

# SERUM ADENOSINE DEAMINASE LEVELS AS AN INDEX OF TUMOR GROWTH IN HEAD AND NECK MALIGNANCY

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**ABSTRACT :** *This study was conducted on 40 biopsy proved patients of head and neck cancers. 85% of patients presented with squamous cell carcinoma in various grades of differentiation. When serum adenosine deaminase activity was compared between controls and cases, significant increase was found in the activities (control 51.54 ± 12.09 IU/L and cases 106.87 ± 29.75 IU/L). The duration of illness didn't reflect any statistical significance with the adenosine deaminase activity. It was 97.50 ± 62.93 IU/L in case where duration of illness was 98 ± 30.98 IU/L in patient with more than one year of disease. The lymph node showed stronger correlation with adenosine deaminase activity. Its level was 83.41 ± 1.41 IU/L in patients with N<sub>1</sub>. The rise in serum adenosine deaminase activity was found to be directly related to the stage I disease. It was 57.80 ± 4.60 IU/L in patient with stage I disease while in patients with stage IV had 135.87 ± 18.39 IU/L of activity. According to histological grading, highest level was found in patients having squamous cell carcinoma (113.41 ± 32.31 IU/L). The activity of adenosine deaminase decreases with radiotherapy and after surgery. This may help in assessing the decrease in tumour mass and improvement in patient's clinical condition.*

*Key Words : Serum Adenosine Deaminase; Head and Neck Malignancy.*

## INTRODUCTION

A fossil remains of a human jaw kept in the National History Department of the British Museum is perhaps the earliest example of cancer in man (Donaldson, 1967). As early as 600 B.C. carcinoma of the oral cavity was described by Sushrut. Though the disease 'Cancer' has been mentioned in some form or other in ancient literature, its frequency seems to be on an increase in the recent years. Carcinoma of head and neck is quite prevalent in our country due to high consumption of tobacco, lime and betel leaves either alone or in combination with smoking. Adenosine deaminase (ADA) catalyzes the catabolic reaction leading to formation of inosine and ammonia from adenosine. Its principal biological activity is present in T-lymphocytes. In patients with disease causing impairment of immune responses in lymphoproliferative, myeloproliferative and solid tumors, serum level of ADA decreases (Zimmer et al, 1975; Tung et al, 1976; Uberti et al, 1976). Level of ADA increases in infections like tuberculosis where immunity is cell mediated and during mitogenic and antigenic responses of lymphocytes. Raised level of enzyme have been found in tissue fluids in case of tuberculosis e.g. pleural, peritoneal, pericardial and

cerebrospinal fluids (Piras, 1978; Malan, 1984; Ocaña, 1986; Ribers, 1987; Sequera, 1989).

## OBJECTIVES

The present study was undertaken with a view to correlate the changes in adenosine deaminase enzyme activity in untreated patients of cancer of head and neck. An attempt was also made to correlate the changes in the enzyme activity with different types of growths, lymph node status, tumor status and different stages of the disease.

## MATERIAL AND METHODS

The present study was carried out on patients visiting the Department of ENT, Sir Sunder Lal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

### Selection of Patients

Following criterion were used for selection of the patients for the present study.

- Histopathologically proven head and neck malignancies without any definitive treatment for the malignant condition prior to visiting the department.
- Disease limited to the local site and regional lymphnodes

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and without distant metastasis.

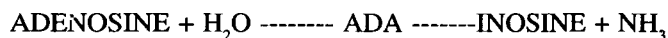
- On first visit a thorough assessment and complete ENT examination of each patient was done.

#### Estimation of Adenosine Deaminase Activity

Serum adenosine deaminase activity was estimated in 40 patients with head and neck malignancies in different stages. Serum from blood samples was separated into clean dry sterile vials, stored at  $-10^{\circ}\text{C}$  and assayed for activity. The samples were centrifuged at 3000 R.P.M. for 10 minutes and the supernatant was used for the assay.

#### Principle

Adenosine deaminase catalyzes the catabolism of adenosine into inosine and ammonia. The enzyme activity is inversely proportional to the degree of cell differentiation.



Adenosine at a wavelength of 265 nm shows characteristic absorption bond. The optical density of a given adenosine solution at this wavelength is directly proportional to the concentration of adenosine in the solution. Therefore the rate of disappearance of adenosine is taken as an index of ADA activity and is followed by the rate of decrease in optical density at 265 nm (Giutai, 1974).

#### OBSERVATIONS

In the present study, 40 patients of head and neck cancer were included alongwith 10 controls. The study was done in the Department of Otolaryngology, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The enzyme estimation was done at the Centre of Experimental Research and Surgery, Institute of Medical Sciences. Only histologically proven previously untreated cases of head and neck carcinoma, in different stages, were included in

**Table II**

**Histopathology Grading (HPG) and Serum (ADA) Activity in Patients with Head and Neck Malignancies.**

HPG	No of Cases	Serum ADA Activity	Range
Squamous Cell Carcinoma	17	41.00± 32.31	65-153
Moderately Differentiated Squamous Carcinoma	8	110.00±29.15	70-150
Poorly Differentiated Squamous Carcinoma	4	111.13± 29.75	55-108
Adenocystic Carcinoma	1	80	-
Large Cell Lymphoma	1	89	-
Well Differentiated Long Lymphoma	1	100	-
Occult Primary	2	147.00± 9.90	-

**Table I**

**Distribution of Cases According to the Site of Involvement**

Site	No of Cases	Percentage
Nose and Maxilloethamoidal complex	5	12.0
Oral Cavity	4	10.0
Nasopharynx	3	7.5
Oropharynx	10	25.0
Larynx and laryngopharynx	12	30.0
Lymphoma	2	5.0
Occult Primary	2	5.0
Others (parotid, External Ear)	2	5.0

this study. Average age in the present series was 49.6 years. The youngest patient was of 20 years while oldest patient was of 75 years. The ratio between males and females was 12 : 3. 33 patients belonged to rural area (92.5%) while only 7 patients (17.5%) belonged to urban area.

In the present study 67.5% presented with growth and swelling in the neck. Table I shows distribution of cases according to site of involvement. 50% cases were of proliferative type followed by ulcerative (25%) and infiltrative types (15%). Table II shows histopathology grading and serum ADA activity. The mean activity in controls below 40 years  $45.58 \pm 10.19$  IU/L while it was  $57.50 \pm 4.09 \pm$  IU/L in controls above 40 years of age, mean ADA activity was 99 while in patients above 40 years of age, it was 114.74 (Table - III).

Table IV shows serum ADA activity according to tumor status.

**Table III**  
**Serum Adenosine Deaminase Activity in Control and Patients of Carcinoma of Head and Neck**  
**(Mean  $\pm$  SD)**

Groups	Age (in years)	No. of Control Cases	Serum ADA Activity IU/L	Range IU/L
Control	A	5	45.58 $\pm$ 10.19	35-58
	B			
Case	A	13	99	55-140
	B	27	114.74	55-154

**Table IV**  
**Distribution of Serum ADA Activity according to Tumour Status in Patients with Head and Neck Malignancies**

Tumour Status	No. of Cases	Serum ADA Activity IU/L	Range IU/L
T <sub>x</sub>	2	147.00 $\pm$ 9.90	140-154
T <sub>1</sub>	13	102.92 $\pm$ 39.14	53-153
T <sub>2</sub>	10	94.90 $\pm$ 22.03	75-107
T <sub>3</sub>	13	120.77 $\pm$ 26.13	70-150
T <sub>4</sub>	1	145.00 $\pm$ 00.00	

## DISCUSSION

Adenosine deaminase is widely distributed in various tissues of the body. The main physiological activity of adenosine deaminase is found in T-lymphocytes and is related to lymphocytic differentiation and proliferation. Mitogenic and antigenic responses of lymphocytes increase its level (Hall, 1963). The significance of this enzyme is shown by its raised level of activity during rapid proliferation of cells under antigenic stimulation to prevent the accumulation of toxic metabolites (Baganha et al, 1990). In infection where cell mediated immunity is increased, its level also increases. It was suggested by Meda et al (1992) a strong suspicion of oral Non-Hodgkin's lymphoma is justified when adenosine deaminase activity in a biopsy specimen is greater than 1000 nmol/h/mg of protein. Different values of serum adenosine deaminase activity were found in patients of carcinoma breast from those suffering from mastopathies (Borzenco., 1991).

When serum activity was compared according to duration

of illness, direct correlation was observed between the increase in enzyme activity and the duration of illness. This indicates an increase in adenosine deaminase level was compared between tumors in different stages, it was found to be 147 $\pm$  9091 IU/L in case of T<sub>x</sub> and 145 in case of T<sub>4</sub>. Therefore it does not seem to be significant. When adenosine deaminase activity was compared in patients with no lymph node status to N<sub>3</sub> status, around two fold increase was found (83.41 $\pm$  26.50 IU/L). When compared with normals or controls, it was found to increase around three fold (control <40 year 45.58  $\pm$  10.19 IU/L and 40 years 57.50  $\pm$  4.09 IU/L).

According to TNM staging of cancer the patients were divided into 4 groups and increase in serum adenosine deaminase activity was directly proportional to advancement in stage of the cancer, the highest being in patients in stage IV (135.87  $\pm$  18.39 IU/L).

It was 57.80  $\pm$  4.60 IU/L in stage I. According to type of the lesion, highest adenosine deaminase activity was found

in ulcerative growths.

Serum adenosine deaminase levels have been shown to be raised nearly one to three fold in various types of cancer. The data in present study demonstrates that serum adenosine deaminase levels were increased by nearly 150% in patients with head and neck cancer, as compared to controls. Increased levels of serum adenosine deaminase activity in malignancy suggests altered adenosine metabolism. Ishii and Green (1973) reported that adenosine is toxic to cultured mammalian cells and interferes with pyrimidine biosynthesis.

In the present study the rise in serum adenosine deaminase activity was found to be directly related to the stage of the cancer indicating that the increase was directly proportional to the primary tumor mass. Sufirin et al, (1978) reported a significant association between an increase in lymphocyte adenosine deaminase activity and the stage of the tumor in patients of transitional cell carcinoma of the bladder. Increase in adenosine deaminase levels may be a result of leakage of the enzyme from the primary tumor cells or from lymphostatic metastases. On comparing the serum adenosine deaminase levels in relation to the type of the lesion, in patients with head and neck cancer, it was observed that rise in serum adenosine deaminase levels was greater in patients with ulcerative growths than in those with proliferative growths.

Various workers have reported that serum adenosine deaminase levels are significantly reduced in patients with lung carcinoma following surgery (Nishihara et al, 1970; Sufirin et al, 1970). Nishihara et al, (1970) reported that patients who were subjected to radiotherapy also exhibited a fall in serum adenosine deaminase activity. After the completion of radiotherapy the decrease in mean adenosine deaminase activity was nearly 85% and the decrease correlated well with a decrease in tumor mass and improvement in the patient's clinical condition.

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