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**Original research article**

# Histomorphological evaluation and classification of carcinoma of breast

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**Abstract**

Invasive carcinoma of no special type(NST) and invasive lobular carcinoma (ILC) are the two most common histological subtypes of invasive breast cancer, with Invasive Carcinoma NST occurring in more than three- quarters of patients. ILC has distinct biologic and prognostic features. Compared with Invasive Carcinoma NST, ILC is less frequent in patients under 35 years of age and associated with more bilaterality advanced tumor stage and nodal involvement. The study has been conducted in the Department of Pathology, in cooperation with the Department of General Surgery. The study material included all the breast specimens (n=180) received as modified radical mastectomy with exclusion criteria of post radiotherapy and post chemotherapy in histologically proven cases of carcinoma of the breast. In the present study, Elston & Ellis modified Bloom & Richardson system was applied for grading of ICNST. Of the 128 cases of ICNST, the majority were of grade II with 60.3% (77/128) followed by grade III with 27% (35/128) and grade I with 12.7% (16/128).

**Keywords:** Carcinoma of breast, NST, ICNST

## Introduction

Breast carcinoma is a heterogeneous disease encompassing a spectrum of subtypes with distinct biological features that lead to differences in response patterns to various treatment modalities and clinical outcomes [1]. Breast cancer is the most common female cancer worldwide and also ranked number one cancer among Indian females. Incidence rates were as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women [2].

Risk factors include inherent factors such as age, sex, race, genetic makeup promoting the familial occurrence of the neoplastic disease or the benign proliferative lesions and extrinsic factors conditioned by lifestyle, diet or long-term medical intervention such as using oral hormonal contraceptives, hormonal replacement therapy and their influence on the neoplastic process [3].

Examination of the routine Haematoxylin - Eosin (H&E) stained sections is the gold standard for the diagnosis of breast lesions and immunohistochemistry (IHC) remains an integral part of this process as it provides clues in diagnostic subtyping and prognostic assessment of breast cancer [4].

Invasive carcinoma of no special type(NST) and invasive lobular carcinoma (ILC) are the two most common histological subtypes of invasive breast cancer, with Invasive Carcinoma NST occurring in more than three- quarters of patients. ILC has distinct biologic and prognostic features [5]. Compared with Invasive Carcinoma NST, ILC is less frequent in patients under 35 years of age and associated with more bilaterality advanced tumor stage and nodal involvement. IHC with E-Cadherin can be used as a diagnostic utility in differentiating between the ILC and Invasive Carcinoma NST [6].

Ductal carcinoma in situ (DCIS) is considered a precursor lesion for the subsequent development of invasive carcinoma with a high-risk index factor than that expected in women without DCIS. Widespread use of screening mammography and increasing awareness of breast cancer in the general population resulted in a tremendous increase in the detection of these lesions since 1983. Death due to pure DCIS is extremely rare, but death occurring after the initial diagnosis of DCIS is either because of an undetected invasive component or due to recurrence of the invasive lesion after the treatment [7]. Cytokeratin 5/6 antibody is very frequently applied to help differentiate invasive from non-invasive lesions [8].

## Methodology

The study has been conducted in the Department of Pathology, in cooperation with the Department of

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General Surgery.
The study material included all the breast specimens (n=180) received as modified radical mastectomy with exclusion criteria of post radiotherapy and post chemotherapy in histologically proven cases of carcinoma of the breast.

**The technique of analysis**

- Specimens were fixed in 10% formalin.
- Tumor size was assessed during grossing of the specimen, and a minimum number of 4 bits were taken from the tumor proper.
- Tumor tissue and all the lymph nodes identified were processed.
- Paraffin blocks were cut at 4 microns thick and stained with Haematoxylin and Eosin.

Classification of tumors was done according to the WHO classification of tumors of the breast. Tumor grade was assessed on H&E using the Elston & Ellis Modified Bloom & Richardson grading system.

- IHC with E-Cadherin was performed in all cases of ILC, selected cases of ICNST, cases of ICNST with foci resembling ILC and Tubular carcinoma.
- IHC with CK5/6 was performed in cases with DCIS component, ILC, Intraductal papillary carcinoma, and Tubular carcinoma.

**The procedure of H&E staining**

- Xylene – 20 minutes
- 70% Ethanol – 5 dips
- Distilled water – 5 dips
- Harris Haematoxylin – 2 minutes
- Washing in running tap water – 30 minutes
- Acid alcohol – 2 to 3 dips
- Washing in running tap water – 30 seconds
- Eosin – 20 seconds
- Washing in running water – 1 minute
- 70% Ethanol – 5 dips
- Absolute Ethanol – 5 dips
- Xylene
- Mounting with DPX.

**Results**

The most common histological type was ICNST accounting for 71.1% of cases followed by ICNST with medullary features.

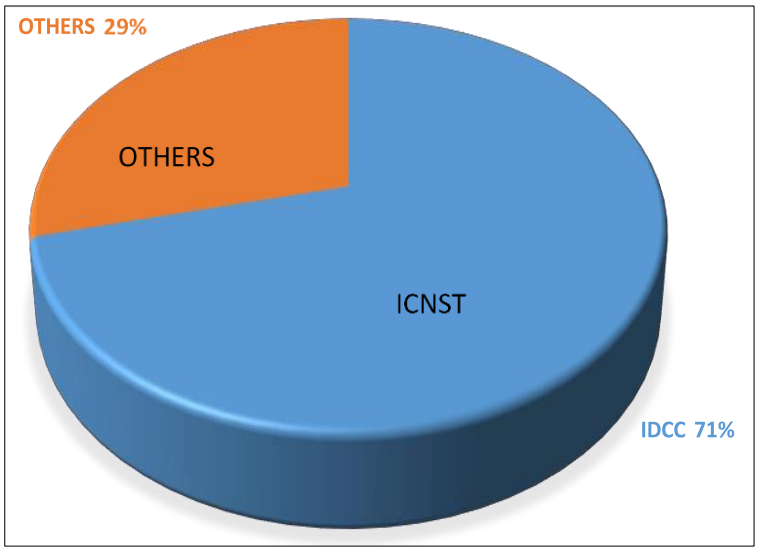


**Fig 1:** Statistics of morphological variants ICNST/others

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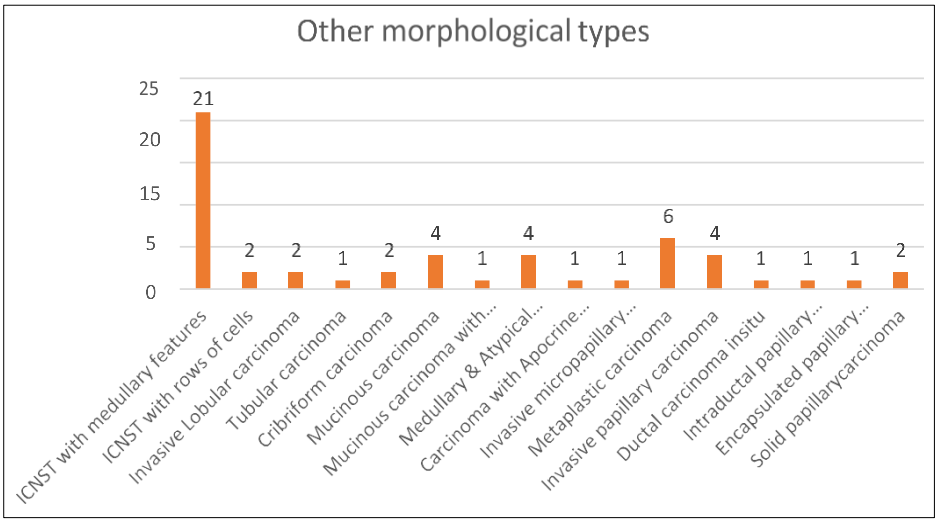


**Fig 2:** Incidence of other morphological types

Measurement of maximum diameter was taken on the surface of the tumor and the size of majority of the tumors were in between 2-5cm.

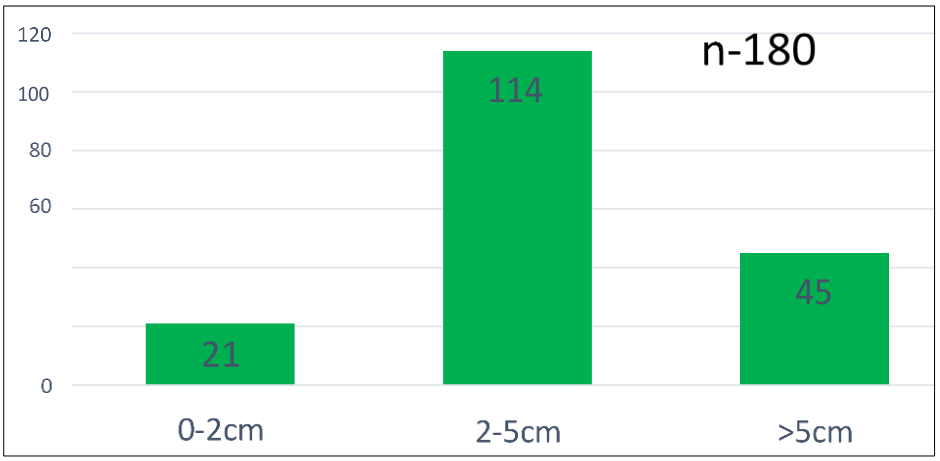


**Fig 3:** Size categorisation in breast carcinoma

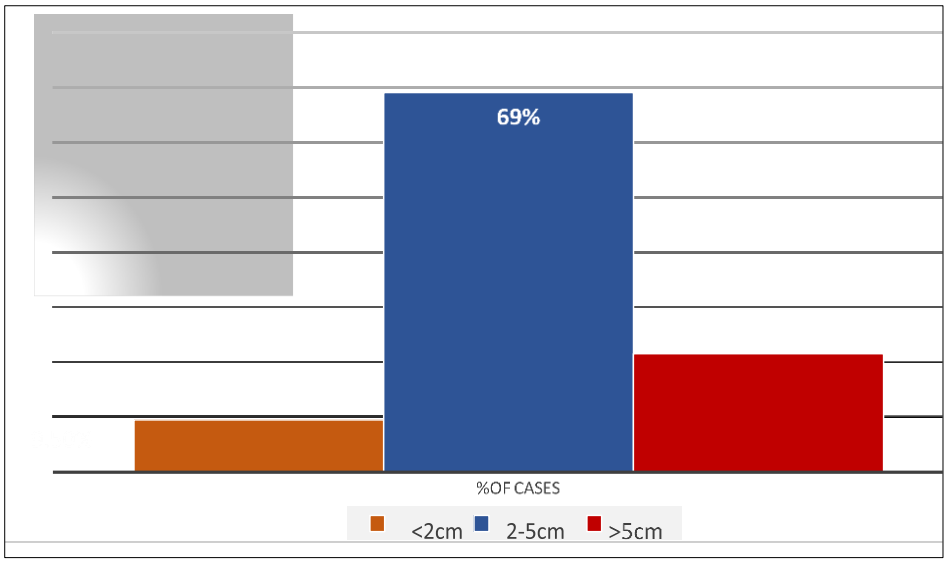


**Fig 4:** Size categorization in ICNST

Out of 180 cases, 8 cases show skin involvement.

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**Table 1:** Skin involvement

| Category | Number of cases |
|---|---|
| With skin involvement | 8 (4.4%) |
| Without skin involvement | 172 (95.6%) |

In the present study 6 cases showed multifocality.

**Table 2:** Multifocality

| Category | Number of cases |
|---|---|
| Unifocal | 174 (96.4%) |
| Multifocal | 6 (3.3%) |

In the present study, 84 cases (46.7%) showed lymph nodal involvement. Of which 45 cases (25%) have ≥ 3 lymph node involvement. 29 cases (16.1%) showed 3-10 lymph node involvement, 10 cases (5.6%) showed >10 involved lymph nodes. 96 cases (53.3%) show no lymph nodal involvement.

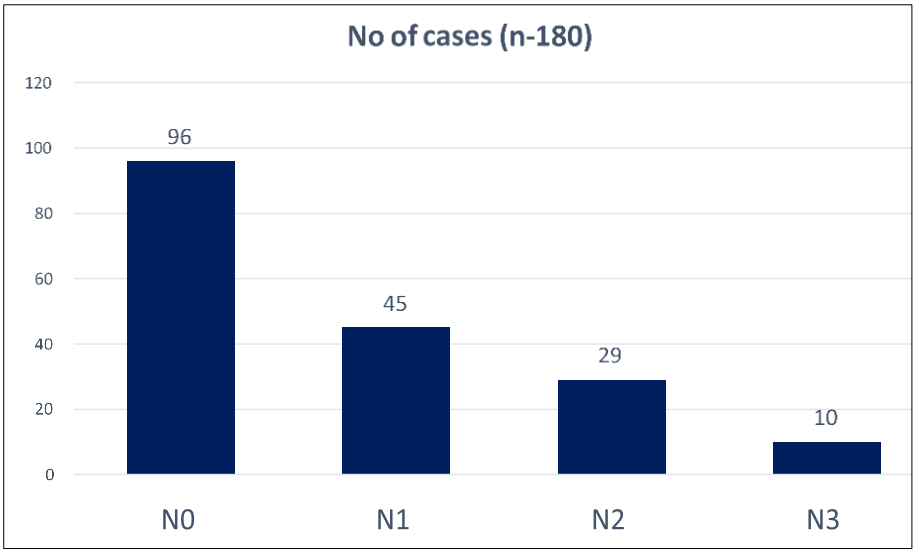


**Fig 5:** Lymph node involvement in breast carcinoma

With increase in size of the tumor there is increase in number of lymph nodes involved.

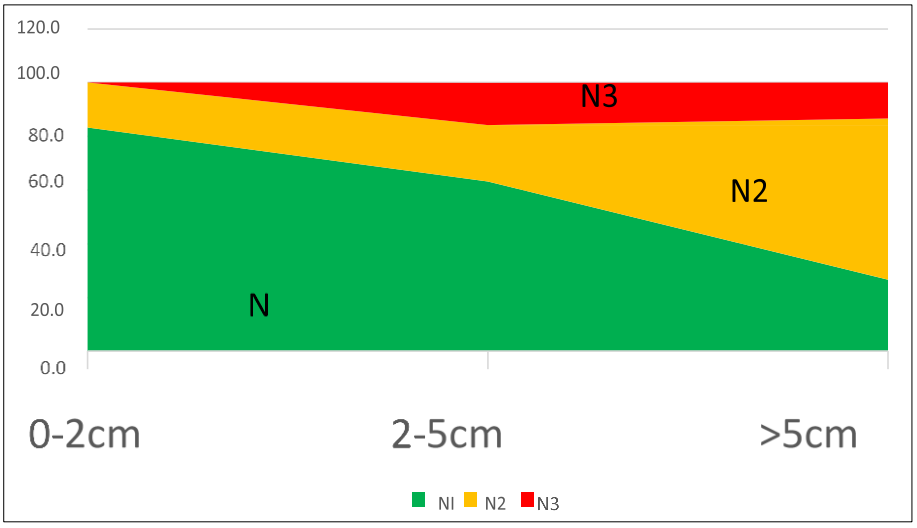


**Fig 6:** Comparison of tumor size with lymph node status

Most of the cases belong to stage group IIA followed by IIB.

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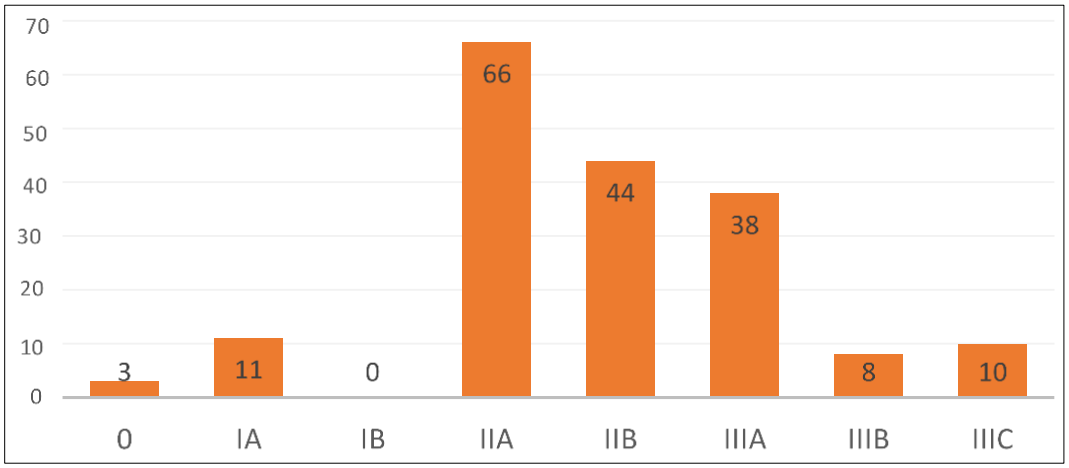


**Fig 7:** Stage distribution in breast carcinoma

Elston & Ellis modified Bloom &Richardson grading system was applied for ICNST.

**Table 3:** Grade wise distribution

| Grade | %OF CASES |
|---|---|
| Grade I | 12.7% (16/128) |
| Grade II | 60.3% (77/128) |
| Grade III | 27% (35/128) |

Present study showed 12.7% (16/128) ICNST cases with grade I, 60.3% (77/128) with grade II, 27% (35/128) with grade III.

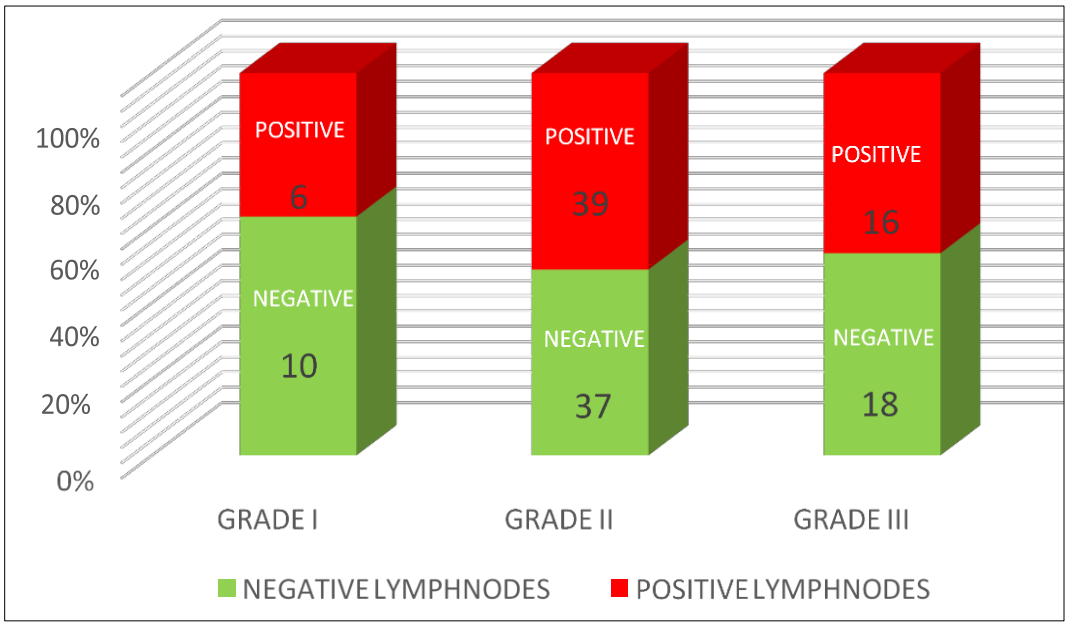


**Fig 8:** Correlation of grade with lymph node status

Grade and lymph node involvement did not show any correlation.

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**Fig 9:** Gross picture of ICNST showing a solid, grey white, circumscribed tumour

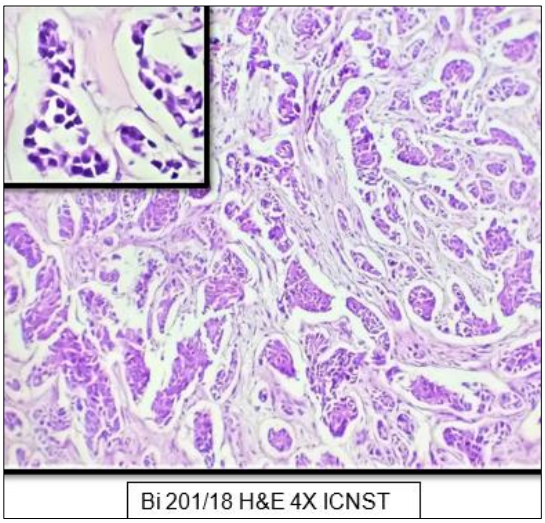


**Fig 10:** Photomicrograph of ICNST showing sheets and cords of pleomorphic cells. Inset highlights hyperchromatic nuclei


**Fig 11:** Gross image of ILC showing poorly circumscribed infiltrative growth

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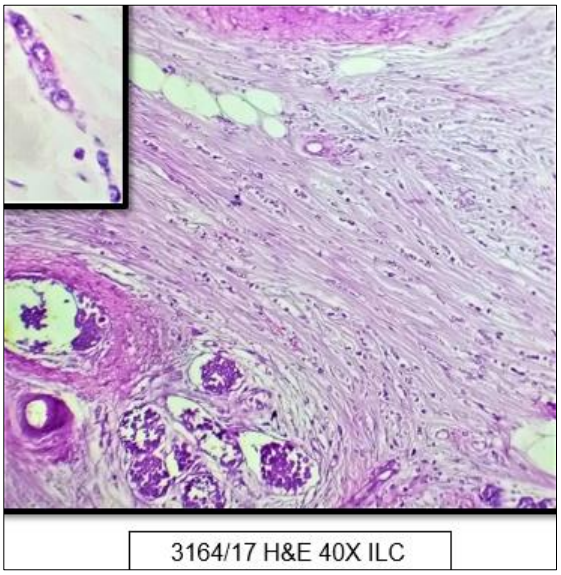


**Fig 12:** Photomicrograph of ILC with Indian file pattern of cells in the inset

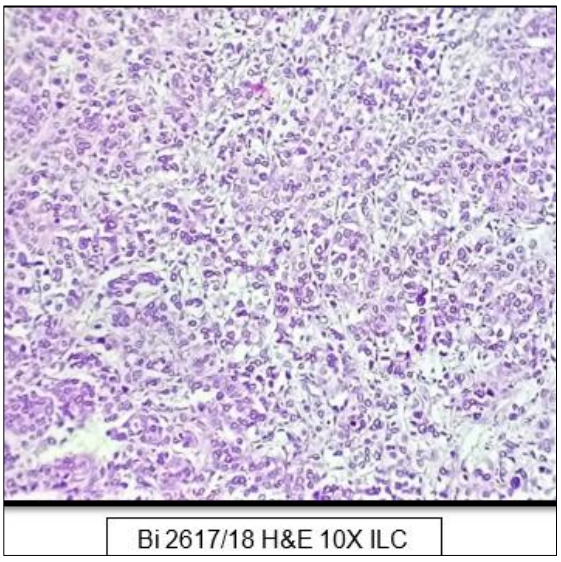


**Fig 13:** Photomicrograph of ILC showing dyscohesive small cells in sheets (solid component)

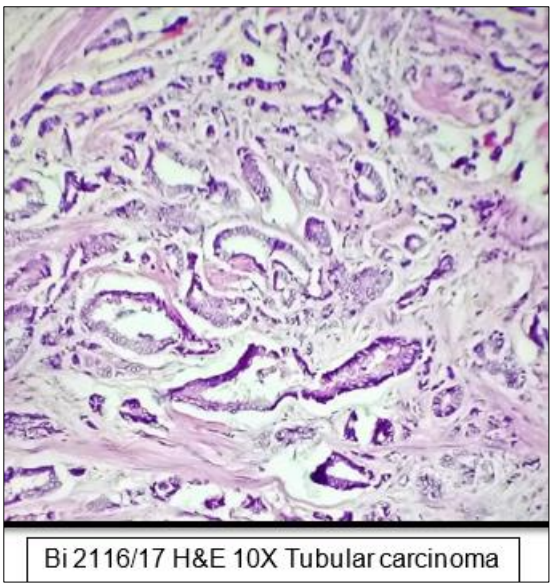


**Fig 14:** Photomicrograph of tubular carcinoma showing cells arranged in predominantly open tubular pattern

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**Fig 15:** Gross image of invasive cribriform carcinoma showing infiltrative grey white growth with small cystic spaces

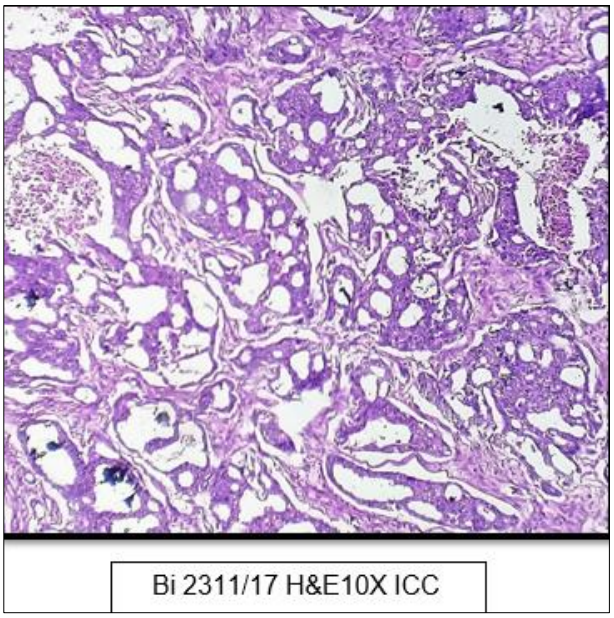


**Fig 16:** Photomicrograph of invasive cribriform carcinoma showing sieve like arrangement of neoplastic cells

**Discussion**

The most common histomorphological variant in the present study was Invasive Carcinoma of No Special Type accounting for 71%. The other morphological variants together constituted 29%.
Two cases, considered as ICNST with focal ILC like features on H&E, were subjected to IHC.

**Table 4:** Comparison of morphological variants

| Morphological type | Present study | Anamika Thakral *et al* [9] | Kiran H. S *et al* [10] | Mohan Rao Nandam *et al* [11] |
|---|---|---|---|---|
| ICNST | 71.1% | 80.64% | 61% | 78.57% |
| ICNST with medullary like features | 11.7% | - | - | - |
| Invasive lobular carcinoma | 1.1% | 0% | 21% | 7.14% |
| Tubular carcinoma | 0.6% | - | - | - |
| Cribriform carcinoma | 1.1% | - | - | - |
| Mucinous carcinoma | 2.2% | 3.47% | - | 7.14% |
| Mucinous carcinoma with | 0.6% | - | 2% | - |

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| | | | | |
|---|---|---|---|---|
| neuroendocrine differentiation | | | | |
| Medullary and atypical medullary carcinoma | 2.2% | 1.16% | 6% | 7.14% |
| Carcinoma with Apocrine differentiation | 0.6% | - | - | - |
| Invasive micropapillary carcinoma | 0.6% | 0.58% | - | - |
| Metaplastic carcinoma | 3.3% | 2.31% | 2% | - |
| Invasive papillary carcinoma | 2.2% | 0.58% | 6% | - |
| Ductal carcinoma in situ | 0.6% | 2.89% | - | - |
| Intraductal papillary carcinoma | 0.6% | - | - | - |
| Encapsulated papillary carcinoma | 0.6% | - | - | - |
| Solid papillary carcinoma | 1.1% | - | - | - |

*- implies these specific entities are not encountered in other studies

In the present study those cases of carcinoma of the breast which lack sufficient characteristics to be assigned to a specific histological type were categorized as ICNST as per the WHO criteria. The incidence of ICNST in the present study was 71.1% (128/180), while Anamika Thakral *et al*. [9] reported 80.64%, and Mohan Rao Nandam *et al*. [11] reported 78.57%. The slight lower incidence in the present study, when compared to other studies, could be due to the classification of ICNST with medullary-like features into a separate entity.

Grossly the tumors were firm to hard with regular as well as irregular borders. Foci of necrosis were observed in 38% of cases in the present study. Microscopically these tumours were composed of cells glands, tubules, cords and sheets of bland to highly pleomorphic cells.

Two cases in the study showed Indian file pattern of arrangement of cells exhibiting moderate pleomorphism. However, the cohesion of tumour cells was observed even in rows of cells and tissue from both the tumors was subjected to IHC workup.

In the present study, Elston & Ellis modified Bloom & Richardson system [12] was applied for grading of ICNST. Of the 128 cases of ICNST, the majority were of grade II with 60.3% (77/128) followed by grade III with 27% (35/128) and grade I with 12.7% (16/128).

In comparison with other studies, the present study showed higher number of grade II cases.

**Table 5:** Comparison of Grading

| | **Present study** | **Blamey *et al* [13]** | **Rakha *et al* [14]** | **Thomas *et al* [15]** |
|---|---|---|---|---|
| Grade I | 12.7% | 29% | 18% | 26% |
| Grade II | 60.3% | 41% | 36% | 45% |
| Grade III | 27% | 30% | 46% | 29% |

The present study showed no correlation between the histologic grade and lymph node involvement.

## Conclusion

Out of 180 cases, 166 cases (92.2%) were of stage IIA and above, this observation highlights the need to improve the screening programmes to detect breast carcinomas at an early stage.

There is an increase in incidence in the younger age indicating the importance of identification of specific risk factors and eliminating them.

It is necessary to differentiate between morphological subtypes as they have different prognostic value and clinical outcome. This can be achieved by histomorphology when the clinching diagnostic features are evident. In some cases, morphology alone is not sufficient to differentiate them into specific subtypes and as such adjunct study with a panel of IHC markers becomes imperative to confirm the histopathological diagnosis.

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