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STUDY ON ADENOSINE DEAMINASE ACTIVITY OF PATIENTS WITH TYPE 2 DIABETES MELLITUS AT AIIMS PATNA: A HOSPITAL BASED COMPARATIVE STUDY.

Biochemistry

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ABSTRACT

Objectives: This present study was to evaluate and compare the adenosine deaminase activity in diabetic and non diabetic subjects.
Methods: Detail history, clinical examination and relevant laboratory investigations were performed to all subjects. The level of serum adenosine deaminase (ADA) was determined by using Erba Mannheim Chem 5X Semiautoanalyser based on Photometry. Lipid profile (total cholesterol, triglyceride and HDL-Cholesterol) were also done using AU 5800 Autoanalyser. VLDL-Cholesterol and LDL Cholesterol were calculated using Friedwald's formula.
Results: Data was analyzed by using latest version of IBM SPSS soft ware. Paired samples T Test was performed. Mean, standard deviation and paired samples correlations were observed. P value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.
Conclusions: Adenosine deaminase activity is significantly increased in diabetic patients when compared to non diabetic subjects. FBS, BMI, TG, VLDL and HDL of diabetic cases are significantly greater with respect to non diabetic subjects. Hence, Increased serum activity of adenosine deaminase activity is a good diagnostic marker of patients with type 2 diabetes mellitus and it might be a marker for insulin therapy indication.

KEYWORDS

Type 2 diabetes mellitus, ADA, FBS, BMI, Lipid profile.

INTRODUCTION

The incidence and prevalence of type 2 diabetes mellitus (T2DM) are increasing globally, and according to a study by World Health Organization, 300 million patients might be affected by the disease by 2030 with the prevalence in developing countries like India and China being estimated to cross 228 million [1,2]. T2DMis the result of a complex interplay between various aetiological, genetic, and environmental factors [2]. A sedentary lifestyle, unhealthy food habits, and the consequent obesity related complications are responsible for the T2DM cases shooting out to epidemic proportions worldwide. However, obesity is not always linked to T2DM as ascertained by studies that indicate that the Asian T2DM phenotype is commonly less obese when defined by Body Mass Index (BMI) and around 20%of north European T2DM cases are of the nonobese type [3, 4]. Insulin resistance and impaired insulin secretion are the main physiological abnormalities associated with T2DM [4]. Immunological disturbances involving the cell mediated immune system and improper T-lymphocyte function also contribute to the pathophysiology of T2DM [5].

Hyperglycemia leads to increased oxidative stress by forming free radicals and superoxide ions and increases adenosine deaminase (ADA) activity [6]. ADA is a purine metabolizing enzyme that catalyzes the deamination of adenosine to inosine regulating intracellular and extracellular adenosine concentration [7]. ADA may play a role in insulin effect and glycemic control as adenosine acts directly to stimulate insulin activity via several processes such as glucose transport, pyruvate dehydrogenase activity, lipid synthesis, leucine oxidation and cyclic nucleotide phosphodiesterase activity [8]. Therefore, the activity of ADA in Type 2 DM is a marker for prognosis in Type 2 DM.

Objectives of our study were to evaluate and compare the adenosine deaminase activity as well as lipid profile of patients with type 2 diabetes mellitus.

MATERIALS & METHODS

This present study was conducted in Department of Biochemistry with the collaboration of Department of Medicine and Department of Pathology of AIIMS, Patna, Bihar, India during a period from October 2018 to January 2019. Entire subjects signed an informed consent approved by institutional ethical committee of AIIMS, Patna, Bihar was sought.

This present study was comprised into two groups (case and control). 30 cases with diabetes were enrolled in cases group. And 30 normal individuals were enrolled in control group. Age groups of all subjects were 30 to 60 years.

METHODS:

A detail history clinical examinations and relevant investigations were performed to all subjects. Inclusion criteria of this study were age 30 to 60 years, and FBS≥126 mg/dL or a patient already on antidiabetic medication.

Exclusion criteria was patients with diabetic complications, hypertension, pregnancy, subjects with history of infectious or alcoholic hepatitis, chronic renal disease, coronary artery disease, disease affecting immune system like rheumatoid arthritis, cancers like leukaemia, chronic infections like tuberculosis and nephrotic syndrome.

Biochemical assays: Fasting blood samples were obtained from the patients as well as the controls. The level of serum adenosine deaminase (ADA) was determined by using Erba Mannheim Chem 5X Semiautoanalyser based on Photometry. Adenosine deaminase hydrolyses adenosine to inosine and ammonia. Ammonia then reacts with a phenol and hypochlorite in an alkaline medium to form a colored blue indophenol complex, using sodium nitroprusside as a catalyst. The degree of blue indophenol complex is directly proportional to the activity of ADA in the sample. ADA activity is described as U/L. One enzyme unit was the amount of enzyme necessary to convert 1 μM of adenosine and ammonia per min at 37 °C. Lipid profile (total cholesterol, triglyceride and HDL-Cholesterol) were done using AU5800 Autoanalyser. VLDL-Cholesterol and LDLCholesterol were calculated using Friedwald's formula.

STATISTICALANALYSIS

Data was analyzed by using latest version of IBM SPSS soft ware. Paired samples T Test was performed. Mean, standard deviation and paired samples correlations were observed. P value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

OBSERVATIONS

A total of 60 subjects (30: case group and 30: control group) of both males and female were enrolled in this study.

Table.1. showing the parameters of diabetic and non diabetic cases.

Variables	Case group (Diabetic) (Mean±S.D.)	Control group (non diabetic) (Mean±S.D.)	R	P-values
Age(Years)	54.160±5.281	46.760±4.675	0.452	0.023 (significant)
BMI(Kg/m2)	23.165±1.420	21.216±1.394	0.799	0.000 (highly significant)
FBS(mg/dL)	183.024±27.909	90.443±6.577	0.591	0.002 (highly significant)

ADA(U/L)	37.832±4.360	21.144±2.943	0.490	0.013 (very significant)
VLDL (mg/dL)	29.087±7.068	22.886±3.438	0.518	0.008 (highly significant)
TG(mg/dL)	160.888±41.454	113.395±18.681	0.042	0.842 (non significant)
TCL(mg/dL)	191.030±32.274	164.786±16.153	0.0426	0.034 (significant)
HDL(mg/dL)	41.908±4.092	40.108±3.942	0.433	0.030 (significant)
LDL(mg/dL)	137.380±15.408	122.486±9.401	0.128	0.541 (non significant)

When mean ± S.D of subjects of cases and control groups was compared. We were seen that age, TCL, HDL were significant differences. ADA was very significant differences. BMI, FBS and VLDL were highly significant differences. And TG and LDL were non significant differences.

DISCUSSION

Diabetes mellitus type 2 is a heterogeneous disease characterized by altered carbohydrate, fat and protein metabolism secondary to insulin resistance. It is characterized by hyperglycemia leading to increased oxidative stress and dyslipidemia. Identifying the resistance of insulin helps in minimizing the complications at an early stage. [9]

In this present study, FBS was highly significantly increased in diabetic patients of case group as compared to non diabetic control group subjects.

(ADA) is an enzyme that has been suggested to be important for modulating the bioactivity of insulin. It is a metalloenzyme which catalyzes the irreversible deamination of adenosine and deoxyadenosine to inosine and deoxyinosine and has an important role in regulating adenosine concentration. [10]

ADA distribution varies between different tissues, but highest concentration occurs in lymphoid and fatty tissues [11]. Adenosine is involved in insulin mediated glucose uptake in skeletal muscle and high ADA activity tends to decrease glucose uptake into cells and thus contributes to insulin resistance [12]. It has been shown in some in vivo and in vitro studies that adenosine increases gluconeogenesis and glycogenolysis and stimulates glucose formation [13]. It also interacts withA1 and A2 adenosine receptors modulating myocardial functions [14]. DPP-4 is an enzyme that acts as an important immune regulator by interacting with CD3 and acting as a costimulator for CD4+ T cells. It also regulates glucose homeostasis by hydrolysing integrins. DPP-4 binds ADA with high affinity and as adenosine causes apoptosis and inhibits differentiation of T lymphocytes by activating P1 adenosine receptors, interaction of ADA with DPP-4 can lead to T cell proliferation and increased cytokine production which can interfere with insulin signalling [15]. Moreover, ADA plays an important role in lymphocyte maturation and activity, whose deficiency is associated putatively with impaired immune function. Thus, suppression of ADA activity may help improve insulin sensitivity and inflammation, cell proliferation, and T-lymphocyte activity, all of which are associated with the pathophysiology of T2DM. Several reports also suggest that ADA modulates insulin action [16].

In this present study, adenosine deaminase (ADA) activities were very significantly increased in all diabetic groups as compared to control group. Our results were in agreement with results obtained in previous studies that concluded the increased in adenosine content make similar effect to insulin on glucose and lipid metabolism in adipose tissue [17]. The increasing of Serum ADA levels in our study may be due to insulin resistance or increased secretion of adenosine [18]. Decreased tissue adenosine levels is due to increased ADA activity which is related to the degree of hyperglycemia and lipid peroxidation in diabetes mellitus due to insulin resistance in the target organs and also the increased in production of free radicals and oxidative stress. [9]

Our study also correlated with the finding of Kaur et al. [19] They were found that there is a significant increase in ADA levels in type 2 DM.

In this present study, BMI of diabetic case group was highly significantly increased as compared with non diabetic control groups. Age groups of diabetic cases were significantly greater when compared to non diabetic subjects.

Lipid profile derangement was an obvious feature in the present study among the studied groups with type2 DM. Triglyceride and LDL were non significant increased in diabetic cases as compared to non diabetic subjects. But total cholesterol, HDL and VLDL were significantly elevated when compared to non diabetic control group subjects.

CONCLUSION

This present study concluded that adenosine deaminase activity is significantly increased in diabetic patients when compared to non diabetic subjects. FBS and BMI of diabetic cases are significantly greater with respect to non diabetic subjects. TG, VLDL and HDL are also significantly increased in diabetic cases when compared to non diabetic control subjects.

Elevated ADA activity, and increased triglyceride levels may associate with the insulin resistance.

Thus, that increased serum activity of adenosine deaminase activity is a good diagnostic marker of patients with type 2 diabetes mellitus and it might be a marker for insulin therapy indication.

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