ORIGINAL ARTICLE

# Clinical Significance of Serum Adenosine Deaminase Levels in Breast Cancer Patients

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**ABSTRACT**

**Objective:** To compare serum adenosine deaminase (ADA) levels in untreated and treated cases of breast cancer patients.

**Study Design:** It was an Analytical, observational study.

**Place and Duration of study:** The study was carried out in the Department of Biochemistry, Islamic international Medical College in collaboration with Department of Surgery, Holy Family Hospital, Rawalpindi during one year period from April 2017 to March 2018.

**Materials and Method:** Total 150 subjects were selected for the study using convenient non probability sampling technique. Selection criteria for patients were both untreated and treated cases of breast cancer. Selection criteria for controls were healthy individual without having any malignancy and all the diseases in which adenosine deaminase is raised. Out of total 150 subjects, we took 70 controls and 80 cases. Of 80 cases, 44 were untreated and 36 were treated breast cancer patients. Serum adenosine deaminase levels of both controls and cases were measured and entered into SPSS version 21 for analysis. Descriptive data were given in the form of mean ± standard deviation (SD). "Independent *t* test" was applied and "p" values less than 0.05 were considered statistically significant.

**Results:** Mean of serum adenosine deaminase level was compared among controls and untreated cases. It was found that serum ADA levels were high in untreated cases as compared to controls (17.75 ± 4.17 VS 14.92 ± 3.73) with p-value 0.001. Mean of serum ADA levels were also compared among untreated and treated cases. It was found that serum ADA levels were markedly low in treated cases as compared to untreated cases (13.18 ± 4.18 VS 17.75±4.17) with p-value <0.0001.

**Conclusion:** It is concluded that serum adenosine deaminase levels are significantly raised in female patients of breast cancer; however these levels get lowered after treatment such as chemotherapy, radiotherapy, hormonal therapy and surgical excision.

**Key Words:** *Adenosine Deaminase (ADA), Breast Cancer, Malignancy, miRNA, Tumor Grades.*

## Introduction

Breast cancer is malignancy in the tissues of breast.[1] It is the most common cancer among females out of all types of cancers. Worldwide approximately 1 million newly diagnosed cases are reported. It is the 2nd leading death cause in females. In women, it is the most common invasive cancer.[2] On overall ranking of deaths caused by cancers, breast cancer ranks 5th.[3] In Pakistan, breast cancer is the most frequently diagnosed cancer among females. It is reported that as compared to Iran and India, Pakistan has 2.5 times greater incidence of breast cancer. This means that almost one in nine female patients suffer from it.[4] Approximately 90,000 women suffer from breast cancer every year in Pakistan.[1] Fortunately, if cancer is diagnosed at an early stage, it can be prevented and treated.[5]

Studies from Lahore and Karachi have shown that breast cancer comprises up to 1/3rd of all malignant tumors in females.[6]

"Adenosine deaminase (ADA) is an important enzyme of the purine-inactivating chain. It helps in catalyzing the irreversible deamination of adenosine and 2'-deoxyadenosine to inosine and 2'-deoxyinosine respectively". Adenosine deaminase

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converts a component which is toxic to lymphocytes i-e deoxyadenosine, to another molecule called deoxyinosine, which is not harmful to the body.[7] Breast carcinoma includes a chain of events that are very inflammatory.[8] Adenosine is a significant molecule that plays an important role in signaling. It employs prominent anti-inflammatory effects in tumorous conditions like prevention of tumor invasion in lymphoid cells. Amplified adenosine deaminase activity diminishes the protective molecule adenosine.[9] A study has shown the diagnostic value of ADA activity in malignant and benign breast tumor patients. According to that study the serum ADA activity in benign tumors was observed to be greater than the normal (noncancerous) breast tissues and it was highest among serum of patients with malignant tumors.[10]

To the best of our knowledge there is no study at national and local level regarding the relationship of serum ADA levels in breast cancer patients. This research will help us to determine the clinical significance of serum adenosine deaminase levels estimation in breast cancer patients. A study was planned to compare serum adenosine deaminase (ADA) levels in untreated and treated cases of breast cancer patients.

## Materials and Methods

It is an analytical, observational study carried out in the Department of Biochemistry, Islamic International Medical College in collaboration with Department of Surgery, Holy Family Hospital, Rawalpindi during a period of one year from April 2017 to March 2018. In this study ADA levels were measured in blood samples from patients and controls.

Approval from the ethical review committee of the institute was obtained. An informed written consent regarding participation in the study was taken from the patients. Total 150 subjects, who fulfilled the inclusion criteria, were included in the study. Convenient non probability sampling technique was adopted. Selection criteria for patients were both untreated and treated cases of breast cancer and selection criteria for controls were: healthy individual without having any malignancy and all the diseases in which serum ADA is raised i.e. tuberculosis, sarcoidosis, chronic obstructive pulmonary disease, HIV, chronic heart failure, psoriasis and rheumatoid arthritis. Out of 150 cases studied, 70 were controls and 80 were cases. Cases were further divided into two groups i.e. untreated cases which were 44 and treated cases which were 36. Treated cases included cases of breast cancer that had gone through any of these treatments: chemotherapy, radiotherapy, hormonal therapy and surgical excision.

Blood was drawn from peripheral veins, transferred to EDTA tube, gently mixed and made to stand upright. The blood samples were centrifuged at 2200 RPM for 10 minutes. The separated plasma was stored at -70°C till completion of sample collection. The invitro quantitative determination of Human ADA concentrations in serum were carried out by ELISA in accordance with the instructions given by manufacturer[11], in the research laboratory of Department of Biochemistry in Islamic international medical college. The data was entered into SPSS version 21 and analyzed. Descriptive data were given as mean ± standard deviation (SD). "Independent *t* test" was used and "p" values of less than 0.05 were considered statistically significant.

## Results

Out of 150 cases studied, 70 were controls and 80 were cases. Cases were further divided into two groups i.e. untreated which were 44 and treated which were 36. Among cases 45 individuals were < 50 years of age and 35 individuals were > 50 years of age. Whereas among controls, 47 individuals were < 50 years of age and 23 were > 50 years of age. Similarly premenopausal women were more in both cases and controls. Among breast cancer cases 59 individuals had sporadic disease whereas 21 had familial.

Mean serum ADA levels were compared among controls and untreated cases. It was found that mean serum ADA levels were high in untreated cases as compared to controls. This difference of mean serum ADA was found statistically significant with "p-value" 0.001.

Mean of serum ADA levels were also compared among controls and treated cases. It was found that serum ADA levels were slightly low in treated cases than the controls. This difference of mean serum ADA was found statistically not significant with "p-value" 0.087.

Mean of serum ADA levels were also compared among untreated and treated cases. It was found that serum ADA levels were markedly low in treated case as compared to untreated cases. This difference of mean serum ADA was found statistically very significant with "p-value" <0.0001. (Table I)

**Table I: Mean Adenosine Deaminase Activity (ADA) In Controls, Untreated and Treated Cases**

| Study Group | ADA levels (ng/ml) | p-value |
|---|---|---|
| Controls (n=70) | 14.92±3.73 | 0.001 |
| Untreated cases (n=44) | 17.75±4.17 | |
| Controls (n=70) | 14.92±3.73 | 0.087 |
| Treated cases (n=36) | 13.18±4.18 | |
| Untreated cases (n=44) | 17.75± 4.17 | <0.0001 |
| Treated cases (n=36) | 13.18± 4.18 | |

## Discussion

In the past few years, the interest has increased regarding the utilization of hormones, enzymes and antigens for diagnosis and prognosis of different tumors (i.e both benign and malignant). In addition to this, researchers are using hormones, enzymes and antigens as assessment tools for assessing the treatment response in patients. They have conducted experiments to assess and check the effect of different enzymes on breast cancer, and correlations between some of the enzyme activities in malignant cells and the carcinogenic processes are also explored.

Total serum ADA activity has been observed in patients with different types of tumors. Some studies suggest that increased ADA activity play an active role in the salvage pathway activity of neoplastic cells and tissues.[12,13] Whereas others are of the opinion that accelerated pyrimidine and purine metabolism in necrotic cells and tissue cause an increase of adenosine concentration, which in turn increase the activity of ADA through compensatory mechanism.[14,15]

Aghaei in 2005 reported that the total ADA activity in serum of breast cancer patients was significantly higher than healthy individuals.[16] Similarly increased activity of serum total ADA had been confirmed by "Mini Walia" and Archana Choudhari in breast cancer patients.[17,18] In present study we have found that mean serum ADA is significantly raised in patients of breast cancer as compare to healthy individuals (p = 0.001). Similar results were also documented by, Borzenko BG and Aghaei M.[19,20,10]

Walia.M in her study concluded that in breast cancer patients after mastectomy, serum ADA levels were decreased significantly.[17] Similarly Borzenko bg mentioned in his study that serum ADA was significantly changed after surgery.[20] In the present study we have found that ADA levels are significantly less in treated cases as compare to untreated cases of breast cancer with p= <0.0001.

There are few limitations of the study as well, which are mainly related to shorter duration of the study. The study parameters are reduced to complete the trial in stipulated time period, otherwise the information related to other diagnostic parameters and detailed clinical presentation could have been more informative.

This study may prove helpful in further research at molecular level like considering the role of ADA in predicting the successful breast cancer treatment, circulating miRNA and RNA expression of ADA gene in local tissue.

## Conclusion

Based on the current results, it is concluded that low serum ADA levels in treated cases as compare to untreated cases can be considered as a prognostic marker for breast cancer treatment and high serum ADA levels in breast cancer patients can prove a valuable marker for early detection and diagnosis of breast cancer along with other established markers. For this purpose a diagnostic accuracy study by comparing serum ADA with gold standard test for the diagnosis of carcinoma breast ie. Histopathological examination of breast tissue will be useful.

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