Assess the role of serum adenosine deaminase as a glycaemic status indicator, among patients with type 2 Diabetes in a tertiary care centre, Telangana state

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Abstract

Introduction: Most common and many people around world and in India are vulnerable to diabetes mellitus and in this diabetes the commonest is type 2 diabetes mellitus and it is a metabolic disorder which is characterized by high blood glucose levels. Metabolic disorders mainly relay upon enzymes and their functions or dysfunctions, one among that enzyme is Adenosine Deaminase (ADA). The ADA is an enzyme which catalyses the irreversible deamination of adenosine to inosine. Adenosine is known to exert potent metabolic effects acting through its receptors. Increased levels of serum ADA has been shown in individuals with type 2 diabetes mellitus. This study aims to understand the relationship between serum ADA and blood glucose levels.

Methodology: Hospital based observational study, which was conducted at RVM Hospital, Siddipet district, Telangana state. It involved 50 cases of uncomplicated type 2 diabetes mellitus and 50 controls. Study was conducted after obtaining an informed written consent from cases and controls.

Results: It is observed that there is gross elevation of serum ADA in diabetic subjects as compared to controls and moreover a positive correlation was found between serum ADA and blood glucose levels.

Conclusion: This study shows ADA level is significantly related to the glycaemic status in type 2 diabetes mellitus. This study highlights the importance of this metabolite and the need for further studies.

Keywords: Adenosine deaminase, adenosine, type 2 diabetes mellitus, glycaemic status

Introduction

The prevalence of type 2 diabetes mellitus and obesity is increasing rapidly. In 2020, 463 million people have diabetes worldwide, by 2045 the estimated prevalence of diabetes is 700 million people (World Health Organization; WHO). Regarding overweight and obesity, 1.9 billion adults were overweight and over 650 million were obese in 2016, and the WHO estimates that approximately 2.7 billion people will be overweight and over one billion will be effected with obesity by 2025. Obesity is associated with increased risk of type 2 diabetes, cardiovascular diseases, respiratory failure and renal dysfunction, cancer [1]. Type 2 Diabetes Mellitus has two hallmark features: 1) insulin resistance, defined here as an impaired ability of the hormone to suppress hepatic glucose output and to promote peripheral glucose disposal and 2) dys- function of the pancreatic β-cell such that insulin secretion is insufficient to match the degree of insulin resistance [2]. In addition to hyperglycaemia, the type 2 diabetic individual almost invariably manifests a serious breakdown in lipid dynamics, often reflected by elevated levels of circulating free fatty acids (FFAs) and triglycerides (TG). Adenosine deaminase (ADA) is an enzyme involved in the metabolism of purine nucleosides, catalyses the irreversible hydrolytic deamination of adenosine (Ado) and 2’-deoxyadenosine (2’-dAdo) to inosine and 2’-deoxynosine, respectively. Adenosine is an anti-lipolytic factor and lowers free fatty acid levels. Several studies have demonstrated elevated levels of adenosine deaminase in individuals with type 2 diabetes mellitus, but the exact pathogenic role of elevated ADA activity in type 2 DM remains to be elucidated. Insulin administration has been shown to reduce the elevated ADA levels in type 2 diabetes [3]. Adenosine Deaminase exerts its effects predominantly by regulating the concentration of intracellular and extracellular adenosine. Conditions which lead to elevated adenosine formation and release (e.g. hypoxia) have been shown to increase the expression of ADA [4].

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The objectives of this study is to estimate the value of serum adenosine deaminase (ADA) in patients with uncomplicated type 2 diabetes mellitus and to know if any correlation exists between serum ADA and blood glucose values.

**Methodology**
Hospital-based, cross sectional study conducted at RVM Hospital from June 2019 to June 2020. Total number of study participants are 100 out of which 50 are case of type 2 diabetic patients without complications and 50 healthy matched controls in relation with age and sex. Inclusion Criteria: Individuals with uncomplicated type 2 diabetes mellitus including both male and female, of age group 30-80 years were included in the study. Exclusion Criteria: Individuals with diabetic complications like vascular / neuropathy / retinopathy / nephropathy etc. hypertension / acute or chronic infection / addictions / pregnancy were excluded from the study. Prior to the study institutional ethical committee acceptance and clearance was taken. A thorough clinical examination and appropriate investigations were done before selecting the cases and controls for the study. Pre-structured and pre-tested questionnaire was used to collect the data. Informed consent was taken from all cases and controls. For all the study participants standing height and weight were measured. BMI was calculated as per the formula: Weight (Kg)/Height (meters)^2. Statistical Data & Analysis: The variables are spread over excel and based on the observations the results are represented in the form of tables and graphs wherever necessary - t-test and Chi-Square tests are used for finding out the significance between any two variables where required. SPSS version 21.0 is used for analysis of data.

**Results**

**Table 1:** Showing age distribution among the study participants (Cases & Controls)

| S. No | Age (Years) | Cases | | | Controls | | |
|---|---|---|---|---|---|---|---|
| 1 | 30-40 | 03 (06) | | | 03 (06) | |
| 2 | 41-50 | 20 (40) | | | 24 (48) | |
| 3 | 51-60 | 12 (24) | | | 11 (22) | |
| 4 | 61-70 | 09 (18) | | | 08 (16) | |
| 5 | 71-80 | 06 (12) | | | 04 (08) | |
| Total | | 50 | 100 | | 50 | 100 |
| Mean+ SD | | 58.10 + 06.44 | | | 56.84 + 05.60 | |

**Table 2:** Showing gender distribution among the study participants

| S. No | Gender | Cases | | | Controls | | |
|---|---|---|---|---|---|---|---|
| 1 | Male | 29 (58) | | | 29 (58) | |
| 2 | Female | 21 (42) | | | 21 (42) | |
| Total | | 50 | 100 | | 50 | 100 |

**Table 3:** Mean and SD of BMI in male and female cases and controls among study participants

| Variable | Cases | | | | Controls | | |
|---|---|---|---|---|---|---|---|
| | Male | Female | P-Value | Male | Female | P-Value |
| BMI | 22.34 + 2.98 | 23.02 + 2.46 | 0.796 | 23.11 + 2.81 | 24.22 + 2.69 | 0.762 |

Observed results are not statistically in significant

**Table 4:** Blood Glucose levels in cases and controls among study participants

| S. No | Sugar Parameters | Cases | | | Controls | | |
|---|---|---|---|---|---|---|---|
| 1 | FBS (mg/dl) | 175.47 + 74.66 | | | 86.12 + 8.71 | < .0011** |
| 2 | PPBS (mg/dl) | 225.26 + 94.60 | | | 112.58 + 9.69 | < .0023** |

Observed results are statistically significant

**Table 5:** Comparison of ADA (U/L) in control and cases among the study participants

| S. No | Cases (ADA (u/L) | Controls ADA (u/L) | P-Value |
|---|---|---|---|
| 1 | 40.60 + 8.65 | 19.75 + 2.65 | < .00036** |

Observed results are statistically significant

**Table 6:** Mac-Pearson correlation of blood glucose with ADA in controls and cases

| S. No | Correlation | Cases | | | Controls | | |
|---|---|---|---|---|---|---|---|
| | R value | P value | R value | P value |
| 1 | FBS vs ADA | 0.889 | <0.0016 | 0.712 | <0.0012 |
| 2 | PPBS vs ADA | 0.791 | <0.0011 | 0.844 | <0.0018 |

Observed results are statistically significant
Table 7: Correlation between ADA and HbA1c

| S. No | Variable | Mean ± SD | Correlation/P-Value |
|-------|----------|-----------|---------------------|
| 1     | ADA      | 32.47±11.68 | 0.81                |
| 2     | HbA1C    | 7.24 ± 3.02  | < 0.0001            |

Observed results are statistically significant.

Table 8: Showing Correlation of Age, BMI, and duration DM with ADA among study participants

| S. No | Correlation | Controls | Cases |
|-------|-------------|----------|-------|
|       | R value | P value | R value | P value |
| 1     | Age vs ADA | 0.181 | 0.39 | 0.159 | 0.49 |
| 2     | BMI vs ADA | 0.022 | 0.75 | -0.314 | 0.11 |
| 3     | Duration of DM vs ADA | - | - | -0.221 | 0.252 |

Discussion

The present study found an elevated serum Adenosine Deaminase (ADA) activity in cases of Type 2 Diabetes Mellitus when compared to age and sex matched controls. This is a common observation in several studies. A strong correlation was found between the blood glucose values and serum ADA level. In this present study there is a strong statistical association between the long term index of glycaemic control viz. Glycated haemoglobin (HbA1c) and serum ADA. This finding is also similar with some previous studies which show a significant correlation of serum ADA with HbA1c. The correlation of serum ADA values with age, BMI, and duration of diabetes was found to be insignificant. In the present study the mean age of study group is 58.10 ± 06.44 and in the control group is 56.84 ± 05.60. Anjali C et al. [5] mean age of study group was 53.25±8.39 and control group was 51.5±6.86. Mustafa Araz et al. [6] mean age of study group was 54.52±10.66 and control group was 52.42±5.79. The Mean age of present study is near with similar with these two studies. In the present study the mean FBS in study group is 75.47 ± 74.66 and in the control group is 86.12 ± 8.71. et al. Mustafa Araz the mean FBS of study group was 167.4±60.3 (<0.001) and in the control group was 80.9±8.55, this observation is similar to the present study and the mean FBS is slightly higher when compared with Anjali C et al. where the mean FBS of study group was (149.6±12.78) (<0.0001), Shiva Prakash M et al. [7] the mean FBS of study group was (146.8±16.2) (<0.001), Gorden M et al. [8] the mean FBS of study group was (156.7±10.3) (<0.0001), Sarah de Ferranti et al. [9] the mean FBS of study group was (129.32±21.10) (<0.01). In the present study the mean BMI in study group is 22.34 ± 2.98 and in the control group is 23.11±2.81 which near similar to the studies reported by Mustafa Araz et al. the mean BMI in study group was 23.68±2.9 and control group was 24.53±3.2, Shiva Prakash M et al. the mean BMI in study group was 22.47±1.79 and control group was 24.15±1.47. In the present study the mean HbA1c of study group is 7.56±3.68 and in the control group is 4.67 ± 0.63. et al. the mean HbA1c of study group was 7.88±1.08 (<0.001) and in the control group was 4.82±0.43, Anjali C et al. the mean HbA1c of study group was 10.47±1.48 (<0.001) and in the control group was 5.12±0.39, Sarah de Ferranti et al. the mean HbA1c of study group was 8.21±1.12 (<0.001) and in the control group was 4.98±0.56, the reported results are similar with the present study. In the present study the mean ADA in study group is 39.77±10.88 and in the control group is 18.95±3.53, Sarah de Ferranti et al. the mean ADA in study group was 40.79±18.12 (<0.01) and in the control group was 19.94±7.89, Anjali C et al. the mean ADA in study group was 32.77±7.36 (<0.001) and in the control group was 15.06±1.21, Mustafa Araz et al. the mean ADA in study group was 37.24±5.0 (<0.001) and in the control group was 18.2±5.6 and in Naciye Kurtul et al. [10] the mean ADA in study group was 22.44±7.420 (<0.0001) and in the control group was 14.0±7.66 all this results are correlating with this study results.

Conclusion

Serum levels of ADA were found to be significantly higher in type 2 diabetics when compared to controls. A strong correlation was found between serum ADA and blood glucose values. Statistical association was found between serum ADA and the long term index of glycaemic control, HbA1c. Body Mass Index, Age, Sex, duration of diabetes was not found to be an influencing factors on the ADA levels. The above findings show that serum Adenosine Deaminase reflects the current glycaemic status in the diabetic individual, indicating involvement of the enzyme Adenosine, in the type 2 diabetes.

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