

## PROGNOSTIC SIGNIFICANCE OF CALRETININ IN BREAST CARCINOMA

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### ABSTRACT

**Background:** Breast cancer is a leading cause of cancer deaths among women worldwide. Elucidation of pathogenesis of breast carcinoma by molecular mechanisms lead to the development of targeted therapies especially in triple negative cancers. In this study a new marker Calretinin is used to assess the prognosis of breast carcinoma and its significant association is demonstrated based on histopathological types, molecular subtypes, and hormonal marker expression. The aim and objective is to evaluate the expression of Calretinin and to correlate the marker expression with tumor grade, histopathological types, molecular subtypes, ER, PR and HER2 expression. To determine the prognosis of breast cancer based on Calretinin expression. To prove Calretinin as a prognostic indicator in breast carcinoma. **Materials and Methods:** A total of 70 patients of breast cancer were included in the study. Representative sections were taken and stained with Hematoxylin and Eosin. Immunohistochemistry was done with ER, PR, HER2 and Calretinin. Necessary grading was done as per marker expression. **Results:** Calretinin expression was correlated with various clinicopathological parameters. The statistical significance was seen with Calretinin staining with Progesterone expression (P value<0.05). **Conclusion:** Calretinin could be a reliable prognostic indicator of breast carcinoma associated with adverse prognosis.

## INTRODUCTION

Breast cancer is the leading cause of cancer deaths among women both in developed and developing countries with mortality being 12.7/100,000 women.<sup>[1]</sup> Among all breast cancers 25% develop metastasis which is responsible for more than 90% of deaths. Grading of the tumors is based on histology and immunophenotyping.

Morphological examination along with Immunohistochemistry plays a vital role in diagnosis and prognostication of breast carcinomas. The stage of the breast cancer is assessed by lymph nodes and histopathological examination. Molecular subtyping done by markers ER, PR, HER2 in both trucut samples and mastectomy specimens. The management is based on the marker status.

Additional IHC markers identified in basal like phenotype which includes cytokeratin14 & 17, vimentin, Calretinin, laminin, Caveolins 1&2 and integrin.<sup>[2]</sup> Calretinin is a calcium buffer of calmodulin superfamily.<sup>[3]</sup> has numerous functions depending on various parameters. Calretinin, a mesothelial marker is expressed in epithelial and mesenchymal malignancies including breast cancer. High level of Calretinin expression was seen in basal-like, HER2 and unclassified tumors.

Triple negative cancers exhibit atypical medullary and metastatic pattern with high incidence of early visceral metastasis.<sup>[4]</sup> Additional diagnostic markers may be required to confirm of breast origin and to explain molecular mechanism involved in pathogenesis which is required for development of novel therapy.

### Aims and Objectives

1. To study the prognostic significance of Calretinin in correlation with other prognostic factors like tumor grade, histopathological types, hormone receptor expression.
2. To evaluate Calretinin expression in Molecular subtypes of breast cancers.

## MATERIALS AND METHODS

**Study Place:** Department Of Pathology, Chengalpattu Medical College, Chengalpattu.

**Study Design:** The Present Study Is A Prospective And Retrospective Study Conducted In The Department Of Pathology During The Period Of June 2017-June 2020.

Ethical Clearance For The Study Was Obtained From The Institutional Ethics Committee Of Chengalpattu Medical College, Chengalpattu.

**Study Population:** A Total Sample Of 70 Cases Were Analysed During The Period Of June 2017- June 2020.

#### Inclusion Criteria

1. Tissue Blocks Of Known Patients Diagnosed As Having Invasive Breast Cancers.
2. Modified Radical Mastectomy Specimens, Toilet Mastectomy
3. Biopsy Specimens-Lumpectomy, Trucut Biopsy, Wide Local Excision

#### Exclusion Criteria

1. Tissue Blocks of Known Patients of Breast Carcinomas Who Underwent Neoadjuvant Chemotherapy and Radiotherapy.
2. All Mesenchymal and Metastatic Breast Cancer.

#### Materials Used

Tissue Sections Prepared From Paraffin Embedded Formalin Fixed Tissues  
Hematoxylin and Eosin Staining Kit  
ER, PR, HER2, Calretinin Monoclonal Antibody Kit  
Secondary Antibody Kit  
Positive Control  
Negative Control

#### Method

Formalin Fixed Paraffin Embedded Blocks and Hematoxylin Eosin Stained Sections of 70 Mastectomy and Biopsy Specimens Are Taken Up For the Study. On Histopathological Examination, They Were Categorized As Invasive Breast Carcinoma With Grades Based On Modified Scarff Bloom Richardson Criteria. Immunohistochemistry Was Performed On The Sections Taken From The Block Together With Suitable Control.

#### Grading of Estrogen and Progesterone Receptor Positivity

Includes:  
Number of Tumor Cell Nuclei Positive and Intensity of Staining.

Allred/Quick Score System  
Score for Proportion

- 0- No Staining
- 1- <1% Nuclei Staining
- 2- 1-10% Nuclei Staining
- 3- 11-33% Nuclei Staining
- 4- 34-66% Nuclei Staining
- 5- 67-100% Nuclei Staining

Score for Intensity

- 0- No Staining
- 1- Weak Staining
- 2- Moderate Staining
- 3- Strong Staining

Both Scores Are Added

Total Scores Range from 0-8

Scores Less Than 2 – Negative

More Than 2- Positive.<sup>[5]</sup>

#### IHC Interpretation HER2:

Pathologists (ASCO/CAP) Have Formulated the New Guidelines in 2007 on A Scale of 0-3+

0 – No Staining /<10% Membrane Staining

1-Faint Staining In > 10% of Tumor Cells, Only Part of The Membrane Stained

2-Weak/Moderate Complete Membrane Staining In More Than 30% of Tumor Cells.

3-Strong Complete Membrane Staining In More Than 30% of the Tumor Cells.

#### IHC Interpretation Calretinin:

Immunoreactivity Is Assessed Using a Combined Score Which Comprises the Distribution and Intensity of Staining

Score Comprising Distribution:

0-0% of Positive Tumor Cells

1-<25% Of Positive Tumor Cells

2-25-50% of Positive Tumor Cells

3->50% of Positive Tumor Cells

Score Comprising Intensity:

0-0

1-1+

2-2+

3-3+

Overall Score Obtained By Multiplying both Intensity and Extent Scores.

Thus Overall Score Graded From 0-9

0-Negative

1-2-Weak Staining

3-6-Moderate Staining

9-Strong Staining

Both Moderate And Strong Staining Are Considered As High-Level Of Calretinin Expression.

Both Negative And Weak Staining Are Considered As A Low Level Expression Of Calretinin.<sup>[6]</sup>

## RESULTS

The present study included a sample of 70 breast carcinoma. The data collected includes the following

- Tumor grade
- Histopathological types
- ER expression
- PR expression
- Her2 expression
- Molecular subtypes

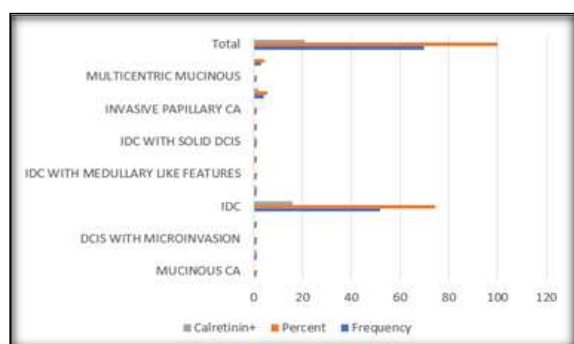
The marker status was assessed and its correlation with the above mentioned parameters were noted. Suitable statistical tests were applied for all datas and presented as charts, graphs and tables.

**Table 1: Correlation of Calretinin with clinical parameters of the patients**

| Clinicopathological parameter |              | CALRETININ |            |      |          |        | P-value |
|-------------------------------|--------------|------------|------------|------|----------|--------|---------|
|                               |              | n(70)      | Expression |      |          |        |         |
|                               |              |            | 0          | WEAK | Moderate | Strong |         |
| Histo Pathological Types      | IDC          | 52         | 36         | 14   | 1        | 0      | 0.3     |
|                               | IDC+(MIXED)  | 5          | 4          | 0    | 2        | 0      |         |
|                               | Medullary    | 2          | 0          | 1    | 1        | 0      |         |
|                               | Papillary    | 1          | 1          | 0    | 0        | 0      |         |
|                               | Multicentric | 1          | 1          | 0    | 0        | 0      |         |

|                    |                         |    |    |    |   |   |      |
|--------------------|-------------------------|----|----|----|---|---|------|
|                    | Mucinous                | 1  | 1  | 0  | 0 | 0 |      |
|                    | Apocrine                | 1  | 0  | 0  | 0 | 1 |      |
|                    | Positive For Malignancy | 1  | 1  | 1  | 0 | 0 |      |
| Molecular Subtypes | Luminal A               | 4  | 4  | 0  | 0 | 0 | 0.5  |
|                    | Luminal B               | 10 | 7  | 2  | 0 | 1 |      |
|                    | Basal                   | 22 | 13 | 6  | 3 | 0 |      |
|                    | Her2 Enriched           | 10 | 7  | 2  | 1 | 0 |      |
| Grade              | I                       | 31 | 23 | 7  | 1 | 0 | 0.2  |
|                    | II                      | 26 | 19 | 4  | 3 | 0 |      |
|                    | III                     | 4  | 1  | 3  | 0 | 0 |      |
| ER                 | Present                 | 36 | 27 | 8  | 0 | 1 | 0.4  |
|                    | Absent                  | 34 | 22 | 8  | 4 | 0 |      |
| PR                 | Present                 | 23 | 20 | 2  | 0 | 1 | 0.03 |
|                    | Absent                  | 47 | 29 | 14 | 4 | 0 |      |
| HER2               | Score 2                 | 11 | 8  | 3  | 0 | 0 | 0.8  |
|                    | Score 3                 | 9  | 6  | 2  | 1 | 0 |      |
|                    | Absent                  | 41 | 30 | 9  | 1 | 1 |      |

## Microscopic Variants



**Figure 1: Distribution of Microscopic Types**

Of the 70 cases, infiltrating ductal carcinoma constitutes 74.3%, Medullary carcinoma constitutes 5.7%, biopsies (trucut, incisional) with positive for malignancy constituted 4.3% and other variants like

Mucinous, Apocrine, Papillary and Micropapillary constituted 1.4% each. [Figure 1]

Out of 52 Infiltrating ductal carcinomas 15 showed Calretinin expression constituting 71%, of which 14 were weakly expressed and 1 case showed moderate expression of Calretinin. Out of the remaining 6 cases, 2 were Infiltrating ductal carcinoma with mixed features both showing moderate expression, 4 were biopsy specimens of which 2 were Medullary carcinoma one showing weak and other showing moderate expression of Calretinin, 1 case of Apocrine carcinoma showing strong expression, 1 case positive for malignancy showing weak expression of Calretinin. [Table 1]

The Statistical analysis based on Calretinin expression with that of different histopathological subtypes showed no significance with P value of 0.3. [Table 1]

## Grade

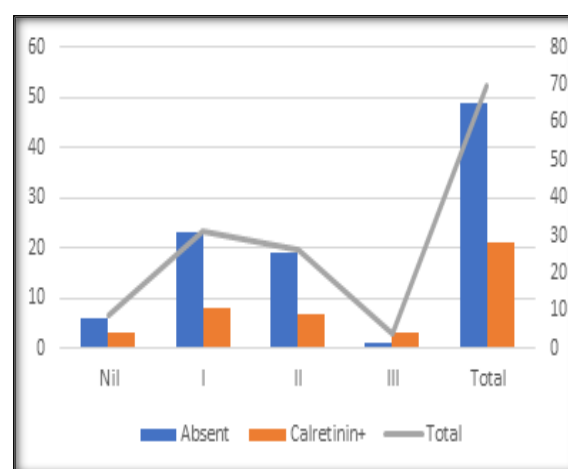
**Table 2: Grade wise distribution and frequency**

| Grade | Frequency | Percent |
|-------|-----------|---------|
| Nil   | 9         | 12.9    |
| I     | 31        | 44.3    |
| Ii    | 26        | 37.1    |
| Iii   | 4         | 5.7     |
| Total | 70        | 100     |

Out of the 70 cases, Grade I constituted 44.3%, Grade II 37.1% and Grade III constituted 5.7%. [Table 2] Out of 31 grade I cases 8 showed Calretinin expression of which 7 showed weak expression and 1 case showed moderate expression. (Table 2 & Figure 2)

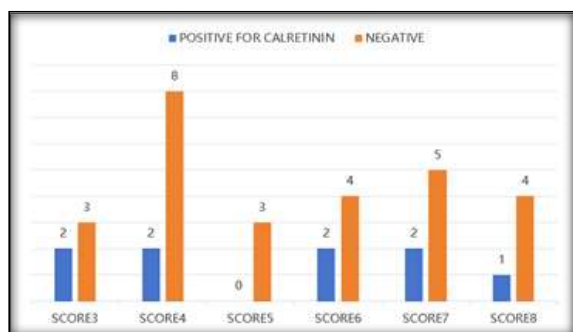
Out of 26 grade II cases 7 showed Calretinin expression, of which 4 showed weak expression and 3 showed moderate expression of calretinin. [Table 2 & Figure 2]

Out of 4 grade III cases 3 showed weak expression of Calretinin. 10 out of 21 cases showing calretinin expression were both grade II and III constituting 48%. (Table 2 & Figure 2). Based on Calretinin expression with that of grade of the tumor, the statistical analysis showed no significance with P value of 0.2 [Table 1 & 3]



**Figure 2: Tumor grade and Calretinin expression**

## Estrogen Receptor Status



**Figure 3: Showing Calretinin expression in Estrogen positive cases**

Out of 70 cases ER positivity was observed in 51.4% of which Score 4 constituted 14.3%, Score 7 constituted 10%, Score 6 constituted around 8.6%, score 8 and Score 3 constituted around 7.1% each, Score of 5 constitutes 4.3%. ER negativity was observed in 48.6%. [Figure 3, Table 4]

Out of 70 breast carcinomas 36 cases on the whole showed estrogen receptor expression which constituted 51.4% and was negative in 34 cases which constituted 48.6%. [Table 4]

Out of 34 cases which were ER negative, 12 cases showed Calretinin expression constituting 57%, of which 8 showed weak expression and 4 cases showed moderate expression of Calretinin. [Table 1 & 5]

Out of remaining 47 cases that showed no progesterone expression 18 showed Calretinin expression constituting 86%, of which 14 cases showed weak expression and 4 cases showed moderate expression of Calretinin. [Table 1, Figure 5]

18 out of 21 calretinin positive cases showed no PR expression constituting 86%. The Statistical analysis based on Calretinin expression and Progesterone expression showed significance with P value of 0.03. [Table 7]

**Table 3: Correlation of Calretinin expression with Tumor grade**

| GRADE | Absent | Calretinin+ | Total | Chi sq | P   |
|-------|--------|-------------|-------|--------|-----|
| Nil   | 6      | 3           | 9     | 4.28   | 0.2 |
| I     | 23     | 8           | 31    |        |     |
| II    | 19     | 7           | 26    |        |     |
| III   | 1      | 3           | 4     |        |     |
| Total | 49     | 21          | 70    |        |     |

**Table 4: Distribution of cases showing Estrogen receptor positivity**

| ER       | Frequency | Percent |
|----------|-----------|---------|
| Positive | 36        | 51.4    |
| Negative | 34        | 48.6    |
| Total    | 70        | 100     |

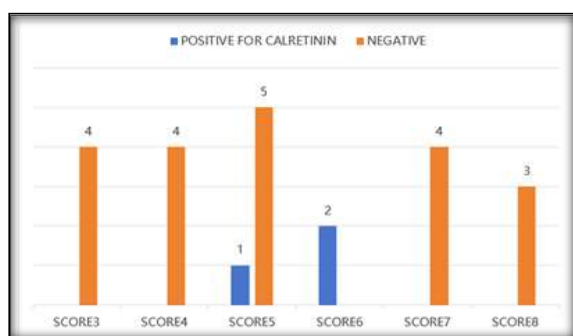
**Table 5: Correlation of Estrogen receptor positive cases showing Calretinin expression**

| ER      | Absent | Calretinin+ | Total | Chi sq | p   |
|---------|--------|-------------|-------|--------|-----|
| Absent  | 22     | 12          | 34    | 0.88   | 0.4 |
| Present | 27     | 9           | 36    |        |     |
| Total   | 49     | 21          | 70    |        |     |

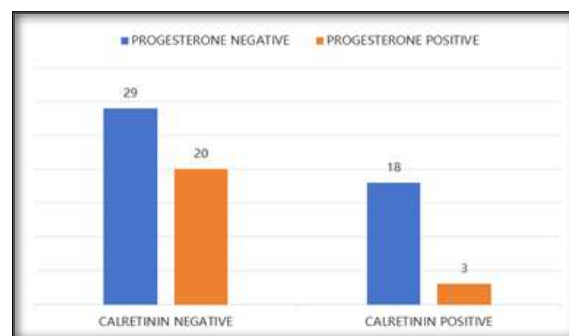
12 out of 21 calretinin positive breast cancers were ER negative constituting 57%. The statistical analysis based on Estrogen receptor positive cases showing Calretinin expression is not significant with P value of 0.4. [TABLE 5]

Out of 70 cases 32.9% showed PR positivity of which Score 5 constituted around 8.6%, Score 3,4 and 7 constituted 5.7% each, Score 8 constituted 4.3% followed by Score 6 constituting 2.9%. (Table 6, Figure 4)

## Progesterone Status



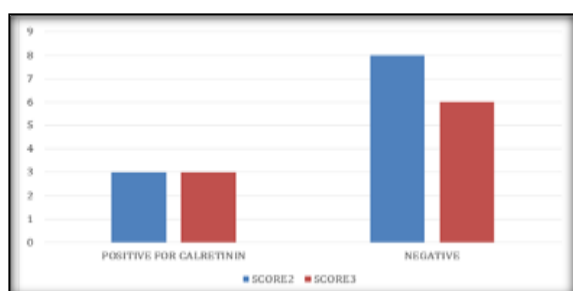
**Figure 4: Showing Calretinin expression in Progesterone receptor positive cases**



**Figure 5: Showing Calretinin expression in Progesterone positive and negative cases**

Out of 23 cases showing Progesterone receptor positivity only 3 showed Calretinin expression, of which 2 showed weak expression and 1 case showed strong expression of Calretinin. (Table 1 & Figure 5] Out of remaining 47 cases that showed no progesterone expression 18 showed Calretinin expression constituting 86%, of which 14 cases showed weak expression and 4 cases showed moderate expression of Calretinin. (Table 1, Figure 5]

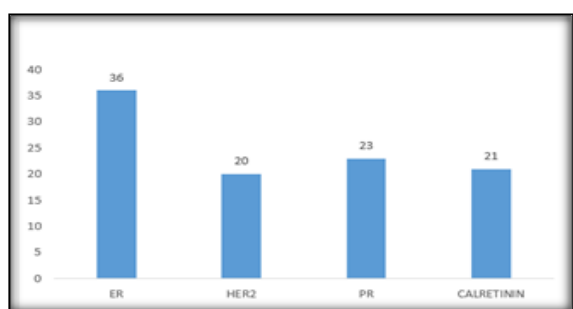
18 out of 21 calretinin positive cases showed no PR expression constituting 86%. The Statistical analysis based on Calretinin expression and Progesterone expression showed significance with P value of 0.03. [Table 7]



**Figure 6: Showing Calretinin expression in Her2 positive and negative cases**

Out of 20 cases showing Her2 positivity 11 belonged to Score 2 and 9 belonged to score 3. Out of 11 Score 2 cases, 3 showed weak Calretinin expression. Out of 9 Score 3 cases, 3 showed Calretinin expression, of which 2 showed weak and 1 case showed strong expression of Calretinin. [Figure 6, Table 1 & 9]

### Calretinin

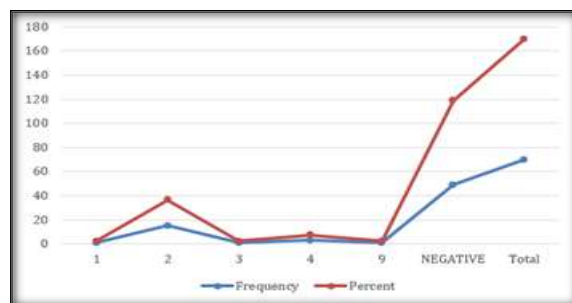


**Figure 7: Showing overall distribution of various markers**

Out of 70 breast carcinoma cases, 21 cases show calretinin expression compared to 36 cases of ER, 20

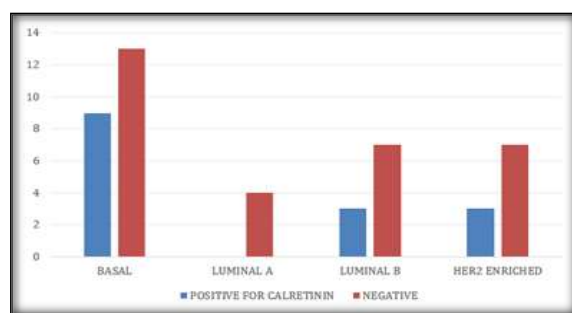
cases of HER2 neu, 23 cases of PR expressions. [Figure 7]

Calretinin is seen in around one third cases of study population. Of the 21 cases showing calretinin expression 16 showing weak expression, 4 cases show moderate expression and 1 case of strong calretinin expression. [Table 1 & 11]



**Figure 8: Calretinin expression**

### Molecular Subtypes



**Figure 9: Molecular subtypes with Calretinin expression**

Out of 70 cases 4 belonged to Luminal A which showed no Calretinin expression, 10 belonged to Luminal B of which 2 showed weak expression and 1 showed strong expression of Calretinin, 22 belonged to Basal subtype, of which 6 showed weak expression and 3 showed moderate expression of calretinin. cases belonged to Her2 enriched subtype, of which 2 showed weak expression and 1 case showed moderate expression of Calretinin. [Table 1 & 12]

Calretinin expression is more in basal subtype (9/21) constituting 43%. The Statistical analysis of Calretinin expression based on molecular subtypes of breast carcinomas showed no significance with P value of 0.5. [Table 12]

**Table 6: Distribution of Progesterone receptor positive cases**

| PR       | Frequency | Percent |
|----------|-----------|---------|
| Positive | 23        | 32.9    |
| Negative | 47        | 67.1    |
| Total    | 70        | 100     |

**Table 7: Correlation of Progesterone receptor positive cases and Calretinin expression**

| PR      | Absent | Calretinin+ | Total | Chi sq | P    |
|---------|--------|-------------|-------|--------|------|
| Absent  | 29     | 18          | 47    | 4.69   | 0.03 |
| Present | 20     | 3           | 23    |        |      |
| Total   | 49     | 21          | 70    |        |      |

**HER 2 STATUS:****Table 8: Distribution of Her2**

| HER2     | Frequency | Percent |
|----------|-----------|---------|
| Positive | 20        | 28.6    |
| Negative | 50        | 71.4    |
| Total    | 70        | 100     |

Cases, HER2 was expressed in 28.6% of which Score 2 was 15.7% and Score 3 was 12.9% while 71.4% showed no HER2 expression. [Table 8]

**Table 9: Expression of Calretinin in Her2 Positive cases**

| HER2 SCORE | Positive for Calretinin | Negative |
|------------|-------------------------|----------|
| Score 2    | 3                       | 8        |
| Score 3    | 3                       | 6        |

Out of 50 Her2 negative cases 15 cases showed Calretinin expression constituting 71%, of which 1 case showed strong expression, 3 showed moderate expression and 11 cases showed weak expression of Calretinin. [Table 1]

**Table 10: Correlation of Calretinin expression in Her2 positive cases**

| HER2 SCORE | Positive for calretinin | Negative | Chi square | p   |
|------------|-------------------------|----------|------------|-----|
| Score 2    | 3                       | 8        | 0.09       | 0.8 |
| Score 3    | 3                       | 6        |            |     |

15 out of 21 calretinin positive breast cancers were Her2 negative constituting 71%. The Statistical analysis of Calretinin expression based on Her2 receptor positivity showed no significance with P value of 0.8. [Table 10]

**Table 11: Distribution of Calretinin expression**

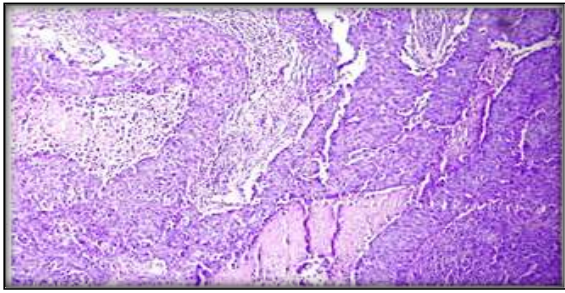
| CALRETININ | Frequency | Percent |
|------------|-----------|---------|
| 1          | 1         | 1.4     |
| 2          | 15        | 21.4    |
| 3          | 1         | 1.4     |
| 4          | 3         | 4.3     |
| 9          | 1         | 1.4     |
| NEGATIVE   | 49        | 70      |
| Total      | 70        | 100     |

**Table 12: Correlation of molecular subtypes with Calretinin expression**

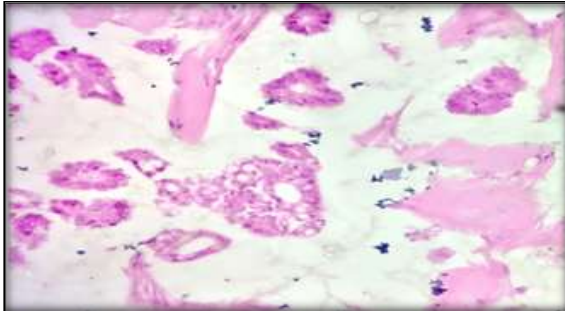
| TYPE          | Positive for calretinin | Negative | Chi square | P   |
|---------------|-------------------------|----------|------------|-----|
| BASAL         | 9                       | 13       | 0.49       | 0.5 |
| LUMINAL A     | 0                       | 4        |            |     |
| LUMINAL B     | 3                       | 7        |            |     |
| HER2 ENRICHED | 3                       | 7        |            |     |

Overall more number of basal subtypes showed Calretinin expression 9 out of 22 cases.

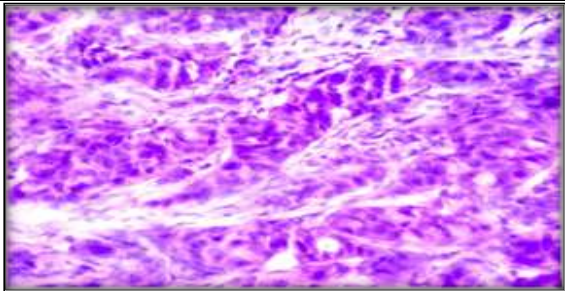
**Figure 3: Medullary Carcinoma****Figure 2: Mucinous Carcinoma**



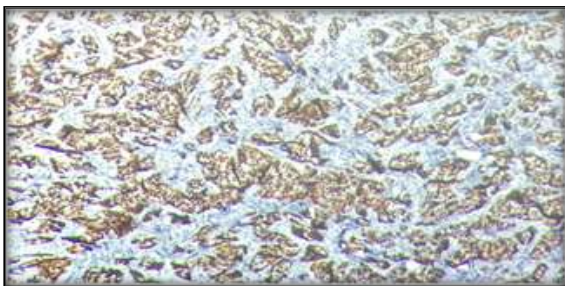
**Figure 4: G 258/2020 Medullary Carcinoma (40x)**



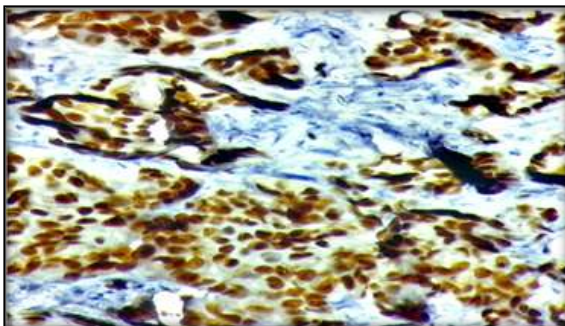
**Figure 5: G 592/2020 Mucinous Carcinoma (40x)**



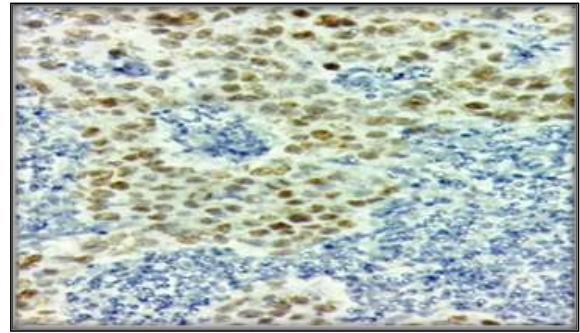
**Figure 6: G 617/2020-Positive for Malignancy (40x)**



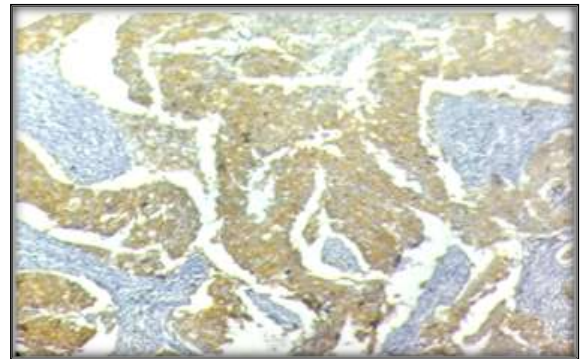
**Figure 7: G/617/2020 ER-10x Strong Positive**



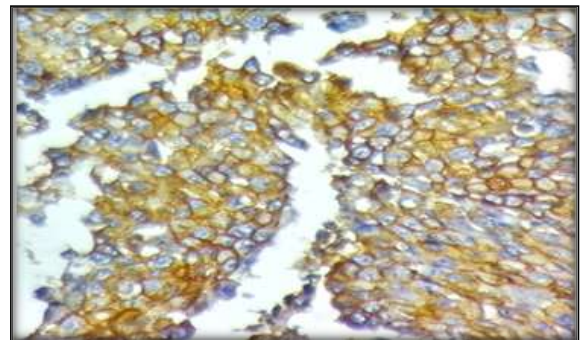
**Figure 8: G 617/2020 ER 40x-Strong**



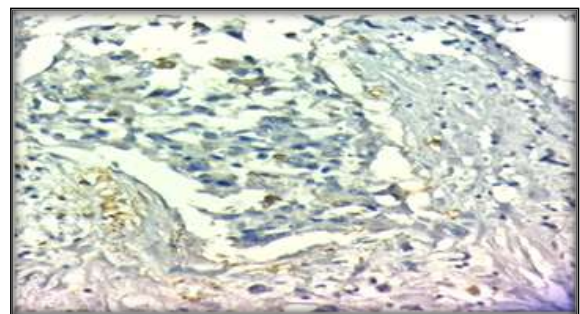
**Figure 9: G 1265/19 ER (40x) Moderate**



**Figure 11: G 467/2018 HER 3+ 10x**



**Figure 12: G 467/2018 HER 2 3+ 40x**



**Figure 13: G 878/2017 Calretinin Weak (40x)**

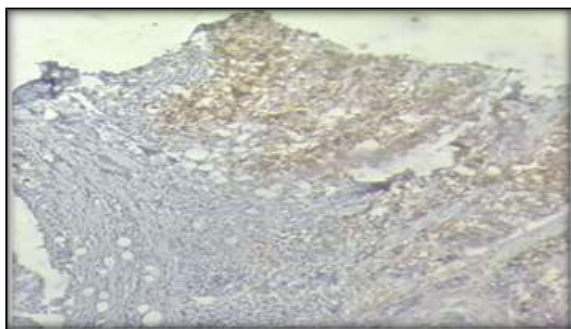


Figure 14: G 941/2017 Calretinin Moderate 10x

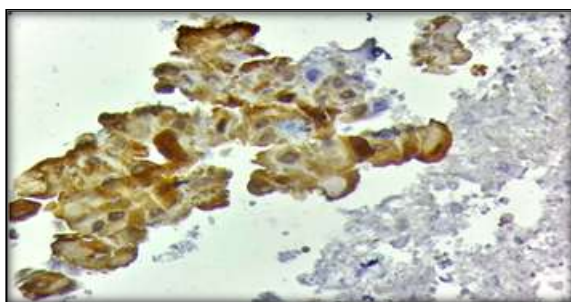


Figure 17: G 431/2018 Calretinin Strong (40x)

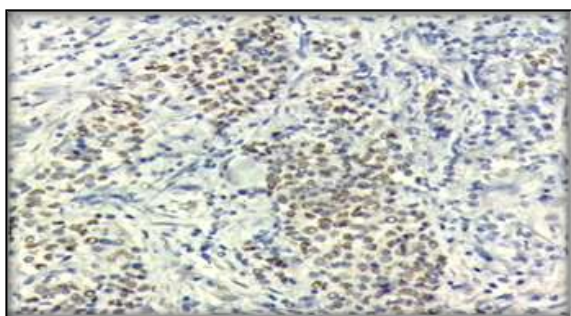


Figure 19: G 1955/2017 ER Control (40x)

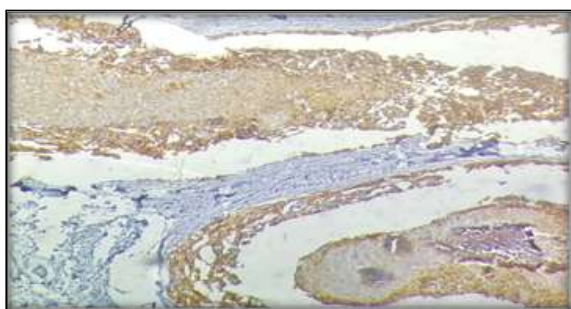


Figure 21: G 1838/2018 HER 2 Internal Control (40x)

## DISCUSSION

### Comparison of Calretinin with histopathological type

Out of 70 breast carcinoma cases, 52 were Invasive breast cancers constituting 74.3%, 4 were Medullary carcinoma constituting 5.7%, and rest were Mucinous, apocrine, Invasive papillary, Micropapillary IDC with medullary like features, IDC with pagets disease of nipple constituting 1.4% each. Out of 52 Invasive ductal carcinomas 15 showed Calretinin expression, of which 14 showed weak expression and 1 showed moderate expression.

Mayada Saad Farrag et al showed a significant association of calretinin with invasive ductal carcinoma of NST where 69 cases constituting 34.8% of No special type carcinoma.<sup>[4]</sup> In our study 21 out of 70 cases showed positive for Calretinin expression of which 15 cases were Invasive ductal carcinoma constituting 71% and showed no significance.

### Comparison of Calretinin with grade

Out of 70 cases, 8 out of 31 were grade I, 7 out of 26 were grade II and 3 out of 4 were grade III and 9 were biopsy cases, 4 out of which showed positive for calretinin expression. Grade I-8 tumors showing Calretinin expression, 7 showed weak expression and 1 case showed moderate expression. Grade II-7 tumors showing Calretinin expression, 4 showed weak expression and 3 showed moderate expression. All the 3 Grade III tumors showed weak Calretinin expression.

Ross James Taliano et al studied Calretinin expression in high-grade invasive ductal breast carcinoma and found no high-level expression seen in grade 1 or 2 carcinomas.<sup>[6]</sup>

Mayada Saad Farrag et al studied expression of calretinin and found significant association with Grade 3 breast carcinoma.<sup>[4]</sup>

In our study out of 21 Calretinin positive cases 10 were from both grade II and III constituting 48%, though not statistically significant.

### Comparison of calretinin with molecular subtypes

Out of 70 breast carcinoma cases, 13 were Basal subtype, were Luminal B and Her 2 enriched, 4 were Luminal A subtypes respectively.<sup>[9]</sup> out of 13 Basal subtype cases showed positivity for calretinin expression, of which 6 showed weak and 3 showed moderate expression.<sup>[3]</sup> out of 7 Luminal B showed calretinin expression of which 2 showed weak and 1 showed strong expression. 3 out of 7 HER2 enriched subtypes showed calretinin expression, of which 2 showed weak expression and 1 showed moderate expression.

Out of 46 breast carcinoma cases that has been classified as different molecular subtypes 22 were classified as Basal subtype, 9 of which showed Calretinin expression constituting 43% of total calretinin expression. Remaining 24 cases have been kept as unclassified type, among which 6 showed Calretinin expression which were all weak.

George Powell et al studied significant association of Calretinin with Basal molecular subtypes.<sup>[7]</sup>

Suryagayathri Venugopal et al studied 107 cases showing calretinin expression in different molecular subtypes and found that among basal like subtype 68.4% of cases showed high level calretinin expression and significant association.<sup>[8]</sup>

In our study 9 out of 22 Basal like subtype showed calretinin constituting 43% of total calretinin expression, though not statistically significant

### Comparison of Calretinin with ER expression

George Powell et al studied 53 breast carcinomas, found 8 were positive for calretinin out of which only 1 was ER positive. Also calretinin positive tumors

were ER negative, high grade and display a basal like phenotype.<sup>[7]</sup>

In our study, out of 36 ER positive cases only 9 showed calretinin expression. Out of 21 cases with calretinin positivity 12 were negative for ER constituting 57% though not statistically significant with P value of 0.4.

#### **Comparison of Calretinin with PR**

Amr El-Karef et al studied the clinicopathological correlation of Calretinin expression in breast cancer in 225 cases and showed high calretinin expression with negative ER, PR and positive HER2neu.<sup>[9]</sup>

In our study out of 23 cases which were PR positive only 3 showed calretinin expression. Also 18 out of 47 PR negative cases showed calretinin expression constituting 86%. The statistical analysis of calretinin expression based on PR expression showed significance with P value of 0.03.

#### **Comparison of Calretinin with Her2neu**

Only 6 Her 2 expressing cancers were positive for calretinin out of 21 cases constituting 29%. While 14 cases with HER2 expression were negative for Calretinin. 15 out of 21 calretinin expressing cancers were negative for Her2 constituting 71% though not statistically significant.

Suryagayathri Venugopal et al 107 breast carcinoma cases and found high Calretinin expression in 30% of Her2 overexpressed tumors but found no statistical significance similar to our study.<sup>[8]</sup>

## **CONCLUSION**

Breast carcinoma is the leading cause of cancer deaths among women which accounts for significant morbidity and mortality. Triple negative tumors are high grade ones with poor overall survival.

The aim was to study the expression of Calretinin in correlation with clinical parameters like with other factors like grade, morphological types, grade of tumors etc, to evaluate the expression of Calretinin with different molecular subtypes.

A total of 70 breast carcinoma cases were studied retrospectively and prospectively in Chengalpattu Medical College for a period of 3 years from June 2017 to June 2020. Immunohistochemistry was done on paraffin section and expression of ER, PR, HER2 and Calretinin was documented and analysed.

Based on the proportion and intensity of nuclear staining ER and PR were scored from 0-8 of which less than 2 is considered negative. Based on percentage of HER2 membrane staining scoring was done 1-3 of which 1+ considered negative. Calretinin showed both nuclear and cytoplasmic staining and based on intensity and percentage of cells stained was grouped into 1-9 of which 1,2 considered weak expression, 3-6 moderate expression and 7-9 considered strong expression.

The marker positivity of Calretinin was analysed and statistical correlation was done with all other clinicopathological parameters taking them as

individual parameters Calretinin expression was more in PR negative cases 18 out of 21 constituting 86% with significant P value of 0.03.

Based on the histopathological types 17 out of 21 calretinin expressing tumors were IDC constituting 71%, of which 8 were of grade I, 7 were of grade II though not statistically significant. 10 out of 21 calretinin positive cases were of grade II and grade III constituting 48%, though not statistically significant.

12 out of 21 ER negative cases and 15 out of 21 Her2 negative cases showed calretinin expression constituting 57% and 71% respectively though not statistically significant. Calretinin expression is more in basal subtype, 22 out of 70 cases of which 9 showed calretinin expression constituting 43% though not statistically significant.

More studies with increased sample size is required to establish Calretinin as an independent prognostic factor for recurrence of breast cancer which may be helpful in devising aggressive treatment strategy. Also it may serve as a new target to breast cancer therapy.

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