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ORIGINAL RESEARCH

Assessment of Serum ADA Activity in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to insulin resistance and impaired insulin secretion. Adenosine deaminase (ADA), an enzyme involved in purine metabolism and immune function, is increasingly recognized for its potential role in the pathophysiology of T2DM through modulation of glucose uptake and insulin sensitivity. **Methods:** A prospective case-control study was conducted in the Department of Biochemistry, a tertiary care center in Northern India, from January to August 2024. The study included 200 participants divided into two groups: 100 diagnosed T2DM patients (cases) and 100 healthy, age- and sex-matched individuals (controls). Fasting and postprandial plasma glucose, serum ADA activity, and lipid profile were analyzed using an automated clinical chemistry analyzer. Data were statistically evaluated using Student's t-test, with a significance threshold set at $p < 0.05$. **Results:** The case group exhibited significantly elevated levels of fasting plasma glucose (187.45 ± 52.78 mg/dL), postprandial plasma glucose (321.80 ± 89.45 mg/dL), and serum ADA activity (38.96 ± 5.63 U/L) compared to controls (91.25 ± 14.90 mg/dL, 134.10 ± 20.32 mg/dL, and 18.24 ± 2.48 U/L, respectively), all with **p = 0.0001**. Lipid profile analysis revealed significantly higher total cholesterol, triglycerides, and VLDL levels in cases ($p = 0.0001$), and lower HDL levels ($p = 0.001$). LDL cholesterol was higher in cases but not statistically significant ($p = 0.173$). **Conclusion:** Elevated ADA levels in T2DM patients may reflect altered glucose metabolism, immune dysregulation, and oxidative stress. ADA could serve as a potential biomarker for monitoring glycemic status and early metabolic complications in type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus, Adenosine deaminase, Hyperglycemia, Insulin resistance, Lipid profile, Biomarker, Glycemic control.

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INTRODUCTION

Diabetes mellitus is a significant metabolic disorder characterised by hyperglycemia, which is increasingly prevalent worldwide, resulting in 4.8 million deaths and morbidity affecting 371 million individuals annually.[1] India possesses the second highest population of individuals with diabetes globally, totalling 62.4 million, with a prevalence of 3.8% among rural adults and 11.8% among urban adults; this figure is projected to escalate to 100 million by 2030. [2, 3, 4]. Chronic hyperglycemia results in glucotoxicity, which subsequently impairs glycaemic control and increases the risk of long-term microvascular and macrovascular complications.

Insulin resistance and compromised insulin secretion are the primary physiological abnormalities linked to T2DM [5]. Immunological anomalies affecting the cell-mediated immune system and dysfunctional T-lymphocyte activity also contribute to the pathophysiology of Type 2 Diabetes Mellitus. [6] Adenosine deaminase (ADA) catalyses the irreversible deamination of adenosine to form inosine [7]. Peak ADA activity has been observed in lymphoid and adipose tissues, liver, skeletal muscle, and cardiac tissue.[8] Adenosine facilitates the enhancement of glucose absorption into cells [9]. Consequently, elevated ADA activity in insulin-sensitive tissues will reduce adenosine levels, subsequently diminishing glucose uptake into cells. Adenosine has been demonstrated to enhance gluconeogenesis and glycogenolysis by elevating cyclic AMP (cAMP) through the stimulation of hepatic adenylate cyclase via adenosine A2a receptor binding in the liver. Both or either of these actions

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leads to an increase in local insulin resistance and hepatic glucose output.[10] ADA is essential for lymphocyte proliferation and differentiation, exhibiting significant activity in T-lymphocytes [11]. Consequently, inhibiting ADA activity may enhance insulin sensitivity and inflammation, cell proliferation, and T-lymphocyte activity, all of which are linked to the pathophysiology of T2DM.

Numerous studies have indicated elevated ADA activity in patients with type 2 diabetes relative to healthy controls. [10, 11, 12] To our knowledge, there is no research on the activity of ADA in the Vidarbha region concerning diabetes. This study seeks to assess the serum total ADA activity in type 2 diabetic patients.

MATERIALS AND METHODS

This prospective case-control study was conducted in the Department of Biochemistry at a tertiary care center in Northern India from Jan 2024 to Aug 2024. Informed written consent was obtained from all participants.

The study included a total of **200 subjects**, divided into two equal groups:

1. **Cases (n = 100):** These were patients diagnosed with type 2 diabetes mellitus, aged between **30 to 60 years**, including both males and females. Demographic details such as age, weight, height, duration of disease, duration of treatment, medical history, and blood pressure were recorded for each subject.
2. **Controls (n = 100):** Age- and sex-matched healthy individuals without a history of diabetes were selected from the general population. These subjects had normal fasting and postprandial blood glucose levels and no known chronic illnesses.

The diagnosis of diabetes mellitus was established based on **World Health Organization (WHO) criteria**, including any of the following:

- Symptoms of diabetes with a random plasma glucose level ≥ 200 mg/dL
- Fasting plasma glucose level ≥ 126 mg/dL
- Two-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test (OGTT)

Exclusion Criteria

Subjects with the following conditions were excluded from the study:

- Type 1 diabetes mellitus or gestational diabetes
- Use of uricosuric drugs
- Chronic arthritis, gout, or autoimmune disorders affecting ADA levels
- Hypertension, dyslipidemia, or smoking history
- Patients on antioxidant vitamin supplementation

Sample Collection and Biochemical Analysis

From each participant, **3 ml of fasting venous blood** was collected under aseptic conditions. Blood was drawn into clean, EDTA-coated tubes and centrifuged at **3,000 rpm for 10 minutes** to separate plasma. The plasma samples were analyzed for the following biochemical parameters:

- Fasting plasma glucose (FPG)
- Postprandial plasma glucose (PPPG)
- Total cholesterol
- HDL cholesterol
- LDL cholesterol
- Triglycerides
- Serum adenosine deaminase (ADA) activity

All biochemical analyses were performed using an **automated clinical chemistry analyzer**, following the manufacturer's protocols.

RESULT

In our study we have 62% male and 38% female in cases and 56% male and 44% female in controls. Maximum subjects belong to age group 41 – 60 years. Both the groups are age matched.

Table 1: Distribution of Subjects According to Age and Sex

Variable	Cases (n=100)	Controls (n=100)
Sex		
Male	62 (62%)	56 (56%)
Female	38 (38%)	44 (44%)

Table 2: Comparison of Fasting and Postprandial Plasma Glucose and Serum ADA in Two Groups

Clinical Parameters	Cases (n=100)		Controls (n=100)		*t*-value	*p*-value
	Mean	SD	Mean	SD		
FPG (mg/dl)	187.45	52.78	ninety-one.25	14.90	11.64	0.0001
PPPG (mg/dl)	321.80	89.45	134.10	20.32	14.01	0.0001
ADA (U/L)	38.96	5.63	18.24	2.48	23.75	0.0001

Note: $p < 0.05$ = significant; $p = 0.0001$ = highly significant

In our study, the comparison of fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), and serum adenosine deaminase (ADA) levels between the case and control groups revealed highly significant differences. The mean FPG in cases was 187.45 ± 52.78 mg/dl, significantly higher than 91.25 ± 14.90 mg/dl in controls ($t = 11.64$, $p = 0.0001$). Similarly, the mean PPPG was elevated in cases at

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321.80 ± 89.45 mg/dl compared to 134.10 ± 20.32 mg/dl in controls (t = 14.01, p = 0.0001). Serum ADA levels were also markedly higher in cases, with a mean of 38.96 ± 5.63 U/L versus 18.24 ± 2.48 U/L in the control group (t = 23.75, p = 0.0001). These findings indicate a strong association between elevated glucose and ADA levels in the case group, underscoring their potential relevance in disease pathophysiology.

Table 2: Comparison of lipid profile in two groups

Clinical Parameters	Cases (Mean ± SD)	Controls (Mean ± SD)	*t*-value	*p*-value
Total cholesterol	202.45 ± 47.26	172.18 ± 30.90	3.89	0.0001
Triglyceride	210.34 ± 63.82	93.45 ± 39.67	10.78	0.0001
HDL Cholesterol	32.84 ± 7.12	41.08 ± 11.56	3.28	0.001
LDL Cholesterol	122.63 ± 36.91	112.76 ± 27.45	1.37	0.173
VLDL cholesterol	41.18 ± 12.94	18.69 ± 7.45	10.61	0.0001

In our study, lipid profile analysis revealed significant differences in most parameters between the case and control groups. The mean total cholesterol was higher in cases (202.45 ± 47.26 mg/dl) compared to controls (172.18 ± 30.90 mg/dl), with a t-value of 3.89 and a highly significant p-value of 0.0001. Triglyceride levels were also markedly elevated in cases (210.34 ± 63.82 mg/dl) compared to controls (93.45 ± 39.67 mg/dl), with a t-value of 10.78 (p = 0.0001). HDL cholesterol was significantly lower in cases (32.84 ± 7.12 mg/dl) than in controls (41.08 ± 11.56 mg/dl), indicating a significant inverse association (t = 3.28, p = 0.001). LDL cholesterol showed a higher mean in cases (122.63 ± 36.91 mg/dl) compared to controls (112.76 ± 27.45 mg/dl), but this difference was not statistically significant (p = 0.173). VLDL levels were significantly elevated in cases (41.18 ± 12.94 mg/dl) versus controls (18.69 ± 7.45 mg/dl), with a t-value of 10.61 (p = 0.0001). These findings highlight a strong dyslipidemic profile in the case group, particularly concerning triglycerides and VLDL.

DISCUSSION

The correlation between serum adenosine deaminase and glycaemic parameters (FBS, PPBS) as well as lipid profile parameters (TG, TC, LDL cholesterol, HDL cholesterol) in type 2 diabetes mellitus was assessed. A significant increase ($p < 0.001$) in serum ADA was observed in individuals with type 2 diabetes mellitus compared to the control group. The findings of our study are corroborated by numerous prior studies. Comparable studies conducted by Bhavita Patel et al[14], Vineet Kumar Khemka et al[15], Shaikh Sahema M et al[16], and Mohammed A. Al-Duais et al[17] yielded analogous results. ADA is an enzyme that irreversibly deaminates adenosine to produce inosine. Adenosine is hypothesised to exhibit insulin-like activity on glucose and lipid metabolism, particularly in adipose tissue and skeletal muscles. [18] ADA is identified as a generator of reactive oxygen species (ROS), a promoter of lipid peroxidation, and an indicator of T-cell activation and glycaemic status in diabetes mellitus (DM)[19,20,21]. An elevation in ADA activity among T2DM patients has been documented, yet the mechanism underlying the augmentation of serum and tissue ADA activity remains poorly understood. Increased ADA activity in insulin-sensitive tissues will diminish adenosine levels, thereby reducing glucose uptake into cells.[22,10] Bhavita Patel et al. [14] elucidated that the pathogenesis of elevated ADA levels in Type 2 Diabetes Mellitus is mediated by the extracellular cAMP-adenosine pathway. Adenosine deaminase (ADA) inactivates adenosine and promotes lipolysis. Nonetheless, it is challenging to determine whether alterations in ADA activity are the cause or consequence of genuine insulin resistance. Adenosine enhances insulin- and contraction-stimulated glucose transport in skeletal muscles by promoting the translocation of GLUT-4 to the cell surface, suggesting that elevated levels of adenosine deaminase, which may reduce adenosine production or action, could contribute to insulin resistance.[23]

The current study revealed a significant elevation of serum ADA and insulin levels in type 2 diabetic patients ($p<0.0001$) compared to healthy individuals. Our findings corroborated those of prior studies, which concluded that the elevation of adenosine levels exerts effects on glucose and lipid metabolism analogous to those of insulin.

CONCLUSION

Due to its role in oxidative stress, as a marker of cell-mediated immunity, and its effects on insulin by altering levels of adenosine, ADA has been regarded as a parameter of interest associated with type 2 diabetes. In conclusion, ADA has been viewed as a parameter of interest in type 2 diabetes. Early detection of complications is critical, and the identification of these complications requires only a single marker. Because of this, the ADA has the potential to serve as a significant parameter that can be utilised as a marker of glycaemic status in patients who have type 2 diabetes mellitus.

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