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RESEARCH ARTICLE

An assessment on the Clinicopathological profiles in patients of breast carcinoma attending Surgical OPDs of Secondary & Tertiary Care centres situated in Urban & rural areas .

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Abstract

Introduction : Breast cancer is by far one of the most frequent cancer in female, both in developed and developing regions. Early diagnosis and treatment will reduce the morbidity and mortality of the disease and thus it prolongs the survival of the patient. Aim of the study is to assess the various type of clinical and pathological patterns of presentation of operable carcinoma breast cases in local region. Methods: This was a Retrospective analytical study of 200 cases of Breast Carcinoma. Relevant clinical features like age, parity , laterality of the tumor, mode of presentation, history of breast cancer in 1st degree relative, fixity of the tumor and skin, and nipple-areola changes were assessed. Size, number, and location of tumor in mastectomy specimens were noted macroscopically. Microscopically, histological type, histological grade lymphatic and blood vessel invasion, and lymph node involvement were evaluated. Results: Most of the patient belongs to 41-50 years age group. 61% were presented with left-sided breast Cancer. 52% presented with UOQ lump, 57% presented with 2-5cms2 sized tumor. Maximum patients complain of Lump and Pain .Around 91% of the patients Histopathological report showed Invasive Ductal Carcinoma. Mostly were histological grade 3 tumors with Lympho-vascular invasion was identified in 28%. Lymph nodes were involved in 54% cases. 41% of the patient were of stage II B, followed by 22% with stage II A. Conclusion: Invasive ductal carcinoma (IDC), not otherwise specified (NOS), is the most common histologic type. Its frequency of occurrence far exceeds that of the other histological types. Most commonly affected age group by breast cancer is 41-50 years, and most of the patients are from post-menopausal age group. Size of the mass was more than 2 cm involving multiple quadrants of breast and with positive lymph nodes. Histologically, grade 3 tumor is most prevalent in study population. Stage II A & II B Comprise maximum patients.

Key Word : Breast Cancer , Invasive Ductal Carcinoma, retrospective , grade , management .

1 | INTRODUCTION

One of the commonest cause of death in adult women is carcinoma breast and it is the commonest leading cause of death among aged 20-59 years.[1]

Mortality rates from breast cancer have increased during the past 60 years in every country. International variation in both incidence and mortality is one of the most striking features of breast cancer. [1,2]The age-standardized rates of breast cancer in India are significantly lower, almost one quarter to

one-third of those in North America and Europe, respectively.[1,3] The postulated reasons for the lower incidence of this disease are believed to be lower socio-economic status, delayed menarche (14 years vs. 12.6 years in white women), relatively early age at birth of first child, high parity, and nearly universal and prolonged breast-feeding. The high socioeconomic status will increase the incidence of carcinoma breast. Now it is reported in the younger age group also. Early diagnosis and treatment will decrease the morbidity and mortality of the disease significantly.[2,4] The treatment depends upon the patient at which stage they are presenting to the health services. Screening mammography above 50 years, if used as a routine will reduce the mortality from cancer by 33%. If they are diagnosed early, the breast conservation surgery can be planned.3 If the patient present at the advanced stage, they have to be treated aggressively having a severe complication after treatment.[4]

The triple approach to the diagnosis of breast carcinoma, involving clinical examination, imaging (mammography), and fine needle aspiration cytology, has an accepted place in the assessment of patients presenting with solid breast mass.[4,5,]The traditional pathological factors of lymph node status, tumor size, histological type, and histological grade are the most useful prognostic factors in breast cancer patients

The breast cancer management requires a multimodality approach, which includes surgery, radiotherapy, chemotherapy.[5] In this study an attempt to study that patient who is eligible for surgery i.e. Operable carcinoma breast. It includes both early breast cancer patient (stage I, stage II A, II B) and Operable LABC patients (111A, Stage 111B) either directly taken for surgery or after neoadjuvant they are eligible for surgery. It accounts for 5-10% of all breast cancer cases. 40% other cases due to mutation in BRCA 1 and BRCA 2 and others are HER2 mutation and P 53 mutation. Genetic counselling and DNA testing can identify the high risk cases. 80% of chance of developing breast cancer.5

Aim of the study was to assess the clinical profiles of the patients of breast carcinoma as well as their relevant macroscopic and microscopic features of the mastectomy specimens.

2 | METHEDOLOGY

This was a Retrospective analytical study which involved Prior Consent from Hospital Authorities / Medical Superintendents of randomly selected local secondary & tertiary care hospitals to see the records of the patients. Case files / records of 200 Patients attended and admitted in the Surgical Units of various Randomly selected tertiary care hospitals located locally in the last 4 years were selected for study.

Clinically suspected and pre-operative FNAC (fine needle aspiration cytology) confirmed patients of breast cancer, who were admitted in the surgical units / department of surgery for mastectomy in randomly selected local Tertiary care hospitals during the study period of last 4 years were included in the study.

This Retrospective & Analytical study involved Prior Consent to see the records of the patients from Medical Records Department (MRD) with the disclosure that we will use the data for study purpose only Identity(Names) were hidden & Medical record numbers were used to generate the data for analysis.

The study was conducted within ethical standards & doesn't involved any direct Intervention to any mentioned subjects nor any physical Examination was performed. Randomization was done using computer tables in selecting data. All Patients data had details of standard clinical examinations, routine biochemical and haematological investigations, For the purpose of the present study, data of 200 of the randomly selected patients (candidates / study subjects) were retrospectively identified. The medical records for these patients were reviewed for the collection and

Supplementary information The online version of this article (10.15520/ijmhs.2016.vol6.iss3.11389) contains supplementary material, which is available to authorized users.

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classification.

Inclusion criteria were

• Female Patient aged between 20 to 80 yrs

• All patients with breast lump with FNAC positive report

• Patients who belong to the clinical stage I, stage II, stage III.

The patients with breast carcinoma, who attended the surgery OPD but not admitted in the department of general surgery for mastectomy in the study period, patients having history of pre-operative chemotherapy or radiotherapy for breast carcinoma, and male patient with breast carcinoma, were excluded from the study.Relevant clinical features like age, laterality of the tumor, mode of presentation, menstrual and reproductive history, history of breast cancer in 1 st degree relative, fixity of the tumor and skin, and nipple-areola changes were assessed. Size, number, and location of tumor in mastectomy specimens were noted macroscopically. Microscopically, histological type, histological grade by Nottingham modification of Scarff Bloom Richardson (SBR)'s method, lymphatic and blood vessel invasion, and lymph node involvement were evaluated in Hematoxylin and Eosin (H and E)-stained sections.Observed Histology procedure in all case files: After doing primary slicing of the mastectomy specimen on the first day, recommended sections were taken on the second day of receiving the specimen. The tissues were then processed following the routine steps of dehydration in ethyl alcohol, clearing in Xylene, and impregnation with paraffin. The processed tissues were embedded in paraffin wax. Sections were cut at 3-5 μm thickness and stained with Hematoxylin and Eosin (H and E) stain. Mitotic figures were scored using an microscope .

It was observed & made sure that all the case files have the Local Examination well explained & divided into four parts; inspection, palpation, percussion and auscultation. On inspection the site, size, shape, surface, extent, borders, skin over were noted.

Patient with Early breast cancer underwent surgery followed by adjuvant chemotherapy(AC), hormonal therapy (HT) and radiotherapy(RT). Chemotherapy is used as adjuvant (AC) or neoadjuvant chemotherapy (NAC).

Patient with stage III disease undergoes neoadjuvant chemotherapy (NAC) followed by surgery , then adjuvant chemotherapy , hormonal therapy (HT), radiotherapy(RT).

All surgeries / Modified Radical Mastectomy (MRM) were performed by general / Onco surgeons.

Continuous data were expressed as mean ± standard deviation (SD) . The data were analysed by IBM SPSS Statistics 23. All quantitative data were coded and transformed into an excel master sheet for computer programming. A chi-square test was used to evaluate categorical variables for analysis. Overall, < 0.05 was proposed to represent statistical significance after correction.

3 | RESULTS

The distribution of age in my study ranges people from 18 -80 years. The lowest age limit in the study was 24 and the highest age limit was 79. The mean age of presentation is 46.5 years. Most of the patient belongs to 41-50 years age group (Table No.1). In the study out of 100 patient records 21 % of them having Diabetes Mellitus (DM), 9% of them having Hypertension(HTN), and 23% of patients having both DM & HTN. This shows those having DM and HTN have a high-risk factor for the development of carcinoma breast .

TABLE 1: Age distribution

Age class intervals	Observations (Percentage) (n=200)
21-30	02
31-40	09
41-50	46
51-60	22
61-70	18
71-80	03
Total	100

Out of 100 patients, most of the patient (61%) belongs to 1 or 2 childbirth. Higher the parity lesser the occurrence of carcinoma breast. Nulliparous was observed in 16% patients. Parity 1was observed in

TABLE 2: Correlation with Parity

Parity	Percentage (%) (n=200)
Nulliparous	16
Parity 1	22
Parity 2	39
Parity 3	11
Parity 4	08
≤5 Parity	04
Total	100

22% patients & parity 2 in 39%.patients. Parity 3 in 11% patients. Parity 4 in 8% patients. ≤5 Parity seen in 4% patients. (Table 2).

In our study 61% were presented with left-sided breast Cancer & 39 % patients had right side breast cancer (Table 3).

TABLE 3:

The side of breast involved	Percentage (%) (n=200)
Left	64
Right	36
Total	100

TABLE 4: Quadrants Involved

Quadrant of involvement	Percentage (%) (n=200)
Upper Outer Quadrant (UOQ)	52
Upper Inner Quadrant (UIQ)	11
Lower Outer Quadrant (LOQ)	07
Lower Inner Quadrant (LIQ)	06
Central	21
Multicentric	03
Total	100

In the present assessment study , 52% presented with UOQ lump, followed by central, UIQ, LIQ, LOQ and multicentric. The commonest occurrence of carcinoma breast is UOQ (Table 4).

In the study 7% patient presented with size less than 2cms^2, 57% presented with 2-5cms^2 sized tumor and

TABLE 5: Size oftumour.

Size of tumour in cms^2	Percentage (%) (n=200)
≤2 cms^2	07
2-5 cms^2	57
>5 cms^2	36
Total	100

36% of them with >5 cms^2 tumor (Table 5).

Presenting Complains and symptoms – Maximum patients complain of Lump and Pain (Table – 6)

TABLE 6: Showing distribution of presenting complains among cases.

Presenting Complains	Percentage % (n=200)
Lump	100
Pain	27
Nipple Retraction	21
Nipple Discharge	03
Skin Dimping	09
Peaud'orange	08
Skin tethering	03

Around 91% of the patients Histopathological report showed Invasive Ductal Carcinoma. Most of the patients presented with breast lump with or without other features, and nipple retraction was also common finding. The tumor mass mostly fixed to the deeper structures.

TABLE 7: Distribution of cases according to Histopathological Examination report.

HPE report	Percentage (%)
Intraductal Carcioma - NOS	91
Lobular	04
Mucinous	02
Tubular	01
Medullary	01
Invasive Papillary	01
Total	100

8% had the positive family history of breast cancer in first degree relatives.Mean tumor size in the study population was 4.53 cms^2 with standard deviation ± 1.87.

Most of the cases i.e 91% were diagnosed as IDC, NOS (Infiltrating ductal carcinoma, not otherwise

specified , See figure 1) Mostly were histological grade 3 tumors (Figure -2) followed by grade 2. Lympho-vascular invasion was identified in 28% (see figure 3) . Lymph nodes were involved in 54% cases (see figure 3). Skin and nipple areola was involved in 13% cases .

Receptor status, in study receptor negative were 46 %, ER –ve PR +ve were 24 % & HER 2 neu +ve were 16% , In rest the status could not be identified.

TABLE 8: The distribution of stages in various cases

Staging of Ca Breast [6]	Percentage % (n=200)
I A	03
II A	22
II B	41
III A	18
III B	16
Total	100

In my study, 41% of the patient were of stage II B, followed by 22% with stage II A, 18% them with III A and 16% stage 111B and least were of stage 1A i.e 4%.

In present study 23% patient under gone Neoadjuvant Chemotherapy followed by MRM then AC,RT,HTs. 66% patient under gone MRM+AC+HT.

4(8%) undergone MRM+AC+RT+HT. (Table - 9)

TABLE 9: Showing treatment given to cases.

Treatment Given	Percentage % (n=200)
MRM + AC+HT	62
MRM+AC+RT+HT	15
NAC+MRM+AC+RT+HT	23
Total	100

(NAC = Neoadjuvant Chemotherapy , MRM = Modified Radical Mastectomy , AC = Adjuvant Chemotherapy , HT = Hormonal Therapy , RT = Radiotherapy)

4 | DISCUSSION

Breast cancer is one of most common cancer in females. Locally advanced breast cancer refers to a diverse and heterogeneous group of breast cancers and represents only 2-5% of all breast cancers in the United States; however, locally advanced breast cancer is more prevalent in India. Subdividing these patients into three broad groups those with the operable disease at presentation-cancer/American Joint Committee on Cancer (AJCC) clinical Stage T3N0 to N1M0,2) inoperable disease at presentation-AJCC clinical Stage T4 or N2 to 3M0 or both, and 3) inflammatory disease- AJCC clinical Stage T4dN0 to N3M0 facilitates clinical management.[6] Generally, clinically operable breast cancer is treated first by surgery followed by adjuvant therapy including RT to the chest wall and supraclavicular region with or without axillary RT depending on disease burden in the axilla. Although, the other two groups are treated with neoadjuvant chemotherapy first followed by local treatment.[7] Breast cancer with ipsilateral SCLN (AJCC Stage IIIC) is a unique clinical entity comprising of 1% of all breast cancer. SCLN drainage is a part of continuum drainage of Level I, II and III axillary lymph node drainage. Skip metastasis can occur commonly from upper quadrant tumor or patients with internal mammary node metastasis.[8] Patients with breast cancer who present with supraclavicular metastases have a poor prognosis, especially when treated with surgery or RT alone. The presence of supraclavicular metastases was one of the original signs of inoperability identified by Akhtar.[9,10] In 1987, the International Union Against Cancer/AJCC tumor-node-metastasis staging system changed the classification of patients with supraclavicular metastases from N3 to M1 to reflect the poor prognosis of patients with this presentation. Recently, Greenall et al reported on a pooled analysis of three M.D. Anderson Hospital protocols and found that patients with regional Stage IV disease had better outcomes than patients with visceral Stage IV disease.[11] Recently, the AJCC has further amended the staging classification to include patients with supraclavicular metastases at diagnosis in the IIIC category. This staging change came into effect from January 1, 2003. However, there is no consensus on the treatment of supraclavicular lymph node metastasis.[12] The retrospective study by Kakarala et al attempted to define the risk factors for SCLN metastasis and select high-risk patients for whom aggressive local

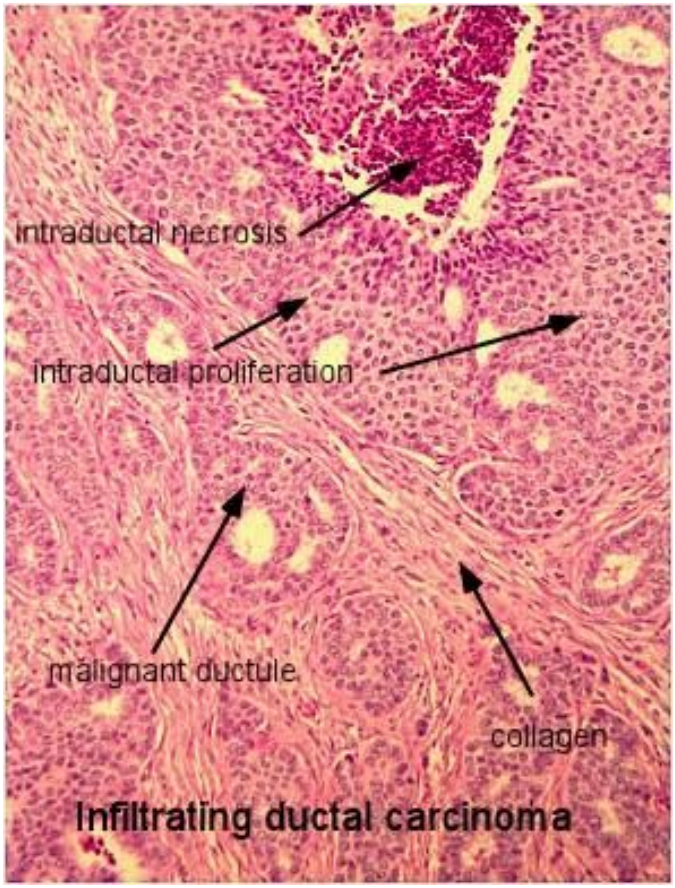

FIGURE 1: Showing salient features of Invasive Ductal Carcinoma (tumor mass of breast)

treatment such as RT is indicated.[13] Toniolo in their study, 113 (4.3%) out of 2658 patients developed SCLN metastasis during this period. Young age (<or = 40 years), tumor size >3cm, high histologic grade, angiolymphatic invasion, negative estrogen receptor status, synthetic phase fraction >4%, >4 positive nodes, and Level II or III involved nodes were all significant for predicting neck metastasis in the univariate analysis. Of these three predictive factors were significant after multivariate analysis: High histologic grade, >4 positive nodes and axillary Level II or III involved nodes.[14]

However, in the study, none of the clinicopathological factors excluding axillary nodal burdens such as including age, menopausal status, and clinical T stage, the location of tumor, high histologic grade, angiolymphatic invasion, negative hormone or Her2 neu receptor status were associated with occult SCLN metastasis.[15]

Receptor status with respect to ER PR – ve , PR +ve & Her 2 neu +ve , in comparison to another study is about 47%, 23%, and 30%.[16,17]

Frequencies of symptoms in breast carcinoma reported by WHO are 60-70% for breast lump, 14-18% for pain, 7-9% for nipple problems, 1% for deformity, 1% for inflammation. [18] In a study by Raina, et al.[19] , most of the patients i.e., 96.5% presented with breast lump. 15.8% patients had pain, and 4.9% had nipple discharge in addition. Mode of presentation of the patients in the present study shows almost similar picture of the other studies.Raina, et al.[19] noticed 7% patients with history of breast cancer in first degree relative. Rosen et al.[20] observed 31% of the patients reported with one or more relatives who were known to have had breast cancer in a study on 1024 patients.Meena, et al.[21] observed that 58% of the breast lumps were freely mobile while remaining were fixed. There is an inadequacy of the data in recent literature regarding this parameter.Nipple retraction was present in 43% of the cases, Peau d' orange appearance in 18% of the cases, and ulceration of the skin in 13% of cases in the study

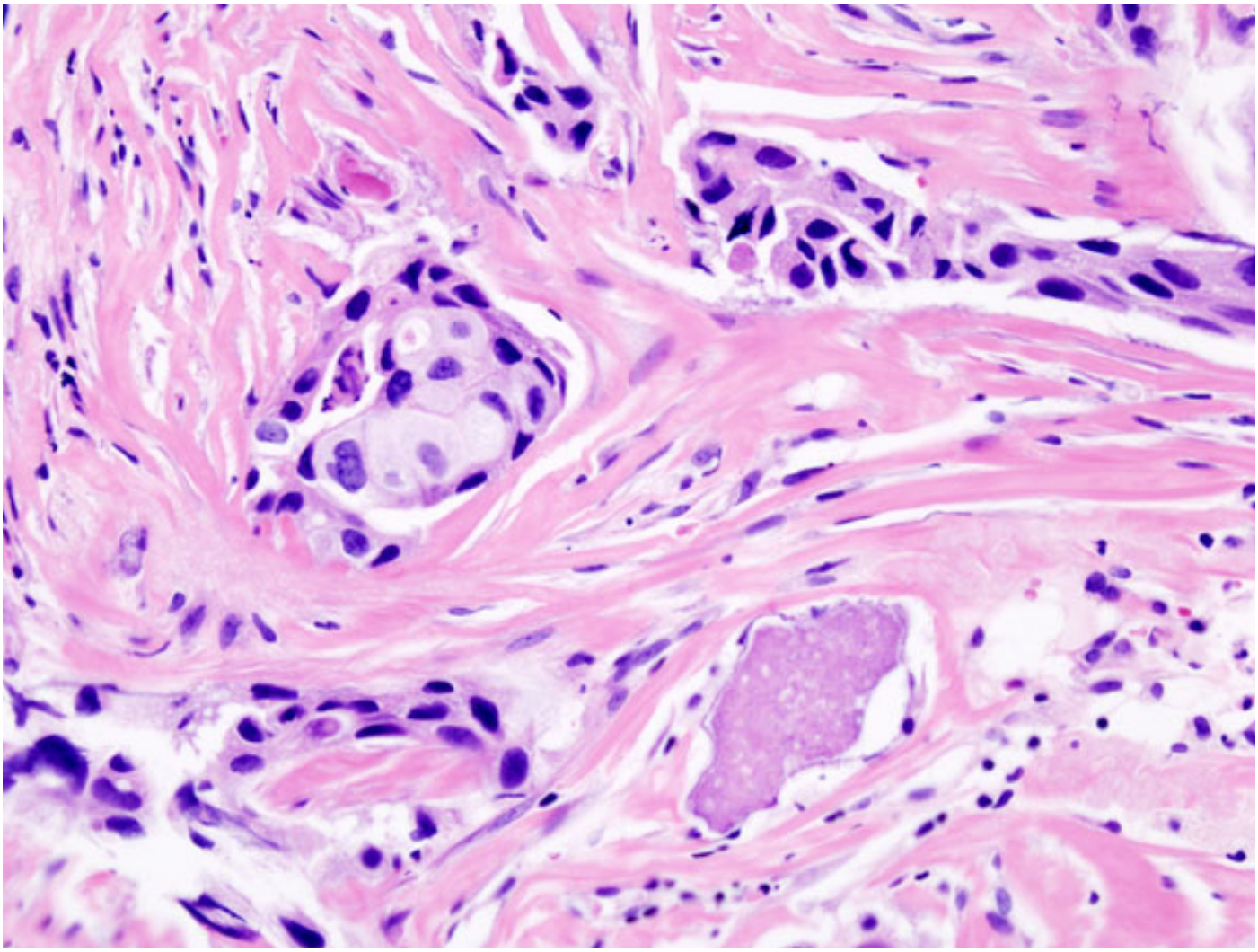

FIGURE 2: –Showing salient features of Invasive Ductal Carcinoma

by Meena et al.[21] The findings of this study are comparable with that of other available studies.The study conducted in Singapore general hospital on the patients aged 35 years or younger revealed the tumor size in 80 cases with values ranging from 0.3 to 11.5 cm (mean 2.7 cm, median 2.1 cm). Of these, 16 (20%) cases were $\leq$ 2 cm (T1), 48 (60%) were 2-5 cm (T2), 14 (17.5%) measured from above 5 cm to 10 cm (T3), and two cases (2.5%) were more than 10 cm in maximum dimension. [22] Of 97 cases with recorded measurements of the size of the tumor, 36 cases (37.1%) were less than 2.5 cm in maximum diameter, and 61 cases (62.9%) were more than 2.5 cm in a large study in Saudi Arab But, these variations can be concluded by the fact as stated by WHO is that there are marked variations in the size from under 10 mm to over 100 mm. [18]

According to WHO literature, 40-50% of the tumors occur in the upper outer quadrant, and there is a decreasing order of frequency in the other quadrants from the central, upper inner, lower outer to the lower inner quadrant. [18] Baily Love's textbook [23]says breast cancer most frequently involves the upper outer quadrant (60%) followed by 12% in both central zone and upper inner quadrant, 10% in lower outer quadrant, 6% in lower inner quadrant. The lump was found in upper outer quadrant in 54% cases followed by lower outer quadrant (12%), lower inner quadrant (12%), upper inner quadrant (5%), and central (7%) and diffuse (10%) in a study conducted in SMS medical college, Jaipur. [21]The discrepancies of probably arouse due to two reasons. Most of the reported series are from countries where breast cancer screening is a routine proce-

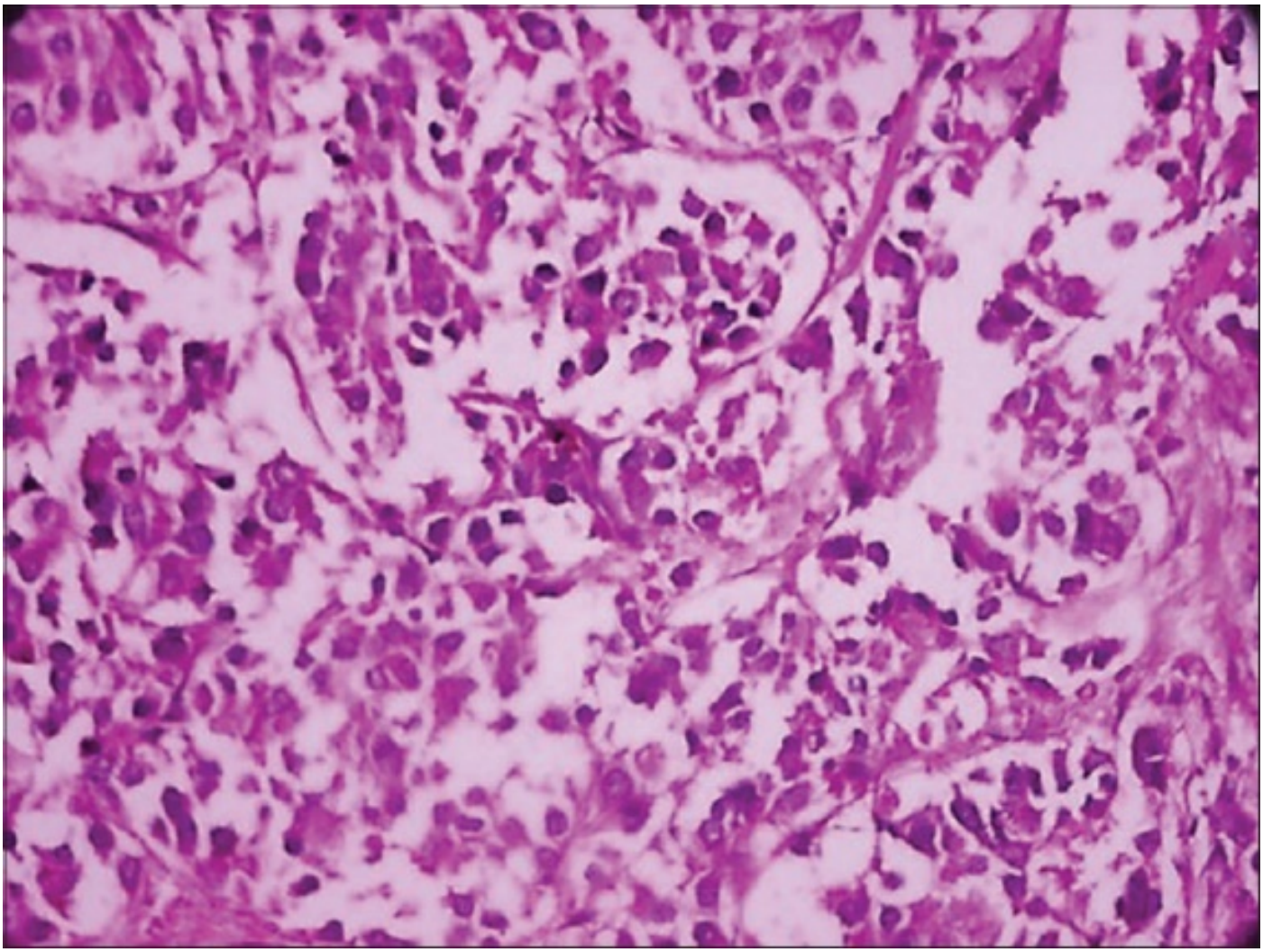

FIGURE 3: H and E-stained section fromtumor mass of breast shows histopathological features of IDC (NOS type) Grade 3 (×40 view)

dure, and early detection is usual in contrast to this study population in which screening has not yet been implemented. Lack of awareness and poor socio-economic status also compelled the patients to come at later stage with larger tumor involving multiple quadrants.WHO stated IDC, NOS is the most common type of invasive carcinoma in breast comprising between 40% and 75% in different published series followed by invasive lobular carcinoma in 5-15% cases. [18] In all the large studies by Rosen, et al.[24] , Ellis, et al.[25] , Page and Anderson[26] , IDC, NOS came out as the most common invasive carcinoma of the breast followed by invasive lobular carcinoma. Raina, et al.[19]observed invasive ductal carcinoma in most (92.8%) of the patients followed by invasive lobular carcinoma (2.9%) and medullary carcinoma (1.4%).Histological subtyping in a study in Singapore disclosed 92.3% ductal, 2.2% lobular, 2.2% mucinous, 2.2% atypical medullary, and 1.1% with both ductal and lobular features in 91 patients with invasive carcinomas. [22] The distribution of histological types of breast carcinoma in this study population is almost similar to that of other reported series.Pinder, et al.[27] observed definite vascular invasion in 22.8% of cases, and concurrence between pathologists was high in this study. Vascular invasion was strongly associated with lymph node stage, tumor size, histological grade, and type of tumor. Vascular invasion was proved as independent prognostic factor for both survival and for local recurrence of tumor.Lymphatic vessel invasion was present in 34.2% of cases, and blood vessel invasion in 4.2% cases in a

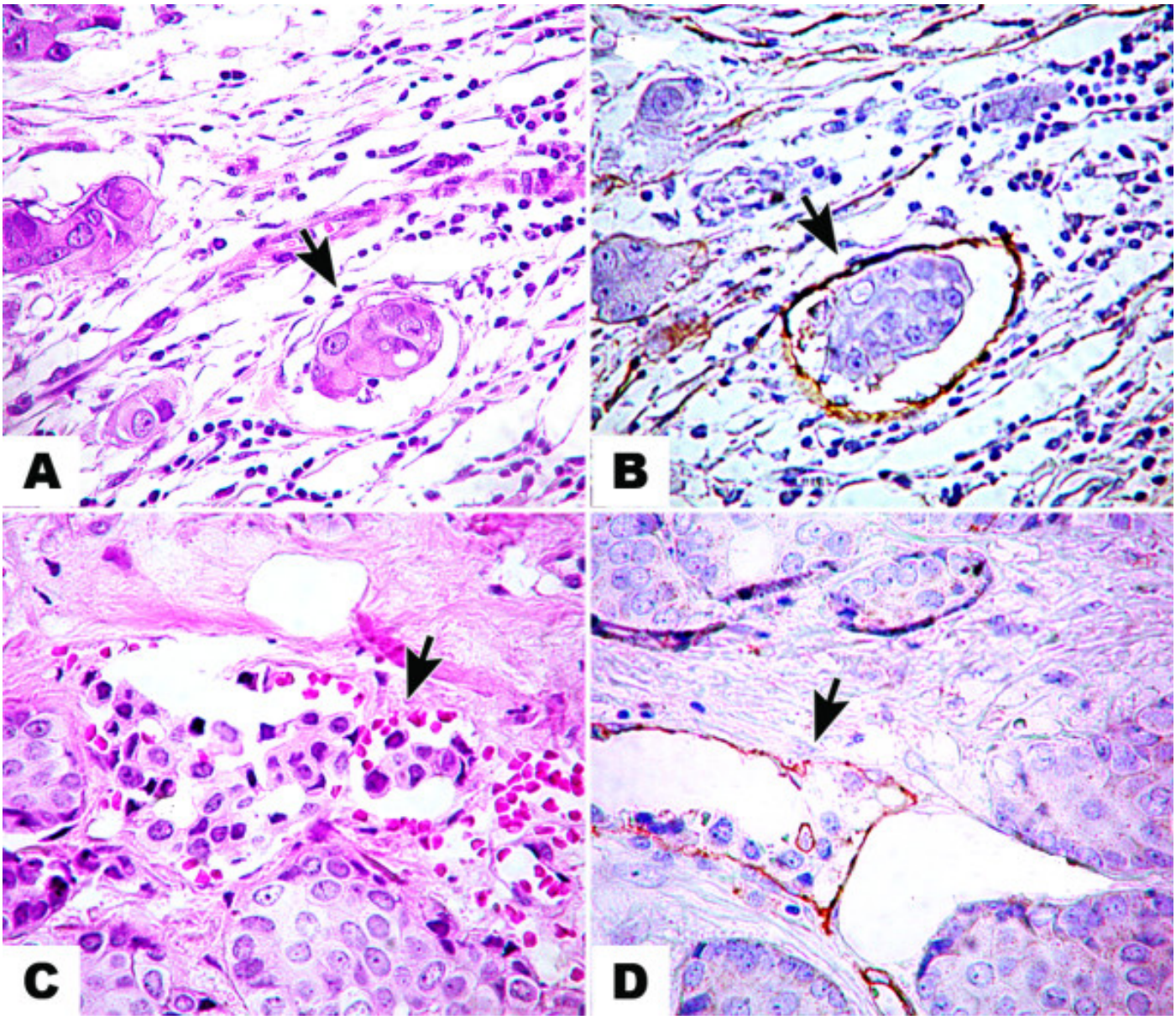

FIGURE 4: Lymphatic and blood vascular invasion in invasive breast cancer in H&E andimmunostained slides. Lymphatic vascular invasion (arrow) seen in H&E (A) and D2-40 (B) stained sections of breast tumors from the same case; ×400; Blood vessel invasion (arrow) seen in H&E (C) and CD31 (D) stained sections; ×400.

study in Italy. Lymphatic vessel invasion correlated with blood vessel invasion, and both were correlated with metastatic axillary lymph nodes and increasing tumor size and grade. [28]The frequency of lympho-vascular invasion in the present study appears to be more or less similar to the reported frequency in several other studies.In a large study [18] , 81 patients out of 137 underwent mastectomy with axillary lymphadenectomy. Thirty-one cases (38.3%) had negative lymph nodes for metastatic deposits, and 50 cases (61.7%) had positive lymph nodes. Of the latter group, 17 cases (21%) had metastases in one to three lymph nodes and 33 cases (40.7%) in more than three lymph nodes.

The study by NSABP (National Surgical Adjuvant Breast and Bowel Project) on 505 patients with primary breast cancer with histologically proven positive lymph nodes observed the relationship between the number of positive lymph nodes and 5-year disease-free survival. The disease-free survival (DFS) of the lymph node negative cases was 85%,

and single node positive cases were 63%. Greater numbers of involved nodes were associated with a progressively worse prognosis. They established the validity of previous observations, indicating the appropriateness of grouping primary breast cancer patients into those with negative, 1 to 3, or ≥4 positive nodes. [29]Khan, et al.[30] observed the overall frequency of nipple-areola involvement in 19.1% cases (26 cases out of 136). The frequencies of occurrence of Paget's disease and direct malignant invasion were 2.94% (4 cases) and 16.17% (22 cases), respectively.The observations of this study are comparable to the other contemporary studies.The largest and most well-known study on histological grading by Elston and Ellis [31] found 342 cases (19%) of grade 1, 631 cases (34%) of grade 2, and 857 cases (47%) of grade 3 tumors. Another very well-known and large long-term follow up study was performed by Rakha, et al.[32] on 2,219 cases in Nottingham, UK. In this study, 18.6% were grade 1, 35.6% were grade 2, and 45.6% were grade 3 breast cancers. Data on the pathology of breast cancer in Asian women revealed a pattern of a higher proportion of patients with high tumor grade (grade 3 of the Bloom and Richardson grading system), and hormone receptor-negative tumors. [33]In the present study, we got more cases of grade 2 and grade 3 tumors and very few cases of grade 1 tumors , it might be due to grade progression as a consequence of late presentation.

The limitations of the present study was the the study was Retrospective one and sample was relatively small.

5 | CONCLUSION

Invasive ductal carcinoma (IDC), not otherwise specified (NOS), is the most common histologic type of breast cancer in the study population. Its frequency of occurrence far exceeds that of the other histological types. Most commonly affected age group by breast cancer is 41-50 years, and most of the patients are from post-menopausal age group. In most of the cases, size of the mass was more than 2 cm involving multiple quadrants of breast and with positive lymph nodes. Histologically, grade 3 tumor is most prevalent in this population. Stage II A & II B Comprise maximum patients.

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Compliance With Ethical Standards.

Conflict Of Interest – None.

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