Research Article

Serum Adenosine Deaminase in patients with Type-2 Diabetes Mellitus and its Relation with Blood Glucose and Glycated Haemoglobin levels

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Abstract

Background: Diabetes mellitus is a metabolic characterized by deficiency of insulin and insulin resistance. Adenosine deaminase (ADA) catalyzes the deamination of adenosine and modulates the bioactivity of insulin and Adenosine receptors has been reported to stimulate glucogenesis and gluconeogenesis. But its role in Type 2 diabetes mellitus is not yet characterized.

Aim & Objectives: The present study aimed to evaluate the serum Adenosine Deaminase level and to correlate ADA levels with Blood Glucose and Glycated hemoglobin levels in Type-2 Diabetes Mellitus patients.

Material and Method: The study populations of 120 patients were divided into 3 groups: Group A which consisted of 40 normal healthy individuals without any complication or history of Diabetes. Group B included 40 patients of Type 2 Diabetes Mellitus both with HbA1c < 7%. Group C consisted of 40 patients of Type 2 Diabetes Mellitus with HbA1c >7% (n=40). Fasting blood sugar, HbA1c, ADA, and body mass Index were estimated in all the subjects under study.

Results: The study showed that mean Fasting Blood Sugar, Post prandial Blood sugar and HbA1c concentration was significantly higher in Group C & Group B compared to Group A. Compared with the well-controlled Type-2 Diabetes Mellitus patients (HbA1c < 7%), the poorly controlled group (HbA1c > 7%) showed significantly increased ADA activity (49.79± 18.12 U/L vs. 90.10± 32.75; P<0.001). The correlation between Adenosine Deaminase and HbA1c was positive and significant in both Group B (r = 0.389; p= 0.007) and Group C (r = 0.430; p<0.001).

Conclusion: Serum ADA levels increase with increase in FBS and glycated haemoglobin levels which may have an important role in determining the glycemic status in Diabetics. A positive correlation between ADA level with short and long term glycemic control suggest its important role in glucose and lipid metabolic derangements seen in Type 2 Diabetes Mellitus patients.

Keywords: Adenosine Deaminase, Glycated Hemoglobin, Hyperglycemia, Type-2 Diabetes Mellitus

1. Introduction

The prevalence of diabetes is rapidly rising at an alarming rate all over the world. Over the past 30 years, the status of diabetes has changed from being mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. The rise in prevalence is seen in all six inhabited continents of the globe. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025.1 It is a common endocrinological disorder characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism.2 Chronic Hyperglycemia in diabetes causes long-term damage, dysfunction, and failure of various organs specially the eyes, kidneys, nerves, heart and blood vessels. Type-2 diabetes is characterised by insulin resistance where there is impaired ability of hormone to suppress hepatic glucose output and to promote peripheral glucose disposal and compromised function of pancreatic β-cells such that insulin secretion is insufficient to match the degree of insulin resistance.3 The main physiological abnormalities associated with Diabetes Mellitus Type-2 is insulin resistance and impaired secretion of insulin . Also Immunological disturbances such as the cell mediated immune system and improper T-lymphocyte function play a role in the pathophysiology of T2DM.3

Adenosine Deaminase (ADA), catalyses the irreversible deamination of adenosine to inosine and 2‘-deoxyadenosine to 2‘-deoxyinosine. Adenosine increases glucose uptake inside the cells. Thus, higher ADA activity will decrease adenosine levels and this inturn decreases glucose uptake into cells. Thus, a suppression of ADA activity may help improve various factors associated with the pathophysiology of T2DM like insulin sensitivity and inflammation, cell proliferation and T-lymphocyte activity.4 Moreover chronic hyperglycemia leads to increased oxidative stress by forming enediol radicals and superoxide ions by NADPH oxidase system and increases ADA levels, both leading to insulin resistance.5 Various reports showing an increase in ADA activity in T2DM patients has been reported. The mechanism that increases serum ADA activity is not well known, but it is assumed that with higher ADA activity in insulin-sensitive tissues, the level of adenosine, which increases glucose uptake into cells, will be reduced. If activity of ADA is suppressed, insulin sensitivity may be improved, and cellular proliferation, inflammation and T-cell activity which are associated with the pathophysiology of insulin resistance, can also be improved. Thus insulin resistance may have an important relationship with ADA activity.3

There are reports available on Serum Adenosine Deaminase levels in patients of Type 2 diabetes mellitus but they are still inconclusive. Since a relationship exists between Adenosine Deaminase, cell mediated immunity and Type-2 Diabetes Mellitus, the present study was undertaken to determine Serum Adenosine Deaminase levels in patients with Type 2 diabetes mellitus and to find correlation between blood glucose and Glycated Hemoglobin levels.
2. Materials and Methods

The present study included 80 patients with Type-2 Diabetes Mellitus. The age group of patients was between 35-65 years of either sex and were on oral hypoglycemic drugs, attending the outpatient department of Dhiraj General Hospital, Sumandeep Vidyapeeth University, Piparia, Waghodiya. Ethical clearance was obtained from the institutional ethics committee. Informed consent was taken from Study subjects and they agreed to participate in the study.

2.1 Study Population

A group of 40 age and sex-matched normal healthy individuals served as Controls (Group A). Eighty Type-2 Diabetes Mellitus patients were further divided into Group B (HbA1c <7%, n=40) and Group C (HbA1c >7%, n=40) on the basis of HbA1c levels. The subjects were selected based on the following inclusion and exclusion criteria.

2.1.1 Inclusion Criteria:

Patients with diagnosed with Type-2 Diabetes mellitus not in the age group 30–60 years, both sexes, either freshly diagnosed or on treatment with the oral anti-hyperglycemic agent metformin (biguanides).

2.1.2 Exclusion criteria:

Subjects on insulin treatment, on drugs like sulfonflyureas, thiazolidinediones, glucocorticoids, thyroid hormones, thiazides, diazoxides, pentamidine, phenytoin, a interferons or having a history suggestive of any infections, known complications of diabetes mellitus, liver disease, immunological disorders, trauma or malignancy.

Clinical examination of subjects was done and their serum blood sugar, serum adenosine deaminase and glycated haemoglobin were estimated. Fasting & post-prandial blood sugar estimation was done by GOD-POD Method on Erba EM-200 fully automated Analyser. Gycosylated haemoglobin (HbA1c) estimation by on Mispa-1 nephelometer. Serum ADA levels estimation was done by a commercially supplied kit (Tulip Diagnostics (P) Ltd, Verna Goa, India). The assay was based on the colorimetric method described by Guisti and Galanti. Lipid profile was done on fully automated Erba EM-200 fully automated analyser. BMI For the assessment of BMI, height, and weight measurements were taken. BMI was calculated by Body Mass Index formula - BMI = weight (kg) / Height (m²).

2.2 Statistical Analysis

The data were collected, recorded and analyzed statistically to determine the significance of different parameters by using Med-Calc v11.5.0. Statistical analysis of various parameters was performed by Students’ t-test. All variables were expressed as mean ± SD (standard deviation). Pearson’s correlation coefficient was used to find out the correlation between two variables. A P- value of < 0.05 was considered as statistically significant.

3. Results

The mean age of Group A, Group B and Group C was 50.10 ± 9.25 yrs, 51.09 ± 11.01 yrs and 50.25 ± 12.15 yrs and they were age matched. Out of 40 subjects in Group A, there were 21 (52.5 %) males and 19 females (47.5 %), in Group B there were 23 males (57.5 %) and 17 males (42.5 %) out of 40 and in group C there were 22 males (55.05 %) and 18 females (45 %) and they were sex matched. Subjects with poor glycemic control (Group C) had higher BMI than those with good glycemic control (Group B) & control Group A (BMI 27.67± 3.4 kg/m² respectively). In the present study, it was found that the mean serum ADA levels were significantly higher in both Group B and Group C as compared to Group A (p <0.001). Also there was significant difference between FBS & PP2BS levels between subjects with poor glycemic than subjects with good glycemic control (p <0.001). It was further observed that the mean HbA1c levels in Group A were 4.98±0.56, in Group B were 6.40 ± 0.35 and the corresponding values among Group C were 8.21 ± 1.12. It was observed that there was significant difference in the levels of HbA1c between Group A and Group B (p <0.001) & Group B & C (p <0.001).

In the present study, the levels of FBS, PP2BS, HbA1c and ADA levels were increased in patients with Type-2 Diabetes Mellitus (Group B & group C) than control group. The mean FBS and PP2BS levels was found to be significantly higher in of Group B and Group C than Group A (p <0.001). Also there was significant difference between FBS & PP2BS levels between subjects with poor glycemic than subjects with good glycemic control (p <0.001). It was further observed that the mean HbA1c levels in Group A were 4.98±0.56, in Group B were 6.40 ± 0.35 and the corresponding values among Group C were 8.21 ± 1.12. It was observed that there was significant difference in the levels of HbA1c between Group A and Group B (p <0.001) & Group B & C (p <0.001).

In the present study, it was found that the mean serum ADA levels were significantly higher in both Group B and Group C as compared to Group A (p <0.001). Also the mean ADA serum levels of subjects with poor glycemic control were significantly higher than subjects with good glycemic control. (p<0.001). The correlation coefficient showing the relationship between serum ADA, FBS, PP2BS & HbA1c levels showed positive correlation between ADA, FBS & PP2BS levels in Group B & Group C while no significant correlation was observed between ADA, FBS, PP2BS & HbA1c levels in Group A. (Table 2).

4. Discussion

Diabetes mellitus is a common endocrine metabolic disorder and is a leading cause of death worldwide. It is characterized by hyperglycemia resulting from a variable interaction of hereditary and environmental factors and is due to the combination of insulin resistance. Diabetes Mellitus is a chronic metabolic disorder and it has long term complications which could have devastating consequences. In the present study, the mean serum ADA levels of group C were significantly higher than group B (P<0.001). Also, the levels of ADA were significantly higher in both groups B and C than Group A (P<0.001). Similar results were reported by and Kaur et al. & Kurtal et al. The pathogenesis of...
increased ADA levels in Type 2 DM is explained by extra cellular CAMP – adenosine pathway. ADA inactivates adenosine and enhances lipolysis. It also potentiates increase in CAMP accumulation. In the deficiency of insulin postprandial lipids and glucose circulate through blood and are taken up by Pancreas, to liver and adipose tissue. The adipocytes stores TAG leading to adipocyte hypertrophy. The exposure leads to cellular dysfunction, increased circulating FFA and a proinflammatory state. Exposure of Hepatocytes to excess fats and glucose leads to steatohepatitis and Insulin resistance. Thus, there is elevation of free fatty acids in diabetes which leads to worsening of IR and β-cell dysfunction.12,13 Chronic Hyperglycemia leads to increased oxidative stress by forming enediol radical and super oxide ions with NADPH oxidase system and increases ADA levels both leading to Insulin resistance. GLUT4 receptors are down regulated in the absence of adenosine. This is one of the reasons for Insulin resistance.5

The correlation between serum ADA and HbA1c levels in Group B & Group C showed that there is positive correlation between HbA1c and ADA and this shows with the increase in glycated haemoglobin levels, levels of serum ADA also increases. This positive correlation between ADA level with short and long term glycemic control suggest its important role in glucose and lipid metabolic derangements seen in type 2 DM patients. This finding was similar with the study done by Kurtul et al.11, Ramani et al.5 & Singh et al.5 However, this study has a few limitations. A concomitant lymphocytic/plasma adenosine deaminase and its activity on insulin or vice versa, and a correlation with oral glucose tolerance test (OGTT) are to be carried out to strengthen this concept. Further studies on ADA activity in lymphocytes are required to consider ADA as an effective prognostic and pathological marker in type 2 diabetes mellitus.

5. Conclusion

In conclusion, the study showed that with an increase in blood glucose & HbA1c levels, serum ADA levels also increases and this may play an important role in determining the glycemic status in patients with Type-2 diabetes Mellitus. Elevated adenosine deaminase activity may be an important indicator in the immuno-pathogenesis of type 2 diabetes mellitus. This suggests that ADA plays a role in the pathophysiology of type 2 DM and its complications. Further studies are required to support these facts.

References