A STUDY ON ROLE OF SERUM CA15.3 IN THE BREAST CANCER PATIENTS OF CHHATTISGARH

Biochemistry

Onkar Prasad Kashyap	Assistant Professor, Department Of Biochemistry, Govt. Medical College Rajnandgaon Chhattisgarh, India
Harish Kumar Uraon*	Assistant Professor, Department Of Biochemistry, Late. Shri Lakhiram Agrawal Memorial Medical College Raigarh, Chhattisgarh, India *Correspondence Author

ABSTRACT

INTRODUCTION- Breast cancer (BC) is the most common cancer in women (23% of all new cases in women). In India, Breast cancer is the second most common cancer after carcinoma cervix. CA15.3 is an established tumour marker for the breast cancer. It has the value in early diagnosis in recurrence of breast cancer. CA 15.3 is a better Tumour Marker than CEA and Tissue Polypeptide Antigen (TPA) as it has greater sensitivity than CEA and higher specificity than TPA.

MATERIALS AND METHOD- A prospective cross sectional study was done in 64 individuals from Pt. JNM medical college and associated Bhim Rao Ambedkar Hospital Raipur (C.G.) India. 32 females with histologically diagnosed breast cancer were taken as subjects and 32 healthy individuals with no diagnosed cancer or family history of cancer were taken as control in this study. The institutional ethics committee approved the study and all study participants gave informed written consent before participating in the study. After consent 3 ml blood samples were collected for serum CA 15-3 quantification in a plain tube. CA 15-3 serum level were quantified by two step sequential chemiluminescent immunometric assay with 0.2 U/ml as the lower limit of sensitivity.

RESULTS- The mean age of the case was 45.9+8.7 years and in case of controls it was 44.9+9.11years. Mean value of the Tumour marker CA15.3 was 133.32+ 73.20 (Mean + SD) U/ml among the breast cancer cases and 16.2 + 8.26 (Mean + SD) U/ml. Serum CA15.3 was significantly higher in patients of the breast cancer than that of the healthy individuals and was statistically extremely significant as the P value was < 0.0001. Out of 32 cases in the study, the maximum number of cases was of Invasive Ductal carcinoma (28 out of 32=87.5%). Medullary carcinoma constitutes 6.25% of the total cases (2 out of 32). 92.85% of the total invasive ductal carcinoma had serum CA15.3 level above reference value while 7.15% had below the reference value.

CONCLUSION- CA 15.3 is cost effective & reliable method in diagnosis & prognosis of Breast cancer.

INTRODUCTION Cancer is one of the leading causes of mortality and morbidity worldwide. Carcinoma of lung, female breast, colorectal and stomach accounts for 40% of all cases diagnosed worldwide. In men, lung cancer is the most common cancer (16.5% of all new cases in men). Breast cancer (BC) was the most common cancer in women (23% of all new cases in women) [1]. In India, Breast cancer is the second most common cancer after carcinoma cervix. [2]. Three most common cancers causing death in women are cervical cancer (17.1%), stomach cancer (12.6%) and breast cancer (10.2%) [3]. Appropriate interventions are effective in avoiding fatal outcome following the diagnosis of breast cancer that is why breast cancer which is second most common in incidence is not among the top three causes of cancer related deaths. Greater than 95% of the invasive carcinomas are infiltrating duct carcinoma, which based on invasiveness and staging are divided into-

(1) Carcinoma in situ and
(2) Invasive carcinoma.

In situ carcinoma refers to a neoplastic proliferation that is limited to ducts and lobules by the basement membrane, whereas the invasive carcinoma penetrates through the basement membrane into stroma. Histologically of all the cases of breast cancers 15-30% constitutes carcinoma in situ among which Ductal Carcinoma In - Situ (DCIS) is 80% and Lobular Carcinoma in Situ is 20%.

The invasive ductal carcinoma is most common type of breast cancer. Most common symptoms presented by women in case of breast diseases are painless palpable mass or nipple discharge. Diffuse cyclical pain has no pathological correlation and most effective treatment is hormonal therapy. Carcinoma of the breast presents with painless mass in 90% cases and only 10% of the cancers are painful. Nipple discharge is a less common finding but bloody discharge is the common finding in duct papilloma.

About 50% of the carcinoma arises in the upper outer quadrant, 10% in each remaining quadrant and 20% in the sub-areolar region. Reproductive and menstrual histories are well recognized risk factors for the breast cancer. [4,5]

CA15.3 is an established tumour marker for the breast cancer. It has the value in early diagnosis in recurrence of breast cancer [6]. CEA and CA 15.3 are useful tools for early diagnosis of metastasis, mainly in those

patients with ER+ or PR+ breast cancer [7]. There are multiple physiological factors promoting breast cancer including hormonal imbalance & genetic predisposition. [8]. CA 15.3 is a better Tumour Marker than CEA and Tissue Polypeptide Antigen (TPA) as it has greater sensitivity than CEA and higher specificity than TPA [9].

There are scarcity of resources on the available topic. With the above background, the present study was conducted to determine the level of CA15.3 tumor Marker in the Carcinoma breast patients and its comparison with histopathological types of breast cancer.

MATERIALS AND METHOD

A prospective cross sectional study was done in 64 individuals from Pt. JNM medical college and associated Bhim Rao Ambedkar Hospital Raipur (C.G.) India. 32 females with histologically diagnosed breast cancer were taken as subjects and 32 healthy individuals with no diagnosed cancer or family history of cancer were taken as control in this study. The institutional ethics committee approved the study and all study participants gave informed written consent before participating in the study. After consent 3 ml blood samples were collected for serum CA 15-3 quantification in a plain tube. CA 15-3 serum level were quantified by two step sequential chemiluminescent immunometric assay with 0.2 U/ml as the lower limit of sensitivity. [7,8,9]

Statistical analysis

Data were expressed as percentage for qualitative data. The association of qualitative & quantitative data with different subgroups were assessed by Chi Square & t test. A p value < 0.05 was considered significant and p<0.01was considered highly significant. All statistical analysis was performed with SPSS statistical software version 13.0.

RESULTS

Table 1-age Distribution Of Case Group And Control Group

Age Distribution in years	Cases			Controls		
	Number	%	Mean age (Mean+SD)	Number	%	Mean age (Mean+SD)
21-30	2	6%	45.9+ 8.7	3	9.3%	44.9 + 9.11
31-40	5	16%		4	12.5%	
41-50	16	50%		17	53.1%	
51-60	9	28%		8	25.1%	
Total	32			32		

The study consisted of 32 histopathologically diagnosed breast cancer patients and 32 healthy individuals. All the cases were below 60 years. Maximum number of cases (50%) was in the age group of 41-50yrs. Minimum number of cases (6%) was in the age group of 21-30 years. The age distribution was matched with controls. The mean age in of the case was 45.9+8.7 years and in case of controls it was 44.9+9.11years.**[TABLE – 1]**

Table-2- Comparison Of Tumour Marker Ca15.3 Between Cases And Controls

TUMOR MARKER	CASES	CONTROLS	SIGNIFICANCE
CA15.3 (U/ml) Mean $\pm$ SD	133.32$\pm$ 73.20	16.2 $\pm$ 8.26	P < 0.0001

Mean value of the Tumour marker CA15.3 was 133.32+ 73.20 (Mean + SD) U/ml among the breast cancer cases and 16.2 + 8.26 (Mean + SD) U/ml. The standard error of difference was 13.022.

Serum CA15.3 was significantly higher in patients of the breast cancer than that of the healthy individuals and was statistically extremely significant as the P value was < 0.0001. **[TABLE – 2]**

Table-3- Distribution Of Histological Type Of Breast Cancer (out Of Total 32 Cases).

HISTOLOGICAL TYPE	NUMBER OF CASES	PERCENTAGE
Invasive ductal	28	87.5%
Medullary	2	6.25%
Lobular	1	3.125%
Metaplastic	1	3.125%

Out of 32 cases in the study, the maximum number of cases was of Invasive Ductal carcinoma (28 out of 32=87.5%). Medullary carcinoma constitutes 6.25% of the total cases (2 out of 32). Lobular and Metaplastic carcinoma accounts for 3.125% each. **[TABLE – 3]**

Table- 4. Percentage Distribution Of The Breast Cancer Cases With Serum Ca15.3 Above And Below Reference Value.

SERUM LEVEL	INVASIVE DUCTAL (28)	OTHER (4)
CA15.3 > 30U/ml	26 (92.85%)	2(50%)
CA15.3 < 30U/ml	2 (7.15%)	2(50%)
Chi square value-2.612 , df-1, p > 0.05		

92.85% of the total invasive ductal carcinoma had serum CA15.3 level above reference value while 7.15% had below the reference value. Among the other histological type of breast cancers 50% of the patient had serum CA15.3 level above the reference value and 50% had below the reference value (Reference value is 0-30U/ml). **[TABLE – 4]**

DISCUSSION

In the current study among 32 cases, 5 were familial breast cancer cases and 27 were sporadic, all the cases were below the age of 60 years. Out of 32 cases, highest incidence of breast cancer was seen in the age group of 41 to 50 years. The mean age at the diagnosis of the breast cancer patient was 45.9+8.7 years. Total number of breast cancer patients below 40 years was 7. Fourteen out of 32 cases were postmenopausal (43.75%) and 18 were premenopausal (56.25%). Table-1 shows the distribution of the breast cancer cases and controls with their Mean age. The age distribution finding was in agreement with the following studies.

Parvin Mehdipour et al. [10] in their study enrolled 400 primary breast cancer patients with the mean age of 48.8 +11.3 years. **Kannan Vaidyanathan et al** [11] took 61 breast cancer patients in their study from the Kidwai Memorial Institute of Oncology Bangalore, India. They found that, the median age of the 39 patients with breast cancer was 42 years and 12 patients with breast and ovarian cancer was 43.5years. **A.Vijayalakshmi et al** [12] included 136 patients in their study with 9 familial and 105 sporadic breast cancer cases. Mean age at diagnosis was 57.4 +4.97 for the familial cases and 50.2 +10.43 for sporadic breast cancer cases. **Valarmathi et al** [13] in their study found that the mean age at diagnosis of 43 breast cancer patient was 44.86 yrs.
In our study we found maximum cases to be Invasive Ductal type of breast cancer. Twenty eight out of 32 patients were invasive ductal carcinoma (87.5%). **Ana Krepischi CV et al** [14] also found the invasive ductal carcinoma, the most common type of breast cancer in their study. **Chakraborty et al** [15] also found the Invasive ductal carcinoma as the most common type of breast cancer among 92 patients they investigated.

Serum CA15.3 is a well established tumour marker for breast cancer. It is more specific as compared to CEA and Tissue Polypeptide Antigen (TPA) (specificity of CA15.3 is 95.7%, CEA is 95.5% and that of TPA is 81.9%).Also it is more sensitive than the CEA (sensitivity of CA15.3 is 64.1% and that of CEA is 44.4%) [9]**.**

The cut off value for serum Ca15.3 was 30U/ml. Mean serum CA15.3 among the case was 133.32+ 73.20 U/ml and that of the control was 16.2 + 8.26 U/ml. Serum level of CA15.3 was significantly higher in cases than control with P value < 0.0001. Out of 18 patients undergoing chemo or radiotherapy, serum CA 15.3 value in 4 patients were less than 30U/ml and 5 were between 30 to 60U/ml. Freshly diagnosed, cases with metastasis and relapse cases had CA15.3 level highly elevated and was above 100U/ml . This finding in the present study is supported by the study of **Ebling et al** [16]. In their study they found that, elevated pre-operative values of CEA and CA 15-3 were associated with early death from disease (*P*=0.0001 for both markers) and in relapse cases serum level of CA 15-3 were also significantly high (*P*=0.0003). In a study done by **Chourin et al** [17], out of 2036 patients initial CA 15-3 concentration was >30 U/ml in 200 patients (9.8%), with 75 who had metastases at diagnosis (M+). CA 15-3 concentrations <30U/ml had strong negative predictive value for metastases at diagnosis (97.5%). Conversely, 37.5% of patients with initial CA 15-3 concentrations >30 U/ml had metastases.

CONCLUSION

In the current study, level of CA 15-3 was significantly higher in cases than control & also higher in invasive ductal carcinoma cases but association was found non significant. CA 15.3 is cost effective & reliable method in diagnosis & prognosis of Breast cancer. Early diagnosis & treatment of Breast cancer cases will not only reduce the mortality & morbidity but also improve the quality of life among these patients.

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