

Evaluation of Plasma Glucose Control in Diabetic Patients on Hemodialysis a Single Center Study

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Abstract

Objectives: The aim of study is to evaluate plasma glucose control in diabetic patient on hemodialysis by measure plasma glycated albumin and HbA1c and correlate them with parameters like serum electrolytes blood urea, serum creatinine, hemoglobin, serum albumin, total serum bilirubin, serum uric acid, parathyroid hormone, serum ferritin; to evaluate the effects of these parameters on the level of diabetic control.

Methods: This is a cross sectional study which included type 2 diabetic patients on hemodialysis these patients are currently undergoing hemodialysis and are on hemodialysis for more than three months. Total 50 type 2 diabetic patients on hemodialysis; between ages of 47–62 years of either gender were selected randomly and comparison done between the effect of different factors on HbA1c and glycated albumin.

Results: There were 50 patients enrolled in this study with a mean age of 54.5 ± 4.7 (range: 47–62) years. Males represented 58% (29 patients) while female represent 42% (21 patients) of the studied group with male to female ratio of 1.38 to one. The duration of diabetes (DM) ranged 4–20 years and two thirds of the cases had duration of 15 years or less. Regarding the treatment of DM, 35 patients (70%) were on soluble insulin while 15 patients neither receive insulin nor oral antidiabetic agent and their treatment was off. Poor glycemic control was significantly associated with younger age, patients aged <50 years were more frequent among the poor glycemic. Good glycemic control had significantly lower HbA1C% level.

Conclusion: Most of our diabetic patient on HD has controlled diabetes reflected by the level of HbA1c and GA. Serum ferritin levels is positively correlate with HbA1c levels in diabetic patient on hemodialysis which suggests that serum ferritin levels can be a marker of glycemic control in type 2 DM.

Keywords: Plasma glucose, diabetic patient, renal dialysis

Introduction

Diabetes mellitus is one of the most common diseases worldwide; diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia and several distinct types of DM are caused by a complex interaction of genetics and environmental factors.¹ Type 1 diabetes is generally considered to result from autoimmune destruction of insulin producing cells (β cells) in the pancreas, leading to marked insulin deficiency, whereas type 2 diabetes is characterized by reduced sensitivity to the action of insulin and an inability to produce sufficient insulin to overcome this 'insulin resistance'.² Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population.³⁻⁵ The excess cardiovascular morbidity and mortality among diabetics have not been fully explained by major risk factors such as hypertension, cigarette smoking and hypercholesterolemia.⁶ Diabetes is the most common cause of end-stage renal disease (ESRD) worldwide, accounting for 44.2% of end stage renal disease patients thus blood glucose levels need to be fairly controlled in these patients with end stage renal disease.⁷ Diabetes is challenging to manage in patients who have end-stage renal disease (ESRD), as both uremia and dialysis can complicate glycemic control by affecting the secretion, clearance, metabolism and peripheral tissue sensitivity of insulin so blood glucose values can be unpredictable in diabetic patients with

ESRD; blood glucose levels can fluctuate widely due to various and opposing effects of ESRD and dialysis.⁸ The aim of study is to evaluate plasma glucose control in diabetic patient on hemodialysis by measure plasma glycated albumin and HbA1c and correlate them with parameters like serum electrolytes blood urea, serum creatinine, hemoglobin, serum albumin, total serum bilirubin, serum uric acid, parathyroid hormone, serum ferritin; to evaluate the effects of these parameters on the level of diabetic control.

Methods

This is a cross sectional study which included type 2 diabetic patients on hemodialysis who were admitted to the Iraqi Hemodialysis Center Baghdad Teaching hospital/Medical City from May 2019 to October 2019, these patients are currently undergoing hemodialysis and are on hemodialysis for more than three months. Total 50 type 2 diabetic patients on hemodialysis; between ages of 47–62 years of either gender were selected randomly and comparison done between the effect of different factors on HbA1c and glycated albumin. Treatment of diabetic mellitus in all patients was soluble insulin but in 15 patients the treatment was stopped. Verbal consents were taken from all patients enrolled in this study. Data were collected by standard questioner about name, age, gender, duration of diabetes, type of diabetes, type of treatment (diet, oral hypoglycemic agents, insulin or combination or on no treatment) and efficacy of haemodialysis session (Kt/v) which is one method of measuring dialysis adequacy

where K mean dialyzer urea clearance, mean time of dialysis in hours, v mean urea volume of distribution.

Exclusion Criteria

1. Thyroid disease
2. Chronic liver disease
3. Serum albumin less than 3 g/dl
4. Active malignancy
5. Acute sever infections or inflammatory disease
6. Active major bleeding in the prior month
7. Pregnancy
8. Patient with Haemoglobinopathy

All participants were tested by drawing a blood sample for the following:

1. Glycated hemoglobin HbA1c
2. Glycated albumin
3. Serum electrolytes (calcium, phosphate, sodium, potassium)
4. Blood urea
5. Serum creatinine
6. Hb
7. Serum albumin
8. Total serum bilirubin
9. Serum uric acid
10. Parathyroid hormone
11. Serum ferritin
12. Fasting plasma glucose (average reading taken over last week)
13. Random plasma glucose (average reading taken over last week)

Statistical analysis done by SPSS 22, frequency and percentage used for categorical data, mean, median and SD for continuous data. Chi-square used for assessed association between variables, person correlation shows the correlation between continuous data. T test used for evaluation differences between mean and median of continues variables. *P*-value less or equal to 0.05 is consider significant.

Results

There were 50 patients enrolled in this study with a mean age of 54.5 ± 4.7 (range: 47–62) years. Males represented 58% (29 patients) while female represent 42% (21 patients) of the studied group with male to female ratio of 1.38 to one. The duration of diabetes (DM) ranged 4–20 years and two thirds of the cases had duration of 15 years or less. Regarding the treatment of DM, 35 patients (70%) were on soluble insulin while 15 patients neither receive insulin nor oral antidiabetic agent and their treatment was off. Regarding the duration; since the initiation of hemodialysis (HD), it ranged between 4–24 months with a mean of 9.2 ± 3.7 months, moreover, 11 patients (22%) on HD for 6 months or less, 68% for 6–12 months and 10% on HD for more than 12 months, these findings are shown in (Table 1).

According to the level of HbA1c%, the studied group categorized into two subgroups; to have fair or poor glycemic control, using a level of HbA1c of 7% as cutoff point. Patients with HbA1c of higher than 7% considered to have poor glycemic control, those with HbA1c of 7% or less considered to have fair glycemic control. This distribution revealed that 32 patients with fair glycemic control giving a control rate of 64% while those with poor glycemic control were 18 represented 36%, (Figure 1).

Table 1. Distribution of baseline characteristics of the studied group (N = 50)

Variable		No.	%
Age (year)	<50	10	20.0
	50–59	27	54.0
	≥60	13	26.0
	Mean (SD*)	54.5 (4.7)	–
	Range	47–62	–
Gender	Male	29	58
	Female	21	42.9
Duration of DM (years)	≤10	12	24.0
	11–15	21	42.0
	16–20	17	34.0
	Mean (SD*)	14.1 (4.3)	–
	Range	4–20	–
Treatment of DM	Soluble Insulin	35	70.0
	None (off)	15	30.0
Duration of HD (month)	≤6 months	11	22.0
	7–12 months	34	68.0
	>12 months	5	10.0
	Mean (SD*)	9.2 (3.7)	–
	Range	4–24	–

SD: standard deviation.

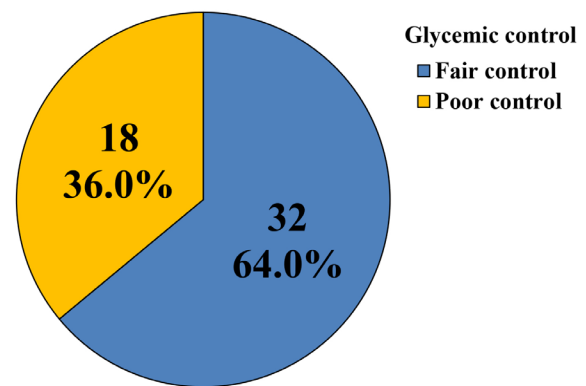


Fig. 1 Distribution of the studied group according to the glycemic control estimated by HbA1c level (7% or more indicated poor control).

To assess the differences in the mean values of the studied parameters across the glycemic control categories, a comparative analysis was performed using the cross-tabulation and chi-square test which revealed that poor glycemic control was significantly associated with younger age, patients aged <50 years were more frequent among the poor glycemic control group represented 38.9% compared to only 9.4% in those with fair glycemic control, (*P*-value < 0.05). Other variables including gender, duration of DM and duration on HD did not show significant differences between both subgroups, in all comparison, (*P*-value > 0.05), (Table 2).

The Comparison of HbA1c%, across the glycemic control subgroups revealed that patients with good glycemic control had significantly lower HbA1c% level, compared to those with

poor glycemic control; 5.9 ± 0.7 vs. 8.1 ± 1.6 , respectively, (P -value < 0.001). Other parameters including Glycated albumin (GA)%, Fasting plasma glucose (FPG), random plasma glucose (RPG), hemoglobin were not significantly different across the glycemic control subgroups, ($P > 0.05$), (Table 3).

Among the biochemical parameters, only Serum ferritin showed significant difference between both subgroups, where patients with poor glycemic control had significantly higher S. Ferritin level, (246.9 ± 63.9) ng/mL compared to 167.4 ± 58.3 ng/ml in those with fair glycemic control, (P -value < 0.001), (Table 4).

Further analysis was performed using bivariate Pearson's correlation test testing for further assessment of the

inter-correlation of different parameters with HbA1c% level, this analysis revealed similar results to that obtained in univariate analysis when t test and chi square were applied, in the correlation matrix, age showed a significant inverse correlation with HbA1c level, (correlation coefficient (R) value = -0.279 , P -value = 0.018), S. Ferritin was also significantly and positively correlated with HbA1c, ($R = -0.687$, $P < 0.001$), (Table 5). From other point of view, when similar correlation analysis applied between the studied parameters from one side and glycated albumin on the other side, no significant correlation had been found between GA and any of these parameters, in all correlations the correlation coefficient was not significant, ($P > 0.05$), (Table 6).

Discussion

Glycemic control in patients on hemodialysis has been shown to improve outcomes and reduce the incidence of complications in these patients; the efficacy of glycemic control depends in part upon the stage at which it is begun and the degree of normalization of glucose metabolism.⁹ It can reverse the

Table 2. Comparison of demographic characteristics of the studied group according to glycemic control

Variable	Glycemic control depending on glycated Hb				P-value	
	Fair control (n = 32)		Poor control (n = 18)			
	No.	%	No.	%		
Age (year)	<50	3	9.4	7	38.9	0.041 sig
	50–59	19	59.4	8	44.4	
	≥60	10	31.3	3	16.7	
Gender	Male	20	62.5	9	50	0.299
	Female	12	37.5	9	50	ns
Duration of DM (year)	≤10	8	25.0	5	27.8	0.675 ns
	11–15	14	43.8	9	50.0	
	16–20	10	31.3	4	22.2	
Duration of HD (month)	≤6 months	7	21.9	4	22.2	0.979 ns
	7–12 months	22	68.8	12	66.7	
	>12 months	3	9.4	2	11.1	

sig: significant difference, ns: no significant difference.

Table 3. Comparison of HbA1c, GA, FBG, RBG and hemoglobin according to the glycemic control of the studied group

	Glycemic control				P-value
	Fair control (n = 32)		Poor control (n = 18)		
	Mean	SD	Mean	SD	
HbA1c%	5.9	0.7	8.1	1.6	<0.001 sig
Glycated albumin%	17.3	6.2	19.8	3.0	0.878 ns
FPG (mg/dL)	169.7	32.1	182.8	56.6	0.341 ns
RPG (mg/dL)	224.7	56.5	226.1	67.5	0.694 ns
Haemoglobin (g/dL)	8.0	0.9	7.8	0.8	0.338 ns

sig: significant difference, ns: no significant difference, SD: standard deviation.

Table 4. Comparison of biochemical parameters according to the glycemic control assessed by HbA1c level of the studied group

Parameter	Glycemic control				P-value
	Fair control		Poor control		
	Mean	SD	Mean	SD	
S. Potassium (mEq/L)	5.8	0.9	6.0	0.9	0.448 ns
SPO ₄ (mg/dL)	4.1	0.9	4.2	0.7	0.730 ns
Blood urea (mg/dL)	94.1	25.5	93.9	14.0	0.969 ns
S. creatinine (mg/dL)	7.2	1.4	7.4	1.6	0.612 ns
S. Ferritin (ng/mL)	167.4	58.3	246.9	63.9	<0.001 sig
S. Albumin (g/dL)	3.4	0.3	3.5	0.4	0.353 ns
TSB (mg/dL)	0.4	0.1	0.5	0.2	0.416 ns
S. Sodium (mEq/L)	140.2	3.6	140.1	4.3	0.969 ns
S. Calcium (mEq/L)	8.7	0.4	8.8	0.5	0.141 ns
S. Uric acid mg/dL	7.2	1.3	6.5	1.2	0.059 ns
PTH	203.9	110.0	207.8	104.2	0.904 ns

sig: significant difference, ns: no significant difference, SD: standard deviation.

Table 5. Correlation matrix of the studied parameters versus HbA1c level of the studied group (N = 50)

Correlation variables	Correlation vs. HbA1c%	
	Correlation coefficient (R)	P-value
Age (year)	-0.279	0.018 sig
Glycated albumin	0.005	0.972 ns
FPS (mg/dL)	0.187	0.217 ns
RPS (mg/dL)	0.124	0.422 ns
Hemoglobin (g/dL)	-0.149	0.312 ns
S. Potassium (mEq/L)	-0.132	0.360 ns
SPO ₄ (mg/dL)	-0.038	0.795 ns
Blood urea (mg/dL)	-0.012	0.932 ns
S. Creatinine (mg/dL)	-0.179	0.219 ns
S. Ferritin (ng/mL)	0.606	0.003
S. Albumin (g/dL)	0.174	0.226 ns
TSB (mg/dL)	-0.050	0.731 ns
S. Sodium (mEq/L)	-0.254	0.075 ns
S. Calcium (mEq/L)	0.275	0.061 ns
S. Uric acid mg/dL	-0.230	0.120 ns
PTH	-0.146	0.317 ns
Efficiency of dialysis (Kt/v)	0.005	0.972 ns

Sig: significant, ns: not significant correlation.

Table 6. Correlation matrix of the studied parameters versus Glycated albumin level of the studied group (N = 50)

Correlation variables	Correlation vs. Glycated albumin%	
	Correlation coefficient (R)	P-value*
Age (year)	-0.051	0.727
HbA1c%	-0.005	0.972
FPS (mg/dL)	0.079	0.741
RPS (mg/dL)	0.074	0.812
Hemoglobin (g/dL)	-0.127	0.388
S. Potassium (mEq/L)	0.090	0.535
SPO ₄ (mg/dL)	0.099	0.498
Blood urea (mg/dL)	0.162	0.260
S. Creatinin (mg/dL)	0.028	0.849
S. Ferritin (ng/mL)	0.079	0.584
S. Albumin (g/dL)	0.157	0.276
TSB (mg/dL)	0.224	0.118
S. Sodium (mEq/L)	0.086	0.554
S. Calcium (mEq/L)	0.090	0.545
S. Uric acid mg/dL	-0.112	0.454
PTH	-0.046	0.754
Efficiency of dialysis	0.078	0.588

*All correlations were not significant, $P > 0.05$.

glomerular hypertrophy and hyperfiltration that involved in the pathogenesis of diabetic nephropathy and reduces the incidence of newly-onset microalbuminuria, on the other hand, progression of overt nephropathy can be stabilized or attenuated via strict glycemic control; therefore monitoring and assessment of glycemic control in diabetic patients with renal disease on hemodialysis is so important factor in assessment of the progression of disease and to control the outcomes.¹⁰ The current study included 50 diabetic Iraqi patients on hemodialysis with a mean age of 54.5 years (range: 47–62), this age distribution agreed the epidemiological profile of diabetic patients on hemodialysis where DM reduces the lag time to get advanced stages of renal disease. These findings are close to that reported by Halle et al. from Cameron who found a mean age of 47.3 years, and Park C from South Korea who reported that kidney disease started at earlier age (≥ 40 years) in diabetic patients compared to non-diabetic.¹¹ Among our studied group, males were relatively dominant with a male to female ratio of 1.33 to one. These findings agreed that reported in previous studies, where the prevalence of ESRD and frequency of males among hemodialysis patients are higher than females, indicated a sex-specific difference as it was reported by Hecking et al. from Austria in 2014 who found that males represented 59% of patients on hemodialysis, this could be attributed to the differences in socio-economic factors beyond biology such as educational level and employment.¹² The dominance of males in our study could be explained by the fact that majority of our patients were middle age (mean age is 54.5 years) and those male patients had more frequent comorbidities. On the other hand, the progression of renal diseases has been shown to be faster in men to reach end stage and need hemodialysis.^{13–16}

From other point of view, sex-specific differences are also recognized in several prevalent comorbidities such as type two diabetes which is a main risk factor for renal diseases, which coexist with or may have contributed to chronic kidney diseases.^{17,18} In our study almost two thirds of the patients had duration of DM of more than 10 years. With a mean duration of 14.1 years, which is long duration; our finding was close to that reported in a Saudi study was conducted by Alwakeel et al.¹⁹ in 2011 who found the mean duration of DM of 15.4 years and after follow up they found that duration of DM was significantly longer in cases with progressive nephropathy and that duration longer than 10 years was significantly associated with progression of diabetic nephropathy and chronic kidney disease.¹⁹ The duration of DM is an important factor contributed to the progression of chronic kidney disease and there is an inter-correlation between DM and chronic kidney disease, where insulin resistance (IR) as one of the key determinant of development of type 2 DM has been shown to be exist across all chronic kidney disease stages and get exacerbated with deterioration of renal function, on the other hand uremia itself induces IR.²⁰

The present study found that 70% of cases were on soluble insulin therapy, this was expected as those patients had higher IR than diabetic patients without chronic kidney disease, and these findings consistent with other studies from other countries like Hahr and Molitch from USA recommended the use of insulin in ESRD patients particularly rapid acting form to reduce postprandial plasma glucose peak.²⁰ On the other hand, Rajput et al. recommended a reduction in the insulin dose in dialysis patients according to patient's age, in patients younger than 15 years, insulin dose should be reduced to 50%, in those aged 15–60 years by 25% while in patients older than 60 years,

no reduction was recommended.²¹ In the present study, we categorized the patients according to their HbA1c level into two subgroups, we found that 36% of the patients had poor glycemic control; HbA1c more than 7%, and the remaining 64% with fair control; HbA1c < 7%. These findings consistent with previous study conducted in London by Creme and McCafferty who reported a rate of poor glycemic control of 39%.²² The present study found two significant correlations across the glycemic control. Regarding correlation between serum ferritin and HbA1c in our study S. Ferritin was significantly and positively correlated with HbA1c, this result is consistent with Madhura who reported same correlation that is Serum ferritin levels positively correlate with HbA1c levels in both complicated and uncomplicated diabetics, which suggests that serum Ferritin levels can be a marker of glycemic control in Type II DM; thus estimating serum Ferritin levels routinely in all Type II DM patients with nephropathy and setting a cutoff value of serum Ferritin will act as a reliable surrogate marker for good glycemic control and will help prevent patients from progressing to overt nephropathy and other complications.²³ Regarding correlation between HbA1c and Age in our study age showed a significant inverse correlation with HbA1c level, where poor glycemic control was significantly associated with younger age group, these

findings reflected by higher HbA1c level among patients aged less than 50 years compared to those older, these findings consistent with previous studies conducted by Rhee JJ et al. which have shown similar significant correlation.²⁴ According to the glycated albumin (GA) level, the mean glycated albumin % in our patients was $17.9 \pm 5.3\%$ which was close to that reported by Peacock et al. who measured glycated albumin in 258 diabetic patients on hemodialysis and found a mean GA% of $18.7 \pm 7.3\%$.²⁵

Conclusion

Most of our diabetic patient on HD has controlled diabetes reflected by the level of HbA1c and GA. Serum ferritin levels is positively correlate with HbA1c levels in diabetic patient on hemodialysis which suggests that serum ferritin levels can be a marker of glycemic control in type 2 DM. The choice which test to use should be guided by the clinical features of the patient and test availability.

Conflict of Interest

None. ■

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