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A Prospective Study on Analysis of Ca 15-3 in Breast Cancer Patients as Prognostic Marker

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Abstract
Background: *Cancer antigen 15-3 (CA 15-3) is used to monitor response to breast cancer treatment and disease recurrence.The range of serum CA 15-3 is less than 30 U/mL. The upper limit of the reference range varies depending on the laboratory and kit used for the test. Values of CA 15 -3 obtained with different assay kits, methods, or laboratories cannot be used interchangeably.CA 15-3 levels are most commonly used to monitor metastatic carcinoma breast during active therapy. Tumor marker 15-3 levels must be used in conjunction with the history, physical examination, and diagnostic imaging. A decrease in marker levels during management can indicate tumor response, whereas stable or increasing levels despite adequate treatment can indicate that the tumor is not responding to treatment or that the tumor is recurring.CA 15-3 tumor marker measurement can also be used to survey disease recurrence after treatment of metastatic breast cancer. In the absence of measurable disease, an increase in CA 15-3tumor marker levels could indicate treatment failure.*
Methods: *Our study entitled "Prospective study on the analysis of CA 15-3 in breast cancer patients as prognostic marker" was conducted on 50 Patients admitted in department of general surgery C.R.. Gardi hospital of R D Gardi Medical College Surasa, Ujjain for management of breast cancer between November 2018 to March 2020*
Sample size taken was 50
Results: *Our study Signifies that with value of CA 15-3>24.95u/ml after full treatment modality 18.75% died due to breast cancer, 3(18.75%) came with recurrence, 3(18.75%) with residual tumor, 4(25%) with distant metastasis and only 18.75% recovered from breast cancer in our follow up of 6 months. And with value of CA 1<24.95u/ml after full treatment modality 88.2%were recovered from breast cancer and no patient died due to breast cancer. In our study we found that decreased serum levels of CA 15-3 in these patients were statistically significant.*
Conclusions: *our study suggests serum CA 15-3 as an independent prognostic factor as well as having additive effect with other poor prognostic factors in breast cancer patients and Elevated pre-treatment concentrations of CA 15-3 may be a useful prognostic factor for cancer progression in patients. Emphasing the cut off value of CA15-3 as 24.95 to finally determine the prognostic importance So our study conclude that every patient of suspected and diagnosed breast cancer must be screened for CA 15-3 tumor marker.*
Keywords: *CA15-3, prognostic marker,breast cancer.*

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I. Introduction

Cancer Antigen 15-3 (CA 15-3) is a tumour-associated antigen used as serum marker for breast cancer surveillance in patients and for monitoring the response to treatment. Aim of this study was to prospectively evaluate CA 15-3 as a prognostic factor in early detection of breast cancer relapse, recurrence and early detection of distant metastasis as well as to analyse the statistical correlation between CA 15-3 levels and clinical-pathological parameters including tumour size, lymph node, histological type, pre and post operatively.

Breast cancer is a leading cause of cancer related morbidity and mortality among females worldwide. Breast cancer itself accounts for 25% of all cancer cases and 15% of all cancer deaths among females worldwide. The tumour marker antigen CA 15-3, which corresponds to an immuno-dominant epitope in the extracellular portion of the membrane bound mucin MUC1, is shed into the bloodstream. An increase in the serum CA 15-3 shed ectodomain is associated with progression of carcinoma in patients.

The high level of CA 15-3 associated with larger burden of occult disease. There are many studies showing worse prognosis in patients with high concentration of CA 15-3. The CA 15-3 is independent predictor of recurrence and advanced breast cancer. During follow-up of patients, this CA 15-3 marker used in surveillance of patient with diagnosed breast cancer and monitoring of treatment.

Cancer antigen 15-3 (CA 15-3) is used to monitor response to breast cancer treatment and disease recurrence.

The reference range of serum CA 15-3 is less than 30 U/mL. The upper limit of the range varies depending on the laboratory and kit used for the test. Values obtained with different assay kits, methods, or laboratories cannot be used interchangeably. CA 15-3 levels are most commonly used to monitor metastatic breast cancer during active therapy. Tumor marker levels must be used in conjunction with the history, physical examination, and diagnostic imaging. A decrease in marker levels during treatment can indicate tumor response, whereas stable or increasing levels despite adequate treatment can indicate that the tumor is not responding to treatment or that the tumor is recurring.

Higher CA 15-3 levels have been correlated with more advanced stages of breast cancer [1] or with larger tumor burden. If the tumor produces CA 15-3, marker levels will increase as the tumor grows. The highest levels may be seen in metastatic breast cancer, particularly when metastases to the liver or bones exist.

II. Aims And Objectives

PRIMARY OBJECTIVES :A Prospective study on the analysis of CA 15-3 In breast cancer patients as prognostic marker.

SECONDARY OBJECTIVES: 1.To clinic-pathological study of breast cancer patients.

2.To study the level CA 15-3 tumor marker in breast cancer patients.

3.To correlate the prognosis in breast cancer patients with the changes in the level of CA 15-3 marker.

AIM OF STUDY**:** Aim of this study was to prospectively evaluate CA 15-3 as a prognostic factor in early detection of breast cancer relapse, recurrence and early detection of distant metastasis as well as to analyse the statistical correlation between CA 15-3 levels and clinical-pathological parameters including tumour size, lymph node, histological type, pre and post operatively.

III. Materials And Methods

The present prospective study entitled "Prospective study on the analysis of CA 15-3 in breast cancer patients as prognostic marker" carried out at department of general surgery C.R.GARDI Hospital of RD GARDI MEDICAL COLLEGE Surasa, Ujjain.

STUDY DESIGN- Hospital based prospective observational and analytical study.

PLACE OF STUDY -Surgical OPD and ward -Department of Surgery RDGMC and C.R.GardiHospital,Surasa Ujjain district of M.P.Ujjain district Is located on tropic of cancer latitude.

The climate is usually tropical.

STUDY GROUP- 50 patients admitted from surgery OPD in surgery ward of RDGMC for surgery, chemotherapy and follow up for carcinoma breast were selected for study.

STUDY PERIOD- November 2018 to MARCH 2020

INCLUSION CRITERIA**:**

1.Patients with breast cancer.

2.Patients with positive radiological and histopathological findings for breast cancer.

EXCLUSION CRITERIA:

1.Patients with benign breast disease

IV. Methodology :

This study included 50 patients with breast carcinoma and analysed serum samples obtained from patients who underwent full treatment modality (neo-adjuvant chemotherapy, modified radical mastectomy or conservative surgery [quadrantectomy + axillary dissection], adjuvant chemotherapy, radiotherapy) according to patients profile at Department of Surgery, C.R.GARDI Hospital of RD GARDI MEDICAL COLLEGE Surasa, Ujjain, MP, INDIA from November 2018 to march 2020. All breast cancer patients were staged according to AJCC staging system (7th Edition) classification: Information concerning age, diagnosis, type of surgery, therapy administered, and clinical pathology such as tumour size (T), lymph node status (N), grade and hormonal status, for each patient were collected through clinical charts .

Serum CA 15-3 concentration was determined by Enzyme Immunoassay Kit based on the principle of a solid phase enzyme-linked immunosorbent assay (ELISA), The lower limit of sensitivity was 1.2 U/ml and the established cut-off was 24.95U/ml determined by 95 percentile of 25 benign breast disease and mastitis patients and upper normal limit of CA 15-3 was calculated (24.95U/ml).

STATISTICAL ANALYSIS

- The observed data was compiled in an excel sheet for all patient
- All statistical analysis was done by the help of statistical software SPSS 23 version and Microsoft Excel
- For quantitative data frequency distribution , measures of central tendency ,dispersion and graphical representation was applied .
- For qualitative data frequency distribution,percentage and various diagrammatic representation was applied.
- For comparison of quantitative variables t test fisher test and for qualitative variables various chi-square test applied.
- Thus results of the study was evaluated using sensitivity, specificity, positive predictive value ,mean, standard deviation and other relevant statistical parameters.

V. Observation And Results

The present study entitled "A Prospective study on the analysis of CA 15-3 In breast cancer patients as prognostic marker" in R.D,G.M.C. UJJAIN was carried out in department of surgery from November 2018 to march 2020. This prospective observational study carried out on 50 patients of breast cancer came to surgery OPD and admitted for diagnosis and definitive treatment in surgical ward of RD Gardi Medical college and associated CRGH hospital Ujjain (MP). After estabilising diagnosis of breast cancer blood sample taken from each patients before treatment,after 7 days of full modality of treatment and on follow up of 6 months of full moadility of treatment . All data were collected, compiled, and analysed

TABLE NO. 1
Distribution of cases according to age

S. No.	Age group	No. of patients	%
1	21-30	1	2
2	31-40	2	4
3	41-50	24	48
4	51-60	19	38
5	>60	4	8

Table shows distribution of cases according to age group.Maximum number of patient are in age group of 41-50 yrs and less number of patient seen below age of 30 yrs .Youngest patient is 26 yrs of age and oldest patient is 71 years

TABLE NO. 2
Distribution of cases as per rural and urban area

Rural	**40**	**80**
Area of residence	**No. of patient**	**%**
Urban	**10**	**20**

Maximum number of patient in our study group are from near rural villages i.e.40(80%) rest 20 are from urban area.

TABLE NO. 3
Treatments administered to 50 breast cancer patients.

Treatment	No. of patients	%
Surgery	**4**	**8**
Surgery + adjuvant chemotherapy	**24**	**48**
Neo-adjuvant chemotherapy + surgery + adjuvant	**22**	**44**

chemotherapy +radiotherapy		
Total	**50**	**100**

Treatments administered to breast cancer patients are summarized in Table 4. 24 patient out of 50 were treated by surgery with adjuvant chemotherapy i. e. around 48%,22(i.e.44%) patient were treated by neo-adjuvant chemotherapy surgery adjuvant chemotherapy and radiotherapy,4(8%) patient were treated by surgery

TABLE NO. 4
Surgery performed.

Surgery	**No.**	**%**
Modified radical mastectomy	**48**	**96**
Quadrantectomy+axillary dissection	**2**	**4**
Total	**50**	**100**

Out of 50 patient 48(i.e.96%) were treated by modified radical mastectomy and 2 (i.e.4%) were treated by quadrantectomy with axillary dissection.

TABLE NO.5
Histological diagnosis.

Histological diagnosis	**No.**	**%**
Infiltrating ductal carcinoma(IFDC)	**46**	**92**
Infiltrating lobular carcinoma(IFLC)	**4**	**8**
Total	**50**	**100**

46 out of 50 patients (i.e.92%) were diagnosed histologically as ductal infiltrating carcinoma,and 4/50(i.e.8%) were diagnosed as infiltrating lobular carcinoma.

TABLE NO. 7
Tumor size.

Tumor size (cm)	No.	%
<2	15	30
2-5	23	46
>5	9	18
Tumor involving chest wall or skin	3	6
Total	50	100

Tumour size was classified as T1 (Tumour size less than or equal to 2cm) in 15/50 (30%), T2 (Tumour size between 2 and 5cm) in 23/50 (46%), T3 (Tumour more than 5cm) in 9/50(18%%) and tumor involving chest wall or skin in 3/50(6%)

TABLE NO.8
Clinical lymph nodes status.

Lymph nodes	No.	%
N0	16	32
N1	24	48
N2	8	16
N3	2	4
Total	50	100

N0—16/50(32%) paients their were no node involves.
N1— 24/50(48%)Axillary nodes mobile (ipsilateral).
N2— 8/50(16%)Axillary nodes fixed to one another and other structures (or only internal mammary lymph nodes are involved but not axillary nodes).
N3 — 2/50(4%)Supraclavicular nodes. Oedema of arm and internal mammary lymph nodes (ipsilaterally) (or–internal mammary lymph nodes and also axillary lymph nodes are involved).

TABLE NO.9
Pathological lymph nodes

Lymph nodes	N0.	%
<3	30	60
4 to 9	15	30
>9	5	10
Total	50	100

Out of 50 patient 30(i.e.60%) were found less then 3 lymph node positive on histopathological examination,15/50(i.e.30%) 4 to 9 lymph node were positive and in 5 /50(i.e.10%) patient more then 9 lymph nodes were positive on histopathological examination.

TABLE NO.10
Pre-treatment serum CA 15-3 level

CA 15 -3 level	No. of patient	%
>24.95U/ML	41	82
<24.95U/ML	9	18
TOTAL	50	100

Table shows before treatment in 41/50 (82%) breast cancer patient the value of serum CA 15-3 is more then 24.95u/ml and in 9/50 (18%) breast cancer patient the vale of CA 15-3 is less then 24.95u/ml. It signifies that 82 % of breast cancer patient in our study shows higher level of CA 15-3 tumor maker before treat

TABLE NO.11
Post treatment serum CA 15-3 level (After 7 days of full treatment modality)

CA 15-3 LEVEL	No. of patients	%
>24.95U/ML	16	32
<24.95U/ML	34	68
Total	50	100

Table shows in 16/50 (32%) breast cancer patient the value of serum CA 15-3 is more then 24.95u/ml and in 34/50 (68%) breast cancer patient the vale of CA 15-3 is less then 24.95u/ml after 7 days of full treatment modality. It signifies that 32% of breast cancer patients in our study shows higher level of CA 15-3 tumor maker after 7 days of full treatment modality

TABLE NO.12
Serum CA 15-3 level after 6 months of follow up

CA 15-3 LEVEL	**No.**	**%**
>24.95U/ML	**11**	**22**
<24.95U/ML	**39**	**78**
Total	**50**	**100**

Table shows in 11/50 (22%) breast cancer patient the value of serum CA 15-3 is more then 24.95u/ml and in 39/50 (68%) breast cancer patient the vale of CA 15-3 is less then 24.95u/ml after 6 months of follow up It signifies that 22% of breast cancer patients in our study shows higher level of CA 15-3 tumor maker and in 78% of breast cancer patients shows decreased level of CA15-3 tumor marker after 6 months of follow up.

TABLE NO.13
Outcome after full treatment modality in patient with value of CA 15-3 >24.95 U/ML

Outcome	**No. of patients**	**%**
Death	**3**	**18.75**
Recurrance	**3**	**18.75**
Residual tumor	**3**	**18.75**
Distant metastasis	**4**	**25**
Recovered	**3**	**18.75**
Total	**16**	**100**

Table shows that out of 16 patients with value of CA 15-3 >24.95 U/ML 3(18.75%) patients died due to breast cancer, 3(18.75%) came with recurrence, 3(18.75%) with residual tumor, 4(25%) with distant metastasis and 3(18.75%) were recovered. This signifies that in our study with value of CA 15-3>24.95u/ml after full treatment modality 18.75% were died due to breast cancer,and only 18.75% recoverd from breast cancer.

TABLE NO. 14
Outcome after full treatment modality in patients With value of CA 15-3 <24.95U/ML

Outcome	**No. of patients**	**%**
Death	**0**	**0**
Recurrance	**2**	**5.88**
Residual tumor	**1**	**2.94**

Distant metastasis	**1**	**2.94**
Recovered	**30**	**88.23**
Total	**34**	**100**

Above table shows that out of 34 patients with value of **CA 15-3 <24.95 U/ML 30(88.23%) patients were recovered,**2(5.88%) came with recurrence, 1(2.94%) with distant metastasis, 1(2.94%) patient came with residual tumor, and no patient died due to breast cancer.This signifies that in our study with value of CA 15-3<24.95u/ml after full treatment modality 88.23%were recovered from breast cancer and no patient died due to breast cancer.

TABLE NO.15
Sensitivity, Specificity, PPV, NPV, and Accuracy

Measures	
Sensitivity	71.42%
Specificity	90.90%
Positive Predictive Value	87.50%
Negative Predictive Value	97.05%
False Positive Rate	11.76%
False Negative rate	23.07%
Concordance (Accuracy)	80%

In our study in breast cancer patients Sensitivity of CA15-3 as prognostic tumor marker is 71.42%, Specificity of CA15-3 as prognostic tumor marker is 90.90%, PPV of CA15-3 as prognostic tumor marker is 87.50%, NPV of CA15-3 as prognostic tumor marker is 97.05%, Accuracy of CA15-3 as prognostic tumor marker is 80%.

VI. Discussion

The problem of breast cancer has always existed and increasing in most countries. Breast cancer mortality can only be reduced by detecting the tumour at the earlier stage. Serum marker in breast cancer are helpful for clinicians in providing more effective management of the disease.

Main use of CA 15-3 is to monitor the breast cancer patient response to treatment and for early breast cancer recurrence or metastasis. In this study 50 cases of breast cancer, change in the value of serum CA15-3 after full modality of treatment and follow-up were assessed and its relate to outcome of patient (prognostic significance). CA15-3 levels were also compared with tumour size, histological type, and its role in prognostic significance**.**

25 patients with benign breast disease and mastitis included in control group. Upper normal value was calculated 24.95U/ml by 95 percentiles.(15)

The main use of CA 15-3 is to monitor the breast cancer patient response to treatment and for early breast cancer recurrence, residual tumour or distant metastasis. CA 15-3 can be used as a marker only if cancer is producing elevate amounts of it. However, it may be useful as a prognostic marker even in a small percentage of patients with localized breast cancer showing increased levels of CA 15-3. If CA 15-3 is initially elevated may be used to monitor treatment and when repeated on after complete treatment modality and 6 months of follow up , to detect early recurrence and residual tumour; CA 15-3 is not useful when breast cancer is detected early by other examinations. In general, higher levels of CA 15-3 are correlated with a larger tumour burden and a more advanced disease. The serum levels of CA 15-3 increase as cancer develops.

An initial elevation of CA 15-3 that does not return to the normal range, is an indicator of lack of response to treatment and represents an adverse prognostic factor. Present study shows a significant correlation between CA 15-3 and the response to treatment. In fact a continuous increase of the marker in patients with metastatic disease that had subsequently developed relapse, recurrence, distant metastasis and even death by analyzing CA 15-3 serum concentrations in breast cancer patients during follow-up. Similar observations were reported by different authors.(8).

In particular, present study showed that patients presenting CA15-3 levels over 24.95U/ml (cut-off) have poor prognostic significance with concentrations <24.95U/ml in breast cancer patients. The aim of this prospective study was to determine the applicability of serum CA 15-3 assay in the detection of prognostic significance in term of outcome (residual tumour, recurrence, distant metastasis and death) after full treatment modality and during the follow up of 6 months.

Present results demonstrated that CA 15-3 levels are frequently higher before treatment than after treatment of primary tumour. In addition, our study found that higher levels of CA 15-3 in patients prior to treatment are more frequently associated with disease progression and worse prognostic significance (outcome) compared to patients with lower levels of CA 15-3.

The most likely explanation can be that patients with elevated levels of CA 15-3 may harbor micro metastatic disease undetectable with the standard diagnostic procedures like Clinical examination, USG, Mammography, MRI, and Histopathological examinations. Finally, our study demonstrated the important role of this marker in monitoring the efficacy of post-treatment therapies (i.e. Surgery, chemotherapy or radiotherapy).

RESULT: Our study Signifies that with value of CA 15-3>24.95u/ml after full treatment modality 18.75% died due to breast cancer, 3(18.75%) came with recurrence, 3(18.75%) with residual tumor, 4(25%) with distant metastasis and only 18.75% recovered from breast cancer in our follow up of 6 months. And with value of CA 1<24.95u/ml after full treatment modality 88.2%were recovered from breast cancer and no patient died due to breast cancer. In our study we found that decreased serum levels of CA 15-3 in these patients were statistically significant.

DECLARATIONS

Conflict of interest: None

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Referances :

[1]. Swart R. Breast Cancer. Medscape Drugs and Diseases.

[2]. Bon GG et al. Clinical and technical evaluation of ACS™BR serum assay of MUC1 gene-derived glycoprotein in breast cancer, and comparison with CA15-3 assays. *Clinical Chemistry*. 1997.

[3]. Wu JT. Expression of monoclonal antibody-defined tumor markers in four carcinomas . *Ann Clin Lab Sci*. 1989 Jan-Feb.

[4]. Duffy MJ, Shering S, Sherry F, McDermott E, O'Higgins N. CA 15-3: a prognostic marker in breast cancer. *Int J Biol Markers*. 2000 Oct-Dec.

[5]. Klee GG, Schreiber WE. MUC1 gene-derived glycoprotein assays for monitoring breast cancer (CA 15-3, CA 27.29, BR): are they measuring the same antigen?. *Arch Pathol Lab Med*. 2004 Oct.

[6]. Harris L, Fritsche H, Mennel R, Norton L, Ravdin P, Taube S. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. *J Clin Oncol*. 2007 Nov 20.

[7]. Gheybi E, Amani J, Salmanian AH, Mashayekhi F, Khodi S. Designing a recombinant chimeric construct contain MUC1 and HER2 extracellular domain for prediagnostic breast cancer. *Tumour Biol*. 2014 Aug 16.

[8]. Ebeling FG, Stieber P, Untch M, Nagel D, Konecny GE, Schmitt UM. Serum CEA and CA 15-3 as prognostic factors in primary breast cancer. *Br J Cancer*. 2002 Apr 22. 86(8):1217-22.

[9]. Wang G, Qin Y, Zhang J, Zhao J, Liang Y, Zhang Z, et al. Nipple discharge of CA15-3, CA125, CEA and TSGF as a new biomarker panel for breast cancer. *Int J Mol Sci*. 2014 May 28. 15(6):9546-65. .

[10]. Kokko R, Holli K, Hakama M. Ca 15-3 in the follow-up of localised breast cancer: a prospective study. *Eur J Cancer*. 2002 Jun. 38(9):1189-93.

[11]. Nicolini A, et al. Intensive post-operative follow-up of breast cancer patients with tumour markers: CEA, TPA or CA15.3 vs MCA and MCA-CA15.3 vs CEA-TPA-CA15.3 panel in the early detection of distant metastases. *BMC Cancer*. 2006 Nov. 20(6):269.

[12]. Kruse V, Van de Wiele C, Borms M, Maes A, Pottel H, Sathekge M, et al. CA 15.3 measurements for separating FDG PET/CT positive from negative findings in breast carcinoma recurrence. Factors influencing the area under the ROC curve. *Nuklearmedizin*. 2014 Aug 6. 53(4):131-8.

[13]. Cervino AR, Saibene T, Michieletto S, Ghiotto C, Bozza F, Saladini G, et al. Correlation between Cancer Antigen 15.3 Value and Qualitative and Semi-quantitative Parameters of Positron Emission Tomography/Computed Tomography in Breast Cancer patients. *Curr Radiopharm*. 2014 May 15.

[14]. Sturgeon C.Practice guidelines for tumor marker use in the clinic. *Clin Chem*.2002 Aug. 48(8):1151-9.

[15]. Gupta SK, Kumar V, Anees A, Goel A. The study of prognostic significance of CA 15-3 in breast cancer. Int Surg J 2018;5:580-3.//www.ijsurgery.com

[16]. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al.Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2014;136(5):E359-8

[17]. FG Ebeling, P Stieber, M Untch, D Nagel, GE Konecny, UM Schmitt, et al.Serum CEA and CA15-3 as prognostic factor in primary breast cancer. Br Jcancer. 2002;86:1217-22.

[18]. Lagow E, DeSouza MM, Carson DD. Mammalian reproductive tract mucins.Human Reproduction. 1999;15:280-92.

[19]. Agrawal B, Gendler SJ, Longenecker BM. The biological role of mucins in cellular interactions and immune regulation: Prospects for cancer immunotherapy. Molecular Medicine Today. 1998;4:397-403.

[20]. Brayman M, Thathiah A, Carson DD. MUC1: A multifunctional cell surface component of re-productive tissue epithelia. Reproductive Biol Endocrinol.2004;2:1-9.

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