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Evaluation of Glycemic Control among Diabetic Patients with ESRD on Regular Hemodialysis

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Abstract

Purpose: To evaluate the effectiveness of hemoglobin A1c (HbA1C), fructosamine, and glycated albumin (GA) in assessing glycemic control among type II diabetic patients with end-stage renal disease (ESRD) on regular hemodialysis.

Methods: This cross-sectional observational study was conducted on 90 type II diabetic ESRD patients on regular hemodialysis and were classified into good and poor glycemic control based on 8-point glucose testing. Good control required 70% of pre-prandial readings below 130 mg/dl, 70% of post-prandial readings below 180 mg/dl, and glycemic variability under 50 in more than 70% of readings. Based on these criteria, 40% had good control, while 60% had poor control.

Results: The study included 64.4% males and 35.6% females with a mean age of 54 years (SD ±5). Forty percent of patients had good glycemic control and 60% of patients had poor glycemic control. Glycemic control was defined by specific pre-prandial, post-prandial, and variability criteria. The most reliable marker of glycemic control is GA through the ROC analysis with AUC (0.816), followed by fructosamine (0.755) and lastly HbA1c (0.703).

Conclusions: GA is a superior marker for glycemic control in type II diabetic ESRD patients on hemodialysis, offering better predictive power than HbA1c and fructosamine.

Keywords: Diabetes Mellitus, ESRD, Hemodialysis, Glycemic Control, HbA1c

Introduction

Diabetes mellitus (DM) is a significant worldwide health issue, impacting about 463 million individuals in 2017. Projections suggest that this number will rise to 700 million by 2045 [1]. This rise in diabetes prevalence has led to a corresponding increase in cases of end-stage renal disease (ESRD), with the proportion of ESRD attributable to diabetes rising from 22.1% in 2000 to 31.3% in 2015 [2]. This dual burden significantly compromises survival rates and places a substantial economic strain on healthcare systems [3].

Cases with DM who undergo hemodialysis are at a heightened susceptibility to developing additional medical conditions and often encounter inferior health results in comparison to individuals without diabetes. It is essential to closely monitor and regulate blood glucose and hemoglobin A1c (HbA1c) levels in order to slow down the advancement of diabetic nephropathy and reduce the occurrence of cardiovascular problems [4]. Glycemic control is typically assessed using various biomarkers, such as glucose and HbA1c. However, blood glucose levels can fluctuate due to factors like diet and stress, offering only a transient snapshot of glycemic management [5].

In patients suffering from chronic kidney disease (CKD), the reliability of HbA1c as a measure of blood sugar management is diminished because of changes in the lifetime of red blood cells and the effects of medications like iron supplementation and erythropoietin, which can artificially decrease HbA1c values [6]. Human serum albumin, the most abundant protein in the bloodstream, has garnered attention as a potential marker of hyperglycemia because of its susceptibility to glycation, a nonenzymatic reaction between glucose and proteins [7].

Fructosamine serves as a valuable marker for evaluating short-term glycemic control, reflecting glucose levels over the preceding 2-3 weeks. It is a quick, straightforward, and cost-effective test that is unaffected by red blood cell disorders, making it particularly useful for diabetes screening during pregnancy and in resource-limited settings [8]. It is crucial to

comprehend the sociodemographic and clinical aspects that impact glucose control in diabetic patients undergoing hemodialysis. This knowledge is necessary for guiding research and devising ways to enhance patient outcomes [9].

Therefore, this study purpose's is to identify which analyte -including (HbA1C, GA, Fructose amine) is better for assessment of glycemic control among diabetic patients with T2DM and ESRD and receiving regular hemodialysis.

Patients and methods

This cross section observational study was carried at Internal Medicine Department - Benha University Hospitals on 90 type II diabetic ESRD patients on regular hemodialysis.

Ethical approval

Before patients were enrolled in the study, they gave agreement, and the study was granted ethical authorization. The patients were fully informed about all study procedures. The Ethics Committee of Faculty of Medicine, Benha University Hospital's gave its approval to this investigation (Approval number: MS 6-4-2023).

Inclusion criteria were type II diabetic patients aged >18 years of both genders with ESRD under maintenance hemodialysis treatment. Diagnosis of DM was made based on American Diabetes Association criteria [10]: Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L). No caloric consumption for a minimum of eight hours is the definition of fasting. Oral glucose tolerance test (OGTT): 2-hour PG ≥200 mg/dL (11.1 mmol/L). The test was conducted in accordance with the guidelines established by the WHO, utilizing a glucose dose that contained the equivalent of 75 g of anhydrous glucose dissolved in water. An HbA1C level of at least 6.5% (48 mmol/mol). A random plasma glucose level of at least 200 mg/dL (11.1 mmol/L).

Exclusion criteria were type I DM patients, patients received blood transfusion or hospitalized patients within the previous 3 months, patients with known hemoglobinopathy, presence of acute inflammatory state and patients with malignant disease.

All studied cases were subjected to

Thorough history taking of socio-demographic characteristics, medical history, current medication (insulin, oral hypoglycemic agents), CVS risk factors and CVS complications. Clinical examination included anthropometric measurements, vital signs and complete systemic examination. Routine laboratory investigations included complete blood count, INR, lipid profile (total cholesterol, triglycerides, LDL, HDL), albumin, liver enzymes (ALT, AST), post-dialysis serum urea and serum creatinine.

Glucose monitoring:

Eight – point glucose monitoring: Participants used EXACTIVE or ACCU-CHEK Active glucose test strips and devices to measure their blood glucose levels eight times a day, weekly, for eight weeks (extendable to ten weeks if needed). Measurements were taken pre- and 2 hours post-meal (breakfast, lunch, and dinner), at bedtime, and at 3 AM. Glucose monitoring was done on non-hemodialysis days to ensure accurate results.

Glycemic control assessment: At the end of eight-point glucose monitoring, HbA1c, GA and fructosamine levels were measured. These tests offer a comprehensive evaluation of patients' glycemic control over different time frames.

Blood samples (5 ml) were taken under aseptic conditions. Three ml were clotted and centrifuged to assess albumin, urea, creatinine, and eGFR. The remaining 2 ml were in an EDTA vacutainer for Hb and HbA1c tests. GA was measured using an ELISA test.

Statistical methods

The statistical analysis and data administration were conducted using SPSS version 28 (IBM, Armonk, New York, United States). The Shapiro-Wilk test and visualization techniques

were employed to evaluate the normality of the quantitative data. The data were described using either medians and ranges or means and standard deviations, depending on their normality. Numbers and percentages were employed to represent categorical data. Quantitative data were compared according to glycemic control status using either the independent t-test or the Mann-Whitney Utest. Data that were categorical were compared using either the Chi-square test or Fisher's exact test. In order to evaluate the predictive capabilities of glycemic indicators, receiver operating characteristic (ROC) analysis was implemented. This involved the computation of areas under the curve, the establishment of cutoff thresholds, and the evaluation of diagnostic indices. Pearson's correlation was implemented to investigate the correlations between glycemic indicators and other variables. Odds ratios and 95% confidence intervals were reported to predict poor glycemic control in both univariate and multivariate logistic regression models. Statistical significance was determined for P values less than 0.05, and all tests were conducted using a two-sided approach.

Results

This cross-sectional study was conducted on 90 type II diabetic patients with ESRD on regular hemodialysis.

The studied cases showed a mean age of 54 years (SD ±5). The majority were male (64.4%, n=58), with an average post-dialysis body weight of 67 kg (SD ±7) and a mean height of 1.6 meters (SD ±0.05), resulting in a mean BMI of 25.2 (SD ±2.8). Most participants lived in urban areas (64.4%), were married (67.8%), and 58.9% were employed. Educational levels varied, with 36.7% illiterate, 27.8% with secondary education, and 35.6% having higher education. The mean heart rate was 86 b/m (SD ±9), respiratory rate was 21 c/m (SD ±2), and blood pressure averaged 123/75 mmHg (SD ±13/10). Hypertension was present in 66.7% (n=60), and 54.4% (n=49) had cardiovascular diseases. The mean duration of diabetes was 12

years (SD ±2). About twenty-four percent of patients were on insulin, 46.7% were on oral hypoglycemic agents and 28.9% were on both. **Table 1**

Table 1: Demographic and clinical findings of the studied patients.

Demographics		
Age (years)	Mean ±SD	54 ±5
Sex		
Males	n (%)	58 (64.4)
Females	n (%)	32 (35.6)
BMI	Mean ±SD	25.2 ±2.8
Residence		
Urban	n (%)	58 (64.4)
Rural	n (%)	32 (35.6)
Marital status		
Single	n (%)	29 (32.2)
Married	n (%)	61 (67.8)
Employment status		
Yes	n (%)	53 (58.9)
Education		
Illiterate	n (%)	33 (36.7)
2ry education	n (%)	25 (27.8)
High education	n (%)	32 (35.6)
Clinical findings		
Heart rate (b/m)	Mean ±SD	86 ±9
Respiratory rate (c/m)	Mean ±SD	21 ±2
SBP (mmHg)	Mean ±SD	123 ±13
DBP (mmHg)	Mean ±SD	75 ±10
DM duration (years)	Mean ±SD	12 ±2
Diabetes medication		
Insulin injections	n (%)	22 (24.4)
Oral hypoglycemic agent	n (%)	42 (46.7)
Both	n (%)	26 (28.9)

SD: Standard deviation; m: meters; SBP: Systolic blood pressure, DBP: Diastolic blood pressure, DM: Diabetes Mellitus, BMI: Body Mass Index; n: number; %: percent; 2ry: Secondary; b/m: beats per minute; c/m: cycles per minute; mmHg: millimeters of mercury.

The average hemoglobin levels in the studied patients was 9.7 g/dl (SD ±0.9), with a mean platelet count of 215 x10^9/L (SD ±67 x10^9/L) and an International Normalized Ratio (INR) of 1.1 (SD ±0.1). Lipid profiles revealed a mean total cholesterol of 157 mg/dl (SD ±45), triglycerides at 124 mg/dl (SD ±31), LDL cholesterol at 78 mg/dl (SD ±28), and HDL cholesterol at 39 mg/dl (SD ±5). The mean albumin level was 3.5 g/dl (SD ±0.3), and liver function tests showed mean AST and ALT levels of 32 U/L (SD ±5) and 33 U/L (SD ±8), respectively. Post-dialysis renal function markers indicated an elevated mean serum creatinine of 3.1 mg/dl (SD ±0.5) and serum urea level of 65 mg/dl (SD ±12). Mean HbA1c level was

6.8% (SD ±0.3%), mean GA was 21% (SD ±4.5) and mean fructosamine level at 493 µmol/L (SD ±135). **Table 2**

Table 2: Laboratory findings in the studied patients.

	Mean ±SD
Hemoglobin (g/dl)	9.7 ±0.9
Platelets (X10^9/L)	215 ±67
INR	1.1 ±0.1
Total cholesterol (mg/dl)	157 ±45
Triglycerides (mg/dl)	124 ±31
LDL (mg/dl)	78 ±28
HDL (mg/dl)	39 ±5
Albumin (g/dl)	3.5 ±0.3
AST (U/L)	32 ±5
ALT (U/L)	33 ±8
Creatinine (mg/dl)	3.1 ±0.5
Urea (mg/dl)	65 ±12
HbA1c (%)	6.8 ±0.3
Glycated albumin (%)	21 ±4.5
Fructosamine (µmol/L)	493 ±135

g/dl: grams per deciliter; INR: International Normalized Ratio; mg/dl: milligrams per deciliter; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; U/L: units per liter; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; HbA1c: Hemoglobin A1c; SD: Standard deviation.

The 8-point glucose testing revealed elevated fasting blood glucose levels with a mean of 150.3 mg/dl (SD ±36.8). Postprandial levels were higher, averaging 202.8 mg/dl (SD ±49.2) after breakfast and 250.2 mg/dl (SD ±58.3) after lunch. Pre-lunch glucose averaged 230.3 mg/dl (SD ±85). Pre-dinner levels were 156.7 mg/dl (SD ±27.5), rising to 207.6 mg/dl (SD ±29.9) post-dinner. Bedtime levels averaged 168.3 mg/dl (SD ±17.7), and the 3 a.m. measurement showed a mean of 196.9 mg/dl (SD ±43). **Figure 1**

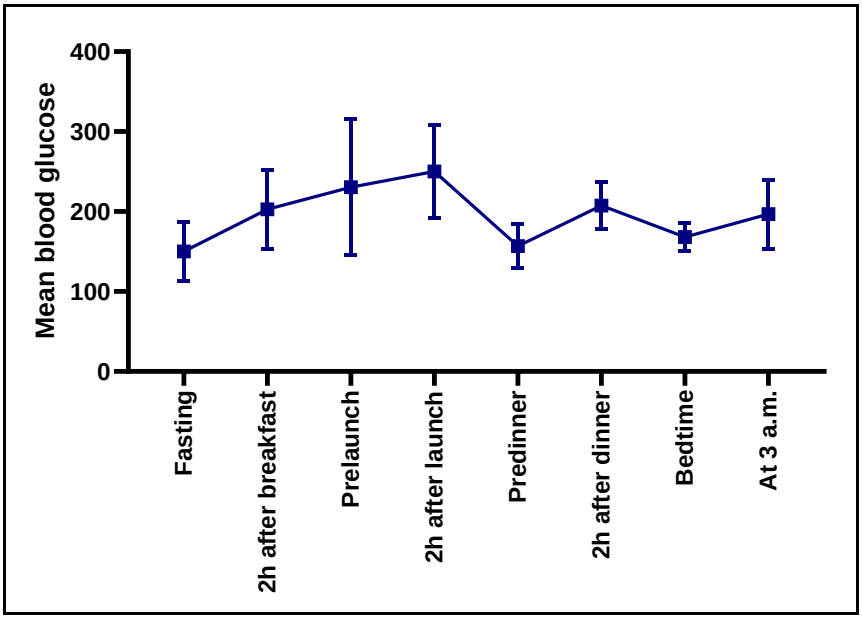

Figure 1: The 8-point blood glucose testing in the studied patients:

Patients were classified into good and poor glycemic control based on the 8-point glucose testing. Good control was defined as having 70% or more pre-prandial readings below 130 mg/dl, 70% or more post-prandial readings below 180 mg/dl, and glycemic variability under 50 in more than 70% of readings. Based on these criteria, 40% of patients had good control, while 60% had poor control. About sixty-eight percent of patients with poor glycemic control were employed. There were no significant differences between both groups regarding age, sex, weight, height, BMI, residence, marital status, education level, cardiovascular disease, diabetes duration, or medication ($P > 0.05$ for all). **Table 3**

Table 3: Demographics and clinical findings according to glycemic control in the studied patients.

Demographics		**Glycemic control**		
		Good (n = 36)	**Poor (n = 54)**	**P-value**
Age (years)	Mean ±SD	53 ±5	54 ±4	0.255
Sex				
Males	n (%)	21 (58.3)	37 (68.5)	0.323
Females	n (%)	15 (41.7)	17 (31.5)	
BMI	Mean ±SD	25.3 ±2.9	25.1 ±2.8	0.653
Residence				
Urban	n (%)	21 (58.3)	37 (68.5)	0.323
Rural	n (%)	15 (41.7)	17 (31.5)	
Marital status				
Single	n (%)	11 (30.6)	18 (33.3)	0.782
Married	n (%)	25 (69.4)	36 (66.7)	

Employment status				
Yes	n (%)	16 (44.4)	37 (68.5)	**0.023***
Education				
Illiterate	n (%)	12 (33.3)	21 (38.9)	0.838
2ry education	n (%)	11 (30.6)	14 (25.9)	
High education	n (%)	13 (36.1)	19 (35.2)	
Clinical findings				
SBP (mmHg)	Mean ±SD	123 ±12	122 ±14	0.773
DBP (mmHg)	Mean ±SD	77 ±10	74 ±9	0.124
DM durations (years)	n (%)	12 ±2	12 ±2	0.920
Diabetes medication				
Insulin injections	n (%)	8 (22.2)	14 (25.9)	0.357
Oral hypoglycemic agent	n (%)	20 (55.6)	22 (40.7)	
Both	n (%)	8 (22.2)	18 (33.3)	

*Significant P-value; SD: Standard deviation; n: number; %: percent; SBP: Systolic blood pressure, DBP: Diastolic blood pressure, DM: Diabetes Mellitus, BMI: Body Mass Index; 2ry: Secondary; SD: Standard deviation; mmHg: millimeters of mercury; n: number; %: percent.

Patients with poor control had higher total cholesterol (172 ± 50 mg/dl), triglycerides (136 ± 33 mg/dl), and LDL cholesterol (89 ± 29 mg/dl), but lower HDL cholesterol (38 ± 4 mg/dl) than those with good control (total cholesterol: 135 ± 22 mg/dl; triglycerides: 108 ± 15 mg/dl; LDL: 61 ± 13 mg/dl; HDL: 42 ± 5 mg/dl), all with $P < 0.001$. Glycemic markers, including HbA1c (6.8 ± 0.2% vs. 6.6 ± 0.3%), GA (23 ± 4.5 vs. 17.9 ± 2.2), and fructosamine (543 ± 146 vs. 417 ± 66), were also significantly higher in the poor control group ($P < 0.001$ for all). No significant differences were found in hemoglobin ($P = 0.566$), albumin ($P = 0.667$), AST ($P = 0.157$), or ALT ($P = 0.592$). **Figure 2**

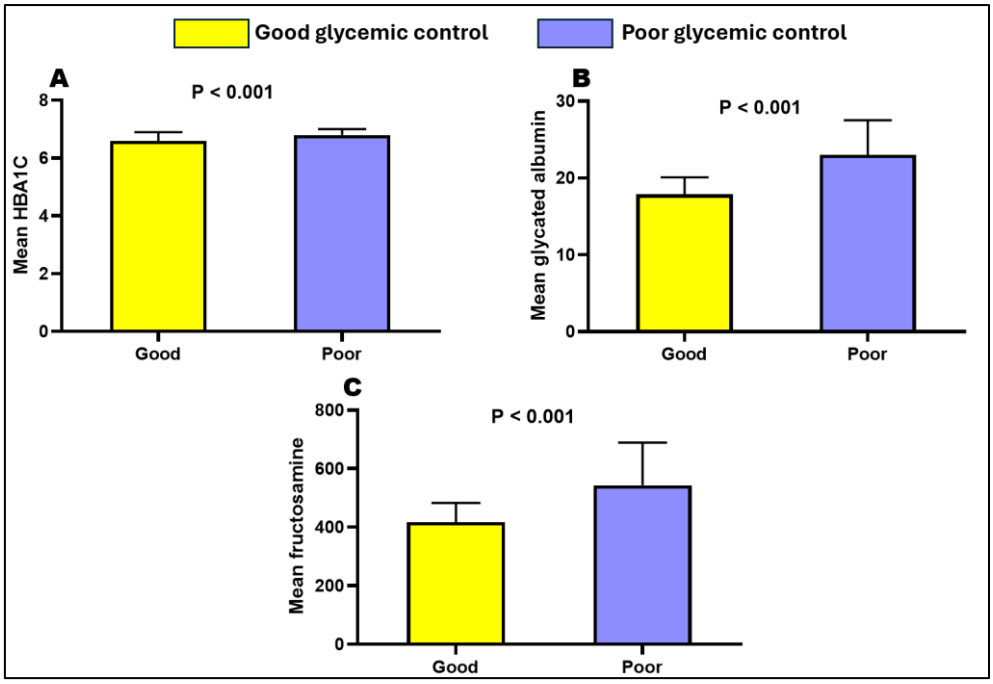

Figure 2: Performance of glycemic markers in predicting glycemic control.

ROC analysis for glycemic markers showed that GA had the best performance with an AUC of 0.816 (95% CI: 0.729–0.904, P < 0.001), indicating very good discrimination between good and poor glycemic control. Fructosamine followed with an AUC of 0.755 (95% CI: 0.645–0.856, P < 0.001), showing good discrimination. HbA1c had the lowest AUC of 0.703 (95% CI: 0.593–0.813), indicating good discrimination. The optimal cutoff points were >6.7 for HbA1c, >20.3 for GA, and >523 for fructosamine. At these cutoffs, HbA1c had sensitivity 64.8%, specificity 66.7%, PPV 74.5%, NPV 55.8%; GA had sensitivity 70.4%, specificity 91.7%, PPV 92.7%, NPV 67.3%; and fructosamine had sensitivity 68.5%, specificity 88.9%, PPV 90.2%, NPV 65.3%. **Figure 3**

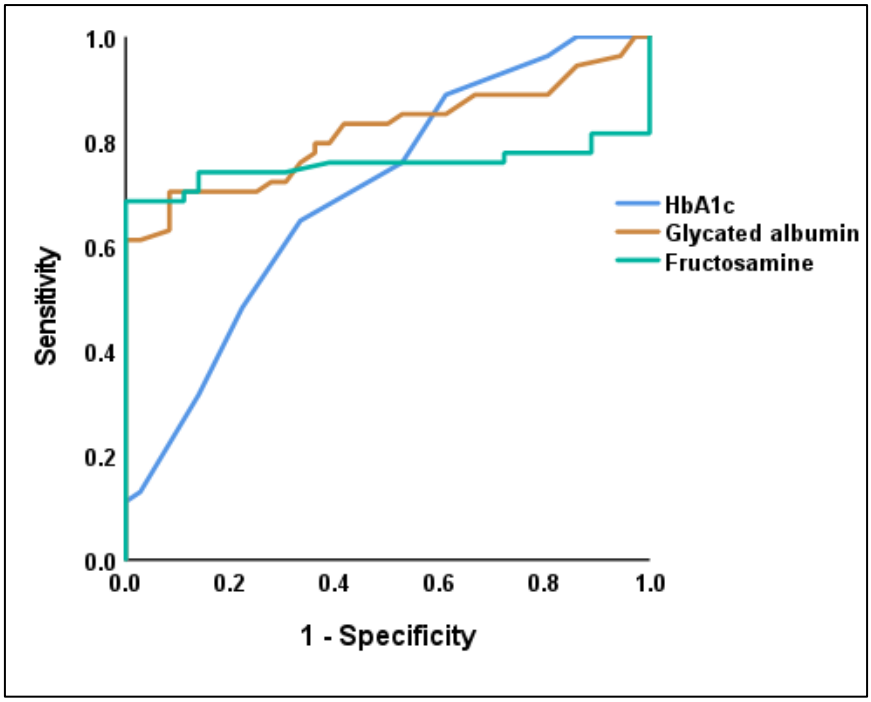

Figure 3: ROC analysis for glycemic markers in predicting poor glycemic control.

Univariate and forward stepwise multivariate logistic regression analyses identified LDL, HDL, creatinine, GA, and employment status as significant predictors of poor glycemic control. Each unit increase in LDL increased the risk of poor control by 14% (OR = 1.141, 95% CI: 1.041–1.251, P = 0.005), while each unit increase in HDL reduced the risk by 32.7% (OR = 0.673, 95% CI: 0.534–0.848, P < 0.001). Each unit increase in creatinine was associated with a tenfold increase in risk (OR = 10.889, 95% CI: 2.034–58.296, P = 0.005), and each unit increase in GA increased the risk by 91% (OR = 1.908, 95% CI: 1.256–2.901, P = 0.002). Employment status increased the risk sixfold (OR = 6.464, 95% CI: 1.033–40.435, P = 0.046).

Table 4

Table 4: Univariate and multivariate logistic regression analysis to predict poor glycemic control.

	Univariate		Multivariate	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Total cholesterol	1.023 (1.01 - 1.036)	**<0.001***	-	-
Triglycerides	1.039 (1.019 - 1.06)	**<0.001***	-	-
LDL	1.056 (1.028 - 1.084)	**<0.001***	1.141 (1.041 - 1.251)	**0.005***
HDL	0.834 (0.752 - 0.924)	**<0.001***	0.673 (0.534 - 0.848)	**<0.001***
INR	0.001 (0 - 0.031)	**<0.001***	-	-
Creatinine	5.484 (1.802 - 16.69)	**0.003***	10.889 (2.034 - 58.296)	**0.005***

Urea	1.043 (1.005 - 1.084)	**0.028***	-	-
HbA1c	28.542 (3.815 - 213.529)	**0.001***	-	-
Glycated albumin	1.433 (1.226 - 1.676)	**<0.001***	1.908 (1.256 - 2.901)	**0.002***
Fructoseamine	1.008 (1.004 - 1.012)	**<0.001***	-	-
Employment status	2.721 (1.136 - 6.513)	**0.025***	6.464 (1.033 - 40.435)	**0.046***

*Significant P-value; OR: Odds Ratio; CI: Confidence Interval; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; INR: International Normalized Ratio; HbA1c: Hemoglobin A1c.

Discussion

In this study we aim to evaluate the effectiveness of HbA1C, GA, and fructosamine in assessing glycemic control among diabetic cases with ESRD on regular hemodialysis. In this study, based on 8-point glucose testing, 40% of patients had good glycemic control, while 60% had poor control. Employment was higher in the poor control group. There were no significant differences between the groups in demographics, clinical characteristics, or medication.

Employment can disrupt diabetes management due to stress, rigid schedules, irregular meal timings, and medication nonadherence. Irregular work hours, stress hormones like cortisol, and limited exercise opportunities worsen glycemic control. Diabetic patients with ESRD need targeted strategies to balance work and medical care [11].

In the present study, patients with poor glycemic control had higher total cholesterol, triglycerides, LDL cholesterol, serum creatinine and urea, but lower HDL cholesterol compared to those with good control. Glycemic markers (HbA1c, GA, and fructosamine) were also higher in the poor control group. No differences were found in hemoglobin, albumin, AST, or ALT levels.

Consistent with our findings, **Rhee et al.,** found that poor glycemic control was associated with increased BMI, elevated WBCs, platelet, higher lipid profiles, blood pressure, and eGFR. It also correlated with abnormal lipid profiles and inflammation. Metabolic syndrome components, particularly obesity and dyslipidemia, were linked to poor control. Higher platelet and white blood cell counts indicated worse diabetes control, while high HDL levels were linked to better outcomes [12].

In the present study, ROC analysis showed that GA had the best performance for discriminating between good and poor glycemic control, with a significant AUC of 0.816 ($P < 0.001$). Fructosamine followed with an AUC of 0.755 ($P < 0.001$), indicating good discrimination. HbA1C had the lowest AUC of 0.703. In agreement with our study, **Gan et al.** found GA is more effective than HbA1c in reflecting true glycemic status, as HbA1c tends to underestimate and does not accurately indicate the glycemic conditions. Unlike HbA1c, GA demonstrates a robust predictor of glycemic control [13].

In conditions that affect the lifecycle of red blood cells, such as iron and/or erythropoietin therapy, uremia, and the necessity for frequent blood transfusions, a variety of factors can contribute to the inaccuracy of HbA1c measurements and the robustness of GA [14].

Additionally, two recent studies conducted by **Inaba et al.** and **Peacock et al.** have identified GA as a more precise indicator of glycemic control, which is consistent with our findings. These studies demonstrated that HbA1c in diabetic hemodialysis patients underestimates blood glucose levels as a result of anemia and the use of erythropoietin, while carbamylated hemoglobin can induce overestimation. GA is a more reliable glycemic control index because it is unaffected by red blood cell lifespan or erythropoietin and correlates more closely with actual glucose levels [15, 16].

GA enables prompt action by detecting rapid glucose changes early. High levels of GA are associated with severe cardiovascular disease and impaired kidney function, rendering it a dependable indicator of glycemic control and a predictor of vascular complications in diabetic nephropathy [13]. In contrast, the KDIGO 2020 guideline asserts that "HbA1c remains the glycemic biomarker of choice in advanced CKD" as a result of the assay biases of GA and fructosamine and their lack of advantages over HbA1c [17].

Nevertheless, the American Diabetes Association and European Association for the Study of Diabetes guidelines assert that "HbA1c may be unreliable in advanced CKD due to anemia and other conditions," and there is substantial evidence that supports the clinical value and reliability of GA over HbA1c [13, 18].

Also, in this study, fructosamine effectively differentiates between good and poor glycemic control with an AUC of 0.755. It provides valuable medium-term assessment (2-3 weeks) and complements HbA1C, especially when short-term changes in glucose control need to be monitored. **Mittman et al.** have demonstrated that fructosamine is a more precise indicator of glycemic control than HbA1c, which is consistent with our findings. In a prospective study of 100 diabetic hemodialysis patients, fructosamine was found to be a more effective predictor of hospitalization and infections than HbA1c [19]. In a more recent study conducted by **Shafi et al.,** a two-fold increase in the risk of all-cause and cardiovascular mortality was observed when fructosamine levels were doubled [20]. This implies that it is capable of accurately reflecting the effects of glycemic control on patient outcomes. **Senapathi et al.** emphasized the unreliability of fructosamine as a glycemic control instrument in nephrotic syndrome. They reported that serum fructosamine levels decreased as nephrotic syndrome advanced and did not correspond with elevated HbA1c levels as a result of substantial albuminuria [21]. The decrease in FA levels was likely a result of the increased protein turnover that was induced by nephrotic syndrome.

Agreeing with our results, research supports the use of GA as a more accurate marker for glycemic control in ESRD due to its independence from factors that typically alter HbA1C levels. Studies by **Inaba et al. and Peacock et al.** have indicated that GA provides a more direct measure of recent glycemic history, reflecting the glycation of serum albumin, which is less influenced by erythropoietin therapy and fluctuations in red blood cell turnover—common

in dialysis patients. This makes GA particularly valuable in this patient population where traditional HbA1C measurements may be misleading [15, 16].

Additionally, meta-analysis done by **Gan et al.** reported that GA is more effective than HbA1c in assessment of glycemic control in ESRD patients on hemodialysis [13]. Further validating the finding, **Divani et al.** have shown that GA correlates better than HbA1c with one week's worth of blood glucose levels obtained by continuous glucose monitoring (CGM) in diabetic patients on hemodialysis [22]. Moreover, a study in Japan by ***Selvin and Sacks*** found guidelines for monitoring glycemic control in diabetes patients on dialysis recommend GA over HbA1c [6].

In our study, univariate and forward stepwise multivariate logistic regression analyses identified LDL, HDL, creatinine, GA, and employment status as significant predictors of poor glycemic control. One unit increase in GA was associated with a 91% increased risk of poor glycemic control.

An increase in LDL by one unit was linked to a 14% higher risk of poor glycemic control, aligning with literature suggesting elevated LDL exacerbates insulin resistance. Conversely, each unit increase in HDL was associated with a 32.7% reduction in risk, supporting HDL's protective role against diabetes complications through improved insulin sensitivity [23]. Elevated creatinine levels, indicative of worsening renal function, were associated with a tenfold increase in the risk of poor control, likely due to the impaired kidney's role in insulin degradation and glucose formation [24].

This study has several limitations that should be considered when interpreting the results. Firstly, the cross-sectional design limits the ability to infer causality between glycemic control markers and patient outcomes. Additionally, the study's sample size was relatively small and drawn from a single center, which may limit the generalizability of the findings to broader populations. The reliance on 8-point glucose testing, while comprehensive, may not

fully capture daily glycemic variability, and the use of self-reported data for certain demographic and clinical variables could introduce bias. Furthermore, the study did not account for potential confounders such as variations in dialysis protocols, nutritional status, or adherence to prescribed medications, which could influence glycemic control. Finally, while GA was found to be the most effective marker in this cohort, the study did not explore the long-term outcomes associated with using GA versus HbA1c or fructosamine in clinical practice, warranting further investigation.

Conclusions

GA is considered to be the most effective analyte for assessing glycemic control in diabetic patients with ESRD on hemodialysis, outperforming HbA1c and fructosamine. It showed superior discriminative ability between good and poor control. Also, significant predictors of poor control included higher LDL and creatinine levels, and employment status, while higher HDL levels were linked to better control.

Conflict of interest: None to declare.

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References

1. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract*. 2019;**157**:107843. https://doi.org/10.1016/j.diabres.2019.107843

2. Cheng HT, Xu X, Lim PS, et al. Worldwide Epidemiology of Diabetes-Related End-Stage Renal Disease, 2000-2015. *Diabetes Care*. 2021;**44**:89-97. https://doi.org/10.2337/dc20-1913

3. Ren Q, Chen D, Liu X, et al. Derivation and Validation of a Prediction Model of End-Stage Renal Disease in Patients With Type 2 Diabetes Based on a Systematic Review and Meta-

analysis. *Front Endocrinol (Lausanne)*. 2022;**13**:825950. https://doi.org/10.3389/fendo.2022.825950

4. Rhee JJ, Zheng Y, Montez-Rath ME, et al. Associations of Glycemic Control With Cardiovascular Outcomes Among US Hemodialysis Patients With Diabetes Mellitus. *J Am Heart Assoc*. 2017;**6**. https://doi.org/10.1161/jaha.117.005581

5. Selvin E, Rawlings AM, Grams M, et al. Fructosamine and glycated albumin for risk stratification and prediction of incident diabetes and microvascular complications: a prospective cohort analysis of the Atherosclerosis Risk in Communities (ARIC) study. *Lancet Diabetes Endocrinol*. 2014;**2**:279-88. https://doi.org/10.1016/s2213-8587(13)70199-2

6. Selvin E, Sacks DB. Monitoring Glycemic Control in End-Stage Renal Disease: What Should Be Measured? *Clin Chem*. 2017;**63**:447-9. https://doi.org/10.1373/clinchem.2016.265744

7. Danese E, Montagnana M, Nouvenne A, et al. Advantages and pitfalls of fructosamine and glycated albumin in the diagnosis and treatment of diabetes. *J Diabetes Sci Technol*. 2015;**9**:169-76. https://doi.org/10.1177/1932296814567227

8. Nansseu JR, Fokom-Domgue J, Noubiap JJ, et al. Fructosamine measurement for diabetes mellitus diagnosis and monitoring: a systematic review and meta-analysis protocol. *BMJ Open*. 2015;**5**:e007689. https://doi.org/10.1136/bmjopen-2015-007689

9. Yusof Khan AHK, Zakaria NF, Zainal Abidin MA, et al. Prevalence of glycemic variability and factors associated with the glycemic arrays among end-stage kidney disease patients on chronic hemodialysis. *Medicine (Baltimore)*. 2021;**100**:e26729. https://doi.org/10.1097/md.0000000000026729

10. ADA C. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2022. *Diabetes Care*. 2021;**45**:S17-S38. https://doi.org/10.2337/dc22-S002

11. Sancini A, Ricci S, Tomei F, et al. Work related stress and blood glucose levels. *Ann Ig*. 2017;**29**:123-33. https://doi.org/10.7416/ai.2017.2139

12. Rhee JJ, Ding VY, Rehkopf DH, et al. Correlates of poor glycemic control among patients with diabetes initiating hemodialysis for end-stage renal disease. *BMC Nephrology*. 2015;**16**:204. https://doi.org/10.1186/s12882-015-0204-4

13. Gan T, Liu X, Xu G. Glycated Albumin Versus HbA1c in the Evaluation of Glycemic Control in Patients With Diabetes and CKD. *Kidney Int Rep*. 2018;**3**:542-54. https://doi.org/10.1016/j.ekir.2017.11.009

14. Zheng CM, Ma WY, Wu CC, et al. Glycated albumin in diabetic patients with chronic kidney disease. *Clin Chim Acta*. 2012;**413**:1555-61. https://doi.org/10.1016/j.cca.2012.04.025

15. Inaba M, Okuno S, Kumeda Y, et al. Glycated albumin is a better glycemic indicator than glycated hemoglobin values in hemodialysis patients with diabetes: effect of anemia and erythropoietin injection. *J Am Soc Nephrol*. 2007;**18**:896-903. https://doi.org/10.1681/asn.2006070772

16. Peacock TP, Shihabi ZK, Bleyer AJ, et al. Comparison of glycated albumin and hemoglobin A(1c) levels in diabetic subjects on hemodialysis. *Kidney Int*. 2008;**73**:1062-8. https://doi.org/10.1038/ki.2008.25

17. Fonseca V, Kohzuma T, Galindo RJ, et al. KDIGO recommendations for the evaluation of glycemic control in advanced chronic kidney disease. *Kidney International*. 2022;**101**:420. https://doi.org/10.1016/j.kint.2021.11.020

18. Copur S, Siriopol D, Afsar B, et al. Serum glycated albumin predicts all-cause mortality in dialysis patients with diabetes mellitus: meta-analysis and systematic review of a predictive biomarker. *Acta Diabetol*. 2021;**58**:81-91. https://doi.org/10.1007/s00592-020-01581-x

19. Mittman N, Desiraju B, Fazil I, et al. Serum fructosamine versus glycosylated hemoglobin as an index of glycemic control, hospitalization, and infection in diabetic hemodialysis patients. *Kidney Int Suppl*. 2010:S41-5. https://doi.org/10.1038/ki.2010.193

20. Shafi T, Sozio SM, Plantinga LC, et al. Serum fructosamine and glycated albumin and risk of mortality and clinical outcomes in hemodialysis patients. *Diabetes Care*. 2013;**36**:1522-33. https://doi.org/10.2337/dc12-1896

21. Senapathi SH, Bhavsar R, Kaur R, et al. A Case Report of Fructosamine's Unreliability as a Glycemic Control Assessment Tool in Nephrotic Syndrome. *Cureus*. 2017;**9**:e1694. https://doi.org/10.7759/cureus.1694

22. Divani M, Georgianos PI, Didangelos T, et al. Assessment of Hyperglycemia, Hypoglycemia and Inter-Day Glucose Variability Using Continuous Glucose Monitoring among Diabetic Patients on Chronic Hemodialysis. *J Clin Med*. 2021;**10**. https://doi.org/10.3390/jcm10184116

23. Al Ghadeer HA, Al Barqi M, Almaqhawi A, et al. Prevalence of Dyslipidemia in Patients With Type 2 Diabetes Mellitus: A Cross-Sectional Study. *Cureus*. 2021;**13**:e20222. https://doi.org/10.7759/cureus.20222

24. Kumar M, Dev S, Khalid MU, et al. The Bidirectional Link Between Diabetes and Kidney Disease: Mechanisms and Management. *Cureus*. 2023;**15**:e45615. https://doi.org/10.7759/cureus.45615