

STUDY OF A STROMAL MARKER CD 10 IN INVASIVE BREAST CARCINOMAS AND ITS CORELATION WITH PROGNOSTIC FACTORS

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ABSTRACT:

Introduction: Breast carcinoma is the most common cancer among women with no regional variations and the second most common cancer worldwide. It accounts for an estimated 167,000 cases/year (2012) worldwide. It is the fifth leading cause of cancer death worldwide accounting for 522,000 deaths/year (2012). It also tops the list of cancer death among women, living in underdeveloped countries. CD10 (common acute lymphoblastic leukaemia antigen, CALLA) is a cell surface zinc dependent protease. CD10 acts as a stem cell regulator in the breast and prevents uncontrolled proliferation of stem cells. It is expressed in breast myoepithelial cells, lymphoid stem cells, neutrophils, and other epithelial cells. CD10 is also expressed in stroma of prostate, lung and colorectal cancers. **Methodology:** Brief clinical details of the patient such as age, gender, clinical diagnosis and surgical procedure was collected from the requisition form. All these surgical specimens were fixed in 10% buffered formalin, routinely processed, paraffin-embedded and stained with haematoxylin and eosin stain. The cases which were diagnosed as breast specimens with Infiltrating ductal carcinoma, NOS and its variants in Haematoxylin and Eosin stain were analysed and immunohistochemical marker CD10 were performed. With the results statistical analysis were done to correlate the positive cases with the prognostic factors. **Result:** This study was carried out in the department of pathology, Sri Venkateshwaraa Medical College and Research Centre, Puducherry in collaboration with the department of General Surgery. Total of 60 patients were included in our study. On comparing CD 10 positivity among invasive breast cancers with age, tumor size and nodal metastasis the following results were observed. Age is not correlating with the CD10 positivity. Tumour size does not correlate with the CD 10 marker positivity. Also in most of the studies there is no correlation between CD10 positivity and tumour size. The presence of lymph node metastasis is not correlating with CD10 marker positivity. The study can be further continued with other prognostic markers with more sample size as a future scope.

INTRODUCTION:

Breast carcinoma is the most common cancer among women with no regional variations and the second most common cancer worldwide. It accounts for an estimated 167,000 cases /year (2012) worldwide. It is the fifth leading cause of cancer death worldwide accounting for 522,000 deaths/year (2012). It also tops the list of cancer death among women, living in underdeveloped countries ^[1,2]. In India the incidence of breast carcinoma is increasing and the mortality rate for breast cancer in India is 11.1 per 10,000 ^[3]. Immunohistochemistry plays a pivotal role in therapeutic categorization. Oestrogen receptor (ER) positive and ER negative breast cancers show obvious differences in patient characteristics, pathological features, response to treatment and prognosis. CD10

(common acute lymphoblastic leukaemia antigen, CALLA) is a cell surface zinc dependent protease. CD10 acts as a stem cell regulator in the breast and prevents uncontrolled proliferation of stem cells ^[4]. It is expressed in breast myoepithelial cells, lymphoid stem cells, neutrophils, and other epithelial cells. CD10 is also expressed in stroma of prostate, lung and colorectal cancers ^[5]. CD10 is gaining importance recently in tumours like renal cell carcinoma, endometrial stromal sarcoma, canalicular pattern of hepatocellular carcinoma apart from Acute Lymphoblastic Leukaemia from where it got its name CALLA.

AIMS AND OBJECTIVES OF THE STUDY:

To correlate the stromal CD10 expression in invasive breast carcinomas with prognostic factors like age of the patient, tumour size and lymph node involvement.

METHODOLOGY:

Brief clinical details of the patient such as age, gender, clinical diagnosis and surgical procedure was collected from the requisition form. All these surgical specimens were fixed in 10% buffered formalin, routinely processed, paraffin-embedded and stained with haematoxylin and eosin stain. The cases which were diagnosed as breast specimens with Infiltrating ductal

carcinoma, NOS and its variants in Haematoxylin and Eosin stain were analysed and immunohistochemical marker CD10 were performed. With the results statistical analysis were done to correlate the positive cases with the prognostic factors.

OBSERVATIONS :

In this study we have included 60 cases diagnosed as Breast carcinoma who are fulfilling inclusion and exclusion criteria.

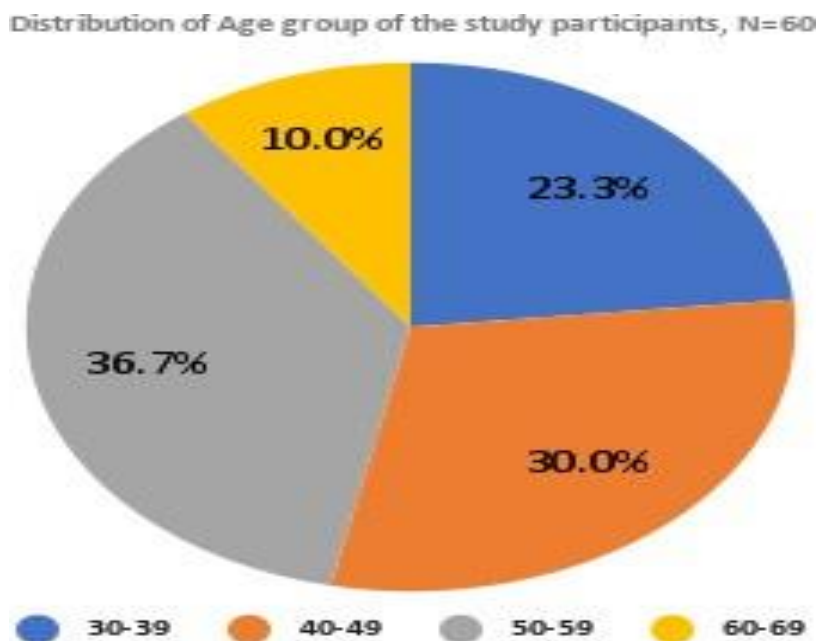
1. Age:

Among these 14 cases were between the age group 30-39, 18 cases were between 40-49, 22 cases were between 50-59 and 6 cases were between 60-69.

Table 1: Age wise distribution of cases; N=60

| Age group | Number | % |
|--------------------|-----------|---------------|
| 30-39 | 14 | 23.3% |
| 40-49 | 18 | 30.0% |
| 50-59 | 22 | 36.7% |
| 60-69 | 6 | 10.0% |
| Grand Total | 60 | 100.0% |

Chart 1: Age wise distribution of cases

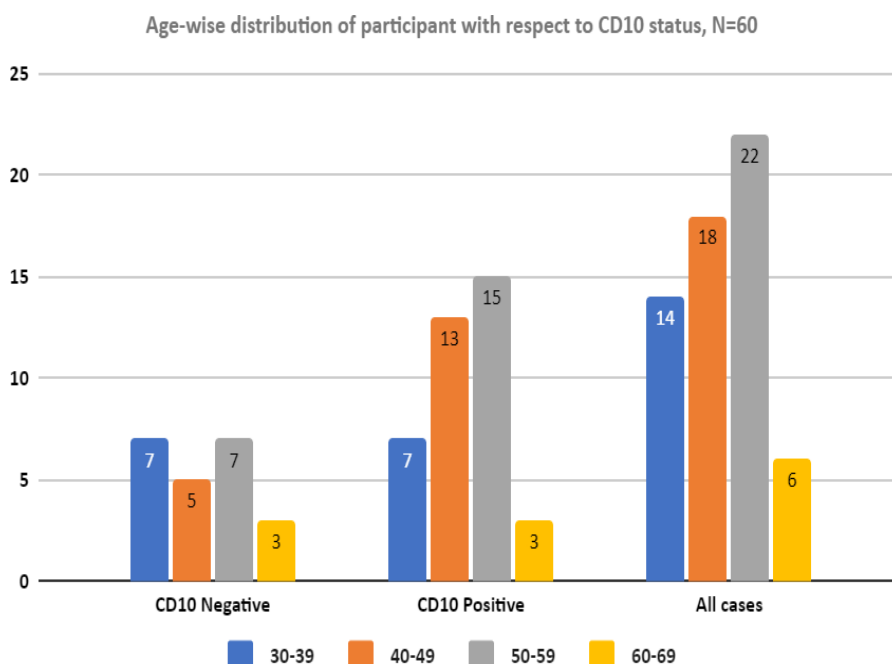


Out of 14 cases between 30-39 age group 7 were positive for CD10, while 13 cases in the age group 40-49 were positive for CD10, 15 cases in the age group 50-59 were positive for CD10 and among 6 cases between 60-69 age group 3 were positive and 3 were negative.

Table 2 : Comparison of CD10 with age

| Age group | CD10 | CD10 | All cases |
|--------------------|-----------|-----------|-----------|
| | Negative | Positive | |
| 30-39 | 7 | 7 | 14 |
| 40-49 | 5 | 13 | 18 |
| 50-59 | 7 | 15 | 22 |
| 60-69 | 3 | 3 | 6 |
| Grand Total | 22 | 38 | 60 |

Chart 2: Comparison of CD10 with age



While dividing the patients in the age group below and above 50 years of age, 62.5% of cases in age group < 50 were found to be positive for CD10 marker while 64.3% cases in the age group >50 were found to be positive, but this distribution was not statistically significant with p-value of 0.89. So age is not correlating with the CD10 positivity.

Table 3: P value for CD10 comparison with age

| Age group(in years) | CD10 marker | | | | p-value (χ^2) |
|---------------------|-------------|------|------------|------|----------------------|
| | Positive N | | Negative N | | |
| | Total N=60 | | Total N=60 | | |
| | (%) | | (%) | | |
| < 50 | 20 | 62.5 | 12 | 37.5 | 0.89 (0.02) |
| ≥ 50 | 18 | 64.3 | 10 | 35.7 | |

2. Tumour size :

Among 60 cases, 3 cases had tumour size of less than 2 cm, while 35 cases were between 2-5 cm and 22 cases were >5 cm in size.

Table 4 : Distribution of tumour size

| Tumour size | Number | % |
|-------------|--------|--------|
| <2 | 3 | 5.0% |
| 2 to 5 | 35 | 58.3% |
| >5 | 22 | 36.7% |
| Total | 60 | 100.0% |

Chart 3 : Distribution of tumour size

Distribution of Tumour Size, N=60

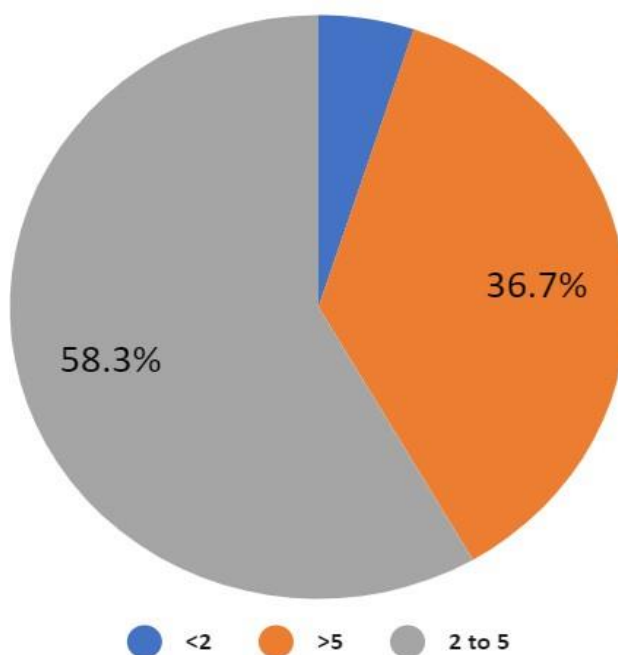


Table 5 : Tumour size comparison with CD10 marker

| Tumour size | CD10 marker | | | p-value (χ^2) |
|-------------|-------------------|-------------------|------------|----------------------|
| | Positive N (%) | Negative N (%) | Total N=60 | |
| <5cm | 23 60.5 | 15 39.5 | 38 | 0.55 (0.35) |
| >5cm | 15 68.2 | 7 31.8 | 22 | |

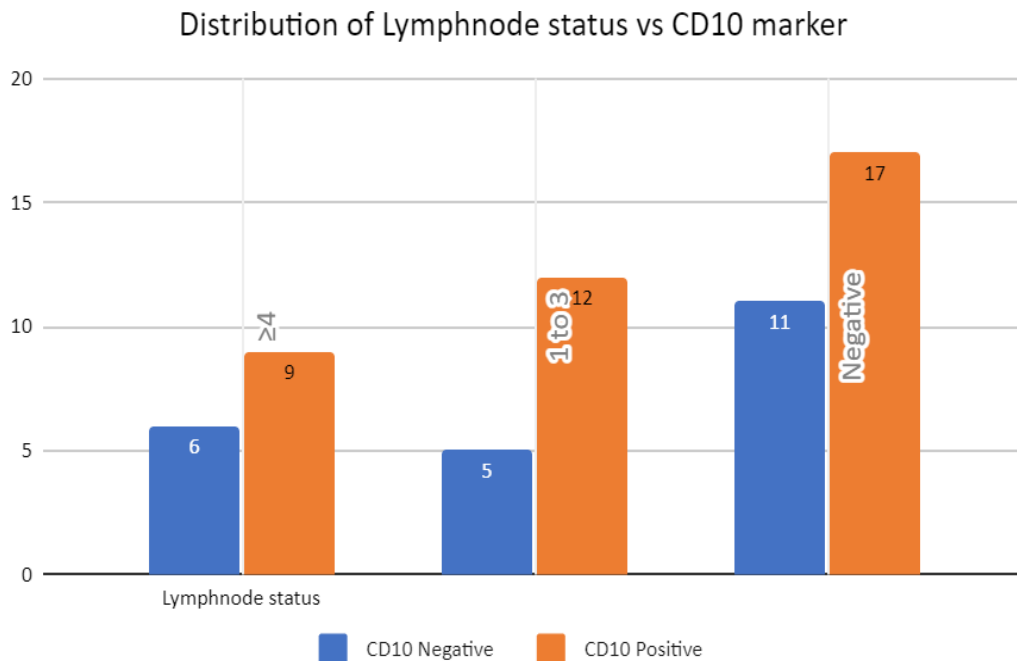
In our study out of 38 cases with tumour size < 5cm, 23 (60.5%) were positive for CD10 markers. While out of 22 cases with tumour size > 5cm, 15 (68.2%) were positive for CD 10 markers. But this comparison is not statistically significant with a p-value of 0.55. So Tumour size does not correlate with the CD 10 marker positivity.

3. Lymph node status:

Table 6 : Comparison of lymph node status with CD10 marker - table 1

| CD10 status | Lymph Node status | | | Total |
|------------------|-------------------|--------|----------|-------|
| | ≥4 | 1 to 3 | Negative | |
| CD10 Negative | 6 | 5 | 11 | 22 |
| CD10 Positive | 9 | 12 | 17 | 38 |

Chart 4: Comparison of lymph node status with CD10 marker - 1



21 cases with positive lymph nodes were positive for CD10 marker while 17 patients with negative lymph nodes status were positive for CD 10 marker.

Table 7: Comparison of lymph node status with CD10 marker - table 2

| CD10 | Lymph Node | |
|----------|------------|----------|
| | Negative | Positive |
| Negative | 11 | 11 |
| Positive | 17 | 21 |

Chart 5: Comparison of lymph node status with CD10 marker - 2

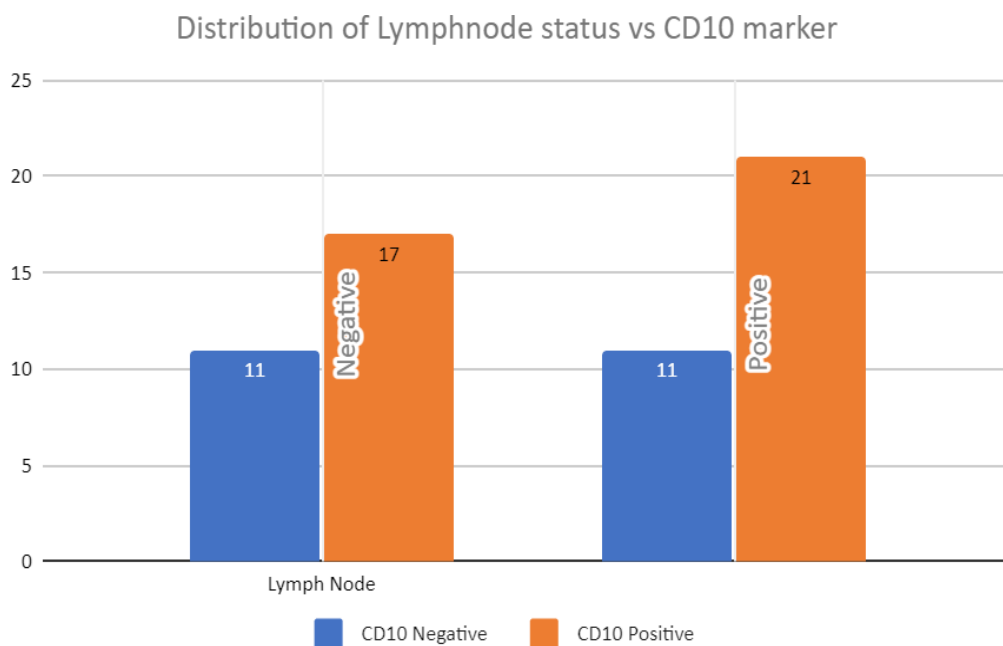


Table 8 : p-value for Comparison of lymph node status with CD10 marker

| Lymph node status | CD10 marker | | | p-value (χ^2) |
|-------------------|-------------|------------|------------|----------------------|
| | Positive N | Negative N | Total N=60 | |
| | (%) | (%) | | |
| Negative | 17 | 60.7 | 28 | 0.76 (0.54) |
| 1-3 | 12 | 70.6 | 17 | |
| ≥ 4 | 9 | 60.0 | 15 | |

In our study of 60 patients 28 were with negative lymph node status, 17 had 1-3 lymph node metastasis while 15 had ≥ 4 lymph nodes positive. Out of these 17 with negative lymph node status were positive for CD 10 marker (60.7%), 12 cases with 1-3 lymph nodes were positive for CD 10 marker (70.6%) and 9 cases with ≥ 4 lymph nodes were positive for CD 10 marker (60%). But this comparison is not statistically significant with a p-value of 0.76. So the presence of lymph node metastasis is not correlating with CD10 marker positivity.

Image 1: CD 10 mechanism of action

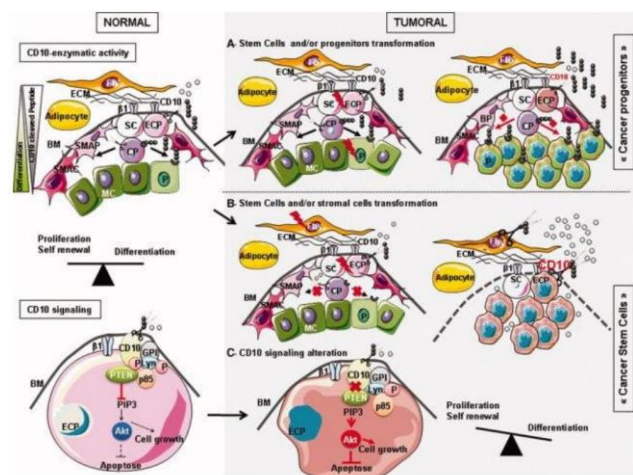


Image 2: Invasive breast carcinoma, NOS



Image 3: High power view of invasive breast carcinoma, NOS

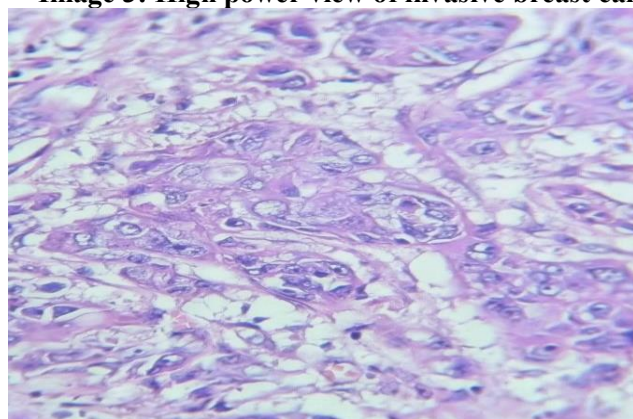
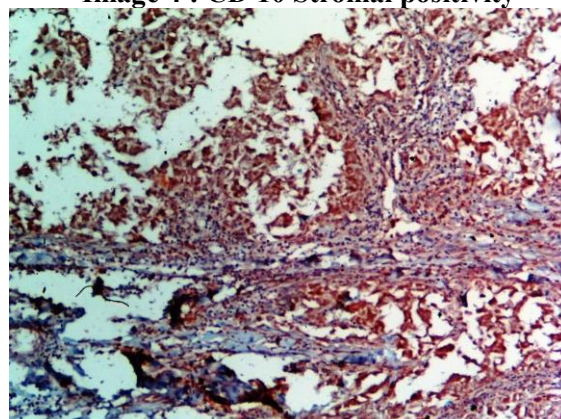


Image 4 : CD 10 Stromal positivity



DISCUSSION:

1. Comparison of CD10 with age :

| Study | CD10 Positive | | | p-value |
|-------------------------|---------------|-----------|---------|---------|
| | Age <40 | Age 40-60 | Age >60 | |
| Our Study | 7 | 28 | 3 | 0.32 |
| Sayantana H. Jana et al | 8 | 19 | 7 | 0.3572 |
| Maria Kamal et al | 28 | 72 | 9 | 0.5092 |
| V. Anuradha Devi et al | 12 | 12 | 5 | 0.52 |

In our study 7 patients of age group <40 were positive for CD10, 28 patients of age group between 40-60 were positive for CD 10 while only 3 patients of age > 60 were positive for CD10 marker. This comparison is not significant with a p-value of 0.32. In a study conducted by Sayantan H. Jana et al 8 patients of age group <40 were positive for CD10, 19 patients of age group between 40-60 were positive for CD 10 while only 7 patients of age > 60 were positive for CD10 marker. This comparison is not significant with a p-value of 0.3572. ⁽⁴⁾ In the study of Maria Kamal et al 28 patients of age group <40 were positive for CD10, 72 patients of age group between 40-60 were positive for CD 10 while only 9 patients of age > 60 were positive for CD10 marker. This comparison is not significant with a p-value of 0.5092. ⁽⁶⁾ B.v. Anuradha Devi et al had 12 patients of age group <40 were positive for CD10, 12 patients of age group between 40-60 were positive for CD 10 while only 5 patients of age > 60 were positive for CD10 marker. This comparison is not significant with a p-value of 0.52. ⁽⁷⁾ So in all the study CD10 positivity is not correlating with age .

2. CD10 positivity Vs tumour size comparison with other studies:

| Study | CD 10 marker Positive | | p-value |
|---------------------------|-----------------------|-----------------------|---------|
| | size <5 cm(%) | Tumour size >5 cm (%) | |
| Our Study | 23(60.50%) | 15(68.2%) | 0.55 |
| Sayantana H. Jana et al | 16(37.5%) | 9(50%) | 0.5325 |
| Maria Kamal et al | 54(65.15%) | 43(61.4%) | 0.0646 |
| B. V. Anuradha Devi et al | 21(46.6%) | 12(85.7%) | 0.003 |
| Ashish Nitin Dhande et al | 31(79.5%) | 8(66.6%) | 0.908 |

In our study 60.5% of patients with tumour size <5cm were positive for CD10 marker while 68.2% of patients with tumour size >5 cm were positive for CD10 marker . But this comparison is not statistically significant with a p-value of 0.55. In a study by Sayantan H.Jana et al 37.5% of patients with tumour size <5cm were positive for CD10 marker while 50% of patients with tumour size >5 cm were positive for CD10 marker . But this comparison is not statistically significant with a p-value of 0.5325. ⁽⁴⁾ In a study by Maria Kamal et al 65.15% of patients with tumour size <5cm were positive for CD10 marker while 61.4% of patients with tumour size >5 cm were positive for CD10 marker . But this comparison is not statistically significant with a p-value of 0.0646. ⁽⁶⁾ In a study conducted by B.V.Anuradha Devi et al 46.6% of patients with tumour size <5cm were positive for CD10 marker while 85.7% of patients with tumour size >5 cm were positive for CD10 marker .This comparison is statistically significant with a p-value of 0.003. ⁽⁷⁾ In a study conducted by Ashish Nitin Dhande et al 79.5% of patients with tumour size <5cm were positive for CD10 marker while 66.6% of patients with tumour size >5 cm were positive for CD10 marker . But this comparison is not statistically significant with a p-value of 0.908. ⁽⁸⁾ So in most of the studies there is no correlation between CD10 positivity and tumour size. But in a study conducted by B.V.Anuradha Devi et al there is increased chances of getting CD10 positivity with increase in tumour size. ⁽⁷⁾

3. CD10 positivity VS lymph node status comparison with other studies -1:

| Study | CD10 Marker Positive | | | p-value |
|---------------|----------------------|------------|------------|---------|
| | Lymphnode | Lymphnodes | Lymphnodes | |
| Our study | 17(60.7%) | 12(70.6%) | 9(60%) | 0.76 |
| dha Devi etal | 10 (35.7%) | 11(73.3%) | 14 (87.5%) | 0.0005 |

In our study 60.7% patients with no lymph node metastasis were positive for CD10 marker, 70.6% of patients with 1-3 lymph nodes were positive for CD10 marker and 60% of patients with >4 lymph nodes were positive for CD10 marker. But this comparison is not statistically significant with p-value of 0.76. In a study conducted by Anuradha Devi et al 35.7% patients with no lymph node metastasis were positive for CD10 marker, 73.3% of patients with 1-3 lymph nodes positive were positive for CD10 marker and 87.5% of patients with >4 lymph nodes were positive for CD10 marker. This comparison is statistically significant with a p-value of 0.0005. So in this study an increase in lymph nodes increases the chances of CD10 marker positivity.⁽⁷⁾ Also in our study 65.6% with lymph node metastasis were positive for CD10 marker while 65.6% of patients without lymph node metastasis were positive for CD10 marker. But this comparison is not statistically significant with p-value of 0.76. In a study conducted by Maria Kamal et al 78.9% with lymph node metastasis were positive for CD10 marker while 54% of patients without lymph node metastasis were positive for CD10 marker. This comparison is statistically significant with a p-value of 0.0016. So in this study the presence of lymph node metastasis correlates with CD10 positivity.⁽⁶⁾ In a study conducted by Ashis Nitin Dhande et al 90% with lymph node metastasis were positive for CD10 marker while 55% of patients without lymph node metastasis were positive for CD10 marker. This comparison is statistically significant with a p-value of <0.01. So in this study also the presence of lymph node metastasis correlates with CD10 positivity.⁽⁸⁾

4. CD10 positivity VS lymph node status comparison with other studies -2:

| Study | CD10 marker Positive | | p-value |
|-------------------|----------------------|---------------------|---------|
| | lymph node positive | lymph node negative | |
| Our study | 21(65.6%) | 21(65.6%) | 0.76 |
| Maria Kamal et al | 75(78.9%) | 34(54.0%) | 0.0016 |
| n Dhande etal | 36(90%) | 11(55%) | <0.01 |

RESULTS:

This study was carried out in the department of pathology, Sri Venkateshwaraa Medical College and Research Centre, Puducherry in collaboration with the department of General Surgery. Total of 60 patients were included in our study. On comparing CD 10 positivity among invasive breast cancers with age, tumor size and nodal metastasis the following results were observed

- Age is not correlating with the CD10 positivity.
- Tumour size does not correlate with the CD 10 marker positivity. Also in most of the studies

there is no correlation between CD10 positivity and tumour size.

- The presence of lymph node metastasis is not correlating with CD10 marker positivity

FUTURE SCOPE:

Role of cd10 a stromal marker can be co-related with other prognostic markers of breast carcinoma and other immunohistochemistry markers like ER, PR, HER2.

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