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Serum ADA and Glycated Hemoglobin in Type 2 Diabetes Mellitus

Dr. Anand Kumar Gupta[*1] **& Dr. Deepika Lahon**[2]

[1]Post Graduate Trainee, Department of Biochemistry, Tezpur Medical College & Hospital, Tezpur, Assam.

[2]Professor & HOD, Department of Biochemistry, Tezpur Medical College & Hospital, Tezpur, Assam.

HIGHLIGHTS

1. Correlating serum ADA with HbA1c in diabetes.
2. ADA levels as an inflammatory marker in diabetes.
3. Investigating serum ADA and glycemic control.
4. ADA and HbA1c in diabetes progression.
5. Evaluating ADA's role in diabetes complications.

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ABSTRACT

Introduction: Diabetes Mellitus (DM) is a global health concern characterized by persistent hyperglycemia. Type 2 Diabetes Mellitus (T2DM), accounting for the majority of cases, is associated with various microvascular and macrovascular complications. This study investigates the correlation between serum Adenosine Deaminase (ADA) levels and Glycated Hemoglobin (HbA1c) in T2DM patients, assessing ADA's potential as a marker for glycemic control. **Objective:** The objective of this study is to estimate serum ADA levels in T2DM patients and explore the correlation between serum ADA and HbA1c, aiming to determine whether ADA can be a reliable marker for glycemic control in T2DM. **Methods:** A case-control observational study was conducted at Tezpur Medical College & Hospital over a year, involving 100 participants: 50 T2DM cases (HbA1c > 6.5) and 50 controls (HbA1c < 6.5). Serum ADA and HbA1c levels were measured and analyzed using standardized biochemical methods. Statistical analysis was performed to assess the correlation between ADA and HbA1c levels. **Results:** The study found significantly elevated serum ADA levels in T2DM patients (mean: 19.148 U/L) compared to controls (mean: 10.144 U/L) with a p-value of 0.0023. HbA1c levels were also significantly higher in the T2DM group (mean: 9.744%) compared to controls (mean: 5.786%) with a p-value of 0.0029. A positive correlation between serum ADA and HbA1c levels was observed, suggesting ADA as a potential marker for glycemic control. **Conclusion:** The study provides evidence that serum ADA levels are significantly elevated in uncontrolled T2DM and strongly correlate with HbA1c levels. These findings suggest that ADA could serve as a reliable marker for poor glycemic control in T2DM, reflecting the underlying immune and inflammatory processes associated with the disease.

* Corresponding author.
Dr. Anand Kumar Gupta, Post Graduate Trainee, Department of Biochemistry, Tezpur Medical College & Hospital, Tezpur, Assam.
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INTRODUCTION

Diabetes Mellitus encompasses a group of metabolic disorders characterized by persistent hyperglycemia, or elevated blood glucose levels. This condition arises from either insufficient insulin production, commonly seen in Type 1 diabetes, or inadequate insulin utilization, which is typical of Type 2 diabetes. In some cases, a combination of both factors contributes to the disorder. Chronic hyperglycemia leads to a cascade of pathophysiological changes that affect various organ systems, imposing significant health burdens on individuals and society[1].

India, as of March 2020, reported over 77 million cases of Diabetes Mellitus, reflecting a prevalence rate of 8.9%. Projections indicate that by 2045, the number of individuals with diabetes in India could soar to over 134 million. This anticipated increase underscores the urgent need for comprehensive public health strategies focused on managing and preventing diabetes. Effective healthcare policies, educational initiatives, and infrastructural developments are essential to mitigate the growing burden of diabetes on both individual health outcomes and national healthcare systems[2].

Globally, diabetes affects approximately 530 million adults, with a prevalence rate of 10.5% among those aged 20 to 79 years. Type 2 diabetes accounts for about 98% of all diabetes cases worldwide, although the distribution varies significantly across different regions. In the United States, data from the National Health Interview Survey (2016-2017) revealed an 8.5% prevalence of diagnosed Type 2 diabetes among adults. The Centers for Disease Control and Prevention (CDC) reported that in 2022, about 11.3% of U.S. adults had diagnosed diabetes, totaling 37.3 million people[3]. Of these, 28.7 million had diagnosed diabetes, while an estimated 8.5 million cases remained undiagnosed. Type 2 diabetes constitutes 95% of all diabetes cases in the U.S. The rising prevalence of childhood obesity further exacerbates concerns, suggesting that the incidence of diabetes may continue to escalate. Globally, the incidence of Type 2 diabetes among adolescents and young adults aged 15 to 39 years increased from 117 to 183 per 100,000 population between 1990 and 2019, highlighting a significant global health challenge[4].

Prolonged hyperglycemia leads to secondary complications affecting multiple organ systems. These complications are broadly categorized into microvascular and macrovascular complications. Microvascular complications include diabetic retinopathy, nephropathy, and neuropathy[5]. Diabetic retinopathy is a leading cause of blindness among adults, while diabetic nephropathy is a primary contributor to kidney failure. Diabetic neuropathy, characterized by nerve damage, often leads to pain, numbness, and an increased risk of foot ulcers and amputations. On the other hand, macrovascular complications involve large blood vessels and include the accelerated development of atherosclerosis. This condition, which results in the narrowing and hardening of arteries, significantly increases the risk of cardiovascular diseases such as coronary artery disease, stroke, and peripheral vascular disease[6].

In addition to physical health impacts, diabetes management requires significant lifestyle adjustments, including dietary changes, regular physical activity, and strict medication adherence. The psychological burden of managing a chronic condition, coupled with concerns about complications and quality of life, can lead to stress, anxiety, and depression for individuals with diabetes and their caregivers. Economically, diabetes imposes substantial costs on individuals, families, healthcare systems, and society at large, including medical expenses, lost productivity, and disability[7].

Effective diabetes management strategies focus on controlling blood glucose levels, managing cardiovascular risk factors, and promoting healthy lifestyles. Early diagnosis, patient education, and access to comprehensive healthcare services are critical in mitigating the impact of diabetes[8]. Regular monitoring for early signs of complications and timely intervention are pivotal in improving outcomes and reducing the overall burden of diabetes-related morbidity and mortality[9].

Hemoglobin A1c (HbA1c) is a crucial marker for managing diabetes, reflecting long-term glycemic control. HbA1c levels provide an integrated view of blood glucose concentrations over the past two to three months, guiding healthcare providers in adjusting treatment plans. Lower HbA1c levels indicate better blood glucose management and a reduced risk of diabetes-related complications[10]. Diabetes Mellitus represents a complex interplay of metabolic dysregulation and systemic complications that profoundly impact individuals and healthcare systems worldwide. Effective management and prevention efforts are essential to mitigate these impacts and improve outcomes for those affected by diabetes[11].

This study aims to investigate the levels of serum Adenosine Deaminase (ADA) and Glycated Hemoglobin (HbA1c) in patients with Type 2 Diabetes Mellitus. The objectives include estimating these levels, comparing serum ADA levels between controlled and uncontrolled diabetes cases, and exploring any potential correlation between serum ADA and HbA1c. Additionally, the study seeks to determine whether ADA activity in serum could serve as a reliable marker for glycemic control in individuals with Type 2 Diabetes Mellitus, thereby providing valuable insights into the management of this chronic condition.

MATERIALS AND METHODS

This case-control observational study was conducted over a year (May 1, 2023 - May 1, 2024) at Tezpur Medical College & Hospital (TMCH) to examine serum Adenosine Deaminase (ADA) and Glycated Hemoglobin (HbA1c) levels in Type 2 Diabetes Mellitus (T2DM) patients. The study included 100 participants—50 cases (HbA1c > 6.5) and 50 controls (HbA1c < 6.5)—selected based on specific criteria. Blood samples were collected and analyzed for various biochemical markers, including ADA and HbA1c, using standardized methods. Data analysis was performed using SPSS software, emphasizing the correlation between serum ADA and HbA1c levels to explore ADA's potential as a glycemic control marker in T2DM.

RESULTS

The age distribution between the control and T2DM case groups is similar, with a mean age of 54.5 years (SD = 13.2) in the control group and 52.4 years (SD = 14.3) in the T2DM group. Both groups have a median age of 54 years, and the age ranges are 28-81 years for the control group and 25-78 years for the T2DM group. The p-value of 0.984 indicates no significant age difference between the groups. Gender distribution is also comparable, with 30 males and 20 females in the control group and 34 males and 16 females in the T2DM group, yielding a p-value of 0.845. Therefore, neither age nor gender is a confounding factor in this study.

Table 1: The Comparison of VLDL in Control and Type 2 Diabetes Mellitus Case

	Control	**Case**
Mean	33.6296	47.783
SD	16.23769223	52.71017724
Median	35.36	41.205
Range	9.0 - 65.79	7.0 - 394.0
		p-value: 0.016

VLDL levels, closely linked to triglycerides, are significantly higher in the T2DM group (mean ± SD: 47.783 ± 52.710 mg/dL) compared to the control group (mean ± SD: 33.63 ± 16.238 mg/dL). The median VLDL is also higher in the T2DM group (41.205 mg/dL) versus the control group (35.36 mg/dL). With a p-value of 0.016, this difference is statistically significant, indicating that T2DM is associated with elevated VLDL levels, potentially increasing cardiovascular risk.

Table 2: The Comparison of LDL in Control and Type 2 Diabetes Mellitus Case

	Control	**Case**
Mean	125.0824	118.4228
SD	56.23183656	42.06290828
Median	114.93	118.5
Range	31.0 - 250.27	20.0 - 203.11
		p-value: 0.039

LDL cholesterol, commonly referred to as "bad" cholesterol, is lower in the T2DM group (mean ± SD: 118.423 ± 42.063 mg/dL) compared to the control group (mean ± SD: 125.082 ± 56.232 mg/dL). Although the median LDL levels are similar between the groups, the p-value of 0.039 indicates a statistically significant difference. This may reflect variations in lipid management between individuals with T2DM and those in the control group.

Table 3: The Comparison of HDL in Control and Type 2 Diabetes Mellitus Case

	Control	**Case**
Mean	34.9424	36.7528
SD	9.136924763	11.2987032
Median	36.945	35.23
Range	14.0 - 46.0	15.0 - 68.0
		p-value: 0.048

HDL cholesterol, known as "good" cholesterol, is slightly higher in the T2DM group (mean ± SD: 36.753 ± 11.299 mg/dL) compared to the control group (mean ± SD: 34.942 ± 9.137 mg/dL). While the median HDL levels are similar in both groups, the p-value of 0.048 indicates a statistically significant difference. This suggests that T2DM might be associated with marginally higher HDL levels, although the clinical significance of this finding may be limited.

Table 4: The Comparison of Triglyceride in Control and Type 2 Diabetes Mellitus Case

	Control	Case
Mean	198.4616	206.4804
SD	99.85572058	83.29847006
Median	172.955	193
Range	70.0 - 355.49	36.0 - 386.0
		p-value: 0.0265

Triglyceride levels are slightly higher in the T2DM group (mean ± SD: 206.480 ± 83.298 mg/dL) compared to the control group (mean ± SD: 198.462 ± 99.856 mg/dL). The median triglyceride levels are also elevated in the T2DM group (193 mg /dL) versus the control group (172.955 mg/dL). The p-value of 0.0265 indicates a statistically significant difference, suggesting that T2DM is associated with higher triglyceride levels, which is a recognized risk factor for cardiovascular disease.

Table 5: The Comparison of Cholesterol in Control and Type 2 Diabetes Mellitus Case

	Control	Case
Mean	227.2664	210.6964
SD	77.95642615	75.85607392
Median	241.535	207.15
Range	66.0 - 362.04	50.0 - 363.49
		p-value: 0.036

Cholesterol levels are lower in the T2DM group (mean ± SD: 210.696 ± 75.856 mg/dL) compared to the control group (mean ± SD: 227.266 ± 77.956 mg/dL). The median cholesterol level is also reduced in the T2DM group (207.15 mg/dL) versus the co--ntrol group (241.535 mg/dL). A p-value of 0.036 indicates this difference is statistically significant, suggesting that T2DM is associated with lower cholesterol levels, potentially due to the disease itself or its management strategies.

Table 6: The Comparison of Un Bil in Control and Type 2 Diabetes Mellitus Case

	Control	Case
Mean	0.674	0.74
SD	0.264042359	0.440315286
Median	0.65	0.6
Range	0.2 - 1.6	0.2 - 2.2
		p-value: 0.081

Unconjugated bilirubin levels are slightly higher in the T2DM group (mean ± SD: 0.74 ± 0.440 mg/dL) compared to the control group (mean ± SD: 0.674 ± 0.264 mg/dL). While the median levels are similar in both groups, with ranges of 0.2 - 2.2 mg/dL in the T2DM group and 0.2 - 1.6 mg/dL in the control group, the p-value of 0.081 indicates that this difference is not statistically significant, suggesting that T2DM does not have a significant impact on unconjugated bilirubin levels.

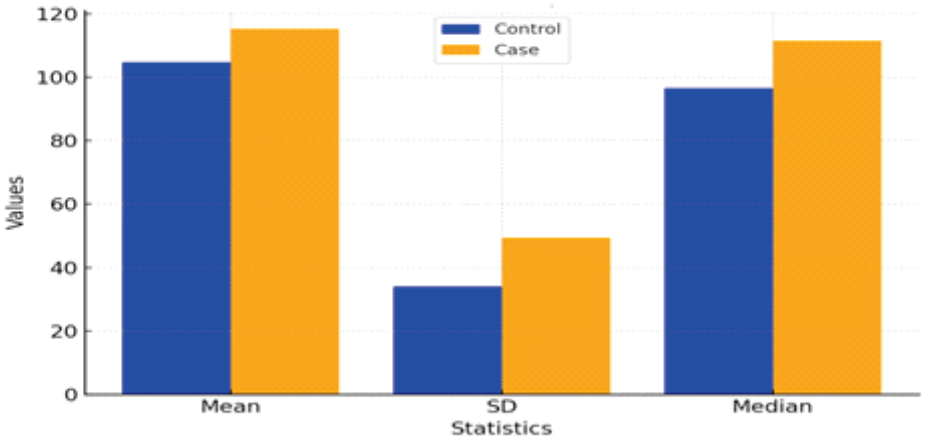

Figure 1 :This bar graph compares the alkaline phosphatase (ALP) levels between the control and case groups.

Alkaline phosphatase (ALP) levels are higher in the T2DM group (mean ± SD: 115.26 ± 49.297 U/L) compared to the control group (mean ± SD: 104.7 ± 33.876 U/L). The median ALP level is also elevated in the T2DM group (111.5 U/L) versus the control group (96.5 U/L), with a broader range in the T2DM group (21 - 353 U/L) compared to the control group (41 - 174 U/L). A p-value of 0.031 indicates a statistically significant increase in ALP levels among T2DM patients, suggesting potential alterations in liver or bone metabolism in this group.

Table 7: The Comparison of ALT in Control and Type 2 Diabetes Mellitus Case

	Control	Case
Mean	45.5	39.78
SD	35.95362659	20.02884654
Median	35	39.5
Range	9 - 188	6-98
		p-value: 0.046

Alanine aminotransferase (ALT) levels are slightly lower in the T2DM group (mean ± SD: 39.78 ± 20.029 U/L) compared to the control group (mean ± SD: 45.5 ± 35.954 U/L). Although the median ALT levels are similar between the groups (39.5 U/L in T2DM cases vs. 35 U/L in controls), the p-value of 0.046 indicates a statistically significant difference, suggesting a modest reduction in ALT levels among T2DM patients.

Table 8: The Comparison of AST in Control and Type 2 Diabetes Mellitus Case

	Control	Case
Mean	51.54	40.84
SD	75.31571915	30.22254868
Median	33	33
Range	19 - 398	17 - 210
		p-value: 0.049

Aspartate aminotransferase (AST) levels are lower in the T2DM group (mean ± SD: 40.84 ± 30.223 U/L) compared to the control group (mean ± SD: 51.54 ± 75.316 U/L). Although the median AST levels are identical in both groups (33 U/L), the range is much broader in the control group (19 - 398 U/L) than in the T2DM group (17 - 210 U/L). The p-value of 0.049 suggests a statistically significant difference, indicating that T2DM may be associated with lower AST levels.

DISCUSSION

Type 2 Diabetes Mellitus (T2DM) is a chronic disorder characterized by insulin resistance, impaired insulin secretion, and hyperglycemia. Effective management requires reliable biomarkers like Glycated Hemoglobin (HbA1c) for long-term glycemic control and Serum Adenosine Deaminase (ADA) for inflammation and insulin resistance. This study explores the correlation between HbA1c and ADA in T2DM patients[12].

Niraula A et al. (2018) and Sharahili AY et al. (2023) both emphasize the predominance of males in Type 2 DM populations, with gender distributions of 103/101 and 53.3% male, respectively. Age also plays a significant role, as Niraula's study showed a higher mean age in T2DM patients (54.82±12.16) compared to controls (45.5±10.4, p=0.01), while Sharahili's study highlighted a high prevalence of T2DM in the 55–64 age group (42.9%). Our study aligns with these findings, indicating a consistent pattern of older age and male gender being associated with Type 2 DM[13,14].

We found significantly elevated ADA levels in the T2DM group (19.148 U/L) compared to controls (10.144 U/L, p=0.0023), consistent with Niraula A et al. (2018), who also reported higher serum ADA levels in T2DM patients (10.55±2.20, p<0.001). Sharahili AY et al. (2023) observed similar patterns, reinforcing the link between increased ADA activity and T2DM[13,14].

Our study also revealed significantly higher HbA1c levels in T2DM patients (9.744%) compared to controls (5.786%, p=0.0029), consistent with findings by Niraula A et al. (2018) and Sharahili AY et al. (2023), further confirming the association between elevated HbA1c levels and poor glycemic control in T2DM populations[13,14].

Our study observed slightly higher urea and creatinine levels in T2DM patients, though not statistically significant, aligning with Lu CF et al. (2021) and Farasat T et al. (2015), suggesting potential kidney function alterations in T2DM. We found no significant difference in total protein and albumin levels between T2DM and control groups, consistent with findings from Lu CF et al. (2021) and Farasat T et al. (2015)[15,16].

Slightly higher globulin levels in T2DM were observed but were not statistically significant, supporting Lu CF et al. (2021) and Caixeta DC et al. (2022). Our study also found lower AST and ALT levels in T2DM, consistent with Cao J et al. (2021) and Alam S et al. (2021). Elevated ALP levels in T2DM, found in our study, align with findings by Alam S et al. (2021) and Cao J et al. (2021). Lastly, total bilirubin levels showed no significant difference, consistent with Alam S et al. (2021) and Kariyawasan CC et al. (2021)[15,17,18,19,20].

Our study found slightly higher unconjugated bilirubin levels in the T2DM group (0.74 ± 0.440 mg/dL) compared to controls (0.674 ± 0.264 mg/dL), though the difference was not statistically significant (p=0.081). This suggests that T2DM does not significantly impact unconjugated bilirubin levels, consistent with findings by Kariyawasan CC et al. (2021) and Alam S et al. (2021), who also observed stable bilirubin levels in T2DM patients[20,19].

We found significantly lower cholesterol levels in the T2DM gr-oup (210.696 ± 75.856 mg/dL) compared to controls (227.266 ± 77.956 mg/dL, p=0.036), potentially due to the disease or its management. This aligns with Choi SW et al. (2012), who reported similar trends, and Sharahili AY et al. (2023), who found that most T2DM patients had normal cholesterol levels, reinforcing the association between T2DM and reduced cholesterol levels[21,14,].

Our study also revealed slightly higher triglyceride levels in the T2DM group (206.480 ± 83.298 mg/dL) compared to controls (198.462 ± 99.856 mg/dL, p=0.0265), consistent with findings by Choi SW et al. (2012) and Sharahili AY et al. (2023), suggesting an increased cardiovascular risk in T2DM patients due to elevated triglyceride levels[21,14].

We observed slightly higher HDL cholesterol levels in the T2DM group (36.753 ± 11.299 mg/dL) compared to controls (34.942 ± 9.137 mg/dL, p=0.048). While statistically significant, the clinical relevance may be limited, contrasting with Choi SW et al. (2012) and Sharahili AY et al. (2023), who reported higher HDL variability in T2DM populations[21,14].

Our study found lower LDL cholesterol levels in the T2DM group (118.423 ± 42.063 mg/dL) compared to controls (125.082 ± 56.232 mg/dL, p=0.039), reflecting possible differences in lipid management. This aligns with Choi SW et al. (2012) and Sharahili AY et al. (2023), who observed similar LDL trends [21,14].

Finally, we found significantly higher VLDL levels in the T2DM group (47.783 ± 52.710 mg/dL) compared to controls (33.63 ± 16.238 mg/dL, p=0.016), suggesting an increased cardiovascular risk, consistent with findings by VinodMahato R et al. (2011) and Sapkota LB et al. (2017). Our study supports the association between T2DM and elevated VLDL levels, further linking T2DM to cardiovascular complications[22,23].

CONCLUSION

In conclusion, this study provides compelling evidence that serum ADA levels are significantly elevated in patients with uncontrolled Type 2 Diabetes Mellitus and strongly correlate with glycated hemoglobin (HbA1c) levels. The findings suggest that ADA could serve as a potential marker for poor glycemic control in T2DM, reflecting the underlying immune and inflammatory processes associated with the disease. The study also highlights the impact of T2DM.

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