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Research article

ADENOSINE DEAMINASE ACTIVITY AND INSULIN IN TYPE 2 DIABETES MELLITUS: DOES ADENOSINE DEAMINASE AFFECTS INSULIN LEVEL?

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ABSTRACT

Aim: Correlation between Adenosine Deaminase activity and Insulin level in patients with Type 2 Diabetes Mellitus. **Material & Method:** We measured the serum level of Adenosine Deaminase (ADA), Insulin and Fasting Plasma Glucose (FPG) in 50 patients with type 2 diabetes and 50 healthy controls. Subjects included in study were known diabetics for 5 years or more. **Results**: The levels of Serum Adenosine Deaminase and Insulin were highly significant ($p<0.001$) in study group in comparison to control group. Adenosine Deaminase was positively correlated with Fasting Plasma Glucose ($r=0.6146$, $p<0.001$) and Insulin ($r=0.3022$, $p<0.05$) in diabetic patients. Insulin was positively correlated with Fasting Plasma Glucose ($r=0.4728$, $p<0.001$) in diabetic patients. **Conclusion:** Present study concludes that serum Adenosine Deaminase activity and Insulin levels significantly increased in type 2 diabetes mellitus. Both Adenosine Deaminase and Insulin positively correlated with each other and also with Fasting Plasma Glucose. As adenosine deaminase can serve as an immunological marker and has a probable role in oxidative stress along with its effect on insulin actions by decreasing levels of adenosine, Adenosine Deaminase can be a useful parameter in the pathophysiology of type 2 diabetes mellitus.

Keywords: Adenosine Deaminase, Insulin, Fasting Plasma Glucose, Adenosine, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes is not one disease, but rather is a heterogeneous group of syndromes characterized by an elevation of fasting blood glucose caused by a relative or absolute deficiency in insulin[1]. According to recent estimates by the International Diabetes Federation (IDF), approximately 285 million people worldwide (6.6%) in the 20–79 year age group had diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. In India, the estimated no. of diabetics was 50.8 million in 2010 and expected to rise to 87.0 million by 2030[2].

Adenosine deaminase (ADA) (Adenosine Aminohydrolase, EC 3.5.4.4) is an enzyme of purine metabolism which acts on adenosine and other adenosine nucleoside analogues and catalyze its hydrolytic cleavage into inosine and ammonia, so it causes reduction in the levels of adenosine. Adenosine mimics the action of insulin on glucose and lipid metabolism in adipose tissue and the myocardium, while it inhibits the effect of insulin on total hepatic glucose output, which suggests that adenosine, causes local insulin resistance in the liver[3]. Adenosine is an agent which primarily decreases cyclic AMP accumulation, whereas insulin acts to

inhibit lipolysis via a noncyclic AMP-dependent mechanism. Under appropriate conditions one can see a marked synergism between the antilipolytic effects of insulin and adenosine. John N. Fain et al. suggested that insulin cannot inhibit lipolysis due to high concentrations of lipolytic agents unless cyclic AMP accumulation is maintained at low levels by adenosine[4].

Main biological activity of ADA is detected in T lymphocyte function, so it was considered as a good marker of cell mediated immunity and it has a crucial role in lymphocyte proliferation and differentiation[5]. Impaired lymphocyte function and enhanced susceptibility to infections is a common feature of human diabetes[6].

Studies have reported elevated ADA activity in type 2 diabetes [3,7,8,18] which concluded ADA as a marker of oxidative stress and lipid peroxidation in diabetes while Anju Gill et al. reported that there is an increase in the serum Insulin level with an increase in HbA1c levels in type 2 diabetes mellitus[6].

In the view of increasing burden of diabetes and as adenosine mimics action of insulin we studied ADA and insulin both in type 2 diabetes mellitus patients.

MATERIALS AND METHODS

In the present cross-sectional study, we included 50 type 2 diabetes mellitus patients having the disease for 5 or more years and were in the age group of 35-74 years and of either sex. The patients were on oral hypoglycemic drugs and were attending the Out Patients Department of Medicine at Sir Takhtsinhji Hospital, Bhavnagar, Gujarat. A group of 50 normal, healthy individuals from the same population served as controls. The study protocol was approved by an Institutional review board of Maharaja Krishna kumarsinhji Bhavnagar University.

Patients on insulin therapy, having complications of Diabetes Mellitus, pre existing infection and use of medications like steroids were excluded from the study. After enrolling in the study, a detailed medical history and the informed consent were obtained. A thorough explanation of the procedure of this study was given to the subjects.

Venous Blood samples were collected in a fasting state for estimation of Fasting Plasma Glucose, Serum Insulin and Serum ADA. Fasting plasma glucose were analyzed by GOD POD method[9], estimation of serum ADA done by Guisti Colorimetric Method[10] on fully auto analyzer I Lab 650 while estimation of serum Insulin was done by Eliza method[11] on Biorad Eliza reader at Clinical Biochemistry Section, Laboratory Services Sir Takhtsinhji Hospital, Bhavnagar, Gujarat.

Statistical analysis: Numerical variables are reported in terms of mean and standard deviation. Comparison between two groups was made with the unpaired student-t test. Correlations were calculated with Pearson product moment correlation coefficient by using graphpad prism version 6.0 statistical software.

RESULTS

Table 1: Comparison of FPG, ADA and Insulin in type 2 diabetes patients and healthy subjects

Parameter	Biological Reference Interval	Diabetic patients	Healthy Subjects	Statistical Significance
FPG (mg/dl)	70-100 mg/dl	165.06±90.60	90.88 ± 6.483	t= 5.774 **p<0.001
Serum ADA (U/L)	0-15 U/L	24.52 ± 9.733	16.51±6.26	t=4.891**p<0.001
Insulin (µIU/mL)	2-25µIU/mL	17.93 ± 10.38	8.75 ± 3.465	t=5.930 **p<0.001

Note: *p < 0.05 – significant, **p < 0.001 – highly significant, #p≥0.05 – not significant

The difference in FPG, ADA and Insulin were highly significant (p<0.001) in type 2 diabetic patients in comparison to control group (table 1).

In diabetic patient's serum ADA levels were positively correlated with FPG (r=0.6146, p<0.001) (Fig.2) and Insulin (r=0.3022, p=0.0330) (Fig 1), While Insulin levels were positively correlated with FPG (r=0.4728, p<0.001) (Fig 3).

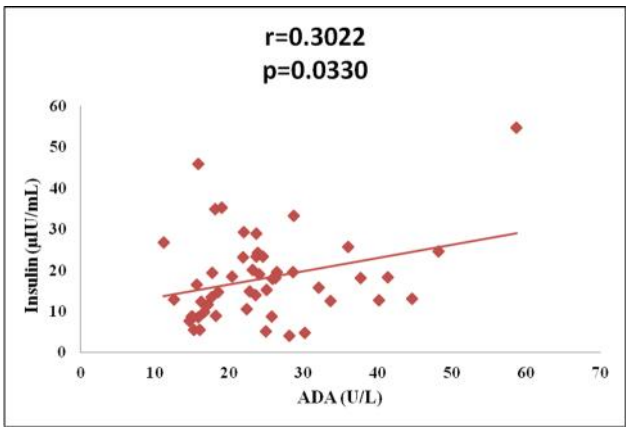

Fig 1: Correlation between ADA and Insulin in type 2 diabetic patients

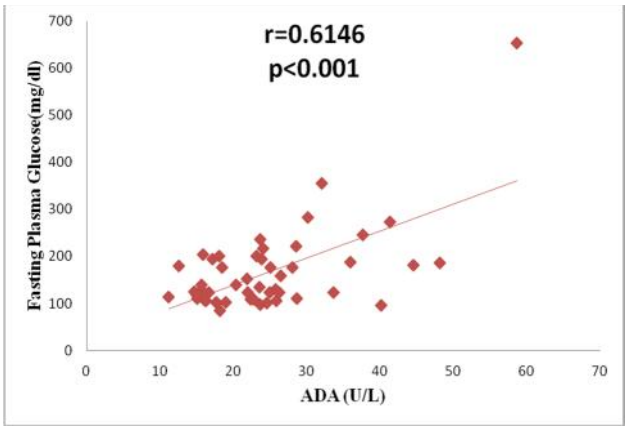

Fig 2: Correlation between ADA and FPG in type 2 diabetic patients

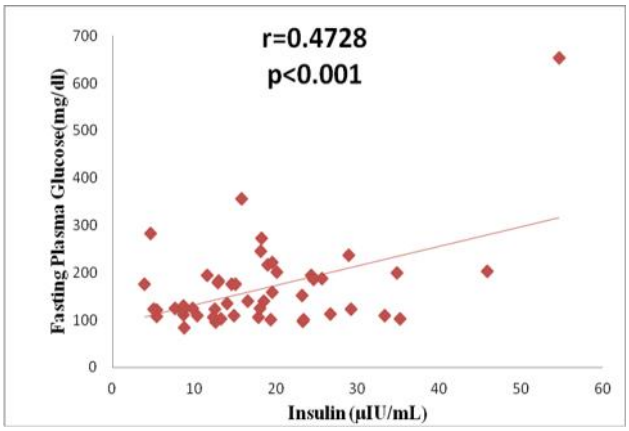

Fig 3: Correlation between Insulin and FPG in type 2 diabetes patients

DISCUSSION

Diabetes Mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycaemia and results from a defect in insulin secretion, insulin action or both. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism[12]. At present due to obesity, the age of onset of diabetes in children and adolescents has been decreased to less than 30 years and it is of great concern as future generations may be burdened with morbidity and mortality at the height of their productivity, potentially affecting the workforce and healthcare resources of the countries across the world[13]. Physiological roles of ADA can be seen in connection with adenosine whose concentration can be modulated by enzymatic action of ADA. Immunological disturbances in type 2 diabetic individuals have an association with cell mediated responses. Adenosine deaminase, an enzyme distributed in human tissues, was considered as a good marker of cell mediated immunity[3]. Hyperglycaemia in type 2 diabetes is associated with increased oxidative stress and according to Gitanjali G et al. ADA has got a role in increasing lipid peroxidation by reactive oxygen species generation, as they observed positive correlation of ADA with Malondialdehyde (MDA) levels[7].

Insulin resistance is the first detectable abnormality found in type 2 diabetes mellitus and it is defined as a reduced response of target tissues such as the skeletal muscle, liver and adipocytes to insulin. Hyperglycemia and hyperinsulinemia themselves can impair insulin secretion and insulin sensitivity. The body becomes more resistant to insulin with increasing duration of diabetes, and according to Meena Verma et al., HbA1c and Insulin levels significantly increase with the duration of diabetes and showed a significant correlation for age, sex and duration of diabetes[14] while Zarghami et al.[15] and Anju gill et al.[7] reported elevated levels of insulin in type 2 diabetes subjects in comparison to healthy controls. Our study supports them.

Adenosine potentiates insulin and contraction stimulated glucose transport in skeletal muscles by enhancing the increase in GLUT-4 at the cell surface and raised the possibility of decreased adenosine production or action by increased level of adenosine deaminase could play a causative role in insulin resistance[16]. Joanna Rutkiewicz et al. in 1990 concluded in their study that insulin is involved in the regulation of activity of adenosine deaminase in different rat tissues[17].

In the present study, serum ADA and Insulin levels were markedly increased in type 2 diabetic patients ($p<0.0001$) in comparison to healthy subjects while ADA ($r=0.6146$, $p<0.001$) and Insulin ($r=0.4728$, $p<0.001$) positively correlate with FPG, which is

highly significant. Positive significant correlation was also present between ADA and Insulin (r=0.3022, p<0.05).Our study found ADA as a marker of glycemic status in type 2 diabetes patients.

CONCLUSION

It is concluded from the present study that serum ADA and insulin significantly increased in type 2 diabetics and correlated with each other and also with FPG. In the present time, ADA has been viewed as a parameter of interest in type 2 diabetes due to its role in oxidative stress, as a marker of cell mediated immunity along with its effects on insulin by altering levels of adenosine. Therefore, ADA can be used as an important parameter in the patients of type 2 diabetes mellitus.

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Conflict of interest: Nil

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