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Assessment of Serum Adenosine Deaminase (ADA) Levels as a Predictive Marker for Diabetes Mellitus in Obese Individuals: A Case–Control Study at a Tertiary Care Center

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ABSTRACT

Background: This study investigated serum adenosine deaminase (ADA) as a potential biomarker for metabolic dysfunction in obesity and type 2 diabetes mellitus (T2DM). **Methods:** A case-control study was conducted with 160 participants (40 per group): Group 1:- non-obese T2DM (BMI <25 kg/m²), Group 2:- obese non-diabetic (BMI ≥25 kg/m²), Group 3:- non-obese healthy controls (BMI <25 kg/m²), and Group 4:- obese T2DM (BMI ≥25 kg/m²). ADA levels and glycemic parameters (FBS, PPBS, HbA1c) were analyzed using ANOVA with Tukey's post-hoc test. **Results**: ADA levels were significantly elevated in obese groups (Group 2: 22.33±16.09 U/L; Group 4: 27.15±20.73 U/L) versus non-obese groups (Group 1: 13.71±6.18 U/L; Group 3: 10.41±4.71 U/L; p<0.01). Obese T2DM showed highest ADA (p<0.001 vs all groups). Notably, obese non-diabetics had higher ADA than healthy controls (p<0.01), while glycemic parameters remained normal. **Conclusion:** Elevated ADA in obese individuals, particularly before diabetes onset, suggests its potential as an early metabolic dysfunction marker. These findings support ADA's role in obesity-related inflammation and insulin resistance.

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INTRODUCTION

Obesity is defined as a state of excess adipose tissue mass that adversely affects health. The direct measurement of fat mass is difficult to assess in routine clinical practice, so a proxy measure that is the body mass index (BMI), is generally used. This is calculated as weight/height^2 (in kg/m2) [1]. BMI more than 25kg/m^2 is defined as obesity in Asian population [2]. According to the WHO, obesity has nearly tripled worldwide since 1975. In 2016, >1.9 billion adults aged ≥18 years old were overweight. Of these, >650 million were obese; 39% of adults aged ≥18 years old were overweight in 2016, and 13% were obese [3].

As people become obese, one of the first and most prominent biochemical abnormalities that develops is the need for increased circulating concentrations of insulin to maintain glucose homeostasis. There are two main theories for the association of obesity with insulin resistance. In the first, products of macrophages and other inflammatory cells that are more abundant in obese adipose tissue can, through paracrine or endocrine routes, disturb insulin's action in muscle and liver cells. In the second, as adipose storage deposits fill up, they become less able to take on excessive calories, which end up being stored as ectopic lipid in tissues such as muscle and liver, which are not primarily designed to store nutrients of this type. The evidence in humans is stronger for the latter hypothesis [4].

The insulin resistance characteristic of the over-nourished state strongly predisposes to the development of type 2 diabetes in people who, largely for genetic reasons, are less able to maintain the high

levels of insulin secretion over many decades. Impaired glucose tolerance and type 2 diabetes are among the most common complications of obesity.

Biochemically, obesity is linked with a low-grade systemic inflammation, where the adipose tissue secretes several chemical mediators like tumor Necrosis Factor-α(TNF-α), Interleukin-6 (IL-6) and leptin [5-7].Further, TNF-α has been shown to have generate insulin resistance by affecting insulin receptors phosphorylation and the insulin receptor substrate [7-9]. Insulin resistance is associated with T2DM. Hence obesity and Diabetes Mellitus show strong correlation. There is also strong evidence that Indians have a greater degree of insulin resistance and a stronger genetic predisposition to Diabetes [9,10].

Adenosine is a nucleotide produced in the body, and has potent anti-inflammatory effects, one of them being its ability to inhibit TNF-α by A3 receptor activation. Adenosine Deaminase (ADA) facilitates irreversible deamination of adenosine to inosine. ADA is present in all mammalian tissues. Glucose uptake into cells is increased by adenosine. Higher ADA activity also decrease adenosine levels in insulin sensitive tissues which ultimately results in decreased uptake of glucose into cells. Hence estimating ADA levels might provide an insight regarding insulin sensitivity and inflammation[11].

Our study was aimed at assessing ADA level as a marker of predicting diabetes among obese individuals. Hence it may help in identifying population at risk or early detection of diabetes among obese population. This helps in early initiation of therapy for diabetes which is one of the major causes of morbidity and morbidity among obese patients.

We believe that this study serves as a roadmap for future researchers who wish to study utility of including ADA levels as part of routine investigations among obese patients to detect diabetes.

MATERIALS AND METHODS

Study population included patients attending OPD/IPD of ESIC MC & PGIMSR, Rajajinagar, Bangalore. Study design is a Case-Control study done for a period of 12 months from November 2023 to November 2024.

The sample size was calculated using the G Power Software V.3.9.7. Considering the effect size to be measured at 0.3 for 'F tests - ANOVA: Fixed effects, omnibus, one-way' among 4 groups with α err prob at 0.05. The total sample size was estimated at 160 with a power of 90%.

Inclusion Criteria:

Age more than 18 years.

The study population was divided into 4 groups

Cases and Controls

Group 1: Obese diabetics Non-obese T2DM (N=40)

Patients with T2DM as per ADA (American Diabetic Association) criteria

BMI < 25kg/m^2

Group 2: Obese non-diabetics T2DM (N=40)

BMI > 25kg/m^2

Group 3: Non-obese diabetics healthy adults (N=40)

Non-diabetic subjects

BMI < 25kg/m^2

Group 4: Non-obese non-diabetic T2DM (N=40)

Patients with T2DM as per ADA (American Diabetic Assication) criteria

BMI > 25kg/m^2.

The exclusion criteria comprised patients with type 1 diabetes mellitus, those on insulin therapy, and individuals with hypertension, ischemic heart disease, renal failure, malignancy, chronic liver disease, tuberculosis, immunological disorders, or pregnancy.

Methodology

Clinical Data Collection: Demographic information, medical history, and anthropometric measurements (e.g., height, weight, BMI) were recorded for all participants. Fasting blood samples were collected from all participants. Serum was isolated for ADA level analysis, with proper handling and storage protocols followed to maintain sample integrity. ADA Level Analysis: ADA levels in serum samples were analyzed using a standardized laboratory method.

Assessment tools included Adenosine deaminase (ADA), Fasting blood sugar (FBS), Post Prandial Blood Sugar (PPBS), HbA1C, Renal function tests, Complete blood count, Liver function test, CRP Serum electrolytes, ESR.

Statistical analysis -The collected data were entered in the Microsoft Excel 2016 and analysed with IBM SPSS Statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp). To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the multivariate analysis the one-way ANOVA with Tukey's Post-Hoc test was used. To find the significance in qualitative categorical data Chi-Square test was used. In all the above statistical tools the probability value . A p-value of < 0.05 was considered statistically significant is considered as significant level.

RESULTS

1. Demographic Characteristics

The majority of participants were aged 41-50 years (28.8%), followed by 61-70 years (19.4%). The mean age was 49.3 ± 14.56 years.

Table 1: Age Distribution of the Study Population

Age Distribution		
Age	Frequency (N)	Percentage (%)
18 - 20	4	2.5
21 - 30	13	8.1
31 - 40	26	16.3
41 - 50	46	28.8
51 - 60	30	18.8
61 - 70	31	19.4
71 - 80	7	4.4
≥ 80	3	1.9
Total	160	

The above table shows Age distribution where Upto 20 yrs is 2.5%, 21 - 30 yrs is 8.1%, 31 - 40 yrs is 16.3%, 41 - 50 yrs is 28.8%, 51 - 60 yrs is 18.8%, 61 - 70 yrs is 19.4%, 71 - 80 yrs is 4.4%, Above 80 yrs is 1.9% and the mean age ± standard deviation is 49.3±14.6 years. The Age between Groups by Pearson's Chi-Square test where χ^2=31.32, p=0.068> 0.05, which shows no statistically significant association between Age and Group.

Table 2:

Gender Distribution		
	Frequency (n)	Percentage (%)
Male	98	61.3
Female	62	38.8
Total	160	

Males constituted a higher proportion 98 (61.3%) of the sample compared to females 62 (38.8%) as in Table 2. **(**Table 2- Gender Distribution of the study population**).**

Table 3: Showing BMI Distribution

Participants	Mean Bmi (Kg/M^2)	SD
Group I	22.26	1.51
Group II	28.05	2.21
Group III	22.06	5.12
Group IV	29.33	3.33

The **c**omparison of Gender between Groups by Pearson's Chi-Square test where χ^2=0.527, p=0.913> 0.05, which shows no statistically significant association between Gender and Groups.

Table 4: ADA Distribution Among Study Population

Variable	Groups	Mean	SD
ADA	Group I	13.71	6.18
	Group II	22.33	16.09
	Group III	10.41	4.71
	Group IV	27.15	20.73

Obese DM has the highest ADA levels.Obese individuals (Groups II and IV) had increased ADA when compared to non-obesity groups (Groups I and III).

The above table (Table 4) shows comparison of ADA between Groups by Oneway ANOVA test where F-value = 12.664, p -= 0.0005<0.01, with mean±SD of Group I is (13.71±6.18), Group II is (22.33±16.09), Group III is (10.41±4.71) and Group IV is (27.15±20.73), which shows a highly statistically significant difference at p < 0.01 level

Table: 5 Showing Comparative Analysis of Individual Groups with ADA Values

Comparison	Mean Difference (I-J)	P-Value	Significance
Non-obese T2DM vs Obese non-diabetic	-8.62	0.028	Significant
Non-obese T2DM vs Healthy control	3.3	0.704	Not significant
Non-obese T2DM vs Obese T2DM	-13.44	0.001	Highly significant
Obese non-diabetic vs Healthy control	11.92	0.001	Highly significant
Obese non-diabetic vs Obese T2DM	-4.82	0.396	Not significant
Healthy control vs Obese T2DM	-16.74	0.001	Highly significant

The Tukey's Post Hoc Test shows a statistical significance difference at p <0.05 level for Group I with Group II, no statistical significance difference at p >0.05 level for Group I with Group III, a highly statistical significant difference at p <0.01 level for Group I with Group IV, a highly statistical significant difference at p <0.01 level for Group II with Group III, no statistical significance difference at p >0.05 level for Group II with Group IV, a highly statistical significant difference at p <0.01 level for Group III with Group IV.

Table 6: Showing Distribution of FBS Among Study Participants

Variable	Groups	N	Mean	SD
FBS	Group I	40	183.50	77.95
	Group II	40	102.15	17.36
	Group III	40	91.03	14.52
	Group IV	40	209.00	67.91

Obesity alone (Group II) does not affect FBS.

The above table shows comparison of FBS between Groups by Oneway ANOVA test where F-value = 49.141, p = 0.0005<0.01, with mean±SD of Group I is (183.50±77.95), Group II is (102.15±17.36), Group III is (91.03±14.52) and Group IV is (209.00±67.91), which shows a highly statistically significant difference at p < 0.01 level.

Table 7: Showing Distribution of PPBS Among Study Participants

	Groups	N	Mean	SD
PPBS	Group I	40	237.68	102.32
	Group II	40	138.05	34.28
	Group III	40	120.45	32.64
	Group IV	40	270.08	100.80

The above table shows comparison of PPBS between Groups by Oneway ANOVA test where F-value = 37.805, p = 0.0005<0.01, with mean±SD of Group I is (237.68±102.32), Group II is (138.05±34.28), Group III is (120.45±32.64) and Group IV is (270.08±100.80), which shows a highly statistically significant difference at p < 0.01 level

Table 8: Showing Distribution of HBA1C- Among Study Participants

Variable	Groups	N	Mean	SD
HBA1C	Group I	40	8.96	3.28
	Group II	40	5.73	0.58
	Group III	40	5.82	0.44
	Group IV	40	9.24	2.55

The above table shows comparison of HBA1C between Groups by Oneway ANOVA test where F-value = 33.208, p = 0.0005<0.01, with mean±SD of Group I is (8.96±3.28), Group II is (5.73±0.58), Group III is (5.82±0.44) and Group IV is (9.24±2.55), which shows a highly statistically significant difference at p < 0.01 level

DISCUSSION

The findings of this study reveal a clear gradient in serum ADA levels across the study groups, with the highest levels observed in obese T2DM patients (Group IV), followed by obese non-diabetics (Group II), non-obese diabetics (Group I), and the lowest in healthy controls (Group III). This pattern suggests that while both obesity and diabetes independently contribute to elevated ADA, their combined presence exerts an additive effect. The significant difference in ADA levels between obese non-diabetics and healthy controls implies that obesity alone-even in the absence of overt diabetes-may drive subclinical metabolic disturbances linked to adenosine metabolism.

A key observation was that ADA levels in obese non-diabetics (Group II) were significantly higher than in non-obese diabetics (Group I), despite comparable glycemic parameters between Groups II and III. This raises the possibility that ADA elevation in obesity may precede hyperglycemia, positioning it as an early marker of metabolic dysregulation rather than merely a consequence of diabetes. Given adenosine's role in suppressing inflammation and enhancing insulin sensitivity, heightened ADA activity could accelerate its degradation, creating a pro-inflammatory and insulin-resistant milieu that predisposes to diabetes.

The glycemic parameters (FBS, PPBS, HbA1c) followed expected trends, with the highest values in diabetic groups (I and IV). Notably, obesity alone (Group II) did not significantly alter FBS compared to healthy controls, reinforcing that hyperglycemia is a later manifestation of insulin resistance. However, the fact that ADA was elevated in Group II suggests that ADA may reflect early metabolic stress before glucose dysregulation becomes apparent.

The strong association between obesity, diabetes, and ADA levels supports the hypothesis that chronic low-grade infla-

-mmation in adipose tissue drives ADA upregulation. Since adenosine inhibits TNF-α-a key mediator of insulin resistance-reduced adenosine due to increased ADA activity could perpetuate inflammation and metabolic dysfunction. This aligns with the observed higher ADA in obese individuals, irrespective of diabetes status, and underscores ADA's potential as a biomarker for "at-risk" metabolic states.

CONCLUSION

This study demonstrates that serum ADA levels are markedly elevated in obese individuals, with the highest levels seen in those with concurrent T2DM. The findings suggest that ADA may serve as an early indicator of metabolic dysfunction in obese individuals before overt diabetes develops. Obesity and diabetes synergistically amplify ADA activity, reflecting compounded inflammatory and insulin-resistant states. Routine ADA measurement in high-risk obese populations could facilitate earlier intervention to prevent diabetes onset.

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