Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.1439
Original Article

ASSESSMENT OF THE RELATIONSHIP BETWEEN SERUM ALBUMIN AND GLUCOSE LEVELS IN HEALTHY, PRE-DIABETIC, AND DIABETIC INDIVIDUALS' CASE-CONTROL OBSERVATIONAL STUDY

*[1]Kanchan Kumari, [2]Swati Sinha, [3]Ajay Kumar Singh, *[4]Vaidehi, [5]Yogesh Krishna Sahay*
[1]Associate Professor, Dept. of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.
[2]Associate Professor, Department of Physiology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.
[3]Tutor, Department of Physiology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.
[4]Tutor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.
[5]Professor &HOD, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.

Abstract

Introduction

Diabetes mellitus is a metabolic disorder characterized by chronic persistent hyperglycemia. If it persists for a prolonged period, it may lead to microvascular and macrovascular complications. Several studies were done to estimate serum albumin in diabetes mellitus, and there is uncertainty about the relationship between serum albumin and diabetes.

Aim and objectives

The aim of this study is to compare serum albumin in normal, pre-diabetic, and diabetic individuals.

Materials and methods

Glucose estimation was done using the Glucose oxidase Peroxidase method, and Albumin estimation was done using the Bromocresol Green method in Pawapuri, Nalanda.

Results

A total of 160 cases of age between 30-80 years were selected out of which 40 each were healthy, pre-diabetic, diabetic with Glucose levels less than 300mg/dl and above 300mg/dl. The mean Serum albumin level with standard deviation in normal individuals was 4.63± 30, in pre-diabetic individuals was 4.38 ± 0.24, in diabetic individuals were 4.23 ± 0.41, in uncontrolled diabetic individuals were3.98± 0.35. There was a significant decrease in serum albumin in pre-diabetic, diabetic, and uncontrolled diabetic individuals from normal individuals.

Conclusion

There was an inverse relationship between serum Albumin and Glucose in diabetic individuals. By regular estimation of serum albumin in diabetic individuals, the development of complications in diabetic individuals can be delayed.

Recommendation

Regular estimation of serum albumin levels in diabetes and keeping serum albumin levels within normal limits is required to delay diabetic complication development.

Keywords: *Pre-diabetic, Diabetic, Serum Albumin, FBG, PPBG.*
Submitted: *2024-10-30* ***Accepted:*** *2024-11-22*

Corresponding Author: *Vaidehi*
Email: *drvaidehiojas@gmail.com*
Tutor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.

Introduction

Diabetes mellitus is a metabolic disease characterized by chronic persistent hyperglycemia. It is mainly classified into type 1, type 2, gestational, and secondary diabetes. In type 1 diabetes etiology is unknown, and results from defective beta cells of the pancreas that affect insulin secretions. Type

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.1439
Original Article

2 diabetes mellitus accounts for 95% of cases in adults, its milder form results from a lack of insulin sensitivity in muscle and adipose tissue due to obesity and a sedentary lifestyle. If diabetes persists for a prolonged period it may lead to many complications that lead to microvascular and macrovascular complications. Microvascular complications include neuropathy, retinopathy, nephropathy, etc. Macrovascular complications include cardiovascular disease, stroke, peripheral vascular disease, etc (1).

In 2020, according to the International Diabetes Federation, about 463 million people had diabetes in the world (2). It has been estimated that 700 million people will have diabetes and 548 million people will have impaired Glucose tolerance by the year 2045. According to the International Diabetes Federation, the burden of diabetes is increasing in low and middle-income groups compared to high-income groups.

In India, the prevalence of diabetes has been increasing since 1990 and more rapidly since year 2000. About 74 million people in India are living with diabetes, the second highest in the world after China. Over half of the people with diabetes in India are undiagnosed (3). Albumin is a small globular protein with a molecular weight of 66.5 KD. In humans, albumin is a major plasma protein that accounts for 50% of plasma proteins synthesized exclusively in the liver. Its normal level is 3.5-5 gm/dl. Major functions of serum albumin include the maintenance of plasma oncotic pressure, transport of endogenous substances such as free fatty acids, bilirubin, steroid hormones, copper, calcium, etc, and exogenous substances such as drugs. It also has buffering action (4). Serum albumin estimation is commonly done to assess liver function and kidney disease. Hyperalbuminemia is rarely seen in clinical practice but hypoalbuminemia is commonly seen. Hypoalbuminemia is usually seen in liver disease, kidney disease, and other conditions such as malnutrition.

Several studies were done to estimate levels of serum albumin in diabetes mellitus. Most authors found an association between serum Albumin and the prediction of diabetes, the development of complications of diabetes, and the effects of diabetes on serum albumin(5). Some studies found an inverse relationship between serum albumin and glycemic status(6,7), while other studies found no association between serum albumin and type 2 diabetes, and there is uncertainty about the relationship between serum albumin and diabetes. This study was done to assess the reality of the relationship between serum albumin and blood glucose levels.

Aim and objective

The aim of this study is to compare serum albumin in normal, pre-diabetic, and diabetic persons. Albumin is more prone to glycation than other proteins. By keeping serum albumin within normal limits, the complications of diabetes can be delayed.

Material and method

Study Design

This is a cross-control hospital-based observational study

Study Location

This study was conducted in the biochemistry unit of the central laboratory of Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda.

Participants

A total of 160 cases of age between 30-80 years were selected out of which 40 were healthy, 40 pre-diabetic, 40 were diabetic with Glucose levels less than 300mg/dl, and 40 were diabetic with Glucose levels above 300mg/dl.

Selection of cases

All the cases and controls were free from liver disease, kidney disease, protein-losing enteropathy, malnutrition, diabetic and hypertensive nephropathy, nephrotic syndrome, and anasarca. All the cases and controls were with normal blood urea, creatinine, serum electrolytes, uric acid, bilirubin, and SGPT levels. All cases and controls were not taking hepatotoxic, nephrotoxic drugs and alcohol. None of them were smokers.

Estimation of blood glucose was done by glucose oxidase peroxide method by a fully automatic analyzer in the Biochemistry unit of the central laboratory in Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda. Serum albumin estimation was done by the Bromocresol Green method in the fully automatic analyzer. Total protein estimation was also done. Urine was examined for proteinuria to exclude kidney disease. Estimation of serum bilirubin and SGPT was also done to exclude liver disease. A detailed history was taken to exclude alcohol consumption, smoking, use of hepatotoxic and nephrotoxic drugs and any other medications, and past medical history.

Procedure

Venous blood was collected from the anticubital vein in a fluoride vial.

Principle

Glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of Glucose oxidase. The hydrogen peroxide then reacted with 4-amino antipyrine and o-hydroxybenzoic acid to form a red color compound and the intensity of the red color was measured at 505 nm wavelength.

Reagent 1- enzyme reagent

Reagent 2- glucose standard 100 mg/dl

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.1439
Original Article

Three clean and dry test tubes were taken and leveled Blank(B), Standard (S) and Test(T)

Table 1: Addition sequence 1

Addition sequence	B	S	T
Enzyme reagent	1ml	1ml	1ml
Sample		10 microlitre	
Standard			10microlitre

Mixed and incubated at 37°C for 10 minutes. Absorbance of S and T was measured against the reagent blank. The whole process was automated in the fully automatic analyzer.
Albumin estimation was done by the Bromocresol Green method.
Assay principle: at pH 3.68 Albumin acts as a cation and binds to the anionic dye Bromocresol Green (BCG), forming a green-colored complex. The absorbance of green colored complex is measured at 630 nm wavelength. The intensity of the colored complex is proportional to the concentration of the albumin in the sample.
Reagent 1Bromocresol Green
Reagent 2 Albumin standard
Procedure: three clean and dry test tubes were taken and labeled as Blank (B), Standard (S), and Test (T).

Table 2: Addition sequence 2

Addition sequence	Blank	Standard	Test
Serum/plasma	_	_	10 microlitre
Reagent 2	_	10 microlitre	_
Reagent 1	1000 microlitre	1000microlitre	1000microlitre

Mixed and incubated at room temperature for 1 minute and then absorbance was measured.

Calculation

Albumin concentration in gm/dl= Absorbance of Test
The absorbance of standard×concentration of standard
The whole process was automated in the fully automatic analyzer.

Bias

There would be a chance of bias but we tried to minimize it by careful selection of cases and control and careful history taking.

Statistical analysis

Statistical analysis was done by using Medical C Statistical software. Mean and standard deviation were calculated. P value <0.05 was taken for a significant difference.

Ethical consideration

Informed and written consent was taken from all participants and the Ethical committee of BMIMS, Pawapuri, Nalanda.

Observations

Table 3 shows a comparison of serum albumin in normal, pre-diabetic, diabetic, and uncontrolled diabetic individuals. In normal individuals mean fasting blood glucose with standard deviation was 86.09±7.54mg/dl and postprandial blood glucose levels were 102.07 ±8.29mg/dl. In normal individuals mean serum albumin levels were 4.63 ±0.30gm/dl. In pre-diabetic individuals mean fasting blood glucose levels with standard deviation were 107.62 ±15.15 mg/dl and mean post-prandial blood glucose levels with standard deviation were 174.45 ±14.75 mg/dl. Mean serum albumin with standard deviation was 4.38 ±0.24gm/dl with a p-value less than 0.0001 concerning normal individuals which was highly significant as also shown in Table 4.

Table 3: Comparison of serum albumin in normal,pre-diabetic, and diabetic individuals

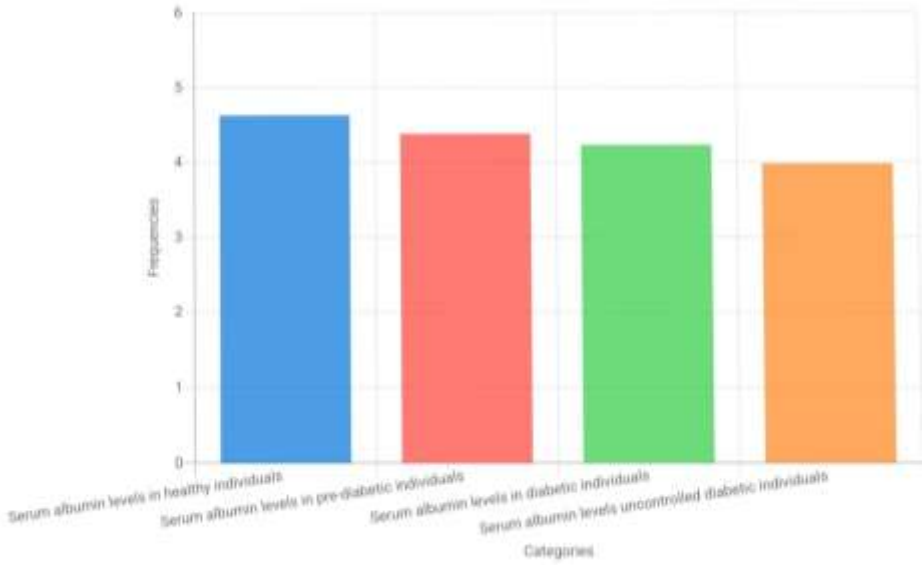
	Normal	Pre-diabetic	Diabetic	Uncontrolled diabetic
Serum albumin in gm/dl	4.63±0.30	4.38±0.24	4.23±0.41	3.98±0.35
FBG(mg/dl)	86.09±7.54	107.62±15.15	132.65±29.22	241±78.52
PPBG(mg/dl)	102.07±8.29	174.43±14.75	248.84±29.46	396.45±108.88

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.1439
Original Article

Table 4: Comparison of serum albumin in normal and pre-diabetic individuals

	Normal	Pre-diabetic	p-values
Serum albumin(gm/dl)	4.63 ±0.30	4.38±0.24	<0.0001
FBG(mg/dl)	86.09±7.54	107.62±15.15	
PPBG(mg/dl)	102.07 ± 8.29	174.45 ±14.75	

Fig 1. Comparison of serum albumin



In Tables 5 and 6, diabetic individuals' mean fasting blood glucose levels were 132.65 ±29.22 mg/dl, and mean post-prandial blood glucose levels were 248.84 ±29.46 mg/dl. Mean serum albumin levels were 4.23 ±0.41mg/dl with p-value <0.0001 concerning normal individuals and <0.0065 concerning pre-diabetic individuals which were significant.

Table 5: Comparison of serum albumin in normal and diabetic individuals

	Normal	Diabetic	p-value
Serum albumin(gm /dl)	4.63±7.54	4.23 ±0.41	<0.0001
FBG(mg/dl)	86.09 ±7.54	132.65 ±29.22	
PPBG(mg/dl)	102.07 ±8.29	248.84 ±29.46	

Table 6: Comparison of serum albumin in normal and uncontrolled diabetic individuals

	Normal	Uncontrolled diabetic	p-value
Serum albumin (gm/dl)	4.63±0.30	3.98±0.35	<0.0001
FBG (mg/dl)	86.09 ±7.54	241 ±78.52	
PPBG (mg/dl)	102.07 ±8.29	396.45 ±108.88	

In Tables 7, 8, and 9, uncontrolled diabetic mean fasting blood glucose levels with a standard deviation was 241 ±78.52 mg/dl, and mean post-prandial blood glucose levels with a standard deviation were 396.45 ±108.88 mg/dl. The mean serum albumin levels with standard deviation were 3.98 ±0.35 gm/dl and the p-values were <0.0001 concerning normal individuals, <0.0001 concerning pre-diabetic individuals, and <0.0004 concerning diabetic individuals which was highly significant.

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol. 5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.1439
Original Article

Table 7: Comparison of serum albumin between pre-diabetic and diabetic individuals

	Pre-diabetic	Diabetic	p-value
Serum albumin (gm/dl)	4.38±0.24	4.23±0.41	<0.0065
FBG(mg/dl)	107.62 ±15.15	132.65 ±29.22	
PPBG(mg/dl)	174.43 ±14.75	248.84 ±29.46	

Table 8: Comparison of serum albumin in pre-diabetic and uncontrolled diabetic individuals

	Pre-diabetic	Uncontrolled diabetic	p-value
Serum albumin(gm/dl)	4.38±0.24	3.98 ±0.35	<0.0001
FBG (mg/dl)	107.62 ±15.15	241±78.52	
PPBG(mg/dl)	174.45 ±14.75	396.45 ±108.88	

Table 9: Comparison of serum albumin in diabetic and uncontrolled diabetic individuals

	Diabetic	Uncontrolled diabetic	
Serum albumin (gm/dl)	4.23 ±0.24	3.98±0.35	0.0004
FBG (mg/dl)	132.65 ±29.22	241±78.52	
PPBG(mg/dl)	248.84±29.46	396.45 ±108.88	

Discussion

This study "Assessment of the relationship between serum Albumin and Glucose levels in healthy, pre-diabetic, and diabetic individuals observational study " shows the relationship between serum Albumin and Glucose levels in healthy, pre-diabetic, diabetic, and uncontrolled diabetic persons. There was a significant decrease in serum albumin in pre-diabetic and diabetic persons from normal individuals. There was an inverse relationship between serum Albumin and Glucose in diabetic persons. Many authors found similar patterns from time to time. According to Folsom AR, MA J, and others, in cross-sectional studies, those with type 2 diabetes had lower serum albumin compared to those without type 2 diabetes (8,9).

Studies of S. Rodr, Iguez-sega de, and others showed serum albumin concentration indirectly reflects insulin reserve and is the indicator of glycemic control (10,11). Schmidt et al also showed lowered serum albumin levels in diabetic individuals (12).In studies of Sandhu Pandiyan and others, in Acute hyperglycemia more than one-third of the patients were hypoalbumenic (13).K. Gunanithi and S. Sakathidasan also showed a significant decrease in serum albumin in type 2 diabetic individuals and there was an inverse relationship between serum Albumin and fasting blood glucose levels in type 2 diabetic individuals (14). Studies of Murtiashaw MH, Barnes JW, and Thorpe SR showed a 30-40% decline in albumin synthesis in uncontrolled diabetics and the basis is a marked decline in transcription of albumin mRNA, albumin degradation, and relative extravascular distribution (15).

Hyperglycemia affects the synthesis, redistribution, oxidative stress glycation function, and distribution of albumin(5). In diabetic individuals uncontrolled blood glucose leads to decreased hepatic albumin synthesis (16). Uncontrolled blood glucose levels in diabetic individuals may aggravate beta-cell dysfunction and insulin depletion (17). Insulin increases the albumin mRNA transcription (18-20). Insulin deficiency decreases albumin mRNA transcription, albumin synthesis, release, and distribution which is responsible for low albumin in uncontrolled diabetic individuals. In patients with hyperglycemia glycation of albumin is preferred over other plasma proteins due to its abundance, longer half-life, and free amino acid binding site available for glycation. Glycated albumin induces an immunological response that reduces the half-life of glycated albumin which is responsible for statistically significantly reduced serum albumin levels in diabetic individuals(21). Low levels of serum albumin in patients with acute hyperglycemia are responsible for the glycation of other plasma proteins, which is responsible for the production of toxic advanced glycation end product. (AGE) that is responsible for complications of diabetes in the long term (22,23,24).

Conclusions

This study concludes that there was an inverse relationship between serum albumin levels and blood glucose in diabetic individuals. A similar result was observed by various authors from time to time. Probable causes of decreased serum albumin in uncontrolled diabetics are due to decreased hepatic synthesis, increased breakdown, and distribution of albumin. Albumin is more prone to glycation than other proteins. Low serum albumin is responsible for the glycation of other proteins and the production of

advanced glycation end product, which is responsible for the development of complications in diabetic individuals.

Limitations

Limitations of this study are small sample size and hospital-based study.

Recommendations

Regular estimation of serum albumin levels in diabetes and keeping serum albumin levels within normal limits is required to delay diabetic complication development.

Acknowledgment

The authors acknowledge the immense help received from the scholars whose articles are cited and included in references to this manuscript. The authors are also grateful to the authors/ editors/publishers of all those articles, journals, and books from where the literature for this article has been reviewed and discussed.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

No funding was received.

References

1. American diabetes association and classification of diabetes mellitus, Diabetes care. 2006; 29: 543-548. https://doi.org/10.2337/diacare.29.s1.06.s43
2. International Diabetes Federation. Org Retrieval 29.04.2020.
3. IDF. Diabetes atlas 9 edition Brussels, Belgium. 2019.
4. Indumati U, Sowbhagya L 1 stedition 2021 ISBN: 978-81. 8191-528-3,p 739-30.
5. K. Gunaithi, S. Sakathidasan, Medpulse International Journal of Biochemistry, Print ISSN:2550-763x. Volume 20, issue 2, November 2021p 13-17.
6. AbbasiA, Banker S, CopeleijinE, et al (2012), Liver function test and risk prediction of incident type 2 diabetes: Evaluation in two cohorts. PLos one 7:e51496. https://doi.org/10.1371/journal.pone.0051496 PMid:23284703 PMCid:PMC3524238
7. Strangest S, Rafatson LB, Dmochowski J et al(2008) Additional contribution of emerging risk factors to the prediction of the risk of type 2 diabetes; evidence from the western New York St.obesity(silver spring) 16: 1370-76. https://doi.org/10.1038/oby.2008.59 PMid:18356828
8. Folsom AR, Ma J, Eckfeldt JH, Neitu FJ, Metcalf PA, Barnes RW; Low serum albumin association with diabetes mellitus and other cardiovascular risk factors but not with prevalent cardiovascular disease or carotid artery intima-media thickness. The atherosclerosis risk in the community (ARIC) study investigators. Ann Epidemiol.1995;5(3): 186-91. https://doi.org/10.1016/1047-2797(94)00105-3 PMid:7606307
9. Castaneda C, BarmudezoI, Tacky KL; Protein nutritional status and function are associated with type 2 diabetes in Hispanic elders. Am J ClinNutr. 2000; 72(1); 89-95. https://doi.org/10.1093/ajcn/72.1.89 PMid:10871566
10. S Rodriguez-sega de, J. Rodriguez, D Mayan, and F Comina, " Plasma albumin concentration is a predictor of HbA1c among type 2 diabetic patients, independently of fasting plasma glucose and fructosamine. "Diabetes care, 2005; Vol 28, no-2, pp 437-439. https://doi.org/10.2337/diacare.28.2.437 PMid:15677811
11. J. C. Bae, S. H. See, K.Y.Hur et al, " Association between serum Albumin, insulin resistance, and incident diabetes in nondiabetic subjects " Endocrinology and Metabolism 2013; Vol 28, no1,pp26-32. https://doi.org/10.3803/EnM.2013.28.1.26 PMid:24396647 PMCid:PMC3811792
12. Schmidt MI, Duncan BB, SharreHS, AjambujaMI, Tracy RP, Heiss G: Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis risk in community study): A cohort s. Lancet 1999; 353: 1649-1652. https://doi.org/10.1016/S0140-6736(99)01046-6 PMid:10335783
13. PandiyanS et al . International journal of Advances in medicine. 2021 June; 8(6) 809-813.
14. K.Gunanithi, S. Sakathidasan; Serum albumin levels in uncontrolled type 2 diabetes mellitus-An observational study Medpulse International Journal of Biochemistry. November 2021; 13-17.
15. Murtiashaw MH, Barnes JW, Thorpe SR. Albumin catabolism in diabetic rats. Arch biochemistry Biophys. 1983; 225(1): 256-262. https://doi.org/10.1016/0003-9861(83)90028-0 PMid:6614922
16. FlaimKE, Hutson SM, Lloyd CE, Taylor JM, Simon R, Jefferson LS. Direct effect of insulin on albumin gene expression in primary culture of rat

Hepatocytes. Am J Physiol1985; 249(Pt1):E447-53.
17. G. Leibowitz, N. Kaiser, and E Carasi, " Beta-cell failure in type 2 diabetes " Journal of diabetes investigation 2011; vol 2, No.2, pp.82-91. https://doi.org/10.1111/j.2040-1124.2010.00094.x PMid:24843466 PMCid:PMC4015541
18. Lloyd CE, Klinyak JE, Hutson SM, Jefferson LS. Stimulation of albumin gene transcription by insult in primary culture of Rat hepatocytes. Am J Physiol1987;252(2pt1): c205-c214. https://doi.org/10.1152/ajpcell.1987.252.2.C205 PMid:3548414
19. PaevyDE, Taylor JM, Jefferson LS. Time course of changes in albumin synthesis and mRNA in diabetic and insulin-treated diabetic rats. AM J Physiol. 1985; 248(6pt 1): E656-E663. https://doi.org/10.1152/ajpendo.1985.248.6.E656 PMid:3890555
20. Kimball SR, Horetsky RL, Jefferson. Hormonal regulation of albumin gene expression in primary culture of rat Hepatocytes. Am J Physiol 1995; 268(pt1): E6-E14. https://doi.org/10.1152/ajpendo.1995.268.1.E6 PMid:7840183
21. Layton GJ, JarmuschG. Effect of glycation of albumin on its renal clearance in normal and diabetic rats. Kidney Int. 1988;33:673-6. https://doi.org/10.1038/ki.1988.52 PMid:3367558
22. Vetter SW. Glycated serum albumin and AGE receptors. AdvclinChem.2015;72:205-75. https://doi.org/10.1016/bs.acc.2015.07.005.PMid: 26471084
23. AlelofarK, Ahmad J. An overview of in vitro and in vivo glycation of albumin: a potential disease marker in diabetes. Glycine 2017;34(5) 575-84. https://doi.org/10.1007/s10719-017-9789-0 PMid:28812216
24. Bhonsle HS,Korwar AM, KoteSs,Golegonkar SB, Chougal AD, Shaik MI et al. Low plasma albumin levels are associated with increased plasma protein glycation and HbA1c in diabetes. J Proteome Res. 2012; 11(2): 1391-6. https://doi.org/10.1021/pr201030m PMid:22181049

PUBLISHER DETAILS:

Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
(ISSN 3006-1059) Print
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256 775 434 261
Location: Wisdom Centre, P.O.Box. 148, Uganda, East Africa