



CLINICAL AND HISTOPATHOLOGICAL REVIEW OF INVASIVE BREAST CARCINOMA IN A TERTIARY CARE CENTRE.

Pathology

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ABSTRACT

BACKGROUND: Breast cancer accounts for 14% of all cancers in Indian women, that can occur at any age. Cancer survival becomes more difficult in higher stages of tumour, hence in order to improve the survival of affected persons, early diagnosis of breast cancer is critical.

METHODS: Retrospective study of 48 mastectomy specimens with relevant clinical details and respective H&E stained slides were reviewed.

CONCLUSION: This review showed that occurrence of Invasive Breast Carcinoma(IBC) peaks in the age group of 41-50years (35.4%) with right and left breast being affected equally in the ratio of R:L – 1 : 1. Most of the IBC (91.6%) were of No Special Type (NST), with 75% of tumours were of Histological Grade II. 58.3% of tumours were of tumour stage T₂ along with lymph node involvement in equal number of cases.

KEYWORDS

Invasive Breast Carcinoma, Histological Grade, Tumour stage, Lymph Node metastasis.

INTRODUCTION:

Breast cancer is the most commonly occurring cancer in women and second most common cancer overall, impacting 2.1 million women each year, and also causes the greatest number of cancer related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer globally, that is approximately 15% of all cancer deaths among women^[1]. In India breast cancer accounts for 14% of all cancers in Indian women. It can occur at any age but the incidence rates in India begin to rise in the early thirties and peak at ages 50-64 years^[2]. Approximately 41,760 women and 500 men died of breast cancer in 2019^[3]. Cancer survival becomes more difficult in higher stages of its growth and more than 50% of Indian women suffer from stage 3 and stage 4 of breast cancer^[4]. In order to improve breast cancer outcomes and survival of affected persons, early diagnosis is critical.

REVIEW OF LITERATURE:

Breasts are modified glandular tissue and functionally of great importance for feeding of the off springs. Breast is a dynamic structure that undergoes changes throughout women's reproductive life. This changes involve disturbances in the breast physiology extending from an extreme of normality to well defined disease process. One fourth women suffer from breast disease in their life time after puberty^[5,6]. Breast cancer is the second most common cancer occurring in women^[1]. Breast cancer frequently present as breast lump in 83% of patients, followed by non-lump breast symptoms, such as nipple abnormalities (7%) and breast pain (6%); and non-breast symptoms like back pain (1%) and weight loss (0.3%)^[7].

Age is the most significant risk factor for breast cancer. The disease is rare in women younger than 25 years and the incidence increases with increasing age, reaching a plateau in women aged 50-69 years. In 2019, 50% of all new cases of invasive breast cancer occurred in women of 50 to 69 years of age^[8]. Breast cancer is more common in the left breast than the right. The left breast is 5 - 10% more likely to develop cancer than the right breast^[9].

The classification of breast tumours continue to evolve, the descriptions of breast tumours follow the familiar systematic approach of sequence from benign epithelial proliferations and precursors, through benign neoplasm, to in-situ and invasive breast cancer, followed by mesenchymal and haematolymphoid neoplasms.

Breast carcinoma has a wide variety of morphological appearances. About one-third can be classified into special histologic types because they have important biologic and clinical associations.

The majority of invasive breast cancers are ductal adenocarcinomas

that are not classified further into a special type(Invasive breast carcinoma of no special type – IBC- NST). They most commonly present as a hard, irregular mass associated with a desmoplastic stromal reaction. When cut, such tumours typically produce a characteristic grating sound due to small, central pinpoint foci of chalky-white desmoplastic stroma and occasional foci of calcification. Less commonly, tumours present as circumscribed masses composed of sheets of tumour cells with scant stromal reaction or comprised of scattered neoplastic glands or single tumour cells infiltrating otherwise unremarkable fibrofatty tissue^[10].

Invasive breast carcinoma is graded using Nottingham Histologic Score. Carcinomas are scored for tubule formation, nuclear pleomorphism and mitotic rate. Grade 1 (well differentiated) carcinomas grow in a tubular or cribriform pattern, have small uniform nuclei and have a low proliferative rate. Grade 2 (moderately differentiated) carcinomas have areas where cells grow as solid clusters or single infiltrating cells and show greater nuclear pleomorphism and high numbers of mitotic figures. Grade 3 (poorly differentiated) carcinomas invade as ragged nests or solid sheets of cells and have enlarged irregular nuclei. A high proliferative rate and areas of tumour necrosis are common in high grade tumours^[10].

Special histologic types of invasive carcinomas can be organised into molecular groups based on expression of ER, PR and HER2, which carry therapeutic implications, harbour unique genetic aberrations, have distinct gene signatures and frequently show associations with clinical behaviour and prognosis^[10].

Lobular carcinoma infiltrates the breast while producing minimal desmoplastic response, making it difficult to detect these cancers by palpation and imaging. The histologic hallmark is the presence of discohesive infiltrating tumour cells, often including signet ring cells containing intracytoplasmic mucin droplets^[10].

Mucinous (colloid) carcinoma is soft or rubbery and has the appearance and consistency of pale grey-blue gelatin. The tumour borders are pushing or circumscribed. The tumour cells are arranged in clusters and small islands of cells within large lakes of mucin. Tubular carcinoma consist of well- formed tubules or cribriform pattern surrounded by sclerotic stroma. Papillary carcinoma produces true papillae, fronds of fibrovascular tissue lined by tumour cells. The tumour cells of apocrine carcinoma resembles the cells that line sweat glands. These cells have enlarged round nuclei with prominent nucleoli and abundant eosinophilic granular cytoplasm. Secretory carcinoma mimics lactating breast by forming dilated spaces filled with eosinophilic material^[10].

Carcinomas with medullary pattern has a good prognosis than poorly differentiated carcinomas. These tumours have large number of infiltrating T lymphocytes (TILs), suggesting that improved outcomes may be related to a host immune response to tumour antigens. These carcinomas are softer due to minimal desmoplasia and often form well-circumscribed masses. Histologic features include solid sheets of large cells with pleomorphic nuclei and prominent nucleoli, frequent mitotic figures, moderate to marked lymphoplasmacytic infiltrate surrounding and within the tumour, and a pushing non infiltrative border^[10].

Metaplastic carcinoma is a heterogeneous group of invasive breast carcinomas (IBCs) characterized by differentiation of the neoplastic epithelium towards squamous cells and/or mesenchymal-looking elements, including but not restricted to spindle, chondroid, and osseous cells. The gross appearance of metaplastic carcinoma is often not distinctive, and the tumours can either present as well-circumscribed masses or display indistinct, irregular borders. Cystic degeneration is not uncommon, in particular in metaplastic carcinomas with squamous differentiation. Pearly, white to greyish, and glistening cut surfaces can be seen in areas of squamous and chondroid metaplasia, whereas the cut surface of areas of osseous metaplasia can be gritty and hard. Metaplastic carcinomas can be monophasic (with only one metaplastic component) or biphasic (with two or more components). The two components can both be of metaplastic histology, such as squamous and/or spindle cells with a mesenchymal/matrix-producing component, or there can be one metaplastic component and one adenocarcinoma component^[11].

Phyllodes tumour is a generally circumscribed fibroepithelial neoplasm showing a prominent intracanalicular architectural pattern with leaf-like stromal fronds, capped by luminal epithelial and myoepithelial cell layers, accompanied by stromal hypercellularity. Phyllodes tumours form circumscribed, firm, bulging mass. The cut surface is tan or pink to grey in colour and may be mucoid and fleshy with cystic degeneration. The characteristic whorled pattern with curved cleft resembling leaf buds is best seen in large tumours, but small ones may have a homogeneous appearance. Malignant phyllodes tumours are diagnosed when all of the following features are present, such as marked stromal nuclear pleomorphism, stromal overgrowth; defined by the absence of epithelial elements in one low-power microscopic field containing only stroma, increased mitoses, increased stromal cellularity; which is usually diffuse and an infiltrative border^[12].

AIM & OBJECTIVES:

To analyse the occurrence of invasive breast carcinoma in relation to age of patient, side and quadrant of tumour location.

To categorise the various types of invasive breast carcinoma presented to our institute and to analyse the stage of tumour, based on tumour size and lymph node metastasis.

MATERIALS AND METHODS:

This retrospective review was done in Department of Pathology, Government Villupuram Medical College & Hospital, Tamil Nadu, India. All modified radical mastectomy and simple mastectomy specimens received in our department from January 2019 to December 2020 over a period of 2 years were analysed. The side of the breast - right/left, temporal orientation of the tumour related to the quadrant such as upper outer/inner, lower outer/ inner and central quadrant were noted. The size of the tumour was measured and the longest axis was considered for staging purpose. The slides relevant to the tumour sections stained with Haematoxylin and Eosin were reviewed for histopathological classification and histological grade. All the slides of lymph nodes dissected from the axillary pad of fat were examined under microscope for metastatic carcinomatous deposit. The tumour size along the longest axis and the number of nodes with metastatic carcinomatous deposit were considered for staging the tumour.

STUDY DESIGN: Retrospective study.

INCLUSION CRITERIA:

All modified radical mastectomy specimens with axillary pad of fat and simple mastectomy specimens.

EXCLUSION CRITERIA:

Trucut (small) biopsy from breast lesions and those cases of recurrent breast carcinoma after mastectomy surgery.

OBSERVATION AND RESULTS:

Review of the 48 cases included in the present study showed that Invasive breast carcinoma affected varied age group from less than 20 years to above 80 years. Most of the reported cases were in the age group of 41-50 years (35.4%), next in the age group of 51-60 yrs (25%). Hence maximum number of cases were presented together in the age group of 41-60 years, that constitutes about 60.4% (Table.1 & Figure.1).

Table.1: Age of presentation of breast carcinoma in the present study.

S.No	Age	Number of Cases	Percentage %
1.	≤ 20 yrs	1	2.1%
2.	21-30	3	6.2%
3.	31-40	7	14.6%
4.	41-50	17	35.4%
5.	51-60	12	25%
6.	61-70	5	10.4%
7.	71-80	2	4.2%
8.	> 80 yrs	1	2.1%

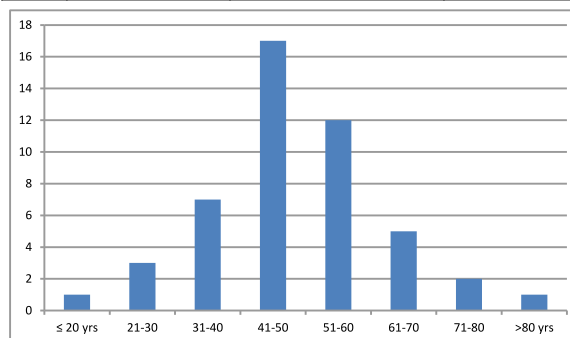


Figure.1: Age of presentation of breast carcinoma in the present study. x-axis : Age, y-axis: Number of patients.

From the present study it was observed that both right and left breast were equally affected by invasive carcinoma, in the ratio of 1 : 1 (Table.2).

Table.2: Tumour involvement in relation to side of breast.

S.No	Side of Tumour Presentation	Number of Cases	Percentage %
1.	Right Breast	24	50 %
2.	Left Breast	24	50 %

The temporal orientation of the tumour in relation to the various quadrant of breast specimen was analysed. The commonest quadrant of breast including both right and left breast presented with tumour was upper outer quadrant (56.3%) followed by central quadrant (25%) (Table.3 & Figure.2).

Table.3: Tumour involvement in relation to various quadrant of breast.

S.No	Quadrant of Tumour presentation (Both Right & Left Breast)	Number of Cases	Percentage %
1.	Upper Outer	27	56.3 %
2.	Upper Inner	4	8.3 %
3.	Lower Outer	2	4.2 %
4.	Lower Inner	3	6.2 %
5.	Central	12	25 %

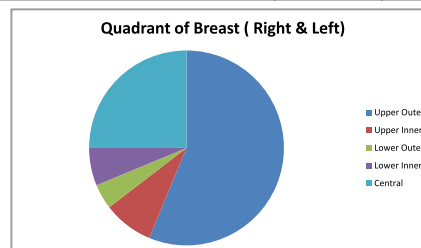


Figure.2: Tumour involvement in relation to various quadrant of breast

Most of the breast carcinoma presented to our institute were in tumour stage T_2 that includes, all tumours of size 2 - 5cms(58.3%). Tumour stage T_3 of tumour size more than 5cms constitutes about 27.1%. Early tumour stage T_1 of tumour size less than 2cms constitutes only 14.6% (Table.4).

Table.4: Staging of tumour based on Tumour size:

S.No	Tumour Size	Number of Cases	Percentage %
1.	T_1 : < 2cms	7	14.6 %
2.	T_2 : 2- 5cms	28	58.3 %
3.	T_3 : > 5cms	13	27.1 %

Histopathological types of breast carcinoma presented to our institute predominantly includes Invasive Breast carcinoma of No specific type(IBC-NST)(Figure.3&5) that constitutes about 91.6%(Table.5). Other few special variants includes metaplastic carcinoma (Figure.4&6), mucinous carcinoma and malignant phylloides tumour.

Table.5: Histopathological types of breast carcinoma.

S.No	Histopathological type of Tumour	Number of Cases	Percentage %
1.	Invasive Breast carcinoma of No special type.(IBC-NST).	44	91.6 %
2.	Metaplastic Carcinoma	2	4.2 %
3.	Mucinous Carcinoma	1	2.1 %
4.	Malignant Phylloides tumour	1	2.1 %



Figure.3. Gross; Cut section of MRM specimen showing an irregular, grey white tumour mass – Invasive breast carcinoma of no specific type (IBC-NST).



Figure.4. The gross appearance of metaplastic carcinoma of breast with a poorly circumscribed tumour mass with areas of cystic degeneration.

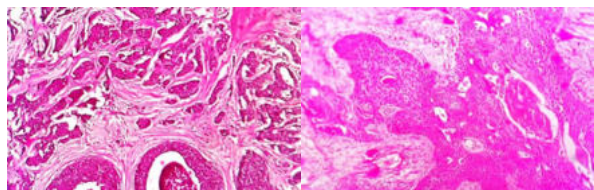


Figure.5.10X Microscopic view of Invasive breast carcinoma of no specific type; the tumour cells are arranged in cords, clusters, trabeculae and glandular pattern surrounded by a desmoplastic stroma.

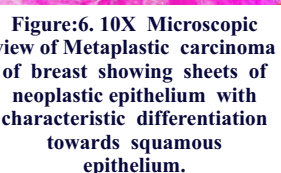


Figure.6. 10X Microscopic view of Metaplastic carcinoma of breast showing sheets of neoplastic epithelium with characteristic differentiation towards squamous epithelium.

Invasive breast carcinoma included in the present study were graded according to Histological Nottingham score. It was observed that histological tumour grade II was the commonest presentation in 75% of cases. Histological grade I was seen in 10.4% and 14.6% of cases showed histological grade III (Table.6).

Table.6: Grade of Invasive breast carcinoma: Based on Histological Nottingham score.

S.No	Histological Grade of Tumour	Number of Cases	Percentage %
1.	Grade I	5	10.4%
2.	Grade II	36	75 %
3.	Grade III	7	14.6%

All the lymph nodes dissected from the attached fibro fatty tissue of mastectomy specimens were examined under microscope for metastatic carcinomatous deposit. No tumour deposit (stage N_0) was observed in 41.7% of cases. Tumour deposit in 1-3 nodes (stage N_1) was seen in 31.2% of cases. 14.6% of cases showed carcinomatous deposit in 4-9 nodes (stage N_2), whereas only 12.5% of cases showed tumour deposit in more than 9 lymph nodes (stage N_3) (Table.7).

Together 58.3% of cases showed metastatic carcinomatous deposit in lymph nodes.

Table.7: Staging : Based on Lymph node status.

S. No	Staging : Number of Lymph Nodes with metastatic carcinomatous deposit.	Number of Cases	Percentage %	Total
1.	N_0 : No metastatic deposit	20	41.7 %	41.7% without tumour deposit in node.
1.	N_1 : 1-3 Nodes	15	31.2 %	58.3% with tumour deposit in node
2.	N_2 : 4-9 Nodes	7	14.6%	
3.	N_3 : > 9 Nodes	6	12.5 %	

DISCUSSION:

From the review of MRM specimens received in our tertiary care teaching hospital over a period of 2 years, it was observed that most of the invasive breast carcinoma were presented in the age group of 41-50 years, extending from as early as less than 20 years and as old as above 80 years. Most of the breast carcinomas were present in the upper outer quadrant followed by central quadrant, equally occurring in both right and left breast. Based on tumour size, it was tumour stage T_2 with tumour size varying from 2-5cms was the commonest presentation. The commonest histopathological type was IBC-NST (Invasive Breast Carcinoma of No Special Type) with minimal number of cases with special morphological patterns. The review of Invasive breast carcinoma based on Histological Nottingham score, showed that most of the tumours were of Grade II tumours. Lymph nodes studied revealed that stage N_0 with no tumour deposit in node and stage N_1 tumour deposit in 1-3 nodes was the commonest presentation. Lymph nodes examined from all specimens revealed that 58.3% of cases had metastatic carcinomatous deposit.

Breast carcinoma can occur at any age, but the incidence rates in India begin to rise in the early thirties and peak at ages 50-64 years^[2]. In our study it was observed that 35.4% of patients were in the age group of 41-50 years which was similar to the observation by Nada et al^[13] and Md Fazlul Rahman Shueb et al^[14]. This observation indicates that the breast carcinoma occurrence peaks 10 years earlier than the national average of 50-64 years^[2].

Similar to Mosammat Mira Pervin et al^[15] study, in our study also it was observed that the predominant quadrant of IBC occurrence was in the upper outer quadrant. Amgiasvasanth A.M et al^[16] stated that IBC was more common in left breast (72.8%), were as Mosammat Mira Pervin et al^[15] observed that, left breast involvement in 52%, right breast in 46% and bilateral involvement in 2% patients. In our review it was observed that both right and left breast were equally affected by invasive carcinoma in the ratio of Right : Left of 1 : 1. Hence both right and left breast are at equal risk of being affected by invasive carcinoma.

Histopathological review of tumour included in our study revealed that the commonest type of invasive breast carcinoma(IBC) was of no special type(NST) (91.6%), which was similar to the observation by Mosammat Mira Pervin et al^[15], Amgiasvasanth A.M et al^[16] and Kavita Gite et al^[17]. The commonest tumour grade in our study was that of Grade II (73.8%) based on Histological Nottingham score, similar to that of the observation by Kavita Gite et al^[17]. Md Fazlul Rahman Shueb et al^[14] observed that 64% patients had axillary node involvement, near similar to the observation in our study where 58.3% patients had presented with tumour deposit in lymph nodes, that included node stages of N_1 , N_2 & N_3 .

CONCLUSION:

This retrospective review showed that the occurrence of invasive breast carcinoma peaks in the age group of 41-50years, which is 10 years earlier than the national average of 50-64years, along with both right and left breast are at equal risk of being affected by invasive breast carcinoma. The commonest histopathological presentation being Invasive Breast Carcinoma of No Special Type(IBC-NST), with histological tumour grade II, in tumour stage T_2 and lymph node stage of N_1 .

Since breast cancer is the major cause of morbidity and mortality among females, delayed disease presentation with late diagnosis of breast cancer increases mortality rate. A multidisciplinary approach to

breast cancer including awareness program, screening for early detection and diagnosis with availability of treatment facilities can reduce the incidence and mortality of breast cancer in Indian women.

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