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Original Research Article

A study of triple negative breast carcinomas

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Abstract

Aim and objectives: To show the incidence of triple negative breast carcinomas in the younger age group (20-40 years) in the study sample and to establish a correlation between expression patterns of estrogen receptor (ER), progesterone receptor (PR) and HER2 /neu with tumour histopathology of breast carcinoma.

Material and methods: A 5 years study, 2 years retrospective and 3 years prospective was conducted in Mahatma Gandhi Memorial Hospital, Warangal, from 2009 to 2014 on triple negative breast carcinomas. All the mastectomy specimens, received in the Pathology Department during this period were considered.

Results: Total of 28 cases of carcinoma breast in females diagnosed histopathologically, were included in the study. In the present study, the patients were in the age group of 20-40 years since most carcinomas in this age group are triple negative. Most of the tumours were of size > 5 cm, 12 cases (43%), followed by 10 cases (36%) of size 2-5 cm. Total 20 (71.4%) were IDC (NOS), followed by 4 (14.2%) were Medullary carcinomas and 2 (7.1%) cases of ILC and each 1 (3.6%) case of tubular and Mucinous carcinomas. Histopathological grading was done according to Modified Bloom Richardson grading and found that 11 (39.3%) were of grade II followed by 5 (17.9%) cases were grade III, 4 cases were of grade I and 8 cases were inassessible. ER and PR were positive in 61% and 47% of tumors respectively. HER-2 over expression was seen in 36% of tumors and was negative in 64% of tumours. Triple negative carcinomas were 4 out of 28 cases, of which 3 were IDC (NOS) and 1 was medullary carcinoma. Triple negative carcinomas are associated with poor prognosis.

Conclusion: ER, PR and HER-2 status correlates well with histopathological grading and other clinico-pathological parameters. Higher grade is associated with HER-2 positivity and ER/PR negativity, larger tumor size, lympho-vascular invasion, lymph node metastasis, and higher clinical stage.

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Key words

Breast carcinomas, Modified Bloom Richardson grading, Triple negative carcinomas, Estrogen receptors, Progesterone receptors, HER-2/neu.

Introduction

Breast cancer is the most common carcinoma in women and accounts for 22% of all female cancers. It is the leading cause of death from cancer for women aged 20 – 59 years. It accounts for 26% of all newly diagnosed cancers in females and is responsible for 15% of the cancer-related deaths in women [1]. Mortality rates from breast cancer have increased during the past 60 years worldwide [2].

The prognostic factors include invasive carcinoma or in situ disease, distant metastases, lymph node metastases, tumour size, locally advanced disease, histological grade, histologic subtype, inflammatory carcinoma and estrogen receptor (ER) /progesterone receptor (PR) status and over expression of HER 2/neu [3].

The immunohistochemistry (IHC) classification provides both therapeutic and prognostic information. These assays have the advantage of allowing only tumour cells to be assessed for receptor status. They can be conducted relatively inexpensively on routinely processed tissue sections with no need for specialized equipment [4].

Triple negative breast cancer, defined as that with negative expression of estrogen and progesterone receptors and HER-2 accounted for 10-17% of all breast carcinomas [5]. Triple negative breast carcinomas are associated with worst prognosis.

Aim and objectives

- To show the incidence of triple negative breast carcinomas in the younger age group (20-40 years) in the study sample.
- To establish a correlation between expression patterns of ER, PR and HER2 /neu with tumor histopathology of breast carcinoma.

Material and methods

A 5 years study, 2 years retrospective and 3 years prospective was conducted in Mahatma Gandhi Memorial Hospital, Warangal, from 2009 to 2014 on triple negative breast carcinomas.

All the mastectomy specimens, received in the Pathology Department during this period were considered.

Inclusion criteria

- Mastectomy specimens of females in the age group 20 – 40 years were included.
- Only samples with definite histopathological diagnosis were considered.
- Only Invasive breast cancers were included.
- Malignant lesions included invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, tubular carcinoma, mucinous carcinoma etc.
- Representative areas in the biopsies were only included.

Exclusion criteria

- All benign and inflammatory lesions were excluded.
- All cases of in situ carcinoma were excluded.
- All lumpectomy specimens were excluded.

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Specimen handling

All mastectomy specimens were fixed in 10% neutral buffered formalin. After adequate fixation, examination of the specimen for gross details was done. Then representative tissue bits were taken and subjected for routine processing and paraffin embedding. Three to four micron thick sections were taken from the paraffin embedded blocks. These sections were routinely stained with hematoxylin and eosin (H & E) and were examined. Histopathological features were noted and the tumors were typed according to the World Health Organization (WHO) classification system. The Nottingham modification of Bloom Richardson grading system was used for grading. **(Photo – 1A, 1B, 2A, 2B, 3A, 3B, 4)**

The paraffin blocks of the samples which had met the inclusion criteria were collected. The details of each case like biopsy number, age, histopathological diagnosis, grading etc. were noted. A total of 28 cases were collected and subjected to immunohistochemistry. **(Photo – 5A, 5B, 5C, 5D, 6A, 6B, 6C, 6D, 7A, 7B, 7C, 7D, 8)**

Results

A total of 28 cases of carcinoma breast were evaluated during this study conducted in Mahatma Gandhi Memorial Hospital, Warangal, from 2009 to 2014.

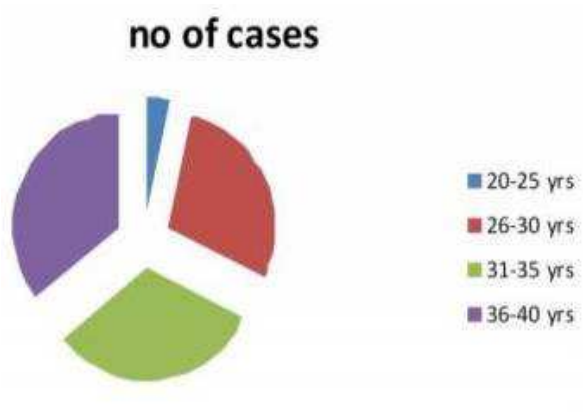
Age distribution

The age of the patients with carcinoma breast in the present study ranged from 20 to 40 years. Mean age was 33.5 years. Age distribution of patients with breast carcinoma was as per **Table – 1** and **Chart – 1**. Distribution of patients according to size of tumor was as per **Table – 2** and **Chart – 2**. Distribution of patients according to histological type of tumor was as per **Table – 3** and **Chart – 3**. Distribution of cases as per IHC results was as per **Table – 4**. Distribution of cases of triple negative breast carcinoma in relation to histologic type and age was as per **Table – 5**. Distribution of cases according to histological grade and IHC results was as per **Chart – 4**. Out of 28 cases studied, only 5 cases were positive for all three markers, 4 cases were triple negative, comprising of about 14.3%. Distribution of cases according to age and IHC results was as per **Chart – 5**.

Table - 1: Age distribution of patients with breast carcinoma.

Age group	No of Cases
20-25 Years	1 (3.6%)
26-30 Years	8 (28.6%)
31-35 Years	9 (32.1%)
36-40 Years	10 (35.7%)
Total	28

Chart - 1: Age distribution of patients with breast carcinoma.



Discussion

Total numbers of breast carcinomas in the present study were 160 cases. Among which 28 cases were in the age group of 20-40 years with the mean age of 33.4 years. Age distribution in comparison with other studies was as per **Table – 6**.

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Table - 2: Distribution of patients according to size of tumor.

Size of tumousr	No. of cases
< 2 cms	6 (21.4%)
2-5 cms	10 (36%)
> 5 cms	12 (43%)
Total	28

Chart - 2: Distribution of patients according to size of tumor.

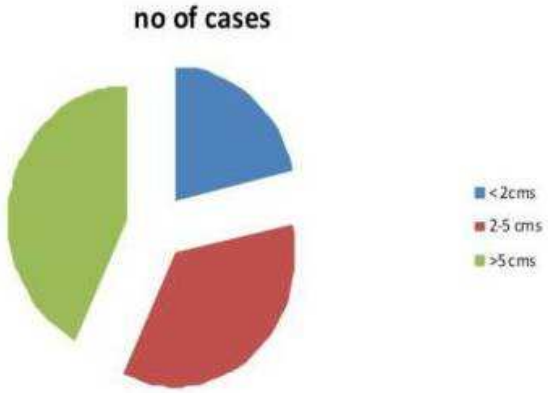

Table - 3: Distribution of patients according to histological type of tumor.

Histological type of tumor	No of Cases
IDC	20 (71.4%)
ILC	2 (7.2%)
Tubular Ca	1 (3.6%)
MC	4 (14.2%)
MUCIN	1 (3.6%)
Total	28

In the present study, age at presentation ranged from 20-40 years with a mean age of 33.5 years. Similar observation was made by Costa, et al. [6] and Joshi K, et al. [7]. Tumor size on gross examination in comparison with other studies was as per **Table – 7**.

Chart - 3: Distribution of patients according to histological type of tumor.

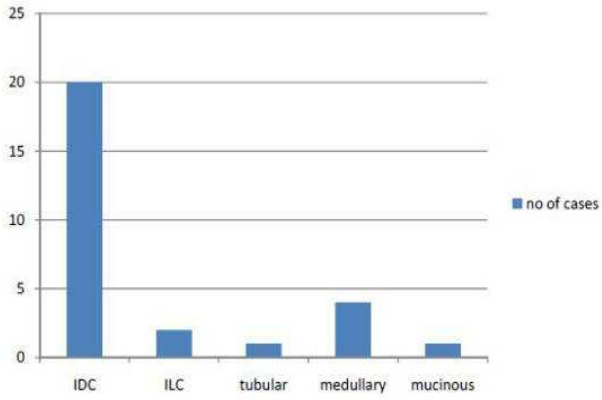

Table - 4: Distribution of cases as per IHC results.

IHC status	Number of cases
ER/PR+,Her2+	5 (17.8%)
ER/PR+,Her2-	17(60.8%)
ER/PR-,Her2+	2 (7.1%)
ER/PR-,Her2-	**4 (14.3%)**

In the present study, total 12 (43%) cases had the tumor size >5 cm, followed by 10 (36%) cases of tumor size of 2-5 cm and 6 (21.4%) cases of <2 cm. In the study by Nisa A, et al. [8], 52.7% of tumors were of size <2 cm and 35.5% were of size from 2-5 cm. In the study of Mona M Rashed, et al. [9], 54% of tumors are of size <2 cm and 36% of tumors were of size from 2-5 cm.

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Table - 5: Distribution of cases of triple negative breast carcinoma in relation to histologic type and age.

	Type of carcinoma	Age (Yrs)
ER/PR/HER2-	IDC	28
	IDC	40
	IDC	27
	MC	35

Chart - 4: Distribution of cases according to histological grade and IHC results.

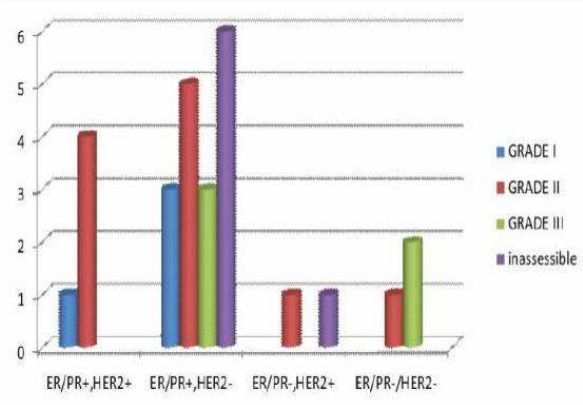

Chart - 5: Distribution of cases according to age and IHC results.

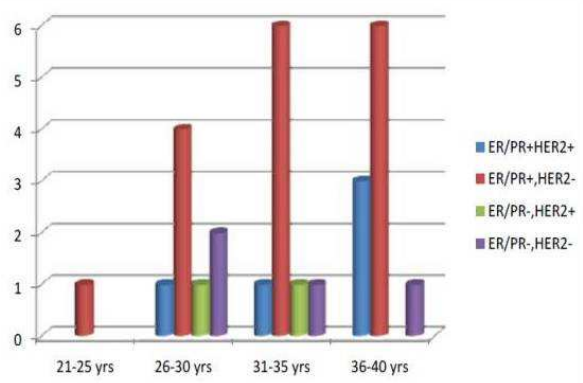

Table - 6: Age distribution in comparison with other studies**.**

Authors	Costa, et al. [6]	Joshi K, et al. [7]	Present study
Mean age (years)	60	35	33.5
Age range (years)	28-95	28-40	20-40

Table - 7: Tumor size on gross examination in comparison with other studies**.**

Size (cm)	Authors		
	Azizium Nisa, et al. [8]	Mona M Rashed, et al. [9]	Present study
<2	52.7	54	21.4
2-5	35.5	36	36
<5	11.8	10	43

Photo – 1A, 1B: Modified radical mastectomy.

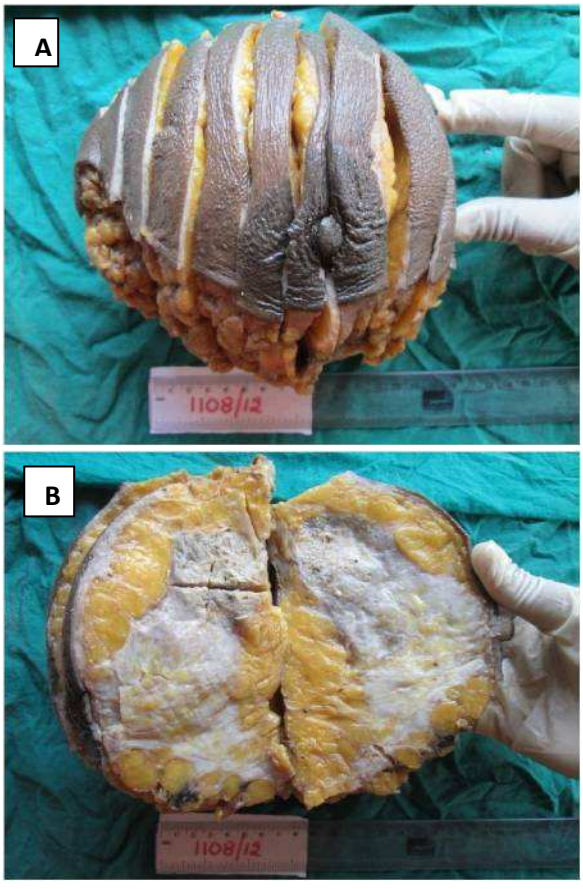

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Photo – 2A, 2B: Modified radical mastectomy.

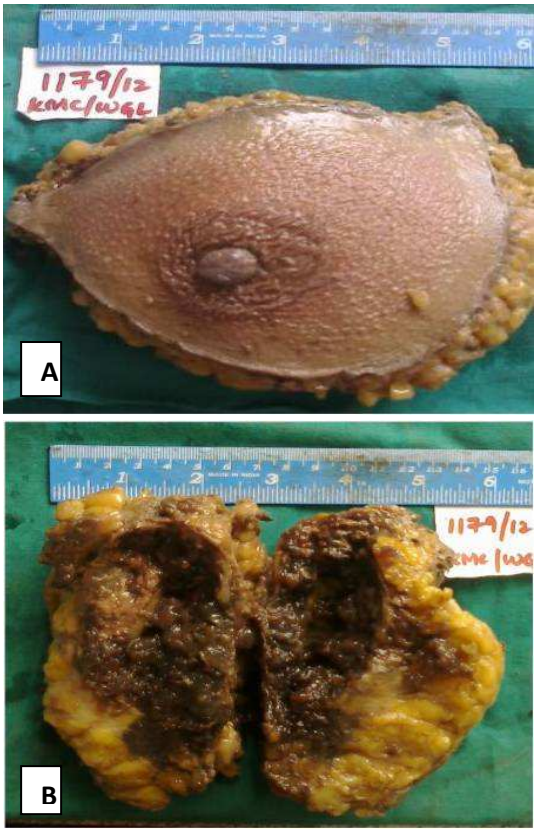
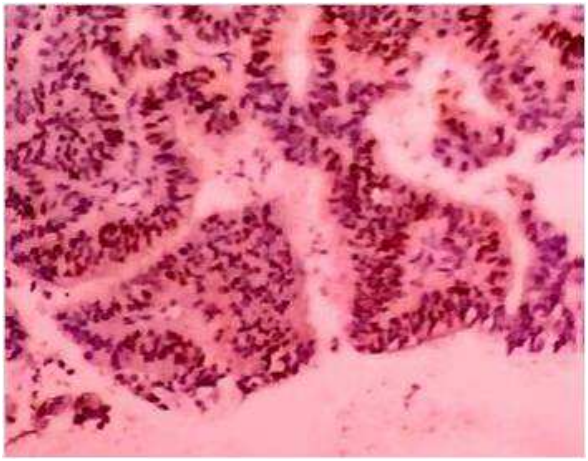


Photo – 3A, 3B: Modified radical mastectomy.

Photo – 4: Positive control: Section from endometrium showing ER positivity. (IHC, 400X)



Histological types in comparison with other studies

In the present study, 20 (71.4%) were Invasive ductal carcinoma (NOS). Similar observation was made by Onitilo AA, et al. [10] and Zafrani B, et al. [11]. Other types of carcinomas had varied incidence in different studies.

Comparison of ER, PR, and HER2 expression with other studies

In the present study, 60.8% were ER/PR+, HER2- and triple negative carcinomas were about 14.3%. Similar observations were seen in Onitilo AA, et al. [10] and Huang JH, et al. [12].

Histological grading of TNBC in comparison with other studies

In the present study, most of the cases were of grade III. Similar observations were noted in in Thike AA, et al. [13] study and Kanapathy Pillai, et al. [14] study.

Conclusion

Breast cancer is one of the most common female malignancies and cause of death among women worldwide. A large number of genetic alterations have been identified in invasive breast carcinomas, many of which are of potential prognostic or predictive value.

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Photo – 5: Invasive ductal carcinoma.
5A: H&E stain, 400X
5B: ER negative. (IHC, 400X)
5C: PR negative. (IHC, 400X)
5D: HER-2 negative. (IHC, 400X)

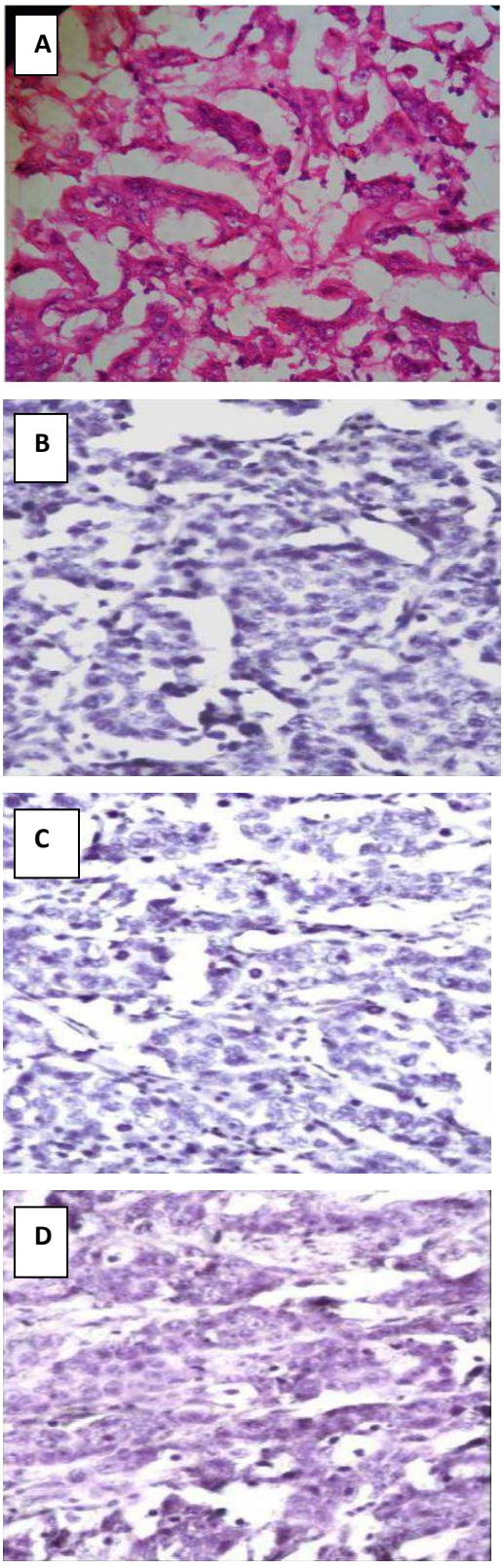

Photo – 6: Medullary carcinoma.
6A: H&E stain, 100X
6B: ER negative. (IHC, 400X)
6C: PR negative. (IHC, 400X)
6D: HER-2 negative. (IHC, 400X)

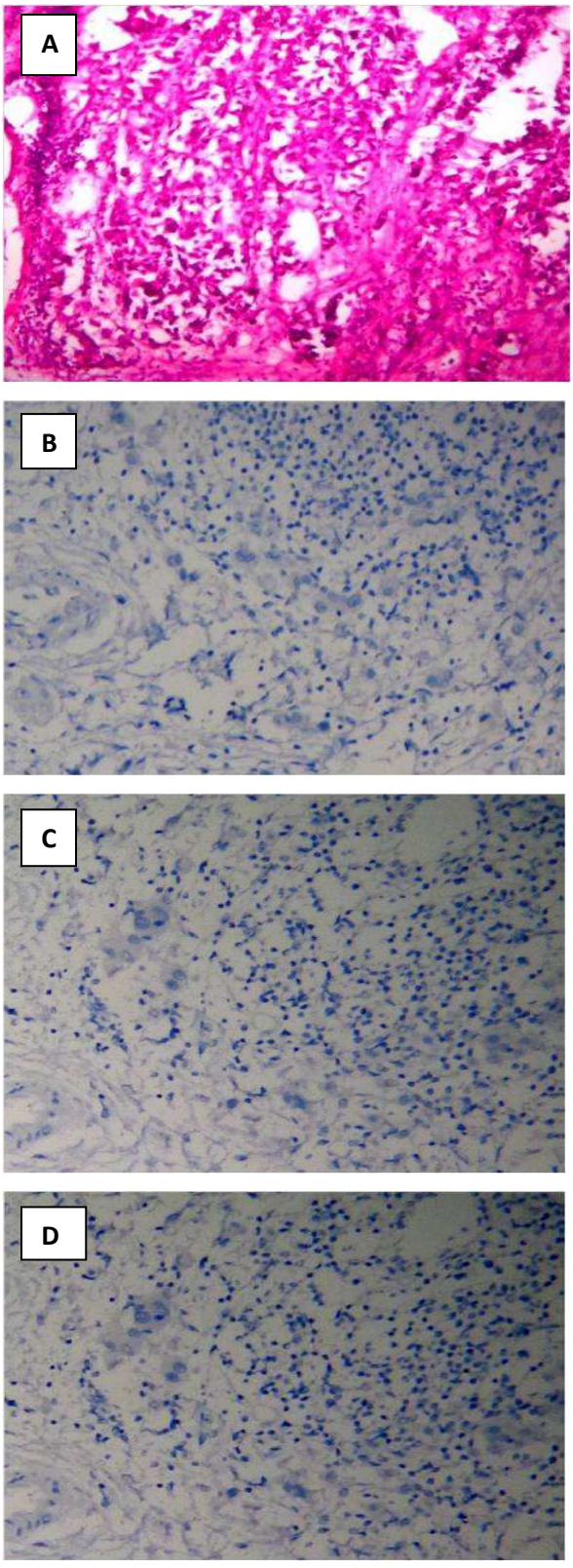

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Photo – 7: Mucinous carcinoma.
7A: H&E stain, 100X
7B: ER negative. (IHC, 100X)
7C: PR negative. (IHC, 400X)
7D: HER-2 negative. (IHC, 400X)

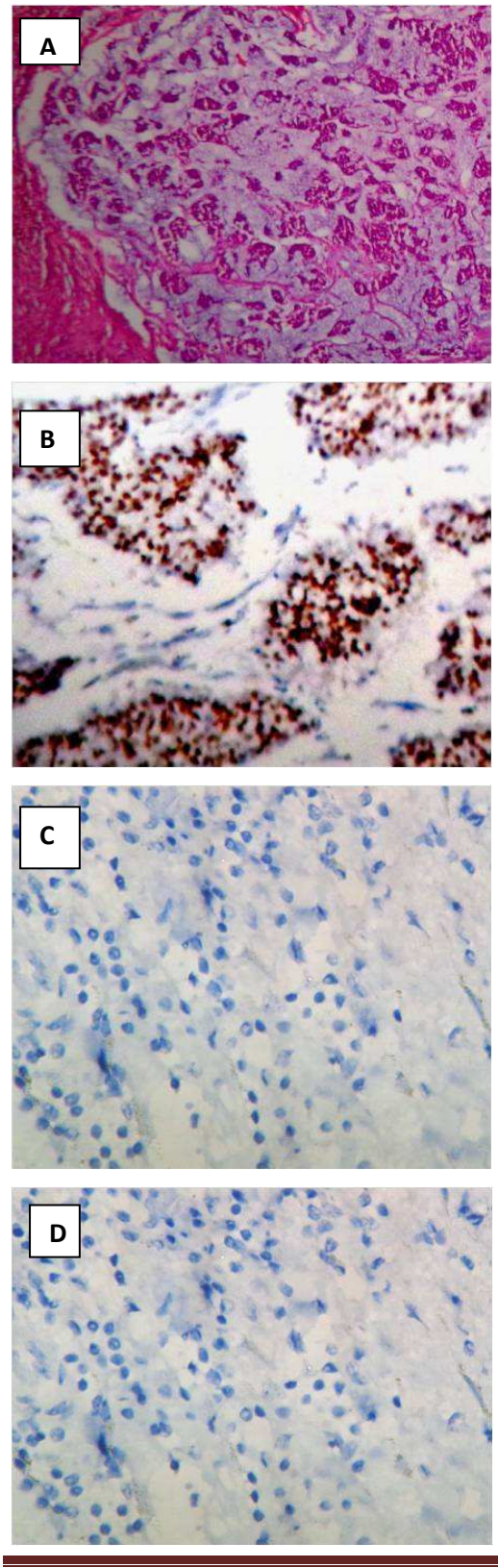
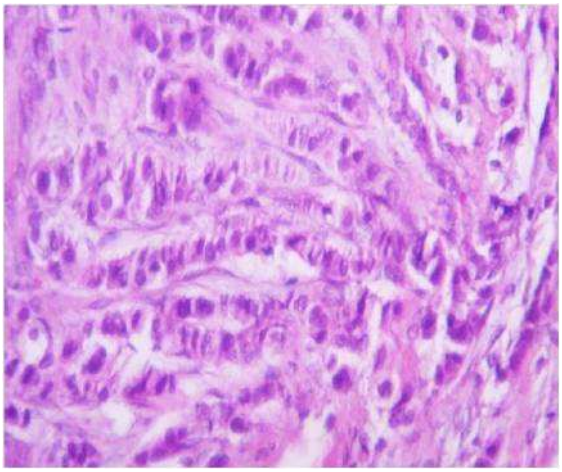


Photo – 8: Lobular carcinoma. (H&E stain, 100X)



Prognosis and management of breast cancer are influenced by classic variables such as histologic type and grade, tumor size, status of hormone receptors - ER, PR and more recently, HER-2 status.

The interrelationship between ER, PR and HER-2 has come to have an important role in the management of breast cancer. Patients with breast carcinoma over expressing HER-2 do not respond to tamoxifen therapy. Recently anti-HER-2 antibodies (Herceptin) have been shown to be effective against HER-2 over expressing breast carcinomas.

In this study an attempt was made to understand the correlation of ER, PR and HER-2 status with histopathological grading and clinic-pathological parameters. In conclusion, ER, PR and HER-2 status correlates well with histopathological grading and other clinico-pathological parameters. Higher grade is associated with HER-2 positivity and ER/PR negativity, larger tumor size, lympho-vascular invasion, lymph node metastasis, and higher clinical stage.

Triple Negative breast carcinomas in younger age group are associated with poor prognosis. Hence, immunohistochemical assessment of ER,

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PR and HER-2 should be incorporated as a routine investigation. This along with histopathological grading and staging will guide the clinicians to make correct choice of treatment protocols.

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