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ORIGINAL ARTICLE

Comparative Study Between Glycated Hemoglobin and Glycated Albumin in Diabetes in Hemodialysis Patients

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Abstract

Background: **The importance of accurately measuring glycemic control in the diabetic people cannot be overstated, since better glycemic control decreases micro- and macrovascular problems in individuals with diabetes mellitus getting renal replacement treatment.**

Aim: **This study's objective was to contrast between glycated hemoglobin and glycated albumin in diabetes in hemodialysis patients.**

Subject and methods: **This was Prospective Comparative research carried out on 100 diabetic patients. Two groups were created out of them: Group (I): that had 50 patients diabetic on hemodialysis. Group (II): included 50 patients diabetic and not on hemodialysis. From March 2022 to September 2022, this research was carried out in the Nephrology Hemodialysis unit at Al-Azhar Hospital.**

Results: **The current research indicated a great statistically substantial enhancement in GA level among group I in comparison with group II (7.2 ± 9.1 vs. 1.8 ± 1.8%, respectively) while there was a statistically substantial reduction in HbA1C level among group I in comparison with group II (6.9 ± 1.6 vs. 7.7 ± 1.3%, respectively) (P value < 0.001). The current study revealed that GA can be used to differentiate between groups I and II at a cut-off level of 1.95, with 76% sensitivity, 90% specificity, 88.4% PPV, 78.9% NPV, and 83.00% accuracy (AUC = 0.84 and P value < 0.001). In addition, HbA1C can differentiate between groups I and II at a cutoff level of 6.65, with 50% sensitivity, 24% specificity, 39.68% PPV, 32.43% NPV and 37.00% accuracy (AUC = 0.33 and P value = 0.003).**

Conclusion: **The present study highlights that in diabetic uremic patients, glycated albumin shows a higher sensitivity and specificity in determining glycemic alterations in comparison with glycemic hemoglobin, thus enhancing their clinical care management.**

Keywords: Diabetes, Glycated albumin, Glycemic control, Hemoglobin A1c, Hemodialysis

1. Introduction

Millions of individuals from all racial and ethnic backgrounds are afflicted with chronic kidney disease (CKD), a global public health problem. One of the main causes of CKD and a significant comorbidity in those who already have the disease is diabetes mellitus.[1]

The percentage of CKD owing to diabetes will continue to climb due to the fast-rising incidence of diabetes globally. In uremic patients receiving hemodialysis, glycemic management may lessen the risk of newly developing microalbuminuria, slow the evolution of diabetic nephropathy, prevent end-organ damage, and lower cardiovascular illness and death.[2]

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Erythrocyte lifespan shortening or a shift in the ratio of young to elderly erythrocytes caused by erythropoietin usage both have a substantial impact on HbA1c readings in HD patients.[3]

It is becoming more well understood that anemia, the use of erythropoiesis-stimulating agents (ESA), and/or iron, irrespective of glycemic management, may cause HbA1c test to understate glycemic status.[4]

Serum glycated albumin (GA), which is unaffected by changes in the erythrocyte survival time in the case of type-2 diabetes with hemoglobinopathy and gives a considerably better assessment of glycemic control in hemodialysis (HD) patients with diabetes mellitus (DM), was proposed to be a stand-in indicator for glycemic control in diabetic individuals.[5]

This study's objective was to contrast between glycated hemoglobin and glycated albumin in diabetes in hemodialysis patients.

2. Patients and methods

This was Prospective Comparative research. Carried out on 100 diabetic patients. Two groups were created out of them: Group (I): that had 50 patients' diabetic on hemodialysis. Group (II): that included 50 patients diabetic not on hemodialysis. From March 2022 to September 2022, this research was carried out in the Nephrology Hemodialysis Unit at Al-Azhar Hospital.

2.1. Inclusion criteria

Only diabetic patients whose blood glucose was stable and whose medication had not changed in the six months before the assessment of GA and HbA1c were allowed to participate in the study.

2.2. Exclusion criteria

The following circumstances precluded study participation for participants: Hemoglobinopathy, anemia caused by conditions other than chronic kidney disease, such as hemolytic anemia (HB less than 8 mg/dl), a history of obvious bleeding or who got a blood transfusion 4 months before the study, as well as hepatic diseases, inflammatory conditions, or thyroid conditions.

2.3. Study intervention

The following was applied to each participant: Full history taking: demographic information, height, weight (dry weight in HD patients), the length of their diabetes, and the length of their HD, complete clinical evaluation and laboratory tests: Complete blood count, serum urea and creatinine, liver function (AST, ALT), serum Na, K, Ca, Po4 and GA assay:

The glycated albumin assay that we evaluated was the Human (GA) Elisa kit (SunRed Company, China), This ELISA kit uses a double-antibody sandwich method as its foundation to identify human GA. We performed the assay according to the manufacturer's instructions on the Chemwell analyser (Awareness, Palm City, Florida, USA).

HbA1c assay: Glycohemoglobin's quantitative colorimetric evaluation in whole blood is done using the Stanbio glycohemoglobin assay.

Utilizing a Cobas c311 analyzer and the turbid metric inhibition immunoassay, Tina-quant Hemoglobin A1c III test, the HbA1c value in the entire blood was calculated (Roche Diagnostics, Basel, Switzerland).

2.4. Dialysis prescription

Type of dialysis: hemodialysis, type of dialysis machine: Fresenius, type of filter: poly flux (high flux membrane). Membrane area: 2.1 m^2, blood pump speed: 300–350 ml/min, dialysis session: 3 sessions/week, each one 4 h, heparin during session: heparin sodium 5000 IU/ML and ultrafiltration: according to dry weight.

2.5. Statistical analysis

Version 24 of the Statistical Program for Social Science (SPSS) was used to analyze the data. Quantitative information was presented as mean SD. Frequency and percentage were utilized to convey qualitative data. **Mean (average):** a discrete collection of numbers' central value, namely the sum of variables divided by the total number of values. **Standard deviation (SD):** is a measure of a collection of values' dispersion. When the SD is low, the values tend to be near to the set's mean; when it's large, the values are dispersed across a broader range.

3. Results

Table 1.

This table shows: There was no statistically substantial age variation (P value = 0.089) between the study groups (groups I and II). In group I, it was 56.8 ± 6.5, whereas in group II, it was 54.5 ± 6.8. There is no statistically substantial variation in regards to sex between the study groups (groups I and II; P value = 0.839). In group I, there were 30

Table 1. Comparison of the demographic information between research groups.

	Group I (N = 50)	Group II (N = 50)	Stat. test	P value
Age (years)				
Mean ± SD	56.8 ± 6.5	54.5 ± 6.8	MW = 1004.5	0.089 NS
Sex				
Male	30 60%	29 58%	X^2 = 0.04	0.839 NS
Female	20 40%	21 42%		
Weight (kg)				
Mean ± SD	78.3 ± 8.07	76.7 ± 7.8	MW = 1107	0.319 NS
BMI (kg/m^2)				
Mean ± SD	25.5 ± 1.5	24.8 ± 1.4	MW = 1016	0.105 NS

BMI, body mass index; MW, Mann Whitney *U* test; NS: *P*-value >0.05, non-significant; X^2, Chi-square test.

Table 2. Comparison between studied groups as regard Creatinine and urea.

	Group I (N = 50)	Group II (N = 50)	Stat. test	P value
Creatinine (mg/dl)				
Mean ± SD	7.75 ± 1.9	0.94 ± 0.26	MW = 0.0	<0.001 HS
Urea (mg/dl)				
Mean ± SD	97.5 ± 41.4	35.8 ± 10.08	MW = 140	0.001 HS

HS, highly substantial; MW, Mann Whitney *U* test.

men (60%) and 20 women (40%) whereas in group II, there were 29 men (58%) and 21 women (42%) There was no statistically substantial age variation (*P* value = 0.319) between the study groups (groups I and II). In group I, it was 78.3 ± 8.07, whereas in group II, it was 76.7 ± 7.8. There is no statistically substantial variation in age between the study groups (groups I and II; *P* value = 0.105). In group I, it was 25.5 ± 1.5, whereas in group II, it was 24.8 ± 1.4 Table 2.

This table reveals: Highly statistical substantial **(*P* value <0.001)** increased Creat in group I (7.75 ± 1.9) when compared with Creat of group II (0.94 ± 0.26). Highly statistical significant **(*P* value <0.001)** increased urea in group I (97.5 ± 41.4) when compared with urea of group II (35.8 ± 10.08) Table 3.

Table 3. Comparison of the study groups' GA and HbA1C levels.

	Group I (N = 50)	Group II (N = 50)	Stat. test	P value
GA (%)				
Mean ± SD	7.2 ± 9.1	1.8 ± 1.8	MW = 392	<0.001 HS
HbA1C (%)				
Mean ± SD	6.9 ± 1.6	7.7 ± 1.3	MW = 819	0.003 S

GA, glycated albumin; HbA1C, glycated hemoglobin; HS, highly substantial; MW, Mann Whitney *U* test.

Highly statistical substantial **(*P* value <0.001)** increased GA in group I (7.2 ± 9.1) when compared with GA of group II (1.8 ± 1.8). Statistically substantial **(*P* value = 0.003)** decreased HbA1C in group I (6.9 ± 1.6) when compared with HbA1C of group II (7.7 ± 1.3) Table 4.

It was shown by the use of the ROC curve that GA may be utilized to distinguish between group I and group II at a threshold level of 1.95 with 76% sensitivity, 90% specificity, 88.4% PPV, 78.9% NPV, and accuracy (AUC = 0.84 and *P* value < 0.001). At a threshold level of 6.65, HbA1C can distinguish between groups I and II with 50% sensitivity, 24% specificity, 39.68% PPV, 32.43% NPV, and accuracy of 37.00% (AUC = 0.33 and *P* value = 0.003) Table 5.

As regard GA in group I there were: Statistically substantial **(*P* value = 0.028)** positive connection **(*r* = 0.31)** between GA and Ca. No statistical substantial **(*P*-value >0.05)** connection between GA and other investigated data. **As regard HbA1C in group I there were:** Statistically substantial **(*P* value = 0.017)** Positive connection **(*r* = 0.34)** between HbA1C and BMI. No statistical substantial **(*P* value >0.05)** connection between HbA1C and other investigated data Table 6.

As regard GA in group II there was: No statistical substantial **(*P* value >0.05)** correlation between GA and other investigated data. **As regard HbA1C in group II there were:** Statistically substantial **(*P* value = 0.009)** Positive connection **(*r* = 0.36)** between HbA1C and PTH. Statistically substantial **(*P* value = 0.046)** Negative connection **(*r* = -0.28)** between HbA1C and Ca. No statistical substantial **(*P* value >0.05)** connection between HbA1C and other investigated data.

4. Discussion

Millions of individuals throughout the globe are impacted by the public health issue known as diabetic kidney disease (DKD). Diabetes mellitus is a significant comorbidity in chronic kidney disease (CKD) and a main cause of DKD. Glycemic management is crucial for extending life and slowing the course of diabetes-related problems in diabetic persistent maintenance hemodialysis (HD) patients.[6]

Table 4. Diagnostic performance of GA and HbA1C in discrimination of group I and group II.

	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P value
GA	1.95	0.84	76%	90%	88.4%	78.9%	83.00%	<0.001
HbA1C	6.65	0.33	50%	24%	39.68%	32.43%	37.00%	0.003

AUC, Area under curve; NPV, negative predictive value; PPV, positive predictive value.

Table 5. Correlation study between (GA and HbA1C) and other studied data in group I.

Group I	GA		HbA1C	
	r	*P*-value	R	*P* value
GA	1.0	–	0.13	0.363 NS
HbA1C	0.13	0.363 NS	1.0	–
Age	−0.05	0.756 NS	−0.03	0.826 NS
Weight	−0.14	0.347 NS	−0.16	0.282 NS
BMI	0.13	0.355 NS	**0.34**	**0.017 S**
Hb	−0.25	0.085 NS	−0.09	0.553 NS
PTH	0.20	0.175 NS	0.08	0.582 NS
Creat	−0.02	0.909 NS	−0.13	0.384 NS
Urea	−0.04	0.784 NS	−0.03	0.848 NS
Ca	**0.31**	**0.028 S**	−0.19	0.196 NS
PO4	0.23	0.114 NS	0.24	0.098 NS
SGPT	0.23	0.117 NS	−0.06	0.681 NS
SGOT	0.18	0.214 NS	−0.06	0.698 NS

(r), Pearson correlation coefficient; NS, non-significant; S, substantial.

Glycemic control over time in the general diabetic population, a number of clinical tests are helpful. Glycemic management in DKD patients is nonetheless more difficult than in the general population due to variations in insulin and glucose homeostasis. Therefore, selecting trustworthy clinical indicators to track glycemic control in patients with diabetes and DKD is crucial.[7]

The most often utilized assay, hemoglobin A1c (HbA1c), calculates the proportion of circulating hemoglobin that has chemically reacting with glucose and represents ambient blood glucose management over the previous 120 days, with the preceding 30 days having the greatest impact.[8]

Therefore, the current study's goal was to compare between glycated hemoglobin and GA among diabetic hemodialysis patients.

Table 6. Correlation study between (GA and HbA1C) and other investigated data in group II.

Group II	GA		HbA1C	
	r	*P* value	*r*	*P* value
GA	1.0	–	0.06	0.685 NS
HbA1C	0.06	0.685 NS	1.0	–
Age	0.24	0.098 NS	0.09	0.549 NS
Weight	0.24	0.092 NS	0.07	0.637 NS
BMI	−0.04	0.796 NS	−0.01	0.948 NS
Hb	0.08	0.607 NS	0.12	0.423 NS
PTH	0.16	0.26 NS	**0.36**	**0.009 S**
Creatinine	−0.12	0.393 NS	0.19	0.182 NS
Urea	−0.17	0.239 NS	0.20	0.165 NS
Ca	0.20	0.168 NS	**−0.28**	**0.046 S**
PO4	−0.11	0.435 NS	−0.21	0.143 NS
SGPT	0.00	0.983 NS	−0.21	0.143 NS
SGOT	−0.07	0.615 NS	−0.23	0.104 NS

(r), Pearson correlation coefficient; NS, non-significant; S, substantial.

In this prospective comparison research, 100 diabetic patients were included who had stable blood sugar levels and whose diabetes medication had not changed in the six months prior to the measurement of GA and HbA1c. There were two equal groups of patients; Group I included 50 diabetic patients on hemodialysis whose mean age±SD was 56.8 ± 6.5 years old and group II included 50 diabetic patients but not on hemodialysis whose mean age±SD was 54.5 ± 6.8 years old. There was non-statistically substantial variation between both groups as regard Sex, age, weight and BMI (P value > 0.05). The studied cases were recruited and assessed for eligibility from the Internal Medicine Department of Al-Azhar University Hospital.

The present study indicated a highly statistically substantial reduce in hemoglobin (Hb) level among group I in comparison with group II (9.7 ± 1.4 vs. 12.02 ± 1.5 g/dl, respectively) (P value < 0.001). There was a high statistical substantial improve in parathyroid hormone (PTH) level among group I in comparison with group II (332.1 ± 181.5 vs. 38.1 ± 15.01 pg/ml, respectively) (P value < 0.001). The increased PTH levels that promote bone marrow fibrosis, reduced erythropoietin synthesis, and resistance to the generated erythropoietin might be the reason for the decreasing hemoglobin level.

Such findings are in agreement with **Tanaka *et al.*** [9] that demonstrated that PTH is a uremic toxin that is thought to have a number of negative consequences, and excessive levels are linked to renal anemia in hemodialysis patients.

Similarly, **Azeem *et al.* (2020)** study on 110 patients on maintenance hemodialysis reported that Anemia commonly occurs in individuals with hyperparathyroidism who are receiving continuous hemodialysis. Patients' mean hemoglobin levels were determined to be 9.75 ± 1.47 g/dl and their mean PTH levels were discovered to be 642 ± 405.9U.

The present study indicated a great statistically substantial rise in creatinine level among group I in comparison with group II (7.75 ± 1.9 vs. 0.94 ± 0.26 mg/dl, respectively) (P value < 0.001). There was a great statistically substantial elevation in urea level among group I in comparison with group II (97.5 ± 41.4 vs. 35.8 ± 10.08 mg/dl, resp.) (P value < 0.001).

Such finding is in agreement with **Kumar and Reddy**,[10] that demonstrated that creatinine levels were higher in diabetic ESRD patients on HD (4.99 ± 0.7) than diabetic non-HD patients (0.9 ± 0.1).

The present research indicated a great statistically substantial improve in PO4 level among group I in comparison with group II (5.5 ± 1.4 vs. 3.4 ± 0.7 mg/dl, resp.) (P value < 0.001). There was non-

statistically substantial variance between both groups regarding Ca level (P value > 0.05).

Such findings are in agreement with recent research by **Ahmed *et al.***[11] that compared diabetic HD patients and healthy non-HD, non-diabetic subjects and demonstrated non-statistical substantial variation between both groups regarding serum Ca level.

The present research indicated a highly statistically substantial elevation in GA level among group I in comparison with group II (7.2 ± 9.1 vs. 1.8 ± 1.8%, respectively) (P value < 0.001). There was a statistically substantial reduce in HbA1C level among group I in comparison with group II (6.9 ± 1.6 vs. 7.7 ± 1.3%, respectively) (P value < 0.001).

Such findings are in line with **Sany *et al.***[12] who found that compared to GA, HbA1c dramatically understates glycemic control in diabetic individuals receiving hemodialysis. There was a great statistically substantial improvement in GA among diabetic HD patients in comparison with diabetic patients without CKD (278.8 ± 43 vs. 190 ± 67 μmol/L, respectively), however, there was a highly statistically significant decrease in HbA1C among diabetic HD patients in comparison with diabetic patients without CKD (5.9 ± 0.5 vs. 6.8 ± 0.8%).

Similarly, **Kumar and Reddy,**[10] In a study with 100 cases, 50 cases of diabetic ESRD patients on HD, and 50 controllers of diabetic patients with typical renal function, HbA1c was significantly lower in cases (7.081.2%) compared to controls (9.26 ± 2.01%).

Moreover, **Peacock *et al.***[13] The percentage GA was statistically substantially greater in ESRD patients compared to those without renal disorder (18.7% 7.3, range: 7.7 ± 52.7 vs. 15.3% 5.5, range: 8.6 ± 33.8%, respectively) and HBA1c was substantially lower (6.8% 1.6, range: 4.1 ± 13.5 vs. 7.3% 1.4, range: 5.1 ± 11.3%). The study included 307 diabetic subjects, 258 of whom were on hemodialysis, and 49were with normal renal function.

The current research found that, at a threshold level of 1.95, GA may be utilized to distinguish between groups I and II with 76% sensitivity, 90% specificity, 88.4% PPV, 78.9% NPV, and 83.00% accuracy (AUC = 0.84 and P value < 0.001). According to the current study's findings, HbA1C may be utilized to distinguish between group I and group II at a cutoff level of 6.65 with 50% sensitivity, 24% specificity, 39.68% PPV, 32.43% NPV, and 37.00% accuracy (AUC = 0.33 and P value = 0.003).

Such findings are in agreement with **Wang *et al.***[14] that compared between diabetic nephropathy and diabetic only patients and demonstrated that the GA had a higher AUC than HbA1c (AUC = 0.580, 95% CI 0.499–0.662, P = 0.058) (AUC = 0.811, 95% CI 0.752–0.8690, P value = 0.005). For the identification of diabetic nephropathy in individuals with type 2 diabetes, the cutoff values of GA with the best sensitivity and specificity were 2.71. (sensitivity 0.676, specificity 0.778).

Moreover, **Miyabe *et al.***[15] indicated that in DM-HD patients, GA offers a more accurate marker of glycemic control than HbA1c. Such a conclusion was reached in light of research demonstrating how the administration of ESA and/or iron without regard to glycemic control might result in an underestimate of glycemic control in DM-HD patients.

A previous investigation by **Martino *et al.***[16] that GA revealed greater sensitivity than HbA1c in HD (84.77 vs. 39.51, respectively), and it would seem to have a stronger predictive ability in detecting new instances of DM, when compared between diabetic and non-diabetic HD patients.

The current research found that among group I, GA and Ca had a statistically substantial positive association (P value = 0.028, r = 0.31) and that there was a positive link between HbA1C and BMI (P value = 0.017, r = 0.34). HbA1C and GA showed no connection (P value > 0.05). According to the results of the current research, there was a statistically substantial negative connection between HbA1C and Ca in group II (P value = 0.046, r = −0.28) and a statistically substantial positive relationship between HbA1C and PTH (P value = 0.009, r = 0.36) among group II.

Conversely, **Martino *et al.***[16] Investigation on 160 HD patients found a strong association between the measured GA and HbA1c levels in the uremic diabetic patients (R = 0.71; P value < 0.0001) when comparing GA and HbA1c regarding the detection of glyco-metabolic abnormalities in non-diabetic and diabetic HD patients.

4.1. Conclusion

The present study highlights that in diabetic uremic patients, glycated albumin shows a higher sensitivity and specificity in determining glycemic alterations in comparison with glycemic hemoglobin, thus enhancing these patients' clinical management.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

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Conflicts of interest

The authors declared that there were NO conflicts of Interest.

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