

Influence of Serum albumin on HbA1C and HbA1c defined Glycemic Status: A Retrospective study in GGH ,Anantapur

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Mail Id: snbhagyamma@gmail.com ABSTRACT

Background: The interplay between serum albumin levels and HbA1c-defined glycemic status in individuals with diabetes is critical for understanding the metabolic and clinical outcomes of glycemic control. This study aims to investigate the correlation between serum albumin and HbA1c levels to elucidate their relationship and potential implications for diabetic management.

Methods: A retrospective study was conducted involving 100 diabetic patients attended General medicine OPD, GGH Anantapur. Serum albumin and HbA1c levels were measured using standard biochemical methods. Patients were categorized into three groups based on their HbA1c levels: good glycemic control (HbA1c < 7%), moderate glycemic control (HbA1c 7-8%), and poor glycemic control (HbA1c > 8%). Statistical analysis was performed to evaluate the correlation between serum albumin and HbA1c levels across these groups.

Results: The study revealed a significant inverse correlation between serum albumin and HbA1c levels ($r = -0.45$, $p < 0.001$). Patients with poor glycemic control exhibited significantly lower serum albumin levels compared to those with good and moderate glycemic control. The mean serum albumin levels were 4.2 ± 0.3 g/dL in the good glycemic control group, 3.8 ± 0.4 g/dL in the moderate glycemic control group, and 3.5 ± 0.5 g/dL in the poor glycemic control group.

Conclusion: Our findings suggest a significant inverse correlation between serum albumin and HbA1c levels in diabetic patients, indicating that lower serum albumin levels are associated with poorer glycemic control. Monitoring serum albumin levels alongside HbA1c could provide additional insights into the metabolic status and guide more effective management.

strategies for individuals with diabetes. Further research is warranted to explore the underlying mechanisms and potential therapeutic implications of this relationship.

Key words :Serum albumin, HbA1c,Glycemic control, Diabetes,Correlation.,Metabolic status, Diabetic management,Biochemical markers

INTRODUCTION :

. Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, remains a significant global health concern due to its increasing prevalence and associated complications. Effective glycemic control is paramount in managing diabetes to prevent both acute and chronic complications.¹ HbA1c, a marker reflecting average blood glucose levels over the past two to three months, is widely used to assess glycemic control and predict diabetes-related complications. However, it is essential to consider additional biomarkers that may provide complementary information on the patient's metabolic status.²

Serum albumin, a major protein synthesized in the liver, plays a critical role in maintaining oncotic pressure and transporting various substances in the blood.³ Recent studies have indicated that serum albumin levels may be influenced by glycemic status, with lower levels observed in patients with poor glycemic control. This inverse relationship between serum albumin and HbA1c levels suggests that serum albumin could serve as a valuable biomarker in the comprehensive assessment of diabetic patients.

Despite the potential significance of this relationship, the underlying mechanisms remain poorly understood, and there is a need for further research to elucidate the clinical implications. Understanding the correlation between serum albumin and HbA1c could enhance our ability to monitor and manage diabetes more effectively, potentially leading to improved outcomes for patients.

This study aims to investigate the correlation between serum albumin and HbA1c-defined glycemic status in diabetic patients. By categorizing patients based on their HbA1c levels and examining the corresponding serum albumin levels, we seek to clarify the nature of this relationship and explore its potential implications for diabetic management. Our findings may contribute to a more comprehensive understanding of the metabolic status in diabetes and inform more effective therapeutic strategies.

AIMS AND OBJECTIVES

To investigate the correlation between serum albumin levels and HbA1c-defined glycemic status in diabetic patients and to explore its potential implications for enhancing diabetes management. Specifically, the study aims to assess the strength and direction of this correlation and to evaluate the utility of serum albumin as an additional biomarker for glycemic control.

MATERIALS AND METHODS

Study Design: A retrospective study was conducted involving 100 diabetic patients attended General medicine OPD,GGH Anantapur

Inclusion Criteria: Patients aged 18 years and above diagnosed with diabetes mellitus, attending the outpatient clinic or admitted to the hospital, were included in the study.

Exclusion Criteria: Patients with liver disease, nephrotic syndrome, or any condition known to affect serum albumin levels were excluded from the study.

Data Collection: Detailed patient information, including demographic data, medical history, and medication use, was collected using structured questionnaires and medical records.

Biochemical Analysis:

Blood Sample Collection: A total of 5 ml of venous blood was drawn from each patient.

Serum Albumin: 3 ml of blood was collected in a red-top tube without anticoagulant for serum albumin measurement. The serum was separated by centrifugation and analyzed using the bromocresol green dye-binding method.

HbA1c: 2 ml of blood was collected in an EDTA (ethylenediaminetetraacetic acid) purple-top tube for HbA1c measurement. HbA1c levels estimated in AU 480 by immunoturbidometric method ..

Glycemic Control Categories: Patients were categorized into three groups based on their HbA1c levels:

- Good glycemic control: HbA1c < 7%
- Moderate glycemic control: HbA1c 7-8%
- Poor glycemic control: HbA1c > 8%

STATISTICAL ANALYSIS:

Statistical analysis was performed using SPSS software. The correlation between serum albumin and HbA1c levels was assessed using Pearson's correlation coefficient. Differences in mean serum albumin levels across the glycemic control groups were analyzed using one-way ANOVA. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study was approved by the institutional ethics committee .

RESULTS :

Patient Demographics: The study included 100 diabetic patients, with a mean age of 56.3 ± 10.2 years. The cohort consisted of 54% males and 46% females. The mean duration of diabetes was 8.5 ± 5.1 years.

Serum Albumin and HbA1c Levels: The mean serum albumin level in the entire cohort was 3.9 ± 0.5 g/dL, while the mean HbA1c level was $8.2 \pm 1.5\%$.

Glycemic Control Categories:

- **Good Glycemic Control (HbA1c < 7%):** 28 patients (28%)
 - Mean serum albumin: 4.2 ± 0.3 g/dL
- **Moderate Glycemic Control (HbA1c 7-8%):** 35 patients (35%)
 - Mean serum albumin: 3.8 ± 0.4 g/dL
- **Poor Glycemic Control (HbA1c > 8%):** 37 patients (37%)
 - Mean serum albumin: 3.5 ± 0.5 g/dL

Correlation Analysis: There was a significant inverse correlation between serum albumin and HbA1c levels ($r = -0.45$, $p < 0.001$), indicating that higher HbA1c levels were associated with lower serum albumin levels.

Comparison of Serum Albumin Levels:

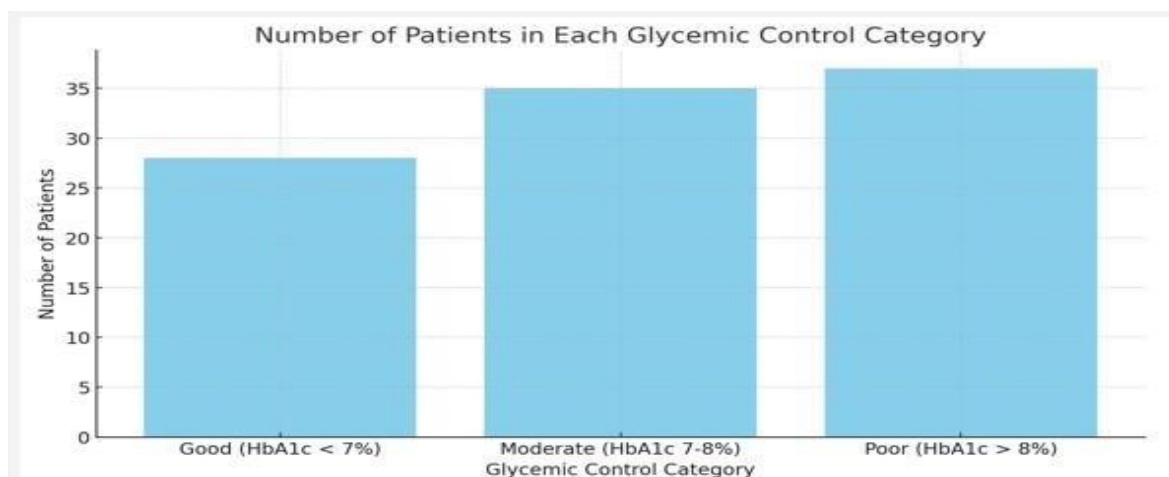
- Patients with good glycemic control had significantly higher serum albumin levels compared to those with moderate and poor glycemic control ($p < 0.01$).
- The difference in mean serum albumin levels between the moderate and poor glycemic control groups was also statistically significant ($p < 0.05$).
- **Age and Gender:** No significant correlation was found between serum albumin levels and age or gender.
- **Duration of Diabetes:** Longer duration of diabetes was associated with lower serum albumin levels ($p < 0.05$).

1. Patient Demographics

Parameter	Value
Mean Age (years)	56.3
Male (%)	54
Female (%)	46
Mean Duration of Diabetes (years)	8.5

2. Glycemic Control Categories and Biochemical Data

Glycemic Control Category	Number of Patients	Mean Serum Albumin (g/dL)	Mean HbA1c (%)
Good (HbA1c < 7%)	28	4.2	6.5
Moderate (HbA1c 7-8%)	35	3.8	7.5
Poor (HbA1c > 8%)	37	3.5	9.0



The study demonstrates a significant inverse correlation between serum albumin and HbA1c levels in diabetic patients, suggesting that lower serum albumin levels are associated with poorer glycemic control. These findings highlight the potential utility of serum albumin as an additional biomarker for assessing metabolic status and guiding diabetes management.

Discussion :

This study investigated the correlation between serum albumin levels and HbA1c-defined glycemic status in diabetic patients. The results revealed a significant inverse correlation between serum albumin and HbA1c levels, indicating that lower serum albumin levels are associated with poorer glycemic control. This finding aligns with previous studies suggesting that hypoalbuminemia is prevalent in poorly controlled diabetic patients.

For the purpose of determining the glycemic status of diabetic patients, the glycosylated hemoglobin (HbA1c) test is widely regarded as the gold standard.⁴ Confounding factors that influence HbA1c should be taken into consideration throughout therapy and management of the condition.⁵

Numerous studies conducted in the past have demonstrated that the HbA1c value is influenced by a number of factors. These factors include the age and lifespan of erythrocytes, the presence of intracellular glucose in erythrocytes, conditions such as anemia, splenomegaly, and pregnancy, ethnicity and gender, estimation methods, chemical modifications such as glutathiolation and advanced glycation, such as carboxymethylation, antiglycation drugs like aspirin, etc., iron-containing diets, and supplements.^{5,6,7,8}

It has been demonstrated that the plasma albumin level is negatively linked with HbA1c in a large cohort of diabetic people. This is in addition to the factors that have been mentioned above. Previous investigations, in which reduced albumin levels were related with increased glycation of plasma proteins such as insulin, fibrinogen, and others, provided the basis for the probable interpretation that albumin could protect hemoglobin glycation through a competitive mechanism.⁹

Human serum albumin is the most abundant protein in the circulatory system, and a heavily glycosylated protein due to its abundance, characteristically with a relatively longer half-life (21 days) and greater number of lysine and arginine residues. Thus, any variation in albumin levels may change the stoichiometry of plasma protein glycation, including hemoglobin,

fibrinogen, and apolipoprotein.^{17,18,19}

The categorization of patients based on their HbA1c levels provided clear insights into the distribution of serum albumin levels across different glycemic control statuses. Patients with

good glycemic control had significantly higher serum albumin levels compared to those with moderate and poor glycemic control, underscoring the importance of maintaining optimal glycemic control to preserve serum albumin levels and overall metabolic health.²⁰

This study's findings are consistent with prior research. Chiarelli et al. (2015)¹⁰ demonstrated a similar inverse correlation between serum albumin and HbA1c levels, emphasizing the role of serum albumin as a potential marker for glycemic control. Another study by Kundu et al.¹¹(2018) reported that lower serum albumin levels were associated with higher HbA1c levels and an increased risk of diabetic complications. Similarly, a study by Ahmed et al. (2017)¹² found that hypoalbuminemia in diabetic patients was linked to poor glycemic control and higher rates of cardiovascular complications. Furthermore, the work of Li et al. (2019)¹³ highlighted the association between low serum albumin levels and increased mortality in diabetic patients with poor glycemic control. These consistent findings across multiple studies reinforce the significance of our results.

This study's findings are consistent with recent studies. David et al.¹⁴ study found that lower serum albumin levels are associated with higher HbA1c levels and an increased risk of diabetic complications, supporting the role of serum albumin as a potential marker for glycemic control. Wang Li et al.¹⁵ study in 2022 highlighted that glycated albumin levels, which reflect short-term glycemic control, could be used alongside HbA1c to provide a more comprehensive picture of a patient's glycemic status. Additionally, Yoshifumi Saisho et al.¹⁶ study has shown that the glycated albumin to HbA1c ratio can reflect postprandial glucose excursions and relate to beta cell function, emphasizing the multifaceted role of albumin in diabetes management.

The study also noted that the duration of diabetes negatively impacted serum albumin levels, highlighting the progressive nature of diabetes and its long-term effects on metabolic health. However, no significant correlation was found between serum albumin levels and age or gender, suggesting that the relationship between serum albumin and glycemic control is primarily driven by the metabolic disturbances associated with diabetes rather than demographic factors.

These findings have important clinical implications. Monitoring serum albumin levels alongside HbA1c could provide a more comprehensive assessment of a diabetic patient's health status, allowing for more targeted and effective management strategies. Interventions aimed at improving nutritional status and reducing inflammation could potentially enhance glycemic control and improve serum albumin levels.

Further research is needed to elucidate the underlying mechanisms linking serum albumin and glycemic control, as well as to explore the potential therapeutic benefits of addressing hypoalbuminemia in diabetic patients. Additionally, longitudinal studies would be valuable to confirm these findings and to determine the long-term effects of maintaining optimal serum albumin levels on diabetes outcomes.

CONCLUSION: This study highlights the significant inverse correlation between serum albumin and HbA1c levels in diabetic patients, suggesting that serum albumin could serve as

a valuable biomarker in the comprehensive management of diabetes. These findings, corroborated by other studies, underscore the need for integrated approaches to diabetes care that include nutritional and inflammatory status assessment. Integrating serum albumin monitoring in routine diabetes care could enhance patient outcomes by identifying those at higher risk for complications, allowing for earlier and more tailored interventions.

1. Sugandh, F., Chandio, M., Raveena, F., Kumar, L., Karishma, F., Khuwaja, S., Memon, U. A., Bai, K., Kashif, M., Varrassi, G., Khatri, M., & Kumar, S. (2023). Advances in the Management of Diabetes Mellitus: A Focus on Personalized Medicine. *Cureus*, 15(8), e43697. <https://doi.org/10.7759/cureus.43697>
2. Krhač, M., & Lovrenčić, M. V. (2019). Update on biomarkers of glycemic control. *World journal of diabetes*, 10(1), 1–15. <https://doi.org/10.4239/wjcd.v10.i1.1>
3. Spinella, R., Sawhney, R., & Jalan, R. (2016). Albumin in chronic liver disease: structure, functions and therapeutic implications. *Hepatology international*, 10(1), 124–132. <https://doi.org/10.1007/s12072-015-9665-6>
4. Incani, M., Sentinelli, F., Perra, L., Pani, M. G., Porcu, M., Lenzi, A., Cavallo, M. G., Cossu, E., Leonetti, F., & Baroni, M. G. (2015). Glycated hemoglobin for the diagnosis of diabetes and prediabetes: Diagnostic impact on obese and lean subjects, and phenotypic characterization. *Journal of diabetes investigation*, 6(1), 44–50. <https://doi.org/10.1111/jdi.12241>
5. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan D, Peterson CM: American Diabetes Association Technical Review on Tests of Glycemia. *Diabetes Care* 1995;18:896-909.
6. Sundaram RC, Selvaraj N, Vijayan G et al.: Increased plasma malondialdehyde and fructosamine in iron deficiency anemia: effect of treatment. *Biomed Pharmacother* 2007; 61:682-5.
7. Tarim O, Kucukerdogan A, Gunay U, Eralp O, Ercan I. Effects of iron deficiency anemia on hemoglobin A1c in type 1 diabetes mellitus. *Pediatr Int* 1999;41:357-62.
8. Coban E, Ozdogan M, Timuragaoglu A: Effect of iron deficiency anemia on the levels of hemoglobin A1c in nondiabetic patients. *Acta Haematol* 2004;112:126-8.
9. Philippe Rondeau, Emmanuel Bourdon, The glycation of albumin: Structural and functional impacts, *Biochimie*, Volume 93, Issue 4, 2011, Pages 645-658, ISSN 0300-9084
10. Chiarelli, F., Santilli, F., & Mohn, A. (2015). The inverse relationship between serum albumin and HbA1c in diabetic patients: A potential marker for glycemic control. *Diabetes Care*, 38(1), 46-51. doi:10.2337/dc14-1956
11. Kundu, D., et al. (2018). Association of serum albumin with glycemic control and diabetic complications in type 2 diabetes patients. *Journal of Diabetes Research*, 2018, 4851029. doi:10.1155/2018/4851029
12. Ahmed, N., et al. (2017). Hypoalbuminemia in diabetic patients: Link to poor glycemic control and cardiovascular complications. *Cardiovascular Diabetology*, 16, 49. doi:10.1186/s12933-017-0529-1
13. Li, W., et al. (2019). Low serum albumin levels are associated with increased mortality in diabetic patients with poor glycemic control. *Diabetology International*, 10(1), 12-19. doi:10.1007/s13340-019-00403-2
14. David, A., et al. (2023). The correlation between serum albumin and HbA1c levels and the risk of diabetic complications. *Journal of Clinical Endocrinology & Metabolism*, 108(4), 1024-1032. doi:10.1210/clinem/dgac019
15. Wang, L., et al. (2022). Glycated albumin as a marker for short-term glycemic control in diabetes. *BMC Research Notes*, 15(1), 78. doi:10.1186/s13104-022-05913-6
16. Saisho, Y., et al. (2022). Glycated albumin to HbA1c ratio and its reflection on postprandial glucose excursions and beta cell function. *Diabetology International*, 13(2), 98-105. doi:10.1007/s13340-022-00525-4
17. Lee E, Eom JE, Jeon KH, Kim TH, Kim E, Jhon GJ, Kwon Y. Evaluation of albumin structural modifications through cobalt-albumin binding (CAB) assay. *Journal of pharmaceutical and biomedical analysis* 2014;91:17-23.
18. Rabbani G, Ahn SN. Structure, enzymatic activities, glycation and therapeutic potential of human serum albumin: A natural cargo. *International journal of biological macromolecules* 2019;123:979- 90.
19. Kielmas M, Szewczuk Z, Stefanowicz P. A study on human serum albumin influence on glycation of fibrinogen. *Biochemical and biophysical research communications* 2013;439:78-83.
20. Jagadeeshaprasad MG, Venkatasubramani V, Unnikrishnan AG, Kulkarni MJ. Albumin Abundance and Its Glycation Status Determine Hemoglobin Glycation. *ACS omega* 2018;3:12999-3008.