Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 2s, https://carcinogenesis.com/

The Study of Comparison between HbA1c% and Glycated Albumin % in Diabetic ESRD Patients on MHD

Dr. Veeresh B Hubballi*[1], Dr. Netra B Hubballi[2], Shruthi K R[3], Avinash[4], Anshu Kumar Yadav[5], Anil Kumar K M[6], Jeyaprakash M R*[7], Chethan kumar B G[8]

[1]Department of Cardiology, Jayadeva Institute of Cardiovascular Sciences and Research Bangalore, Karnataka, India

[2]Department of PG Studies in Kayachikitsa, JSS Ayurveda Medical College and Hospital, Mysuru-570028, Karnataka, India

[3]Department of Biochemistry, Sri Lakshmi College of allied health sciences, Rajeev Gandhi University of Health Sciences, Bengaluru, Karnataka, India-560091

[4]Department of Biochemistry, Shri maruthi group of institutions, Bengaluru, India-560091

[5]Department of Biochemistry, JSS Medical College, Mysuru-570015, Karnataka, India

[6,8]Department of Environmental Science, JSS Academy of Higher Education & Research, Mysuru-570015, Karnataka, India.

[7]MB School of Pharmaceutical Science, Mohan babu University, Sree Sainath Nagar, Tirupathi-517102, India.

Corresponding Author: veerhubballi799191@gmail.com, jpvis7@gmail.com

ABSTRACT

This study investigated the comparative effectiveness of Glycated Hemoglobin and Glycated Albumin as glycemic control markers in diabetic patients with End Stage Renal Disease undergoing maintenance hemodialysis. The research involved a prospective observational design comparing diabetic nephropathy patients on hemodialysis with diabetic patients having normal renal function. Results demonstrated that Glycated Hemoglobin levels were significantly lower in hemodialysis patients compared to controls, while Glycated Albumin levels remained elevated, suggesting that Glycated Hemoglobin may falsely underestimate glycemic control in patients with renal dysfunction. Multivariate analysis confirmed that Glycated Albumin serves as a more reliable and statistically significant indicator of blood glucose control in this population. The findings indicate that factors affecting red blood cell survival, including severe nephropathy, compromise the accuracy of Glycated Hemoglobin measurements. This study concludes that Glycated Albumin represents a superior biomarker for assessing long-term glycemic status in diabetic patients undergoing hemodialysis treatment.

Keywords: *Glycated Albumin, Glycated Hemoglobin, End Stage Renal Disease, Hemodialysis, Glycemic Control*

How to Cite: Dr. Veeresh B Hubballi, Dr. Netra B Hubballi, Shruthi K R, Avinash, Anshu Kumar Yadav, Anil Kumar K M, Jeyaprakash M R, Chethan kumar B G, (2025) The Study of Comparison between HbA1c% and Glycated Albumin % in Diabetic ESRD Patients on MHD, *Journal of Carcinogenesis*, *Vol.24, No.2s*, 1342-1348.

1. INTRODUCTION

Diabetes Mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] Type 2 Diabetes Mellitus is the predominant form of diabetes worldwide, accounting for 90% of cases globally. An epidemic of T2DM is under way in both developed and developing countries. India currently represents 49 per cent of the world's diabetes burden, with an estimated 72 million cases in 20176. 20–40% of patients with diabetes develop diabetic nephropathy.

Measurement of Glycated Haemoglobin (HbA1c) is the standard method for assessing long-term glycaemic control. When plasma glucose is consistently elevated, there is an increase in non-enzymatic glycation of haemoglobin; this alteration reflects the glycaemic history over the previous 2–3 months, because erythrocytes have an average life span of 120 days (glycaemic level in the preceding month contributes about 50% to the HbA1c value). Measurement of HbA1c at the ―point

of care‖ allows for more rapid feedback and may therefore assist in adjustment of therapy. However clinical conditions such Haemoglobinopathies, Anaemias, Reticulocytosis, Transfusions, and Uraemia may interfere with the HbA1c result. The degree of glycation of other proteins, such as albumin, can be used as an alternative indicator of glycaemic control when the HbA1c is inaccurate[2]. Factors that shorten Red Blood Cell (RBC) survival, including severe nephropathy, may reduce HbA1c since the time necessary for glucose to chemically bond with RBCs decreases.

Hence it was hypothesized that Glycated Albumin (GA) which is unaffected by the red cell survival time in Chronic kidney disease patients on haemodialysis, is a better indicator of glycaemic control than Glycated haemoglobin. They evaluated diabetic haemodialysis patients and diabetic subjects without nephropathy and demonstrated that HbA1c severely underestimates true glucose control relative to the GA assay[3,4]. GA measures specifically the glycation product of albumin; it has been developed as an index for glycaemic control[5], but it is not affected by serum albumin levels because its ratio to total serum albumin is calculated[6]. To date, serum GA has been suggested as a more reliable and sensitive glycaemic index to replace HbA1c in diabetic patients with CKD. Thus this study was formulated to compare Glycated Haemoglobin versus Glycated Albumin in terms of their efficacy in assessing the Glycaemic Control, their prognostic values, and to study the clinical significance of Ratio of Glycated Albumin percentage to Glycated Haemoglobin percentage, among patients with diabetic End Stage Renal Disease on Haemodialysis.

2. MATERIALS AND METHODS

The study was carried out in the department of Internal Medicine, KARNATAKA INSTITUTE OF MEDICAL SCIENCES, HUBBALLI, between November 2016 and July 2018. It is a time bound prospective, comparative, observational study which included total of 88 patients (44 cases and 44 controls).
For selection of cases, all patients with Diabetic ESRD on haemodialysis were screened applying Inclusion / Exclusion criteria. For controls, Diabetic Patients with Creatinine Values of less than 1.5 mg% (and NOT on haemodialysis) were considered. Following were the inclusion and exclusion criteria:

INCLUSION CRITERIA:
FOR CASES:
1. Age > 18 years, both male and female patients
2. Type 1 and Type 2 Diabetes patients
3. Diabetic nephropathy- End stage renal disease patients on haemodialysis
   - End stage renal disease was defined by EGFR <15ml/kg/m2 as given by The Cockcroft and Gault formula CCr={((l 40–age) x weight)/(72xSCr)}x 0.85 (if female)
   - Diabetes (both type1 and type2) was defined by

FBS > 126 mg/dl
PPBS > 200 mg/dl
HbA1c > 6.5%
History of diabetes with treatment for the same

FOR CONTROLS:
1. Age > 18 years, both male and female patients

2. Type 1 and Type 2 Diabetes patients
3. Serum creatinine < 1.5 mg/dl

EXCLUSION CRITERIA:
Both for cases and controls
1. Non-diabetic patients
2. Haemoglobinopathy
3. Anaemia due to causes other than ckd
4. Hepatic disorders
5. Heavy proteinuria (24 hours urine protein > 3000mg/day)

ONLY FOR CASES
1. Diabetic ESRD patients on peritoneal dialysis
2. Post renal transplantation status

METHODS OF DATA COLLECTION
1. Patients satisfying both inclusion and exclusion criteria were included in the

Study after taking duly informed written consent.
2. A pre-designed proforma was used to collect the data.
3. Basic demographical details were collected from the paietnts
4. Detailed medical history was taken which included the following information-
5. Releavant investigations were done for all patients included under the study.
6. For the assessment of Glycated haemoglobin and Glycated Albumin 10ml of
venous blood were collected from all patients. Blood was drawn from the dialyzer circuit in subjects with ESRD, before to the initiation of dialysis or administration of heparin anticoagulants. Blood samples were then divided into two parts 5ml each one in EDTA tube and other in plain bulb. One in EDTA tube was sent for HbA1c . From other sample in plain bulb serum was allowed to clot for 10-20 minutes. Then centrifuged (at 2000 RPM) for 20 minutes. The supernatant was collected and stored at -80 degree Celsius for future measurement of GA in MEDICAL RESEARCH DEPARTMENT in the institute.
7. eGFR was measured using the Cockcroft and Gault formula.
8. HbA1c was analysed within 24 h of collection (refrigerated if not immediately assayed) on a cation exchange column chromatograph using an automated high-pressure liquid chromatography instrument.
9. ASSESSMENT OF GLYCATED ALBUMIN : Glycated Albumin ELISA kits were used for the measurement of the same. The kit uses a double-antibody sandwich enzyme-linked immunosorbent one-step process assay (ELISA) to assay the level of Glycated Albumin (GA) in 62 samples. Standard, test sample and HRP-labeled Glycated Albumin (GA) antibodies were added to enzyme wells which are Pre-coated with Glycated Albumin(GA) antibody, then incubation was done. Further washing was done to remove the uncombined enzyme. Upon adding Chromogen Solution A and B, the color of the liquid was changed into blue, and the reaction with the acid caused the color to become yellow. The depth of color was measured interms of OPTIC DENSITY (OD) and the concentration of the Glycated Albumin(GA) was further derived from it by forming a standard curve.
Glycated Albumin percentage is calculated from Glycated Albumin concentration in ng/ml using the formula.92 [7]

RANGES OF GLYCATED ALBUMIN

- Excellent (GA <18%)
- Good (18.0 < GA <21.0%)
- Fair (21.0 < GA <24.0%)
- Poor (GA >24.0%)12 63

STATISTICAL ANALYSIS

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software.
The following methods of statistical analysis have been used in this study

- Patient Characteristics such as age, sex, duration of illness, mode of treatment and target organ damages are summarized as frequencies and percentages.
- Biochemical parameters are summarized as mean with Standard deviation or median with range.
- Outcome and target organ damages between cases and controls were compared using chi square test.
- Biochemical parameters such as blood sugar, HbA1C%, Glycated Albumin percentages between cases and controls are compared using t test or Wilcoxon ranksum test as required depends on normal or non-normal distribution of the data respectively.
- Association of various biochemical parameters within cases and controls were analysed using Pearson's correlation co-efficient.
- Multivariate linear regression was carried out using average blood sugar as dependent variables and patient characteristics such as type of DM, BMI and other biochemical parameters such as HbA1C and Glycated Albumin percentage as explanatory variables for this entire hypothesis testing p value was considered at 0.05 level.

3. RESULTS

Table 1: Distribution of age (in years) and bmi among cases vs controls

AGE	**Type**	**(n=)**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	**P value**
	Control	44	56.52	12.38	58	20	84	0.15
	Case	44	52.7	11.95	54	24	76	
BMI	**Type**	**(n=)**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	**P value**
	Control	44	26.53	2.64	26.81	16.77	32.06	<0.00001
	Case	44	23.57	2.89	23.84	17.85	29.07	

Table 2: Distribution of sex, type of diabetes and type of treatment among cases vs controls*

		Case	%	Control	%	Total	%	P Value
SEX	**Female**	11	25.0	23	52.3	34	38.6	
	Male	33	75.0	21	47.7	54	61.4	0.009
	Total	44	100.0	44	100.0	88		
TYPE OF DIABETES	**Type 2**	42	95.5	42	95.5	84	95.5	
	Type 1	2	4.5	2	4.5	4	4.5	1.00
	Total	44	100.0	44	100.0	88		
TREATMENT	**No Treatment**	1	2.3	3	6.8	4	4.5	
	OHA	37	84.1	0	0.0	37	42.0	**<0.001**
	Insulin	4	9.1	41	93.2	45	51.1	
	Both	2	4.5	0	0.0	2	2.3	
	Total	44	100.0	44	100.0	88		

Table 3: Distribution of hemoglobin, serum creatinine serum albumin and estimated gfr among cases vs controls

	Type	(n=)	Mean	SD	Median	Minimum	Maximum	P value
Hemoglobin gm/dl	Control	44	12.45	1.49	12.45	9.4	15.8	0.00001
	Case	44	8.6	1.76	8.8	3.4	12.4	
S.creatinine mg/dl	Control	44	0.777	0.138	0.8	0.6	1.1	0.00001
	Case	44	8.42	2.94	8.4	4.4	16.8	
S. Albumin g/dl	Control	44	3.01	0.31	3	2.2	3.5	0.0022
	Case	44	2.8	0.279	2.8	2.2	3.4	
eGFR	Control	44	98.01	10.25	97.12	68.78	126.28	0.0001
	Case	44	10.87	3.47	10.76	4.98	18.83	

Table 4: Distribution of various glycaemic control parameters among cases vs controls

Parameter	Type	Mean	SD	Median	Minimum	Maximum	P value
Fasting blood sugar	Case	159.91	52.71	165.5	54	242	
	Control	178.86	77.23	182	84	501	0.45
Post prandial blood sugar	Case	228.32	54.16	242.5	104	364	
	Control	253.07	89.36	224	124	494	0.66
Average blood sugar	Case	196.02	45.49	192	98	286	
	Control	208.09	66.76	186.5	112	421	0.69
HbA1c	Case	6.77	0.952	6.6	5.1	8.9	0.002
	Control	7.6	1.53	7.2	6.2	12.8	
Glyc. Albumin ng/ml	Case	326.35	43.3	328.72	234.12	398.45	0.0017
	Control	352.12	39.84	364.49	256.32	398.65	
Glyc.albumin %	Case	25.6	4.32	25.95	16.87	33.03	0.3
	Control	26.58	4.96	26.46	17.62	34.94	

Majority of the patients (55.7%) were in the age group of 41-60. Below 20 years there was one patient.
The number of males and females in the control group was 21 and 23 respectively, whereas in the case group there were 33 males and 11 females. Male preponderance 75 % was found among cases whereas in controls female preponderance 52.3% was found .

Majority of the patients (33%) were having duration of diabetes in the range of 3.1 to 6 years. Only 17 out of 88 patients were having duration of diabetes between 6.1 to 9 years .

Mean duration of diabetes among cases and controls was 8.82 years and 4.76 years respectively

Only two Type 1 diabetic patients were there among the cases. Thus for the matching of the same only two Type 1 diabetes

patients were selected among controls.

In cases 93.2% i.e., 41 out of 44 patients were on Insulin and remaining 3 patients were deferred from anti-diabetic treatment due to frequent hypoglycaemic episodes. In ESRD the elimination of the insulin will be reduced, hence in the later stages patients will be prone for hypoglycaemic episodes.

In controls 37 out of 44, i.e., 84.1 % patients were on OHA, 4 patients were on Insulin only , 2 were on both insulin and OHA for the treatment. One patient was non-compliant with the treatment.

Mean BMI among cases was 23.57 Kg/m2 where as among controls it was 26.53 Kg/m2
Haemoglobin and S.Albumin levels were significantly higher in controls (12.45±1.49) and 3.01± O.31 respectively) than cases (8.6± 1.76 and 2.8±0.279 respectively). Whereas Creatinine levels were higher in cases (8.42±2.94) than controls(0.77±0.13.

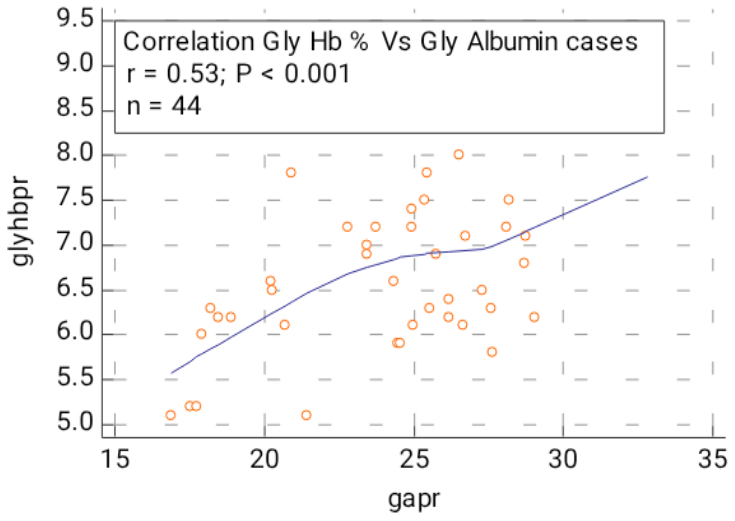
Meam of estimated GFR among cases and controls was 10.87ml/min/1.73m^2 and 98.01 ml/min/1.73m^2 respectively

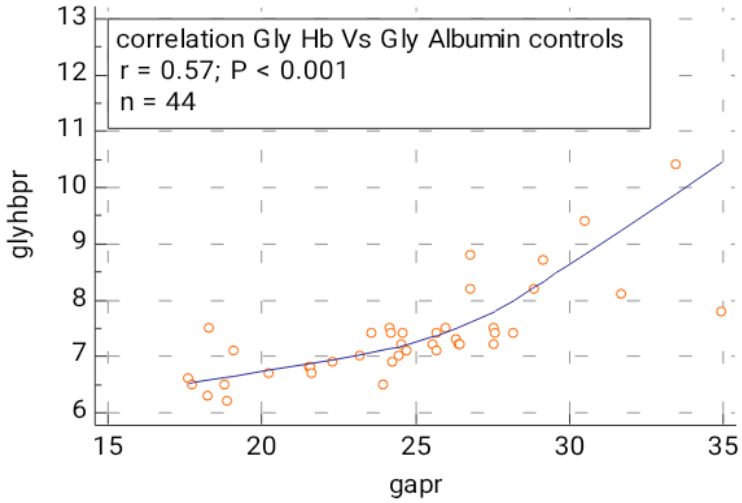
Fasting blood sugar, postprandial blood sugar and average blood sugar among cases was 159.91mg/dl , 228.32mg/dl and 196.02mg/dl respectively where as among controls it was 178.86mg/dl, 253.07mg/dl and 208.09mg/dl respectively. Sugar recordings were higher among cases compared to controls but not statistically significant.

HbA1c in cases was 6.77 % and in controls it was 7.6 %. HbA1c was found to be significantly low among cases compared to controls. Supporting this finding was the ratio of Glycated albumin % to glycated haemoglobin which was 3.8 among the cases and 3.51 in controls, inferring falsely low HbA1c among cases compared to controls.

Table 5: Comparison of correlation coefficient among cases v/s control.

Comparison parameters	Correlation (r)	
	Control	Case
Average blood sugar Vs Glycated Hemoglobin %	0.401	0.456
Average blood sugar Vs Glycated albumin (ng/dl)	0.482	0.441
Average blood sugar Vs Glycated albumin percentage	0.652	0.542
Average blood sugar Vs Glycated albumin to Hemoglobin ratio	0.311	0.210
Glycated albumin Vs Glycated Hemoglobin percentage	0.427	0.441
Glycated Albumin % Vs Glycated Hemoglobin %	0.499	0.611





Multivariate analysis of various factors predicting blood sugar values clearly showed Glycated albumin % is better and statistically significant compared to HbA1c.

4. DISCUSSION

Majority of the patients 49 out of 88 (55.7%) were in the age group of 41-60 . Below 20 years there was one patient. The mean age among cases was 52.7 ± 11.95 years whereas in controls it was 56.52 ± 12.38 years .Thus the mean age was more in controls compared to cases, which was comparable with study done by Dawlat et al[8] in which mean age in cases was 42.3 ± 9 years and controls was 49.6 ± 7 years. However in other studies done by Peacock et al and Freedman et al[9] mean age was more in cases compared to controls The number of males and females in the control group was 21 and 23 respectively , whereas in the case group there were 33 males and 11 females. Male preponderance 75 % was found among cases whereas in controls female preponderance 52.3% was found. Comparable with the present study male preponderance in cases and female preponderance was found in study done by Peacock et al(cases 53% males, controls 40% males), Freedman et al (cases 54.1% males and controls 40.2% males) and Dawlat et al (cases 60% males and controls 30% males) Majority of the patients (33%) were having duration of diabetes in the range of 3.1 to 6 years. Only 17 out of 88 patients were having duration of diabetes between 6.1 to 9 years. Mean duration of duration of diabetes in our study in cases was 8.8 years whereas in controls it was 4.76 years . In other similar studies like Peacock et al and Freedman et al , mean duration of diabetes was higher among cases than in controls .Since greater the duration of diabetes, higher the risk of Diabetic nephropathy. Hence the duration of diabetes was found to be more in cases compared to controls

Comparable to the Dawalat Sany et al study mean BMI in cases was lesser compared to controls as shown in . As compared to controls cachexia occurring due to various mechansims is more commonly seen among ESRD patients, hence in our study too the mean BMI was found to be on higher among cases compared to controls.

Our findings were comparable with to that of study conducted by Dawlat S et al as shown in the table 33. The main EGFR in our study was observed as 10.87 ± 3.47ml/min/1.72m^2 among cases versus 98.01 ± 10.25 ml/min/1.72m^2 among controls. Our mean EGFR among cases was comparable with that of a study by Dawlat et al. However the mean EGFR among controls was found to be slightly higher 121 ± 21ml/min/1.72m^2 in their study compared to ours 98.01 ± 10.25 ml/min/1.72m^2.

- Mean Hemoglobin was low in cases compared to controls in the present study as well as other similar studies like Peacock et al and Dawlat et al. Chronic illness, blood loss , loss of appetite, poor absorption of iron and blood loss etc are the various factors which contribute to anemia as appropriately observed in present stu When Serum albumin was compared among cases and controls in present study
- cases- 2.8 ± 0.279 gm/dl controls- 3.01 ± 0.31gm/dl, Peacock et al study cases - 3.7 ± 0.4 gm/dl controls - 4 ± 0.6 gm/dl and Dawlat et al study cases -6.9 ± 0.6gm/dl
- controls - 7.3 ± 0.26gm/dl was found that serum albumin was less in cases compared to controls, indicating the effect of proteinuria found among diabetic nephropathy patients.
- Serum creatinine was on higher side in cases compared to controls in present study as well as similar two other studies.
- Average blood sugar in present study was more in controls 256.07 ± 66.76 compared to cases 196.02 ± 45.49. Similar to our study, in Dawlat et al study the mean blood sugar that is the the mean values of the three-monthly measurements of casual plasma glucose (PG) obtained during the two months before determination of serum GA and HbA1c , in controls 146.5 ± 35 was on higher side compared to cases 146.5 ± 35. But in Peacock et al study

relative to those without kidney disease, mean (s.d.) serum glucose concentrations were higher (172 (62) vs 146 mg per 100 ml (66); p¼0.024). The other studies took the RBS of preceding 3 months into consideration to estimate average plasma glucose. In the present study we used FBS ,PPBS and Mean blood sugar (average of three RBSs recordings of the patiet within one month)levels which is theoretically more accurate

- The HbA1C levels was drastically lower and GA levels were higher in the cases compared to the control group in present study. The results were similar to the studies done by Peacock et al and Freedman et al wherein the hba1c was paradoxically lower among the cases compared to controls. The GA levels were also higher in the cases than controls , in these studies.
- It is clear that the HbA1c assay has severe limitations in diabetic patients on HD, markedly underestimating recent glycemic control compared to serum glucose concentrations and GA. This report extends the findings of the accuracy of the HbA1c assay in HD and to demonstrate that HbA1c is significantly impacted by ESRD.
- Theoretically, proteinuria can impact GA% based upon reduced exposure of serum albumin to glucose. Freedman et al addressed this issue by comparing GA%/HbA1c in 15 anuric diabetic patients lacking proteinuria (mean ± SD 2.71 ± 0.63, median 2.58) with that in 12 diabetic patients with urine output exceeding 1 L per day (2.81 ± 0.68, median 2.92). Significant differences were not seen in GA%/HbA1c between these groups (p = 0.49), suggesting that proteinuria did not contribute to the results. The present study also showed a negative correlation coefficient between GA and S. albumin.
- The HbA1C levels was drastically lower and GA levels were higher in the cases compared to the control group in present study. The results were similar to the studies done by Peacock et al and Freedman et al wherein the hba1c was paradoxically lower among the cases compared to controls. The GA levels were also higher in the cases than controls, in these studies.

5. CONCLUSION

- Glycated Hemoglobin a standard method for the assessment of long term glycemic control if falsely low in diabetic ESRD patients on HD.
- Glycated Albumin % ia a better indicator of glycemic control among Diabetic ESRD patiets on HD compared to Glycated albumin.

LIMITATIONS:

- As the study had restricted period of time , total number of cases that can be collected were limited.

REFERENCES:

1. Kasper, D Fauci, A., Hauser, S., Longo, D.,Jmaeson, J and Loscalzo, J(2015). Harrison's Principles of Internal Medicine. 19th edition New York: McGraw-Hill Professional Publishing Chapter 417 pp 2399
2. Kasper, D Fauci, A., Hauser, S., Longo, D.,Jmaeson, J and Loscalzo, J(2015). Harrison's Principles of Internal Medicine. 19th edition New York: McGraw-Hill Professional Publishing Chapter 418 pp 2410
3. Inaba M, Okuno S, Kumeda Y, Yamada S, Imanishi Y, Tabata T, Okamura M, Okada S, Yamakawa T, Ishimura E, Nishizawa Y. Glycated albumin is a better glycaemic indicator than glycated hemoglobin values in hemodialysis patients with diabetes: effect of anemia and erythropoietin injection. Journal of the American Society of Nephrology. 2007 Mar 1;18(3):896-903.
4. Peacock TP, Shihabi ZK, Bleyer AJ, Dolbare EL, Byers JR, Knovich MA, Calles-Escandon J, Russell GB, Freedman BI. Comparison of glycated albumin and hemoglobin A1c levels in diabetic subjects on hemodialysis. Kidney international. 2008 May 1;73(9):1062-8.
5. Guthrow CE, Morris MA, Day JF, Thorpe SR, Baynes JW. Enhanced nonenzymatic glucosylation of human serum albumin in diabetes mellitus. Proceedings of the National Academy of Sciences. 1979 Sep 1;76(9):4258-61.
6. Koga M. 1, 5-Anhydroglucitol and glycated albumin in glycemia. InAdvances in clinical chemistry 2014 Jan 1 (Vol. 64, pp. 269-301). Elsevier.
7. Abidin D, Liu L, Dou C, Datta A, Yuan C. An improved enzymatic assay for glycated serum protein. Analytical Methods. 2013;5(10):2461-9.
8. Sany D, Elshahawy Y, Anwar W. Glycated albumin versus glycated hemoglobin as glycaemic indicator in hemodialysis patients with diabetes mellitus: variables that influence. Saudi Journal of Kidney Diseases and Transplantation. 2013 Mar 1;24(2):260.
9. Freedman BI, Andries L, Shihabi ZK, Rocco MV, Byers JR, Cardona CY, Pickard MA, Henderson DL, Sadler MV, Courchene LM, Jordan JR. Glycated albumin and risk of death and hospitalizations in diabetic dialysis patients. Clinical journal of the American Society of Nephrology. 2011 May 19:CJN-11491210