

Correlation of Age, Tumor Size, Grade, Lymph Node Metastasis and Skin Involvement in Breast Carcinoma- Hospital Based StudyShah Mitesh¹, Agrawal Ruchi², Singh Puja³, Gangwani Amar⁴¹Department of Pathology, Assistant Professor, Bundelkhand Medical College, Sagar, M.P. India²Department of Microbiology, Demonstrator, Bundelkhand Medical College, Sagar, M.P. India³Department of Pathology, Associate Professor, Bundelkhand Medical College, Sagar, M.P. India⁴Department of Pathology, Professor & Head, Bundelkhand Medical College, Sagar, M.P. India

Received: 18-09-2023 / Revised: 21-10-2023 / Accepted: 26-11-2023

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Conflict of interest: Nil

Abstract:

Introduction: Breast carcinoma is one of the most common malignancy worldwide. Incidence of the disease is also increasing in India and can cross about 2 million till 2030. Various studies conducted worldwide had shown size of tumor, lymph node status, age and other variables are the prognostic markers for breast cancer. It had found that 4 or more lymph node involvement also affect survival.

Aims and Objectives: To find the correlation of age, tumor size, grade, tumor architecture, nuclear pleomorphism, mitotic activity, lymph node metastasis and skin involvement in breast carcinoma. Method: Retrospective study was conducted in department of pathology, Bundelkhand Medical College, Sagar (M.P.) from 2019- september 2023. Data regarding age, tumor size, grade, tumor architecture, nuclear pleomorphism, mitotic activity, lymph node metastasis and skin involvement in breast carcinoma specimens was collected, assessed and statistically analyzed by Chi-square test.

Result: Statistically significant correlation between tumor size and grade [corrected χ^2 score is 16.93, corrected p value 0.009 (p <0.05)], tumor size and lymph node metastasis [χ^2 score is 6.02, p value 0.049 (p<0.05)] along with mitotic activity and lymph node metastasis [corrected χ^2 score is 6.46, corrected p value 0.04 (p<0.05)] found.

Conclusion: Larger tumor size can have more probability of higher grade and lymph node metastasis. Higher the mitotic activity score more chances of spread to lymph nodes. Age, number of positive lymph nodes, skin invasion are independent risk factors.

Keywords: Breast, Carcinoma, Age, Tumor Size, Grade, Lymph Node, Skin, Metastasis.

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Introduction

Breast carcinoma is one of the most common malignancy worldwide [1,2]. Australia, New Zealand, Northern America, Western and Northern Europe had more rate of incidence (>80/1lac women) than other countries in 2020 [3,4]. Incidence of the disease is also increasing in India and can cross about 2 million till 2030 [1]. Breast carcinoma account for 25% of all cancers in females. [5] In 2016 incident cases of breast carcinoma in India was about 1.2 lac where 98% were females while prevalent cases were about 5.2 lacs [1]. In 2017 incidence rate was 25.8/1 lac women and 12.7/1 lac women was the mortality rate. Delhi, Chennai, Bangalore and Thiruvananthapuram were the top four districts as per the incidence rate [5,6]. In India many patients seek health care in advanced stages with huge

masses, skin changes and after occurrence of other complications [1].

Breast is among the top 5 leading sites of cancer [7]. Age standardized incidence rate of breast cancer has also increased in all the states of India among females in last 25 years [1]. In India incidence of breast carcinoma is increasing in younger women with more cases than earlier are found under 40 years of females [5]. Age adjusted incidence and mortality varies among countries with Northern America, Western and Northern Europe have high postmenopausal mortality rate while Melanesia, Western and middle Africa have high premenopausal mortality rates [3].

Various studies conducted worldwide had shown size of tumor, lymph node status, age and other variables are the prognostic markers for breast

cancer. For breast cancer relation of size of tumor, nodal status and outcome is known long back. Increase in tumor size and nodal involvement both had negative impact on prognosis. It had found that 4 or more lymph node involvement also affect survival [8].

Age, tumor size, grading and lymph node metastasis are important prognostic markers of breast carcinoma [9]. Past studies showed that older postmenopausal women had better prognosis, better differentiation of tumor and had lower stage; while tumor size shows a good correlation with incidence of nodal metastasis and is an easy, quick and cheaply determined parameter to predict relapse and dissemination in node negative breast carcinoma [2,9].

In breast cancer distant metastasis is one of the primary causes of mortality. Distant metastasis can occur even if diagnosis done at early stages. So it will be helpful in management to identify the risk factor associated with distant metastasis. Infiltration of skin and chest wall by tumor along with nodal involvement is the good predictor of distant metastasis [10].

Though tumor size and lymph node involvement both are prognostic factors of breast carcinoma, nodal status is considered better than tumor size especially for N3 cases. For extensive nodal involvement tumor size became independent prognostic marker with worse outcome for T4 tumor stage [11].

Present study is done to find the correlation of tumor size, age, grade and lymph node metastasis in the patients of breast carcinoma of Bundelkhand region by hospital based study.

Aims and Objectives

1. To find the correlation of age with tumor size, grade and lymph node metastasis.
2. To find correlation of tumor size with grade, lymph node metastasis and skin involvement.

3. To find correlation of grade with lymph node metastasis and skin involvement.
4. To find correlation of lymph node metastasis and skin involvement.
5. To find correlation of tumor architecture, nuclear pleomorphism, mitotic activity with lymph node metastasis.

Method:

Study design: Retrospective study

Present study was conducted after approval from institutional ethical committee, and done from specimens received in department of pathology, Bundelkhand Medical College, Sagar (M.P.) from 2019- September 2023. Data regarding age, tumor size, modified Bloom Richardson grade, score for tumor architecture, nuclear pleomorphism, mitotic activity, lymph node metastasis and skin involvement in breast carcinoma specimens and their sections was collected from records, requisition forms and assessed as per objectives. Data regarding tumor size and nodal involvement is categorized as per TNM staging and CAP protocol (12).

Inclusion criteria

1. Only breast carcinoma in female patients were included
2. Data of well-preserved specimen with requisition form and full details were included

Exclusion criteria

1. Breast carcinoma in males, carcinoma in situ and atypical lesions was excluded from study.
2. Carcinoma other than infiltrating duct carcinoma
3. Breast tumor other than carcinoma

Statistical analysis: Statistical analysis was done using Chi-square test. P-value <0.05 was considered statistically significant. William's correction is applied where needed (13)

Result

Table 1: Tumor Size in mm

| Age in years | Tumor Size in mm | | | | | Total |
|--------------|------------------|----------|-------------|----------------|----------------|------------|
| | >1mm - 5mm | ≤ 5mm | >5mm- ≤10mm | >10mm - ≤20 mm | >20 mm - ≤50mm | |
| 20-30 | 0 | 0 | 0 | 2 | 1 | 3 (2.3%) |
| 30-40 | 0 | 1 | 2 | 8 | 15 | 26 (20.3%) |
| 40-50 | 0 | 0 | 2 | 21 | 21 | 44 (34.4%) |
| 50-60 | 0 | 1 | 7 | 17 | 07 | 32 (25%) |
| 60-70 | 0 | 0 | 0 | 10 | 8 | 18 (14.1%) |
| 70-80 | 0 | 0 | 0 | 2 | 2 | 4 (3.1%) |
| 80-90 | 0 | 0 | 0 | 1 | 0 | 1 (0.8%) |
| Total | 0 | 2 (1.5%) | 11 (8.6%) | 61(47.7%) | 54 (42.2%) | 128 |

Table 1 shows distribution of various sizes of tumors of breast carcinoma with the age of the

patients. Out of total 128 samples of breast carcinoma no sample had tumor of >1 to 5 mm

size, maximum samples 61 (47.7%) had tumor size > 20 mm to 50 mm followed by 54 (42.2%) cases with tumor size of >50 mm. Maximum 44 cases (34.4%) were from patients of 40-50 years age group followed by 50-60 age group with 32 cases (25%). Patients with age group 30-40 years had tumor size > 50 mm in 15 out of 26 cases while for rest other age groups most cases had tumor size >

20 mm to \leq 50 mm which either equal are to or more than cases having > 50 mm tumor size in same age group.

For categories age group and tumor size Chi square score (χ^2) is 20.42, p value 0.30, χ^2 Score after William's correction is 19.33, corrected p value 0.37 (p>0.05). Hence association of age and tumor size is not statistically significant.

Table 2: Grade

| Age in years | Grade | | | Total |
|--------------|-------|----|-----|-------|
| | I | II | III | |
| 20-30 | 2 | 1 | 0 | 3 |
| 30-40 | 7 | 15 | 4 | 26 |
| 40-50 | 12 | 24 | 8 | 44 |
| 50-60 | 7 | 20 | 5 | 32 |
| 60-70 | 4 | 6 | 8 | 18 |
| 70-80 | 1 | 2 | 1 | 4 |
| 80-90 | 1 | 0 | 0 | 1 |
| Total | 34 | 68 | 26 | 128 |

Table 2 show distribution of grade of breast carcinoma in various age groups of patients. Grade II was most commonly found in 68 cases out of 128 patients followed by grade I in 34 patients and then grade III in 26 patients. In patients with age group 60-70 years Grade III was most common grade 8 out of 18 cases. Cases of age group 20-30

years were only 3 and grade I was commonest grade in this age group. For age group and grade Chi square score (χ^2) is 13.76, p value 0.32. χ^2 score after William's correction 13.13, corrected p value 0.36 (p>0.05).

Hence association of age and grade is not statistically significant.

Table 3: Lymph node metastasis

| Age in years | Lymph node metastasis | | | | | Total |
|--------------|-----------------------------|-----|------------|----------------|----------|-------|
| | No. of lymph nodes involved | | | Total Positive | Negative | |
| | 1-3 | 4-9 | 10 or more | | | |
| 20-30 | 0 | 0 | 0 | 0 | 2 | 2 |
| 30-40 | 2 | 8 | 3 | 13 (68%) | 6 (32%) | 19 |
| 40-50 | 8 | 13 | 2 | 23 (66%) | 12 (34%) | 35 |
| 50-60 | 7 | 5 | 3 | 15 (55%) | 12 (45%) | 27 |
| 60-70 | 9 | 2 | 2 | 13 (72%) | 5 (18%) | 18 |
| 70-80 | 1 | 0 | 2 | 3 (100%) | 0 | 3 |
| 80-90 | 0 | 1 | 0 | 1(100%) | 0 | 1 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 3 shows distribution of lymph node metastasis with age group of breast carcinoma patients. Lymph node metastasis was found in 68 cases while negative in 37 cases. Lymph node was not sent in 23 lumpectomy cases. Maximum cases of lymph node metastasis though seen in age group 40-50 years patients while proportion of lymph node positive and negative for metastasis is more for higher age group i.e. 60-90 years while no metastasis was found in 20-30 years.

Number of lymph node positive cases was more than lymph node negative cases for age groups 30-40, 40-50 and 50-60 years age group while proportion of lymph node positive cases was lesser as compared to age group above 60 years. For age group and lymph node metastasis Chi square score (χ^2) is 7.42, p value 0.28, χ^2 score after William's correction is 7.06, corrected p value 0.32 (p>0.05).

Hence association of age and lymph node metastasis is not statistically significant. Table 3 also shows distribution of number of positive lymph nodes among various age groups of patients. Out of 68 lymph node positive patients 27 and 29 cases have involvement of 1-3 and 4-9 lymph nodes respectively while 12 out of 68 cases have 10 or more lymph nodes involved.

For age group 30-40 and 40-50 years, 4-9 lymph nodes involvement seen in 8 out of 13 and 13 out of 23 cases respectively while for age group 50-60 and 60-70 years 4-9 lymph nodes involvement seen in 5 out of 15 and 2 out of 13 cases respectively.

For age group 70-80 years 2 out of 3 cases have 10 or more lymph nodes involvement while for age group 70-80 years only 1 case show lymph node involvement which is 4-9 lymph nodes.

For age group and number of positive lymph node Chi square score (χ^2) is 17.89, p value 0.057, χ^2 score after William's correction is 16.58, corrected

p value is 0.08 ($p > 0.05$). Hence association of age and number of positive lymph node though close to 0.05 but is not statistically significant.

Table 4: Grade

| Tumor size | Grade | | | Total |
|---------------|-------|----|-----|-------|
| | I | II | III | |
| >1mm ≤ 5mm | 0 | 0 | 0 | 0 |
| >5mm-≤10mm | 2 | 0 | 0 | 2 |
| >10mm-≤20 mm | 6 | 5 | 0 | 11 |
| >20 mm -≤50mm | 19 | 31 | 11 | 61 |
| >50 mm | 7 | 32 | 15 | 54 |
| Total | 34 | 68 | 26 | 128 |

Table 4 shows distribution of grade for various sizes of tumors. 2, 6, 19 and 7 out of 34 cases with grade I had tumor sizes in >5 mm-10mm, >10mm-20mm, >20mm-50 mm and >50 mm respectively with maximum cases having tumor size >20mm-50 mm.

5 out of 68 cases of grade II had tumor size >10mm-20mm while 63 cases had tumor size >20 mm, i.e. 31 and 32 cases had tumor size >20mm-50

mm and >50 mm respectively. For grade III all cases have tumor size >20 mm with 11 out of 26 cases having tumor size >20mm-50 mm while maximum cases i.e. 15 out of 26 had tumor size >50mm. For tumor size and grade Chi square score (χ^2) is 17.45, p value 0.008, χ^2 score after William's correction is 16.93, corrected p value 0.009 ($p < 0.05$). Hence association of tumor size and grade is statistically significant.

Table 5: Lymph node metastasis

| Tumor size | Lymph node metastasis | | | | | |
|----------------|----------------------------|-----|------------|----------------|----------|-------|
| | No. of lymph node involved | | | Total Positive | Negative | Total |
| | 1-3 | 4-9 | 10 or more | | | |
| >1mm ≤ 5mm | 0 | 0 | 0 | 0 | 0 | 0 |
| >5mm-≤10mm | 0 | 0 | 0 | 0 | 0 | 0 |
| >10mm - ≤20 mm | 1 | 0 | 1 | 2 | 6 | 8 |
| >20 mm -≤50mm | 17 | 11 | 5 | 33 | 16 | 49 |
| >50 mm | 9 | 18 | 6 | 33 | 15 | 48 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 5 shows distribution of lymph node metastasis with tumor sizes. No cases with lymph node metastasis had tumor size ≤10mm. For tumor size >10 mm-20 mm 2 out of 6 cases show lymph node metastasis while for tumor size >20mm-50mm and >50 mm 33 out of 49 cases and 33 out of 48 cases show lymph node metastasis.

For tumor size and lymph node metastasis Chi square score (χ^2) is 6.02, p value 0.049, ($p < 0.05$). Hence association of tumor size and lymph node metastasis though marginal but is statistically significant. Table 5 also shows distribution of positive lymph nodes with various tumor sizes. For tumor size >10 mm-20mm 2 cases show lymph node metastasis, 1 with 1-3 positive lymph node

and 1 with 10 or more positive lymph nodes. For tumor size >20mm-50mm 17 out of 33 lymph node positive cases had 1-3 positive lymph nodes while 11 and 5 cases had 4-9 and 10 or more positive lymph node respectively.

For tumor size >50mm 18 out of 33 lymph node positive cases had 4-9 positive lymph nodes while 9 and 6 cases had 1-3 and 10 or more positive lymph node respectively. For tumor size and number of positive lymph node Chi square score (χ^2) is 6.43, p value 0.17, χ^2 score after William's correction is 6.12 corrected p value 0.19 ($p > 0.05$). Hence association of tumor size and number of positive lymph node is not statistically significant.

Table 6: Skin involvement

| Tumor size | Skin involvement | | Total |
|----------------|------------------|----------|-------|
| | Positive | Negative | |
| >1mm ≤ 5mm | 0 | 0 | 0 |
| >5mm-≤10mm | 0 | 0 | 0 |
| >10mm - ≤20 mm | 0 | 09 | 9 |
| >20 mm -≤50mm | 7 | 42 | 49 |
| >50 mm | 9 | 38 | 47 |
| Total | 16 | 89 | 105 |

Table 6 shows distribution of skin involvement with tumor size. In 23 lumpectomy cases skin was not sent. Skin was positive for tumor metastasis in 16 out of 105 cases while not involved in 89 cases. Skin is positive for tumor deposits in cases with tumor size above 20 mm and not involved in tumors <20 mm size. For tumor size >20 mm-50mm skin is positive for tumor metastasis in 7 out

of 49 cases while not involved in 42 cases. For tumor size >50mm skin is positive for tumor metastasis in 9 out of 47 cases while not involved in 38 cases. For tumor size and skin metastasis Chi square score (χ^2) is 2.21, p value 0.33, χ^2 score after William's correction is 2.15, corrected p value 0.34 ($p>0.05$). Hence association of tumor size and skin involvement is not statistically significant.

Table 7: Lymph node metastasis

| Grade | Lymph node metastasis | | | | | |
|-------|-----------------------------|-----|------------|----------------|----------|-------|
| | No. of lymph nodes involved | | | Total positive | Negative | Total |
| | 1-3 | 4-9 | 10 or more | | | |
| I | 6 | 4 | 0 | 10 | 12 | 22 |
| II | 15 | 19 | 7 | 41 | 18 | 59 |
| III | 6 | 6 | 5 | 17 | 7 | 24 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 7 shows distribution of grade with lymph node metastasis grade I, II and III show lymph node metastasis in 10 out of 22, 41 out of 59 and 17 out of 24 cases respectively while not involved in 12, 18 and 7 cases respectively. For grade and lymph node metastasis Chi square score (χ^2) is 4.56, p value 0.10 ($p>0.05$). Hence association of grade and lymph node metastasis is not statistically significant.

Table 7 also shows distribution of grade with number of lymph nodes involved in lymph node positive cases. For grade I out of 10 cases 1-3 lymph nodes involved in 6 cases, 4-9 involved in 4

cases while no case had 10 or more lymph node involved. For grade II out of 41 cases 1-3 lymph nodes involved in 15 cases, 4-9 involved in 19 cases and 7 cases had 10 or more lymph node involved. For grade III out of 17 cases 1-3 lymph nodes involved in 6 cases, 4-9 involved in 6 cases and 5 cases had 10 or more lymph node involved.

For grade and number of positive lymph node Chi square score (χ^2) is 4.69, p value 0.32, χ^2 score after William's correction is 4.47, corrected p value 0.35 ($p>0.05$). Hence association of grade and number of positive lymph node is not statistically significant.

Table 8: Skin involvement

| Grade | Skin involvement | | Total |
|-------|------------------|----------|-------|
| | Positive | Negative | |
| I | 1 | 21 | 22 |
| II | 10 | 48 | 58 |
| III | 5 | 20 | 25 |
| Total | 16 | 89 | 105 |

Table 8 shows distribution of grade with skin involvement. Grade I, II and III cases had skin involvement in 1, 10 and 5 cases respectively while not involved in 21, 48 and 20 cases respectively. For grade and skin involvement Chi square score (χ^2) is 2.57, p value is 0.28, χ^2 score after William's correction is 1.37, corrected p value 0.50 ($p>0.05$). Hence association of grade and skin involvement is not statistically significant.

Table 9: Skin involvement

| Lymph nodes | Skin involvement | | Total |
|-------------|------------------|----------|-------|
| | Positive | Negative | |
| 1-3 | 7 | 20 | 27 |
| 4-9 | 3 | 26 | 29 |
| 10 or more | 3 | 09 | 12 |
| Positive | 13 | 55 | 68 |
| Negative | 03 | 34 | 37 |

Lymph node is not sent in 23 cases. Table 9 shows distribution of lymph node involvement and skin involvement. Out of 68 lymph node positive cases skin was involved in 13 cases and not involved in 55 cases. While out of 37 lymph node negative cases skin was involved in 3 cases while negative in 34 cases. 3 node negative cases had skin

involvement. For lymph node and skin involvement Chi square score (χ^2) is 2.25, p value 0.13 ($p>0.05$). Hence association of lymph node involvement and skin involvement is not statistically significant. Table 9 also shows out of 13 skins positive cases 7, 3 and 3 cases had 1-3, 4-9 and 10 or more positive lymph nodes respectively. For number of positive

lymph node and skin involvement Chi square score (χ^2) is 2.521, p value 0.28, χ^2 score after William's correction is 2.42, corrected p value 0.30

($p > 0.05$). Hence association of number of positive lymph node and skin involvement is not statistically significant.

Table 10: Lymph node metastasis

| Tumor architecture | Lymph node metastasis | | | | | Total |
|--------------------|-------------------------------|-----|------------|-------|----------|-------|
| | Number of lymph node positive | | | | Negative | |
| | 1-3 | 4-9 | 10 or more | Total | | |
| Score 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Score 2 | 12 | 11 | 3 | 26 | 17 | 43 |
| Score 3 | 15 | 18 | 9 | 42 | 20 | 62 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 10 shows distribution of tumor architecture with lymph node metastasis. Out of 68 lymph node positive cases tumor architecture with score 2 and score 3 found in 26 and 42 cases respectively, no case had score 1.

For tumor architecture and lymph node metastasis Chi square score (χ^2) is 0.59, p value 0.74, χ^2 score after William's correction is 0.58 corrected p value 0.75 ($p > 0.05$). Hence association of tumor architecture and lymph node metastasis is not statistically significant. Among 26 cases with score

2, 12 cases, 11 cases and 3 cases had 1-3, 4-9 and 10 or more positive lymph nodes respectively. And among 42 cases with score 3, 15 cases, 18 cases and 9 cases had 1-3, 4-9 and 10 or more positive lymph nodes respectively.

For tumor architecture and number of positive lymph node Chi square score (χ^2) is 1.33, p value 0.86, χ^2 score after William's correction is 1.27, corrected p value 0.87 ($p > 0.05$). Hence association of tumor architecture and number of positive lymph node is not statistically significant.

Table 11: Lymph node metastasis

| Nuclear pleomorphism | Lymph node metastasis | | | | | Total |
|----------------------|-----------------------------|-----|------------|----------------|----------|-------|
| | No. of lymph nodes involved | | | | Negative | |
| | 1-3 | 4-9 | 10 or more | Total positive | | |
| Score 1 | 5 | 2 | 1 | 8 | 8 | 16 |
| Score 2 | 17 | 22 | 5 | 44 | 20 | 64 |
| Score 3 | 5 | 5 | 6 | 16 | 9 | 25 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 11 shows distribution of nuclear pleomorphism with lymph node metastasis. Score 1, 2 and 3 found in 8, 44 and 16 cases of lymph node positive cases. For nuclear pleomorphism and lymph node metastasis Chi square score (χ^2) is 1.98, p value 0.37 ($p > 0.05$).

Hence association of nuclear pleomorphism and lymph node metastasis is not statistically significant. Out of 8 cases with score 1 5, 2 and 1 cases had 1-3, 4-9 and 10 or more positive lymph nodes. Out of 44 cases with score 2 17, 22 and 5 had 1-3, 4-9 and 10 or more positive lymph nodes.

Out of 16 cases with score 3 5, 5 and 6 had 1-3, 4-9 and 10 or more positive lymph nodes. Score 1 has maximum 1-3 lymph nodes, Score 2 has maximum (22 cases) 4-9 positive lymph nodes and score 3 has maximum (6 cases) 10 or more positive lymph nodes. For nuclear pleomorphism and number of positive lymph node Chi square score (χ^2) is 7.66, p value 0.11, χ^2 score after William's correction is 7.30, corrected p value 0.12 ($p > 0.05$). Hence association of nuclear pleomorphism and number of positive lymph node is not statistically significant.

Table 12: Lymph node metastasis

| Mitotic activity | Lymph node metastasis | | | | | Total |
|------------------|-----------------------------|-----|------------|----------------|----------|-------|
| | No. of lymph nodes involved | | | | Negative | |
| | 1-3 | 4-9 | 10 or more | Total Positive | | |
| Score 1 | 9 | 12 | 1 | 22 | 18 | 40 |
| Score 2 | 15 | 12 | 10 | 37 | 19 | 65 |
| Score 3 | 3 | 5 | 1 | 9 | 0 | 9 |
| Total | 27 | 29 | 12 | 68 | 37 | 105 |

Table 12 shows distribution of mitotic activity with lymph node metastasis. Score 1, 2 and 3 found in 22, 37 and 9 cases of lymph node positive cases. For mitotic activity and lymph node metastasis Chi

square score (χ^2) is 6.61, p value 0.036, χ^2 score after William's correction is 6.46, corrected p value 0.04 ($p < 0.05$). Hence association of mitotic activity

and lymph node metastasis is statistically significant.

Out of 22 cases with score 1, 9, 12 and 1 had 1-3, 4-9 and 10 or more positive lymph nodes. Out of 37 cases with score 2, 15, 12 and 10 cases had 1-3, 4-9 and 10 or more positive lymph nodes. Out of 9 cases with score 3, 3, 5 and 1 case had 1-3, 4-9 and 10 or more positive lymph nodes.

For mitotic activity and number of positive lymph node Chi square score is 6.29, p value 0.18, χ^2 score after William's correction is 6.00, corrected p value 0.20

($p > 0.05$). Hence association of mitotic activity and number of positive lymph node is not statistically significant.

Discussion

Correlation of age with tumor size, grade and lymph node metastasis: Present study shows maximum 44% cases of breast carcinoma in age group 40-50 years followed by 32 cases in 50-60 age group (25%). In study of Łukasiewicz S et al [14] patients of >50 years age comprises more than 80% of all patients, and > 65 years patients were >40 % while in this study > 40 years age group had about 80% cases and patients above 60 years age group comprises only 18%. Thus lower age group has major bulk of patients in present study. About 90 % cases in present study has tumor size >20 mm and in patients aged >60 years age group no patients has tumor size <20mm but no correlation of age found with tumor size in this study.

Study of Clayton F et al [15] showed older patients have lower median mitotic count while younger patients have higher median mitotic count. which is a part of modified Bloom Richardson grading while present study shows in patients >30 years of age most patients have grade II and III, only in patients aged 20-30 years grade I is more common and no patient has grade III though no statistically significant correlation of age of patients found with grade in this study.

Study of Anwar SL et al [10] found statistically significant correlation of distant metastasis with >50 years postmenopausal and <40 years of age in breast cancer while in our study no statistically significant association and lymph node metastasis found, though patient of >60 years age had higher percentage of lymph node positivity.

Correlation of tumor size with grade, lymph node metastasis and skin involvement: In our study cases of grade I have varied tumor sizes, predominant cases of grade II and all cases of grade III have tumor size >20 mm. Present study shows statistically significant association of tumor size and grade while study of Liu Y et al [11] showed T stage is an independent prognostic factor of grade.

Study of Clayton F et al [15] showed Bloom-Richardson grade, nuclear grade and mitotic activity has good prognostic value but had no additional predictive value when associated with size.

Present study has correlation of tumor size and lymph node metastasis though marginal but is statistically significant which is similar to study of Purushottam MK et al [2].

Study of Purushottam MK et al showed significant correlation of tumor size and lymph node metastasis, study of Anwar SL et al [10] showed though larger tumors do not directly correlate but significantly associated with distant metastasis while study of Abner AL et al [16] and Liu Y et al [11] showed no significant correlation between tumor size and lymph node involvement. Study of Sopik V et al [17] showed little correlation of tumor size <10 mm or >50 mm size with lymph node metastasis while for tumor size 11-50 mm it showed positive correlation.

Present study showed no statistically significant correlation of tumor size and number of positive lymph node which is in contrast with study of Carter CL et al [8]. Study of Carter CL et al. showed for tumor <3cm there is higher chances of 1-3 lymph nodes than 4 or more nodes involvement while for tumor >3 cm 4 or more lymph nodes are more often involved.

In present study skin is positive for tumor deposits in cases with tumor size above 20 mm and not involved in tumors <20 mm size. For tumor size >20 mm-50mm skin is positive for tumor metastasis in 7 out of 49 cases and for tumor size >50mm skin is positive for tumor metastasis in 9 out of 47 cases. Correlation of tumor size and skin involvement is not statistically significant in present study which is in contrast to study of Clayton F et al [15] which showed positive correlation of skin invasion and larger tumor size.

Correlation of grade with lymph node metastasis and skin involvement: Correlation of grade and lymph node metastasis is not statistically significant in present study which is contrast to study of Purushottam MK et al [2] and Wasserberg N et al [18] which showed significant correlation of high grade with lymph node metastasis.

Association of grade and number of positive lymph node is not statistically significant in present study which is in contrast to study of Drinka E et al. [19] that showed statistically significant correlation of grade and number of positive lymph nodes.

Grade I, II and III cases have skin involvement in 1, 10 and 5 cases respectively in present study. Correlation of grade and skin involvement is not statistically significant in this study which is similar to study of Anwar SL et al [10] and Wu ZY

et al [20]. Anwar SL et al found though metastatic rate is more for higher grade but not statistically significant.

Correlation of lymph node involvement and skin involvement: In present study out of 68 lymph node positive cases skin was involved in 13 cases while out of 37 lymph node negative cases skin was involved in 3 cases, out of 13 skin positive cases 7, 3 and 3 cases have 1-3, 4-9 and 10 or more positive lymph nodes respectively. Correlation of neither lymph node involvement nor number of positive lymph node with skin positivity is statistically significant in the present study. Study of Anwar SL et al found skin and chest wall invasion as strong predictor of metastasis to distant site.

Correlation of tumor architecture and Lymph node metastasis: In present study out of 68 lymph node positive cases tumor architecture with score 2 and score 3 found in 26 and 42 cases respectively, no case have score 1, among 26 cases with score 2, 12 cases, 11 cases and 3 cases have 1-3, 4-9 and 10 or more positive lymph nodes respectively and among 42 cases with score 3, 15 cases, 18 cases and 9 cases have 1-3, 4-9 and 10 or more positive lymph nodes respectively. Association of tumor architecture with lymph node metastasis and number of positive lymph node is not statistically significant in the present study. Study of Clayton F et al [15] found that in Bloom-Richardson grade tumor differentiation show weak correlation with prognosis.

Correlation of nuclear pleomorphism and lymph node metastasis: In present study score 1, 2 and 3 found in 8, 44 and 16 cases of lymph node positive cases, Out of 8 cases with score 1 5, 2 and 1 cases have 1-3, 4-9 and 10 or more positive lymph nodes, out of 44 cases with score 2 17, 22 and 5 have 1-3, 4-9 and 10 or more positive lymph nodes, out of 16 cases with score 3 5, 5 and 6 have 1-3, 4-9 and 10 or more positive lymph nodes. Score 1 has maximum 1-3 lymph nodes, score 2 has maximum 4-9 positive lymph nodes and score 3 has maximum 10 or more positive lymph nodes.

Though association of nuclear pleomorphism with lymph node metastasis and number of positive lymph node is not statistically significant in the present study. Study of Wasserberg N et al [18] found grade 3 pleomorphism as predictor of lymph node involvement

Correlation of mitotic activity and lymph node metastasis: In present study Score 1, 2 and 3 found in 22, 37 and 9 cases of lymph node positive cases, out of 22 cases with score 1 9, 12 and 1 have 1-3, 4-9 and 10 or more positive lymph nodes, out of 37 cases with score 2 15, 12 and 10 cases have 1-3, 4-9 and 10 or more positive lymph nodes and out

of 9 cases with score 3 3, 5 and 1 case have 1-3, 4-9 and 10 or more positive lymph nodes.

Correlation of mitotic activity and lymph node metastasis is statistically significant in the present study which is similar to study of Aziz S et al [21] and in contrast with study of Clayton F et al [15]. Study of Kwatra A et al [22] found mitotic rate as one parameter of prognosis.

Though present study showed no statistically significant association of mitotic activity and number of positive lymph nodes.

Conclusion

Significant correlation of tumor size with grade and lymph node metastasis suggest that larger tumor size can have more probability of higher grade and lymph node metastasis while correlation of mitotic activity and lymph node metastasis suggest higher the mitotic activity score more chances of spread to lymph nodes. Age, number of positive lymph nodes, skin invasion are independent risk factors. Study over larger population should be done to assess their prognostic significance.

Limitations of study: Most patients attended hospital were of low socioeconomic status and less educated so presented lately.

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