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Evaluation of serum ADA level in type 2 Diabetes Mellitus Patient and its correlation with Glycosylated hemoglobin in a tertiary centre of North India

Authors
Dr Rajkumar Verma, Dr Mridul Chaturvedi, Dr Arti Chaudhary, Dr Akash Bharti

Abstract

Background: *Type 2 diabetes mellitus is a metabolic disease characterized by insulin resistance, reduced production of insulin, and systemic inflammation. Latest studies suggest a link between adenosine deaminase (ADA), an immunomodulatory enzyme, and metabolic dysfunction and glycemic control in patients with type 2 diabetes mellitus[1,2,4].*

Methods: *A cross-sectional observational study was conducted at Sarojini Naidu Medical College (SNMC), Agra. The study included 150 patients with type 2 diabetes mellitus, in whom serum ADA and HbA1c levels were evaluated and correlated using SPSS for statistical analysis, including logistic regression and Spearman's correlation. A p-value below 0.05 was considered significant.*

Results: *The study showed a significant link between HbA1c and fasting glucose ($r = 0.81$, $p < 0.001$) and between ADA and HbA1c ($r = 0.72$, $p < 0.001$). Subjects having inadequate glycemic control (HbA1c ≥ 7%), prolonged diabetes duration, obesity, dyslipidemia, smoking, and systemic hypertension demonstrated significantly elevated levels of ADA. Adenosine deaminase (ADA) also had a negative correlation with HDL ($r = -0.22$) and a positive correlation with total cholesterol levels ($r = 0.34$) and total triglyceride levels ($r = 0.41$).*

Conclusion: *In patients with T2DM, serum ADA levels show a significant positive correlation with HbA1c levels, indicating that ADA levels can be judiciously used as a biomarker in the assessment of glycemic control, inflammation, and metabolic stress, as well as in monitoring the progression of the disease and guiding customised care for diabetes management. ADA levels can be a cost-effective addition in monitoring and guiding treatment protocols in diabetic patients[5,6].*

Keywords: *Type 2 Diabetes Mellitus, Adenosine Deaminase, HbA1c, Glycemic Control, Biomarker, Inflammation, Metabolic Dysfunction.*

Introduction

Type 2 diabetes mellitus is a growing global health concern, accounting for about 90% of all diabetes cases worldwide. The frequency of T2DM has increased rapidly, especially in third-world countries, including India and China[8]. The complexity of the disease is governed by environmental and genetic factors. It results in insulin resistance and decreased insulin production by the beta cells of the pancreas[9]. Recent studies demonstrate the prognostic significance of HbA1c level variability as an important biomarker for long-term glycemic control. Adenosine deaminase (ADA) has now emerged as a potential marker for immunological abnormalities

linked to type 2 diabetes mellitus[1,2,4]. Adenosine, reduced by ADA activity, has a function similar to insulin in promoting glucose uptake by skeletal muscle and adipose tissues and in preventing lipolysis. Thus, high ADA levels can exacerbate insulin resistance by raising free fatty acids and lowering glucose absorption.

Understanding the complex relationship between immune dysfunction and metabolic dysfunction is essential in improving treatment protocols and patient outcomes in this increasingly prevalent disease of global concern.

Objective of the Study

- To determine the level of glycated hemoglobin (HbA1c) in people who have type 2 diabetes (T2DM).
- To evaluate the adenosine deaminase (ADA) levels in the serum of individuals with type 2 diabetes.
- To assess the correlation between ADA and HbA1c levels in patients with type 2 diabetes mellitus at North Indian tertiary centers.

Materials and Methods

Study Design:

The cross-sectional observational study was conducted in the Medicine Department, in cooperation with the Pathology Department and the Outpatient Department of Sarojini Naidu Medical College (SNMC), Agra, over the course of one year (2020–2021).

Methodology

A total of 150 participants with T2DM underwent a comprehensive physical examination, history taking, and laboratory testing after providing proper consent. Glycemic control (HbA1c) was measured using HPLC (NGSP accredited), and serum ADA levels were measured using a colorimetric technique. The primary objective of the study was to evaluate the correlation between ADA and HbA1c levels of the selected participants.

Statistical Analysis

Following the methodical entry and tabulation of data using Microsoft Excel, statistical analysis was conducted using IBM SPSS software. Descriptive statistics were used to summarize the baseline characteristics. Chi-square tests were used to evaluate correlations between categorical variables. To determine the strength and direction of the relationship between serum ADA and HbA1c, logistic regression analysis was used to compute odds ratios (OR) and 95% confidence intervals (CI). A p-value of less than 0.05 was considered statistically significant, and a 5% margin of error was upheld throughout the analysis.

Inclusion Criteria:

1. Adults in the age range of 21 to 69.
2. Individuals who meet the American Diabetes Association's (ADA) criteria for Type 2 Diabetes Mellitus (T2DM), which include any of the following:

- FPG (fasting plasma glucose) ≥ 126 mg/dL (7.0 mmol/L)
- During a 75-g oral glucose tolerance test (OGTT), glucose levels ≥ 200 mg/dL (11.1 mmol/L) two hours after loading
- Random plasma glucose levels of 200 mg/dL (11.1 mmol/L) or higher when accompanied by the typical signs of hyperglycemia or hyperglycemic crisis

Exclusion Criteria

1. Patients diagnosed with Type 1 Diabetes Mellitus
2. Individuals with a known history of chronic alcohol consumption
3. Patients receiving insulin therapy
4. Presence of any acute diabetic complications, such as diabetic ketoacidosis or hyperosmolar hyperglycemic state
5. Individuals undergoing immunosuppressive therapy
6. Patients with other comorbidities like CKD or CLD

7. Participants suffering from other chronic illnesses in which ADA levels are also affected, such as tuberculosis, enteric fever, viral hepatitis, nephrotic syndrome, leprosy, infectious mononucleosis, HIV, or chronic malnutrition
8. Pregnant and lactating women

Results:

1.Correlation between ADA and HbA1c:

Variable Pair	Spearman's correlation coefficient	p-value
ADA and HbA1c	0.72	<0.001
ADA and Fasting Glucose	0.65	<0.001
HbA1c and Fasting Glucose	0.81	<0.001

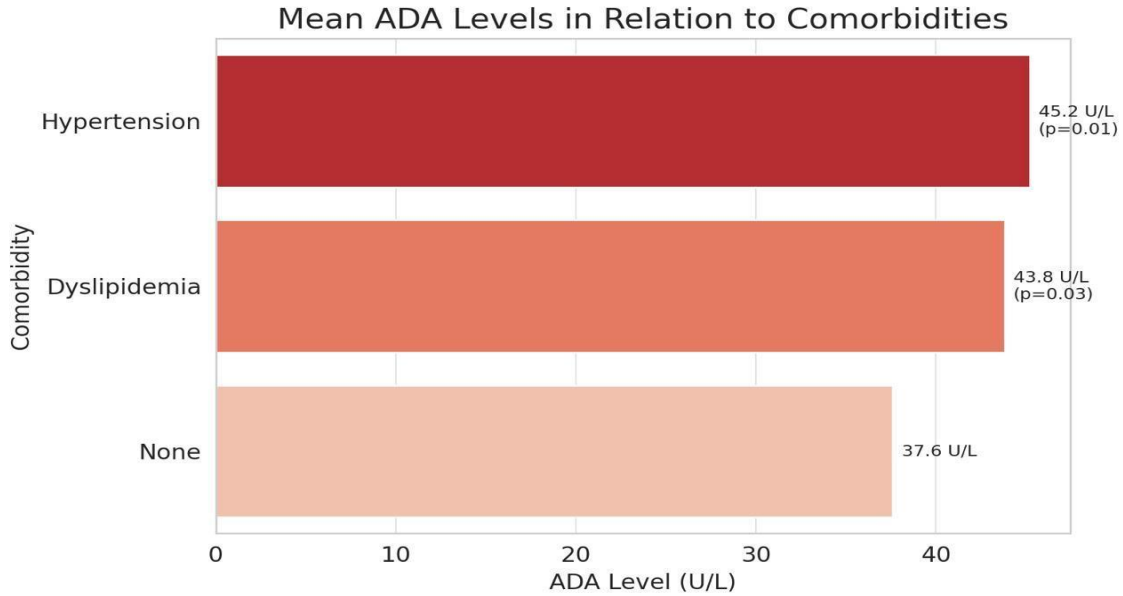
The study shows a strong positive correlation between ADA and HbA1c ($r = 0.72$) and between HbA1c and fasting glucose ($r = 0.81$), both highly significant ($p < 0.001$). This suggests that elevated ADA levels are associated with poorer glycemic control in type 2 diabetes.

2.ADA levels stratified by glycemic control (based on HbA1c Levels):

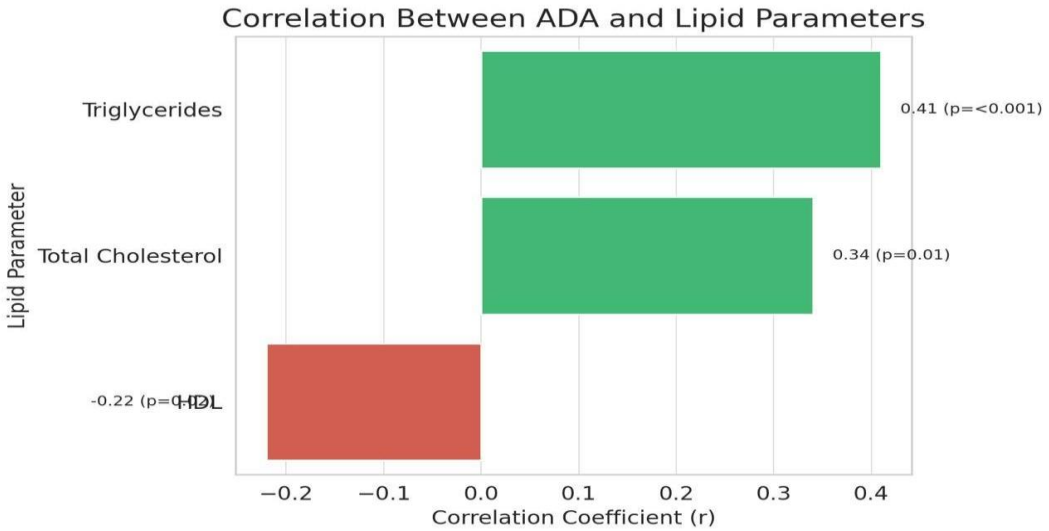
Glycemic Category	Number of Participants [n (%)]	ADA (U/L) Mean ± SD	p-value
HbA1c < 7% (Good Control)	38 (25.3%)	28.4 ± 6.2	<0.001
HbA1c ≥ 7% (Poor Control)	112 (74.7%)	47.9 ± 10.8	

The study shows a strong positive correlation between ADA and HbA1c ($r = 0.72$), and between HbA1c and fasting glucose ($r = 0.81$), both statistically significant ($p < 0.001$). This indicates that higher ADA levels are associated with poor glycemic control in type 2 diabetes.

3.ADA level with comorbidities in study population:



Patients with hypertension and dyslipidemia exhibited significantly higher ADA levels (45.2 and 43.8 U/L respectively) compared to those without comorbidities (37.6 U/L). This suggests a strong metabolic association between elevated ADA activity and common cardiovascular risk factors.



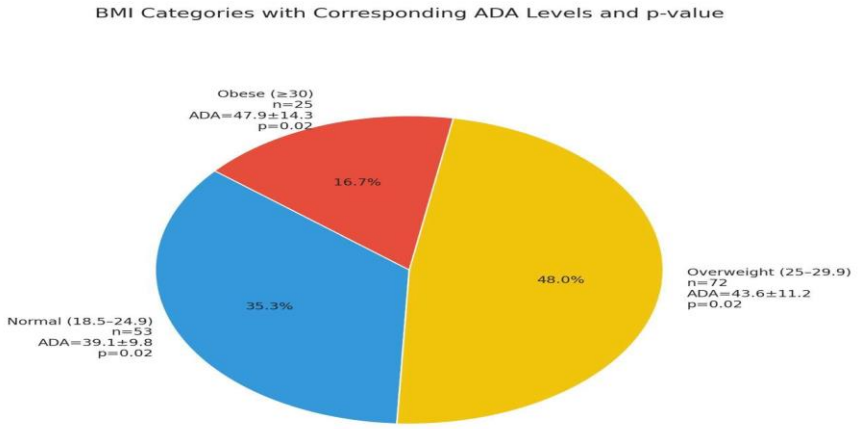
ADA levels showed a positive correlation with triglycerides ($r = 0.41$, $p < 0.001$) and total cholesterol ($r = 0.34$, $p = 0.01$), while a weak negative correlation was observed with HDL ($r = -0.22$, $p = 0.02$). These findings suggest that elevated ADA activity is associated with atherogenic lipid profiles in type 2 diabetes patients.

4.Duration of diabetes and ADA level:

Duration (years)	ADA (U/L) (Mean ± SD)	p-value
<5	38.4 ± 9.7	<0.001
5–10	45.6 ± 11.2	
>10	50.3 ± 14.1	

The study shows a significant rise in ADA levels with increasing duration of diabetes: from 38.4 U/L (<5 years) to 50.3 U/L (>10 years), with $p < 0.001$. This indicates that longer diabetes duration is strongly associated with elevated ADA activity, reflecting progressive metabolic stress

5.Association between BMI categories and serum ADA Level:



The pie chart shows that ADA levels rise progressively with increasing BMI—highest in obese individuals (47.9 U/L) compared to overweight (43.6 U/L) and normal BMI (39.1 U/L). This statistically significant association ($p = 0.02$) highlights the metabolic impact of excess weight on ADA activity.

6.ADA level in smokers vs. non-smokers:

Smoking Status	n (%)	ADA (U/L) (Mean ± SD)	p-value
Smoker	48 (32.0%)	48.3 ± 13.5	<0.001
Non-Smoker	102 (68.0%)	39.7 ± 10.2	

Smokers showed significantly higher mean ADA levels (48.3 ± 13.5 U/L) than non-smokers (39.7 ± 10.2 U/L) with $p < 0.001$, indicating a strong association between smoking and elevated ADA.

This suggests smoking may enhance ADA activity, possibly due to increased metabolic or inflammatory stress.

Discussion

The study aimed to examine the relationship between ADA levels and glycemic control, as measured by conventional HbA1c levels in patients with T2DM. Increased levels of ADA, associated with inflammation and immunological dysfunction, are thought to be a significant marker of metabolic stress in patients with T2DM. This study set out to assess ADA's clinical utility as a relevant biomarker in the management and surveillance of diabetes mellitus [1,2,4].

According to the findings of this study, ADA and HbA1c showed a strong positive correlation ($r = 0.72$, $p < 0.001$), suggesting that elevated ADA levels are a reliable marker for poor glycemic control. ADA is also associated with smoking, comorbidities, lipid profile, BMI, fasting glucose, and duration of diabetes. The findings positively contribute to our understanding of the pathophysiology of T2DM and the potential use of ADA levels as a new modality in the diabetes treatment regimen [2,3,5].

The results of the study are in close agreement with the available literature. A similar association between ADA and HbA1c was found in many independent studies. Consequently, ADA levels were significantly raised in patients with poor glycemic control (HbA1c ≥ 7%) and those with elevated fasting glucose levels. These results lend credence to the link between ADA, immunological activation, and diabetes-related metabolic imbalances [1,4,5].

The study also depicted significantly increased ADA levels in people with systemic hypertension and dyslipidemia. This is in line with studies indicating that glycemic imbalance and systemic inflammation are both reflected in elevated ADA levels[7,8]. Niraula A et al. and other reports indicate that ADA levels increase with age and the duration of diabetes, most likely due to chronic inflammatory burden and cumulative metabolic damage over time[2,3].

Our study's lipid profile correlations, which indicate a negative correlation with HDL and a positive correlation with triglycerides, support the findings of previous studies highlighting the similar metabolic and inflammatory pathways between ADA and lipid abnormalities[9,10]. Interestingly, some research indicates that lifestyle changes can lower ADA levels, even though ADA was higher in patients receiving both lifestyle and OHA interventions. This implies that there might be variance based on sample differences, treatment intensity, or patient compliance [3,4].

Even though the study's findings are generally consistent with the literature, there are a few limitations to be mindful of. The cross-sectional design restricts causal inference, and reliance on a single-center cohort may limit generalizability. Given some contradictory findings, such as the minimal effect of dietary patterns on ADA levels and higher ADA levels in people who have changed their lifestyle, more longitudinal research is required to assess the temporal dynamics and treatment responsiveness of ADA. Additionally, while smoking and renal function were significantly correlated, the correlations were weaker than in previous studies, indicating the influence of population heterogeneity [6,11].

Future studies should aim for multicentric, larger sample sizes with longitudinal follow-up in order to validate ADA as a monitoring tool for glycemic

control and diabetes complications. Integrating genetic, oxidative stress, and inflammatory markers may help clarify the pathophysiological significance of ADA. By identifying differences in ADA behavior across treatment groups, socioeconomic backgrounds, and clinical characteristics, stratified analysis may increase the prognostic utility of ADA in a variety of populations[12].

This study makes a significant addition to the growing body of evidence showing that blood ADA is a reliable, accessible biomarker that captures the burden of comorbidities, glycemic control, and the course of type 2 diabetes. ADA's strong correlation with HbA1c and its associations with modifiable risk factors, such as smoking and BMI, underscore its potential for clinical use in the management of diabetes. With further validation, ADA could serve as an auxiliary marker to guide tailored monitoring and intervention strategies in routine diabetic care[1,2,5,6].

Conclusion

This study demonstrates a significant correlation between serum adenosine deaminase (ADA) levels and HbA1c levels in patients with type 2 diabetes mellitus (T2DM), highlighting the potential role of ADA as a biomarker for glycemic control and metabolic dysfunction. Elevated ADA levels were notably associated with poor blood sugar control, obesity, longer diabetes duration, and dyslipidemia. Multivariate analysis further identified ADA as an independent predictor of poor glycemic control, emphasizing its potential for use as a cost-effective adjunct marker in diabetes monitoring[1,2,4,5].

These findings suggest that ADA reflects not only glycemic burden but also the inflammatory and metabolic disturbances characteristic of T2DM. The study underscores the utility of ADA as a multifaceted marker for monitoring disease progression, assessing complication risk, and guiding personalized diabetes management strategies [1,2,4,5].

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