



## EVALUATION OF DIAGNOSTIC AND PROGNOSTIC ROLE OF SERUM TUMOUR MARKER CA 15.3 IN BREAST MALIGNANCY- A RETROSPECTIVE STUDY WITH THE USE OF 3<sup>RD</sup> GENERATION ELISA .

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**ABSTRACT** **Introduction:** CA-15-3 is also called as Episialin. CA 15-3 is a serum cancer antigen that has been used in the management of patients with breast cancer. CA 15-3 is an indicator of tumor load .CA 15-3 level correlate with the tumor burden in the form of higher values are seen in large sized tumor, higher nuclear grade, more number of lymph nodes involvement and in stage 3 and 4 patients than stage 1 & 2 patients. Very high CA 15-3 levels tend to indicate advanced disease, and a value 5 to 10 times normal could alert a physician to the presence of metastatic disease. CA 15-3 levels are highest in patients with liver or bony metastases.

**Materials and Methods:** The present study was retrospective, observational, analytical type done in Department of Pathology at a tertiary care center. Estimation of serum CA 15.3 level was done by using Indirect Sandwich Enzyme Linked Immunosorbent Assay (ELISA).

**Results:** 100 sample were received out of which 60 cases were followed up postoperatively. Majority of cases involved left sided breast with commonly being invasive ductal carcinoma NOS type. Sensitivity and Specificity for evaluating recurrent and metastatic cases was found to be 83.3% and 98.1% respectively.

**Conclusion:** CA 15-3 values in normal female is < 35 U/ml. values >35 U/ml are considered abnormal. Serial measurement of CA 15-3 are more important to detect recurrence or metastasis at any time after treatment.CA 15-3 is an important prognostic indicator, good predictor for relapse and important for therapeutic monitoring in breast cancer patients.

**KEYWORDS :** Breast carcinoma, CA 15.3, ELISA, liver or bony metastasis.

### INTRODUCTION

CA-15-3 is also called as Episialin. Numerous monoclonal antibodies (mAbs) have been raised against mucins on carcinoma cells. Many of these mAbs are directed against an epithelial sialo – mucin<sup>1-6</sup> that is now referred to as episialin. Episialin is synthesized as a transmembrane molecule with a relatively large extra- cellular domain and a cytoplasmic domain of 69 amino acids.<sup>7</sup>The extracellular domain mainly consists of a region of nearly identical repeats encoding 20 amino acids. The number of repeats is highly variable in the human population, leading to substantial differences in molecular weights of the episialin molecules from different individuals.<sup>8</sup> The CA 15-3 epitope is recognized by two monoclonal antibodies in a double-determinant or sandwich radioimmunoassay.CA 15-3 is a serum cancer antigen that has been used in the management of patients with breast cancer. CA 15-3 is an indicator of tumor load .Multiple studies have shown that the incidence of CA 15-3 elevation increases with an increasing stage of the disease. Low CA 15-3 levels do not exclude metastases, and a given CA 15-3 level cannot be used to determine the stage of disease.<sup>9</sup>CA 15-3 level correlate with the tumor burden in the form of higher values are seen in large sized tumor, higher nuclear grade, more number of lymph nodes involvement and in stage 3 and 4 patients than stage 1 & 2 patients. Very high CA 15-3 levels tend to indicate advanced disease, and a value 5 to 10 times normal could alert a physician to the presence of metastatic disease. CA 15-3 levels are highest in patients with liver or bony metastases.<sup>10,11</sup>Increasing numbers of metastatic sites correlate with increasing CA 15-3 levels.<sup>10</sup> CA 15-3 is a particularly sensitive method for detecting osseous metastases.<sup>10-11</sup> Elevation of CA 15-3 levels can also be seen in healthy individuals, in certain benign conditions, and in other malignant conditions.

### AIMS AND OBJECTIVES

To establish diagnostic and prognostic role of CA 15.3 in breast malignancy and to study its role in monitoring and recurrence of breast carcinoma.

### MATERIALS AND METHOD

Patient's serum was taken as sample. Estimation of serum CA15.3 was done by using ELISA method which is Enzyme immunoassay for the quantitative determination of serum CA15.3.

Calbiotech –ELISA kit was used .Robonik wash well and read well-ELISA instrument were used. Study was done by Indirect Sandwich ELISA method.

**Study Duration:** Sept 2020-Feb 2021

**Sample Size:** Total 100 samples of CA15.3 were received.

### OBSERVATIONS AND RESULTS

Cases from different wards like surgery, radiotherapy etc. presenting with breast lump were studied in detail including proper history. Clinical diagnosis and supportive investigations like USG, mammography, CT scan, FNAC were done. Confirmation of diagnosis was done either by FNAC or histopathological examination of biopsy. For every patient, histopathological type was done. Preoperative value of CA 15-3 was measured in all cases. Postoperative value of CA 15-3 was done in many cases. Patient with raised postoperative CA 15-3 value were further followed up

**TABLE – 1: INFORMATION REGARDING STUDIED CASES (n=100)**

| Sr. No. | Studied Cases   | No.      |
|---------|---|----------|
| 1       | Total cases studied   | 100      |
| 2       | Pre-Tx CA 15-3 value measured                                     | 100      |
| 3       | Post-Tx CA 15-3 value measured                                    | 60       |
| 4       | Duration of Post-Tx value measured after surgical removal         | 7 days   |
| 5       | Duration of Post-Tx measurement for pts taking radio/chemotherapy | 3 cycles |
| 6       | Post op values not measured                                       | 40       |

In present study it was observed that majority of cases i.e. 84% of cases were invasive ductal carcinoma – NOS type and rest cases of other types of carcinoma breast like invasive papillary carcinoma, Medullary carcinoma and mucinous carcinoma of breast. No specific relation was found between histopathological type of carcinoma and serum CA 15-3 values. In present study, it was observed that lesions are more common on left breast compared to right sided breast. In 2% of cases there was presence of carcinoma breast on both the sides. In present study, it was observed that in majority of patients, size of the lesions was between 2 to 5 cm. Mean value of CA 15-3 level was highest i.e. 71.22U/ml in patients with lesion larger than 5 cm. Maximum number of patients among lesion larger than 5 cm showed serum CA 15-3 levels more than 35 u/ml. Thus Mean CA 15-3 level as well as positivity rates increased as size of the lesion increased in carcinoma breast patients.

**TABLE-2 : POSITIVITY RATE OF CA 15-3 IN PATIENTS ACCORDING TO AGE (n=100)**

| Age                | No. of cases | Mean Serum CA 15-3 Levels (U/ml) | Number of patients whose CA 15-3 value is more than 35 | Positivity rate (%) |
|--------------------|--------------|----------------------------------|--|---------------------|
| 20 to 40 years     | 14           | 40.108                           | 6  | 42                  |
| 41 to 60 years     | 54           | 55.62                            | 36   | 66.66               |
| More than 60 years | 32           | 66.55                            | 28   | 87.5                |

**TABLE-3 : COMPARISON OF MEAN CA 15-3 VALUES IN PRE OP, POST OP CASES AND IN METASTATIC, RECURRENT AND OTHER CASES**

| Cases                                     | Number | Mean serum CA 15-3 Values (U/ml) |                     |
|---|--------|----------------------------------|---------------------|
| Pre operative cases                       | 60     | 69.8                             |                     |
| Post treatment cases                      | 60     | 36.85                            |                     |
|   |        | Mean Pre-op CA15.3               | Mean Post-op CA15.3 |
| Metastatic cases                          | 3      | 50                               | 45                  |
| Recurrence cases                          | 2      | 52.2                             | 52                  |
| Other than metastatic or recurrence cases | 1      | 40                               | 37                  |

In all the 100 cases in present study preoperative CA 15-3 levels were measured. Post treatment values were measured in 60 cases following MRM or chemotherapy. In rest of cases (40 cases) postoperative value detection could not be done as some of patients MRM was done in private hospital and few patients did not come for the follow up. 6 out of 60 cases were further followed up regularly with CA 15-3 level detection and clinical and radiological investigations. It was found that 5 out of these 6 cases developed recurrence or metastatic disease in further course of time. Among these, 2 patients showed recurrence of carcinoma, 2 cases had developed metastatic carcinoma in opposite breast and 1 case had developed bone metastasis during the course of time. These patients were clinically normal and metastatic disease was detected by radiological investigations like CT scan, MRI and various serum biochemistry investigations as they had high CA 15-3 values.

There was one patient with normal post op CA 15-3 level, who developed metastasis in opposite breast during the follow up. Thus, serum 15-3 evaluation helped early detection of metastatic disease as compared to their clinical presentation. In present study the role of post treatment value of CA 15-3 value in detection of metastatic disease or recurrent disease was evaluated and observed that post treatment CA 15-3 is 83.3% sensitive and 98.1% specific in detection of recurrent or metastatic disease post treatment. Similarly positive predictive value and negative predictive value was found to be 83.5% and 98.1% respectively. Here p value was calculated and found to be <0.0001. These findings suggest that CA 15-3 has definitive prognostic role (p value <0.0001) in breast carcinoma.

In present study range of patients age was from 35 years to 95 years. Maximum number of patients were seen in post menopausal age group i.e. 76%. Similar other studies, Alsaed<sup>12</sup> 2013 had more number i.e. 83% of patients in pre menopausal age group than post menopausal age group with 17%. While Daniele<sup>13</sup> 2013 and Gion<sup>14</sup> 1991 both the studies showed more number of patients with carcinoma breast in post menopausal age group with 66.1% and 70.8% respectively.

## CONCLUSION

ELISA is rapid, sensitive, reliable and cost effective test for measurement of Cancer Antigen 15-3. CA 15-3 values in normal female is < 35 U/ml. values >35 U/ml are considered abnormal. CA 15-3 value although has definitive diagnostic value, it cannot be used as a sole diagnostic measure and supportive investigations like Radiological diagnosis, FNAC and/or Histopathological study should be used along with it for definitive diagnosis. Higher the grade or stage of the tumor the positivity rate of tumor marker also increases. Elevated CA 15-3 levels correlated with increasing age, size and lymph node status. The sensitivity of CA 15-3 increases to 95% in patients with advanced disease. Tumors with dissemination have more CA 15-3 value than localized tumors. Pre and postoperative CA 15-3 values are important indicators & any decrease in CA-15.3 value after surgery, radiotherapy or chemotherapy correlates with efficacy of treatment.

CA 15-3 is a reliable prognostic predictor for monitoring disease progression. Post operative CA 15-3 value has definitive prognostic

value to detect any metastasis or recurrence after successful surgery or chemotherapy & should normally decrease after any therapy. For this pre-operative CA 15-3 measurement is necessary to correlate difference in pre operative and post operative value. Chances of recurrence are more with tumors with higher pre operative value. Serial measurement of CA 15-3 are more important to detect recurrence or metastasis at any time after treatment but even single CA 15-3 value together with pre operative value is of great importance. If post-operative CA 15-3 level remains stable or increases, it indicates chances of recurrence.

Thus, CA 15-3 is an important prognostic indicator, good predictor for relapse and important for therapeutic monitoring in breast cancer patients.

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