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**Original Article**

# A Study to Assess Correlation of Adenosine Deaminase Activity with Different Predictors and Parameters of Diabetes and Obesity

Authors
**Vivek Sharma[1], Arun Mishra[2], Dr Neeraj Gour[3], Dr Poornima Dey Sarkar[4]**
[1]Demonstrator, Dept of Biochemistry, SHKM Govt Medical College, Nuh, Haryana
[2]Assistant Professor, Dept of Biochemistry, Modern Institute of Medical Sciences, Indore (MP)
[3]Associate Professor, Dept of Community Medicine, SHKM Govt Medical College, Nuh, Haryana
[4]Professor, Dept of Biochemistry, MGM Medical College, Indore
Corresponding Author
**Dr Neeraj Gour**
Associate Professor, Dept of Community Medicine, SHKM Govt Medical College, Nuh, Haryana
Email: *drneerajg04@gmail.com*, Mobile: 08199997935

**Abstract**
**Introduction:** *Obesity is a complex disorder that involves some degree of over-consumption[1] coupled with a metabolic derangement. As ADA has been putatively associated with inflammation, and adipose tissue inflammation is the hallmark of insulin resistance in obese T2DM patients. Our study attempted to evaluate the role of serum ADA in T2DM subjects.*
**Methods**: *This observational cross sectional study was conducted in the Department of Biochemistry at MGM Medical College and MY Hospital. All the patients and controls were clinically examined and routine biochemical tests were analyzed for all subjects.*
**Result**: *Correlations of ADA with different predictors of obesity and diabetes were calculated. ADA was found to be positively correlated with FBS, HBA1C, Insulin, Leptin and HOMA IR whereas negative correlation was found between ADA and Adiponectin.*
**Conclusion:** *This is very much evident through this study that ADA may be treated as prognostic predictor of diabetes either linked to obesity or not.*
**Keywords**: *ADA; Diabetes; Obesity.*

## Introduction

Obesity is a complex disorder that involves some degree of over-consumption[1] coupled with a metabolic derangement. Adipose tissue previously was considered a passive storage depot for fat but is now known to play an active role in metabolism[2]In India, the second most populous country in the world and where under-nutrition has been the major public health concern over the past several decades, little attention has been paid to obesity until recently.

The intimate relationship between diabetes and obesity has given rise to the term "diabesity" to characterize the close association of these two disorders [3] and one study showed that overweight/obesity and central obesity were

significantly associated with diabetes [4] In India, the prevalence of diabetes is expected to increase from 31.7 million in2000 to 79.4 million in 2030[5]. Adenosine deaminase (ADA) is a polymorphic enzyme which is present in all mammalian tissue[6]. ADA catalyses the irreversible deamination of adenosine to inosine contributing to the regulation of intracellular and extracellular concentration of adenosine and is suggested to be an important enzyme for modulation of insulin bioactivity[7]. The physiological function of ADA is crucial in regulating the steady state concentrations of adenosine in a variety of systems, especially immunology, neurological and cardiovascular systems. As ADA has been putatively associated with inflammation, and adipose tissue inflammation is the hallmark of insulin resistance in obese T2DM patients, the serum level of ADA in T2DM is ill-defined. Our study attempted to evaluate the role of serum ADA in T2DM subjects with following objectives:

1. To determine serum adenosine deaminase level in obese subjects and compare it with normal.
2. To correlate adenosine deaminase levels with parameters of diabetes and obesity in the above subjects.

## Material & Methods

### Study Design

This observational cross sectional study was conducted in the Department of Biochemistry at MGM Medical College and MY Hospital.

### Study sample

Cases were divided into three groups namely, Group 1: normal, healthy adults as control group, Group 2: obese subjects, without diabetes, Group 3: obese subjects, with diabetes. 100 cases were selected in each group.

### Sampling technique

Convenient sampling method has been adopted for the recruitment of subjects.

### Data collection

The obese diabetic subjects and obese non diabetic subjects were taken from the outpatient department of Endocrinology, MGM Medical College and MY Hospital while the control subjects were recruited from the subjects coming to the department for a routine health check-up. A written informed consent from the patient and control was obtained after complete explanation of the study. All the patients and controls were clinically examined and routine biochemical tests were analyzed for all subjects prior to selection. The BMI and other anthropometric measurement of all subjects were done. The patients on insulin treatment, obesity, hypertension, ischemic heart disease, neurological disorders, renal failure, chronic liver disease, cancer, and immunological disorders were excluded from this study. The study was approved by the institutional ethics committee.

### Biochemical Assays

3 mL venous blood samples were obtained from the patients as well as controls after 8–10 hours of fasting. All the routine biochemical parameters were analyzed by automated clinical analyzers (Roch P 800 and ELISA). The serum ADA level was measured using a spectrophotometer based on the method by Giusti and Galanti. ADA activity is described as U/L.

### Statistical analysis

Appropriate statistical test were applied for the statistical analysis of data. ANOVA has been applied to assess the variance and correlation coefficients have been calculated to find out correlation between two quantitative variables. Significance level has been set as $P < 0.05$ with 95 % confidence level.

## Results

This study was conducted in the Department of Biochemistry at MGM Medical College and MY Hospital.

Among all three groups maximum males (81%) were in control group whereas majority of females were in other obesity with (33%) and without diabetes (37%) groups.(Table 1)

Mean age of controls was 56.91 years where as mean age in the group of subjects with Obesity

with diabetes was 40.91 years and with Obesity without diabetes was 48.10 years. (Table 2)

Mean BMI of controls was 23.26. Mean BMI in the group of subjects with Obesity with diabetes was 32.43 and of subjects with Obesity without diabetes were 32.06. (Table 3)

Measurement of ADA was done among all three groups and it was maximum among subjects having obesity with diabetes (Mean- 22.71) followed by people having obesity without diabetes (Mean -21.79). (ANOVA F value : 47.14, P< 0.005). (Table 4)

Correlations of ADA with different predictors of obesity and diabetes were calculated. ADA was found to be positively correlated with FBS, HBA1C, Insulin, Leptin and HOMA IR whereas negative correlation was found between ADA and Adiponectin. (Table 5)

**Table 1** Distribution of subjects on the basis of gender

| Groups | Male | | Female | |
|---|---|---|---|---|
| | Number | % | Number | % |
| Controls (n=100) | 81 | 81 | 19 | 19 |
| Obesity with diabetes (n=100) | 67 | 67 | 33 | 33 |
| Obesity without diabetes (n=100) | 63 | 63 | 37 | 37 |

**Table 2:** Distribution of subjects on the basis of age

| Groups | Age(Years) Mean+SD |
|---|---|
| Controls (n=100) | 56.91+9.37 |
| Obesity with diabetes (n=100) | 40.91+8.34 |
| Obesity without diabetes (n=100) | 48.10+10.71 |

**Table 3** Distribution of subjects on the basis of body mass index (BMI)

| Parameters | Controls | Obesity with diabetes | Obesity without diabetes |
|---|---|---|---|
| | (n=100) | (n=100) | (n=100) |
| | Mean+SD | Mean+SD | Mean+SD |
| BMI $Kg/m^2$ | 23.26±3.60 | 32.43±2.27 | 32.06±2.59 |

**Table 4 :** Comparison of ADA in Controls, Obesity with diabetes and Obesity without diabetes

| Parameters | Controls | Obesity with diabetes | Obesity without diabetes |
|---|---|---|---|
| | (n=100) | (n=100) | (n=100) |
| | Mean+SD | Mean+SD | Mean+SD |
| ADA (IU/L) | 17.40±1.97 | 22.71±4.66 | 21.79±5.05 |

ANOVA F value : 47.14, ( P< 0.005)

**Table no- 05:** Correlations of ADA with different predictor of obesity and diabetes

| | | FBS | HBA1C | INSULIN | LEPTIN | ADIPONECTIN | HOMA IR |
|---|---|---|---|---|---|---|---|
| ADA | Pearson Correlation | .290 | .226 | .260 | .336 | -.118 | .327 |
| | P value | .000 | .000 | .005 | .005 | .041 | .005 |
| | N | 300 | 300 | 300 | 300 | 300 | 300 |

## Discussion

The study was conducted in the Department of Biochemistry at MGM Medical College and MY Hospital. Volunteer patients diagnosed with mentioned disorder were selected for the study. Complete care was taken in protecting the anonymity of patients and the privacy of patient medical records. Administration of any

drug/medication or any surgical procedure to the patients was not involved in the study, only analysis was done. The samples were collected by standard procedures under aseptic conditions. Standard procedures were followed for the preservation and storage of samples before analysis. There is a global obesity pandemic. However, the prevalence of overweight and obesity among men and women varies greatly within and between countries, and overall, more women are obese than men. These gender disparities in overweight and obesity are exacerbated among women in developing countries, particularly in the Middle East and North Africa. Yet, in developed countries, more men are overweight than women[8]In our study Healthy subjects (controls) 81 cases are of males which were maximum in comparison of any group, 67 males subjects were in obesity with diabetes and 63 males were there in obesity without diabetes which is minimum in comparison to any group. Elderly obesity worldwide has become a growing public-health concern in developed countries with aging populations. The global epidemic of elderly obesity could be a major risk factor not only for resurgent chronic diseases, such as hypertension, cardiovascular disease, or diabetes, but also for impairing one's quality of life.[9]In our study Mean age of controls, diabetes with obesity and without obesity was 56.91 years, 40.91 years and 48.10 years respectively. Body weight, body mass index (BMI), waist and hip circumferences, waist/hip ratio (WHR), triceps and subscapular skinfolds were all positively predictive of NIDDM independent of age and sex.[10] In our study Mean BMI of controls,diabetes with obesity and without obesity was23.26 , 32.43 and 32.06 respectively. The body mass index (BMI) of subjects was calculated and adenosine deaminase activity was determined in their fasting blood sample. Serum adenosine deaminase activity was significantly increased in overweight and obese subjects and as well as in combined overweight and obese group as compared to control ($P < 0.0001$).[11] our study also reported conforming findings i.e. ADA level was far more higher among obese and diabetic patients than normal so ADA measurement can become early predictor of Insulin resistance and in turn for diabetes linked with obesity either.

We investigated the relationship between adenosine deaminase with BMI and FBS and found that adenosine deaminase level has a positive correlation with BMI and FBS ($P < 0.0001$).We also investigated the relationship between adenosine deaminase with insulin resistance (Homa IR) and found that adenosine deaminase level has a positive correlation with insulin resistance. As level of level of adenosine deaminase increases the insulin resistance also increases ($P < 0.0001$). we measured ADA activity in serum of obese subjects and found that ADA activity was significantly increased in obese subjects compare to control and the increase is proportional to increase in BMI ($P<0.0001$).

Our study supports this mechanism as ADA is increased in obese subjects and the increase is directly proportional to the increase in BMI. By inactivating extracellular adenosine which is spontaneously released by adipocytes, ADA impairs the insulin sensitivity for glucose transport[12] Although adenosine is endogenous anti-inflammatory agent and may limit cytokine production, various studies have proved that production of TNF-α is increased in obesity[13] It has also been proved that inhibition of re-phosphorylation of adenosine by adenosine kinase[14] or its degradation by ADA[15] improves survival from sepsis in various models. It has already been proven that ADA is increased in patients with diabetes mellitus[16] Hence we state that an increase in ADA activity is more than expected and insulin resistance develops in obesity and these obese persons then progress to develop NIDDM and with the background of a country like India, where people are more prone to diabetes[17], drugs used in the treatment of inflammatory disease such as adenosine kinase inhibitors[18] methotrexate sulfasalazine or aspirin[19] which exert their beneficial effects by releasing

adenosine should be given to overweight and obese persons.

**Conclusion**

This is very much evident through this study that ADA may be treated as prognostic predictor of diabetes either linked to obesity or not, though more studies are warranted in same direction to make this finding conclusive and acceptable biochemical evidence.

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**Conflict of interest**: None

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