

A Comparative Study of CA 15.3 Levels in Pre Treated Breast Cancer Patients and Controls

Inderjit Singh¹, Jasmeet Singh², Rupinderjit Kaur³, Raja P.S. Banipal⁴

ABSTRACT

Introduction: Breast cancer is the leading cause of cancer deaths among women worldwide after carcinoma of cervix uteri. CA 15.3 is the chief tumor marker used in the diagnosis of severity of disease and progression from treatment. Study aimed to evaluate tumor marker CA 15.3 in pre-treated breast cancer patients and to compare it with controls.

Materials and methods: the study included 50 breast cancer patients and 50 controls of the same age group and socio-economic status.

Results: CA 15.3 levels were found to be significantly higher in breast cancer patients as compared to controls and CA 15.3 levels significantly increased with increase in tumor grade and advancement of stage.

Conclusions: CA 15.3 levels are significantly increased with advancement of stage and tumor grade indicating its great role in advancement of stage and as an indicator for the improvement from the out-come of treatment.

Keywords: CA 15.3 Levels, Breast Cancer

INTRODUCTION

Cancer is not a new disease. The word cancer is derived from French word “chancre” originally meaning “crab”. There are several descriptions written which can be found on Egyptian papyrus dating back to almost 1600 BC. The Greek physician Hippocrates is believed to be the first person to use the word “carcinoma”, which describes the crab like way that both the ulcer forming and non-ulcer forming tumors spread. Overtime the word shortened to “cancer”.¹

One of the oldest description was discovered in Egypt and dates back to approximately 1600 BC. In Edwin Smith Papyrus it has been described that 8 cases of tumors or ulcers of the breast were treated by cauterization. It has been written about the disease that, “There is no treatment.” During 17th century it was believed that breast cancer was generally caused by imbalances in the fundamental fluids especially excess black bile.¹

Breast cancer is one of the very common cancer among women worldwide, with nearly 1.7 million new cases diagnosed in 2012 (second most common cancer overall). This represent about 12% of new cancer cases and 25% of all cancers in women. Breast cancer is hormone related and the factors that modify the risk of this cancer when diagnosed during pre-menopausal and when diagnosed during post-menopause are not the same.²

Breast cancer originates in the cells of the breast. The breast tissue covers an area larger than just the breast and it further extends up to the collar bone and from the armpit across to the sternum in the center of chest. Each breast is made of

glands, ducts (thin tubes) and fatty tissue. Lobules are group of glands that can produce breast milk. Milk flows from the lobules through ducts to the nipple. The nipple is surrounded by darker area called the areola. Fatty tissue fill the spaces between the lobules and ducts. Besides this it also protects them.³

The size, stage, rate of growth, and other characteristics of a breast cancer determine the kinds of treatment. Treatment may include surgery, drugs (hormonal therapy and chemotherapy), radiation and immunotherapy. Tumor removal by surgery provides the largest benefit and it can cure many cases. Besides this, to increase the likelihood of cure, several chemotherapy regimens are also prescribed in addition to surgery.³

Tumor markers had become very important in breast cancer research because of their impact on prognosis, treatment, survival and also to their relation to breast cancer subtypes. CA15.3 is a mucin belonging to a large family of glycoproteins encoded by the MUC 1 gene that is heterogeneously expressed on the apical surface of normal epithelial cell types, including those of the breast. CA 15.3 is elevated in a proportion of breast cancer patients with distant metastases. Though current American Society of Clinical Oncology⁴ and Cancer Network guidelines do not recommend its use for surveillance purposes, elevated CA 15.3 is used to anticipate detection of recurrences in patients with breast cancer as an additional tool in evaluating therapeutic response of advanced disease.⁵

CA-15.3 is detected by a murine monoclonal antibody DF3 produced against a membrane enriched extract of a human breast cancer metastatic to liver. Circulating DF3 reactive antigen is a heterogeneous molecule with a molecular mass of 300-450 kdal. DF3 peptide core consist of highly conserved 60 nucleotide base pair tandem repeat sequence. Clinical application-CA15.3 is that it is mostly elevated 69% of advanced cases. It is not useful in screening as it is also

¹Associate Professor, Department of Physiology, ²Assistant Professor, Department of Biochemistry, ³Assistant Professor, Department of Microbiology, Chintpurni Medical College and Hospital, Bungal, Pathankot, ⁴Professor, Department of Radiotherapy, G.G.S. Medical College, Faridkot, Punjab, India

Corresponding author: Jasmeet Singh, Assistant Professor, Department of Biochemistry, Chintpurni Medical College and Hospital, Bungal, Pathankot, Punjab, India

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elevated in benign breast disease and ovarian tumors.⁶

In 18th century a wide variety of hypothesis were postulated including injury to the breast, curdled breast milk, nipple discharge and various forms of lymphatic blockages as causative factors for the breast cancer.⁷

Cancer is one of the leading cause of death in both more and less economically developed countries. The burden will also increase due to the growth and ageing, particularly in less developed countries in which about 82% of the world's population resides. There are several life style behaviors that are known to enhance cancer risk, such as smoking, poor diet, physical inactivity, and reproductive changes including lower parity and later age at first birth.⁸

Breast cancer, however, becomes palpable in its advanced stage and often develops into fungating lesion which finally becomes necrotic (die from the inside, causing the tumor to appear to breakup) and ulcerate through the skin.¹

Breast cancer is most frequently diagnosed it is the leading cause of cancer death among females world over, with an estimated 1.7 million cases and 5, 21, 900 deaths in 2012. Breast cancer alone counts for 25% of all cancer cases and 15% of all cancer deaths among females.⁹

Tumor markers have become highly important in breast cancer research because of their impact on prognosis, treatment and survival and also to their relation to breast cancer subtypes. CA15.3 is a mucin belonging to a large family of glycoproteins encoded by the MUC 1 gene that are heterogeneously expressed on the apical surface of normal epithelial cell types, including those of the breast. CA 15.3 is elevated in a proportion of breast cancer patients with distant metastases.¹⁰

Ca15.3 is the most widely used and investigated in the breast cancer follow-up. Initial studies indicate that CA 15.3 is abnormal in majority of the patients with metastatic breast cancer and that antigen levels are correlated with changes in the clinical status of the breast cancer patients. Actually they are important asset to monitor the efficacy of medical therapies after surgery.¹⁰

Study aimed to evaluate tumor marker CA 15.3 in pre-treated breast cancer patients and to compare it with controls.

MATERIAL AND METHODS

This study was conducted in the Department of Radiotherapy and Biochemistry G.G.S. Medical College Faridkot. Ethical clearance was also taken at G.G.S. Medical College and Hospital Faridkot from the Institutional ethical Committee and finally published in collaboration with the Department of Biochemistry, Physiology and Microbiology Chintpurni Medical College and Hospital, Bungal, Pathankot. The study included 50 breast cancer patients and 50 controls. The premenopausal patients were sub-grouped into 21 with metastasis and 29 without metastasis and 19 with early stage and 31 with advance stage breast cancer. All the patients were freshly diagnosed with breast cancer and they had not undergone any form of treatment like Surgery, Radiotherapy, Chemotherapy or any other form of hormone therapy. Proper informed consent was taken from patients and those who

were only willing to participate were included in this study. CA 15.3 levels was evaluated for the patients and samples were run on Fully Automated ACCESS- 2 working on the principle of Chemiluminiscence.

Principle of Chemiluminiscence: The above three parameters will be estimated by using principle of chemiluminiscence in which there is emission of light when an electron returns from an excited or higher energy level to lower energy level. The excitation event is resulted by a chemical reaction and it involves the oxidation of an organic compound iso-luminol, by hydrogen peroxide in the presence of catalyst myelo-peroxidase which produces long lived light emission at 425 nm. Light is emitted from the excited product generated by the oxidation reaction of acridinium ester by alkaline hydrogen peroxide in presence of detergent. It produces a rapid flash of light at 428 nm. Acridinium esters are high specific activity labels with detection limit of 800 zeptomoles.¹¹

STATISTICAL ANALYSIS

Statistical analysis for all the above parameters was done by using SPSS software and the level of significance was evaluated using Man Whitney test.

RESULTS

In this study CA 15.3 levels were compared between premenopausal patients and premenopausal controls. The CA15.3 levels were found to be significantly higher in breast cancer patients as compared to controls with Mean±SD=45.50±30.49 (U/ml) and Mean rank=72.68 as compared to controls with Mean±SD=15.37±4.63(U/ml) and Mean Rank=28.32 with Man Whitney U=141.00 and p value was found to be significant (p<0.05).

Similarly the CA 15.3 levels were compared between premenopausal patients with and without metastasis In this study the CA 15.3 levels were found to be significantly higher in premenopausal patients with metastasis as

CA 15.3 levels (U/ml)	Patients (U/ml)	Controls (U/ml)	p value
MEAN	45.50	15.37	p<0.05
SD	30.49	4.63	Significant
Mean Rank	72.68	28.32	Man Whitney U=141.00

Table-1: Comparison of CA 15.3 In pre menopausal patients and pre menopausal controls

CA-15.3 levels (U/ml)	Pre PAT with metastasis (U/ml)	Pre PAT without metastasis (U/ml)	p-Value
Mean	61.85	33.66	p<0.05
SD	35.93	18.94	Significant
Mean rank	32.24	20.62	Man Whitney U=163.00

Table-2: Comparison of CA 15.3 in pre menopausal patients with and without metastasis

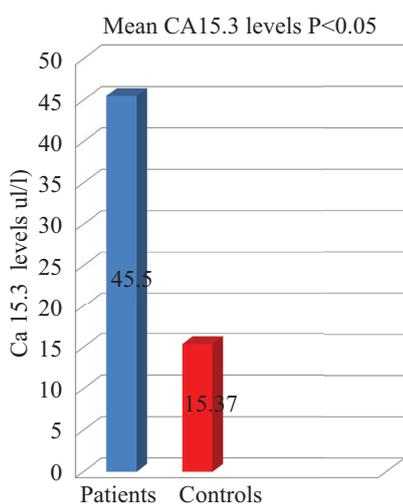


Figure-1: Showing comparison of CA 15.3 levels in premenopausal patients and controls

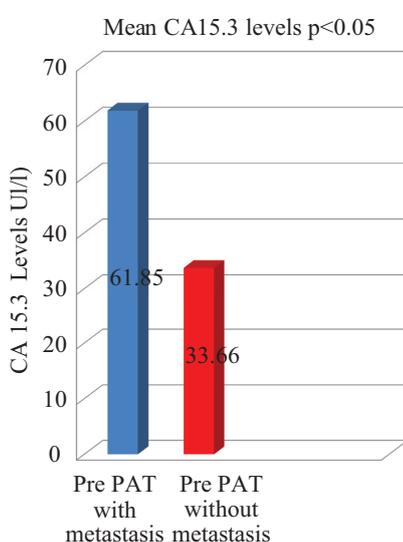


Figure-2: Showing comparison of CA15.3 in premenopausal patients with and without metastasis

compared to premenopausal patients without metastasis with Mean±SD=61.85±35.93 (U/ml) and Mean rank=32.24 as compared to premenopausal patients without metastasis with Mean±SD=33.66±18.94 (U/ml) and Mean rank=20.62 with Man Whitney U=163.00 and p value was found to be significant (p<0.05).

DISCUSSION

In this study CA 15.3 levels were compared between premenopausal patients and premenopausal controls. The CA15.3 levels were found to be significantly higher in breast cancer patients as compared to controls with Mean±SD=45.50±30.49 (U/ml) and Mean rank=72.68 as compared to controls with Mean±SD=15.37±4.63(U/ml) and Mean Rank=28.32 with Man Whitney U=141.00 and p value was found to be significant (p<0.05).

Similarly in this study the CA 15.3 levels were compared between premenopausal patients with and without metastasis In this study the CA 15.3 levels were found to be significantly higher in premenopausal patients with metastasis as

compared to premenopausal patients without metastasis with Mean±SD=61.85±35.93 (U/ml) and Mean rank=32.24 as compared to premenopausal patients without metastasis with Mean±SD=33.66±18.94 (U/ml) and Mean rank=20.62 with Man Whitney U=163.00 and p value was found to be significant (p<0.05).

Breast cancer is the very common malignant disease and is one of the major cause of cancer related mortality among females worldwide.¹² In India, breast cancer is the second most common cancer overall and second most common cancer in incidence and mortality is next only to carcinoma cervix in females.¹³

CA 15.3 have become well established diagnostic tool as fast, non-invasive, reproducible and quantitative parameter in follow up care and monitoring therapy of breast cancer patients. However, the potential role of these factors on prognosis has only been studied in few investigations, which came to inconsistent conclusions.¹⁴

CA 15.3 is also widely used and investigated in breast cancer follow-up and used in conjunction with the history, physical examination and diagnostic imaging. A decrease in marker levels during treatment can indicate tumor response, whereas increasing levels despite adequate treatment can indicate that tumor is not responding to treatment or that the tumor is recurring.¹⁰

CA15.3 levels were also compared between pre menopausal and post menopausal breast cancer patients. The comparison of Mean±SD=60.47±8.59 in pre menopausal breast cancer patients as compared to Mean±SD=63.17±4.58 in postmenopausal breast cancer patients was found to be statistically significant.¹⁵

Similarly CA 15.3 levels were also compared between the metastatic and non-metastatic breast cancer patients. The Median=22.6 was found in non-metastatic and Median=43.5 was found in metastatic breast cancer patients was compared and was found to be statistically significant with p<0.00.¹⁶

CA-15.3 is most widely used and investigated in breast cancer follow-up. Raised values of CA-15.3 were seen with advanced stage of breast cancer with mean in Stage-1=2(U/ml), Stage- 2=14.92(U/ml), Stage-3=34(U/ml) and Stage-4=59.6(U/ml) and the study showed CA-15.3 is significantly helpful in predicting response to the treatment. CA-15.3 is abnormal in majority of the patients with metastatic breast cancer and antigen levels are correlated with changes in clinical status of breast cancer patients. But according to current scenario we can say that CA-15.3 is not very specific or sensitive enough to detect early breast cancer. CA 15-3 can also be elevated in patients with cancer and serial determinations of CA-15.3 may be useful in post-surgical follow-up of breast cancer patients.¹⁰

CONCLUSION

Thus in the end we can conclude by summarizing that CA 15.3 levels are increased in breast cancer and these levels are further increased with the advancement of tumor stage and metastasis as shown by our study and several other studies that support our study also.

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