity to underlying tissue was seen in 38% cases and 62% tumours were mobile.

Normal nipple-areolar complex was noted in 63.2% patients whereas 37.6% had retracted nipple-areola. Overlying breast skin was normal in 67.3% patients where as skin dimpling and peau-d-orange was seen in 11.3% and 9.5% of patients respectively.

Tumour emboli was found present in 58.5% cases and tumour necrosis was present in 44.6% cases. Paget's disease was present in 5.8% cases.

Maximum patients had tumour size ranging from 2.1-5 cms (59.5%) and Grade-III tumor was found in (47.5%) according to modified RB score, tumour necrosis was present in 44.6% cases, tumour emboli in 58.5% and 53% cases had axillary lymph node metastasis (table-1,2,3).

DISCUSSION

Breast cancer carries a lifetime risk of up to 12% and a risk of death of up to 5%.⁷ Due to lack of awareness on early detection and barriers to health services, most women with breast cancer are diagnosed in late stages in low and middle income countries.⁸ The greatest increase in incidence of breast cancer has been in developing Asian countries.⁹ Invasive breast carcinoma-NST is the most common type of breast cancer. In this present study 88.4% breast cases were Invasive carcinoma no special type and 11.6% were other variants.

The age of the patients in present study ranged from 26 to 82 years with the mean age of 50.2 years. This was in concordance to study done by Yucel et al¹⁰ (mean age- 51 years). In this study 7.5% patients were nulliparous and 92.5% had children. Study by Nigam et al¹¹ showed 3.4% to be nulliparous and 96.6% to be multiparous. Present study found 72.6% cases from low socio-economic background, Study by Sandhu et al¹² also reported 89.8% patients belonged to low socio-economic status and rest were middle and upper class patients.

In this study 59% of breast lumps were left sided and 41% were right sided. Majority of lumps (42.7%) were in upper outer quadrant. Rummel et al¹³ reported 51.5% cases in UOQ, 15.6% breast lumps in UIQ, 22.3% in lower quadrants and 10.6% central in location. Senie et al¹⁴ proposed that, higher percentage of breast cancer on left side is due to difference in breast size in an individual. When relative breast volumes were computed from the mammograms of healthy women, 55% were found to have a larger left breast. It has been suggested that the asymmetry of breast carcinoma reflects differences in the sensitivity of the mammary glands to hormonal stimulation, resulting in unequal volumes of tissue at risk to develop carcinoma. Same holds true for upper outer quadrant which is bulkier as compared to other quadrants.¹² In present study 21.2% of patients presented with lump of less than 2 months duration, 34% within 2-6 months and 18.5% with 6 months to 1 year. Similar results were retrieved by a study done by Sandhu et al¹² who found 21.5% patients presenting within 2 months duration, 48.9% patients within 2-6 months duration, 20.6% from 6 months to 1 year and 9% more than 1 year duration. This somehow points out that women neglect lump as it is painless and then present at a later stage when there are secondary changes associated.

In our study 63.2% cases presented with normal nipple areolar complex, 37.6% presented with retracted nipple. Similarly normal overlying skin was present in 67.3% patients and rest 32.7% presented with dimpling/peau-d-orange/ulceration or discoloration of skin.

Both abnormal skin and abnormal nipple areola complex occurs late and suggests long standing and advanced local disease. Ignorance, painless symptoms, poor socio-economic status, lack of medical resources, social barrier can be attributed to late presentation.

In our study, 8.2% presented with tumour size up to 2 cm, 59.5% patients with tumour size between 2.1-5 cm, 28% with size between 5.1-10 cm and 4.3% had size more than 10 cm (Table-1). In a study by Patrana et al¹⁵ found 38% had size up to 2 cm, 44% patients presenting with tumour size between 2-5 cm and 18% patients presented with size larger than 5 cm. Large tumour size at presentation is again attributable to ignorance and low socio-economic status. Non availability of screening mammography and less medical resources also play role in seeking delayed medical advice.

In present study, 9.3% cases were of grade-I, 43.2% cases of grade-II and 47.5% cases of grade-III breast carcinoma. Present study was in concordance with Fisher et al¹⁶ and Elston et al¹⁷ who also reported maximum number of patients in Grade-III followed by Grade-II and minimum in Grade-I. Tumour grade in an inherent property of cancer cells, the histological grading is significantly correlated with the prognosis, patients with grade-I tumours showing a significantly increased survival compared to patients with tumours of grade-II or grade-III.¹⁸ Large number of reports have emphasized the strong significant correlation between histological grade as a measure of differentiation and prognosis.¹⁹

In this study tumour necrosis was present in 44.6% cases

and tumour emboli was present in 58.5% cases. This present study was in concordance with Rezaianzadeh et al²⁰ who also found similar results in studying tumour necrosis in breast carcinoma patients. Tumour necrosis is thought to happen when tumour cells divide more rapidly and overruns the blood supply. Tumor necrosis has been equated in many studies with early treatment failure¹⁶ and reduced overall survival²¹ which suggests that presence of tumour necrosis is a poor prognostic marker. Gilchrist et al²² observed higher percentage of recurrence in patients who had necrosis in tumour. He also concluded that necrosis plays important role in recurrence during the first 2 years of follow-up. For patients who remained disease free beyond 10 years, necrosis in the primary tumour no longer was a significant prognostic factor.

In present study skin involvement by tumour cells was seen in 5.8% of cases and in rest skin was free. Study by Rezaianzadeh et al²⁰ found 7.3% cases had skin involvement by tumour cells. They also observed that skin and nipple involvement were negatively associated with survival, but these factors became non-significant after adjustment as they are further linked to tumour size and grade.

In present study 47% patients were negative for axillary lymph node involvement, whereas 18.3%, 14%, 11.3% and 9.4% were positive for 1-3, 4-7, 8-10 and >10 axillary lymph node involvement respectively. Patrana et al¹⁵ found an association between increasing tumour size with increase percentage of lymph node metastasis with in turn leads to worse prognosis, some other studies also mention the same.⁷ High grade tumours are associated with more incidence of axillary lymph node metastasis. According to Hopton DS high grade tumours are associated with increased incidence of axillary node metastasis with four or more nodes as compared with low grade tumors.²³

Our study showed ER/PR positive in 44.7% cases and ER/PR negative in 49.8% cases (table-4) which was found in concordance with study done by Bharti et al²⁴ who also found maximum number of patients with ER/PR negative, but not in concordance with Fritz et al²⁵ who found more number of ER/PR positive patients. The presence of ER and PR predicts the long term outcome of hormonal therapy⁷, thus they have been more commonly used as a predictive marker rather than as a prognostic marker. Due to treatment by tamoxifen, ER-positive patients have a considerably better prognosis than ER-negative patients. Some studies suggest that steroid hormone receptor status is an important prognostic and predictive factor for breast carcinoma in both early and metastatic disease.²⁶

Present study showed HER2 negativity in 70.8% (table-5) cases which was in concordance with study done by Santos et al²⁷ who also found similar results for HER2 status. HER2 is a pro-oncogene and its overexpression is known to be associated with poor survival and prognosis in early stage diseases.¹⁰ Yung et al. confirmed the relation between HER2 status and mortality.²⁸ HER2 expression has been valuable in predicting treatment responses to trastuzumab, certain endocrine therapies and chemotherapy, adding to its role as

a predictive marker.⁷

CONCLUSION

The present study was undertaken to look into the demographic details of patient and histomorphologic prognostic factors of breast carcinoma. The study showed that women operated in our tertiary care hospital, presented with advance stages of breast carcinoma. Often they present with dimpling, peau-d-orange of skin, nipple retraction and ulceration. In majority of patients tumour sizes is invariably more than 2 cm and already have positive axillary lymph nodes and tumour emboli. All these factors suggest that women in this area do not consult doctor at an early stage of disease. Lack of awareness about breast cancer as well as non-availability of screening mammography precludes early diagnosis.

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