Original Article

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.1242127

Anatolian Curr Med J. 2023;5(3):192-195

Impact of long-term glycemic variability on interdialytic weight gain in diabetic hemodialysis patients

Mustafa Topal[1], Muhammed Hasan Güler[2]

[1]Department of Nephrology, Konya City Hospital, Konya, Turkey
[2]Department of Internal Medicine, Konya City Hospital, Konya, Turkey

Cite this article as: Topal M, Güler MH. Impact of long-term glycemic variability on interdialytic weight gain in diabetic hemodialysis patients. *Anatolian Curr Med J.* 2023;5(3):192-195.

Received: 25.01.2023 ◆ **Accepted**: 10.04.2023 ◆ **Published**: 28.07.2023

ABSTRACT

Aims: Interdialytic weight gain (IDWG) was shown to be associated with mortality and correlated with long-term glycemic indices in diabetic hemodialysis (DHD) patients. The aim of this study was to investigate the association between glycemic variability (GV) and IDWG in DHD patients.

Methods: 82 DHD patients were studied for 6 months. Six measurements of monthly predialysis glucose were used to calculate glycemic indices. The weight gain over the dry weight of the last 10 consequent hemodialysis sessions was measured for each patient to calculate IDWG.

Results: IDWG was positively correlated with GV, HbA1c (p=0.025, r=0.247 and p=0.006, r=0.304, respectively) and inversely correlated with age (p=0.01, r=-0.283). GV was positively correlated with HbA1c (p<0.001, r=0.638), mean predialysis glucose (p<0.001, r=0.737) and negatively correlated with serum sodium (p=0.014, r=-271). HbA1c and age were found to be independently related to IDWG after linear regression analysis.

Conclusion: GV should be taken into account to improve IDWG in DHD patients.

Keywords: Hemodialysis, interdialytic weight gain, diabetes mellitus, glycemic variability, HbA1c

INTRODUCTION

Diabetes mellitus is the leading cause of end-stage renal disease and glycemic control is associated with mortality in diabetic hemodialysis (DHD) patients.[1,2] Glycemic control has been based on long-term glycemic indicators. Recently, not only long-term control, but also glycemic variability (GV) is found to have important clinical outcomes in diabetic patients.[3] GV has been put forth as an alternative glycemic indicator in the past decade and the number of studies about the impact of GV in literature is still increasing. GV is defined as the fluctuations of glucose or long-term glycemic indices over a certain time. GV can be calculated either as short-term (ie by continuous glucose monitoring devices within hours or a few days) or as long-term (ie by visit to visit glucose measurements within weeks or months). GV is found to be related to coroner artery disease, cerebrovascular disease, diabetic neuropathy, retinopathy, nephropathy, and even mortality in diabetic population.[3,4] Even before the onset of diabetes, GV was found to be related to the occurrence of diabetes, macrovascular complications and mortality.[5,6] GV was also studied in end-stage renal disease patients. It was found to be associated with severe hypoglycemia in DHD patients, and also with mortality in both DHD and peritoneal dialysis patients.[7-9]

Interdialytic weight gain (IDWG) is described as the weight gain over the dry weight to express excess water between two dialysis sessions in hemodialysis (HD) patients. It has been recommended that IDWG should be less than 4%-4.5% of dry weight.[10] IDWG was related to intradialytic hypotension, higher blood pressure, increased hospital admissions, extra HD sessions and thereby increased costs in previous studies.[11-13] Moreover, IDWG is shown to be related to poor survival in DHD patients.[14,15] Concordantly, decreased IDWG was associated with less intradialytic cardiac damage.[16] IDWG is found to be higher in DHD patients than non-diabetics and also to be correlated with HbA1c levels.[12,17,18] However, the impact of GV on IDWG has not been studied yet. The aim of our study is to search the association between GV and IDWG in diabetic HD patients.

Corresponding Author: Mustafa Topal, drmustafatopal@yahoo.com

METHODS

The study was carried out with the permission of the KTO Karatay University Medical Faculty Clinical Researches Ethics Committee (Date: 21.09.2022, Decision No: E-41901325-200-43559-024) and carried out in compliance with Helsinki declaration. This study was performed in two HD centers between January and July 2022. 82 DHD patients aged over 18 years who were at least 3 months on HD were enrolled in this study. Patients who were under 18 years, who had blood transfusion in the past 3 months, who had hemoglobinopathies, who had residual diuresis more than 100 ml/day and whose data were missing more than 1 measurement were not included in the study. They were all on a 4 hours, thrice-weekly HD schedule, using low flux membranes. Dialysate fluid glucose concentration was 100 mg/dl and sodium concentration was 138 mEq/L. Dialysis adequacy was calculated as Kt/V. Patient characteristics like gender, age, weight and height were noted. Body mass index (BMI) was calculated for each patient as kilograms/squared meters. Serum creatinine, blood urea nitrogen, sodium, potassium, calcium, phosphorus, albumin, parathormone and complete blood count samples were acquired just before the beginning of the HD session.

Glycemic Indices

Serum glucose samples were obtained predialysis once monthly for six months as spot glucose and were irrelevant of previous meal. Glucose tests were done by Roche COBAS 8000 c 702 module. Mean predialysis glucose (MPG) was calculated by dividing the sum of predialysis glucose (PG) by 6 for each patient. GV was calculated -as visit to visit PG- by the sum of absolute differences of 6 PG dividing by 5. HbA1c was obtained from the fourth month's predialysis samples. HbA1c measurements were tested by Arkray ADAMS HA-8180V system.

Interdialytic Weight Gain

Each patient's predialysis weight was acquired from last month's last 10 consecutive HD sessions. The difference of every measurement from the patients' dry weight was calculated. The sum of 10 absolute weight gain was divided by 10 to find the mean absolute weight gain for each patient. Finally, to find IDWG, mean absolute weight gain was divided by each patient's dry weight and then multiplied by 100.

Statistical Analysis

Statistics were done by SPSS version 22. According to Kolmogorow-Smirnov normality test, normally distributed measure correlations were done by using Pearson correlation. Non-normally distributed measure correlations done by Spearman correlation. After grouping GV according to mean GV, two groups were tested by Mann-Whitney U test. Then, a linear regression using backward elimination was done with IDWG related parameters. A p value of <0.05 was accepted as statistically significant.

RESULTS

82 DHD patients were included in this study, 48 (58.5%) of whom were female. Mean age was 63.23±10.85 years. The mean IDWG was 3.19±1.34%. Some characteristics of patients are shown in **Table 1**. IDWG was statistically significantly and positively correlated with GV (**Figure 1**), HbA1c and negatively correlated with age (**Table 2**). After grouping GV according to mean GV (49.37 mg/dl/month), high GV group had higher IDWG (3.56±1.43% vs 2.95±1.23%, p=0.032). GV was positively correlated with HbA1c (p<0.001, r=0.638), MPG (p<0.001, r=0.737) and inversely correlated with predialysis serum sodium (PSNa) (p=0.014, r=-271). HbA1c was positively correlated with MPG (p<0.001, r=0.706), hemoglobin (p=0.044, r=0.223) and conversely correlated with age (p<0.001, r=-0.401) and PSNa (p=0.024, r=-0.249). MPG was negatively correlated with age (p=0.022, r=-0.252) and PSNa (p<0.001, r=-0.385). Gender did not reveal any statistically significant difference in terms of HbA1c, mean glucose, GV and IDWG. After linear regression analysis, HbA1c was found to be a positive and age was found to be a negative independent predictors of IDWG (p=0.049 each) (**Table 3**).

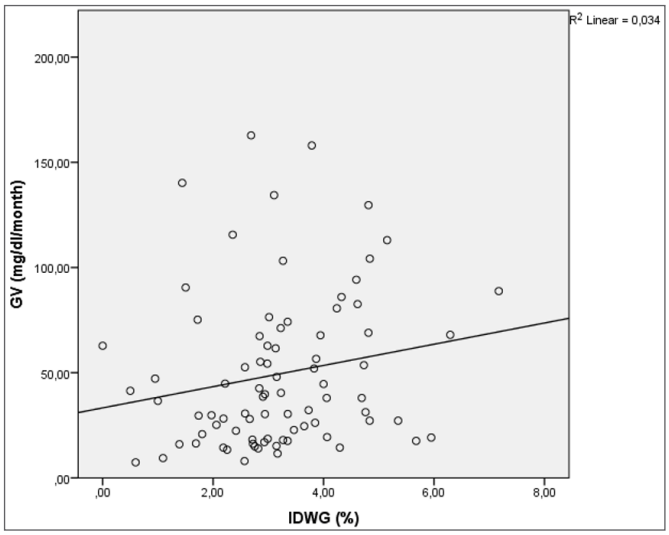

Figure 1. Scatter plot of correlation between GV and IDWG (p=0.025, r=0.247).

Table 1. Demographic and laboratory parameters of patients

Parameters	% or mean values
Female gender	48 (58.54%)
Age (years)	63.23±10.85
BMI (kg/m)	27.6±5.6
HbA1c (%)	6.67±1.73
MPG (mg/dl)	184.63±72.92
GV (mg/dl/month)	49.37±36.56
IDWG (%)	3.19±1.34
PSNa (mEq/l)	139.9±4.3
Hemoglobin (g/dl)	11.18±1.23
Kt/V	1.48±0.21

Table 2. The correlation of IDWG with GV, HbA1c and age by Spearman's rho test

Parameter	IDWG
GV	p= 0.025, R= 0.247
HbA1c	p= 0.006, R= 0.304
Age	p= 0.01, R= -0.283

Table 3. Regression analysis according to IDWG

Parameters	Backwards stepwise Model 1(R2=0.178)		Backwards stepwise Model 2 (R2=0.177)	
	Standardized β (CI%95)	p	Standardized β (CI%95)	p
(constant)		0.010		0.007
Age	-0.238 (-0.059-0.001)	0.055	-0.241 (-0.059-0.000)	0.049
HbA1c	0.252 (-0.034-0.425)	0.094	0.241 (0.001-0.372)	0.049
GV	-0.017 (-0.010-0.009)	0.896		

DISCUSSION

IDWG was found to be correlated with GV in the present study. To our knowledge it was the first study to investigate and find a relationship between GV and IDWG. Hyperglycemia leads to increasing osmolarity, which further leads to thirst via central mechanisms. Thus, chronic hyperglycemia detected by HbA1c in DHD patients leads to higher IDWG. As one end of GV is hyperglycemia, the same scenario may also be valid for GV. On the other hand, when it comes to how hypoglycemic end of GV affects IDWG, it may be more complicated. First, an over eating reaction as a consequence of hypoglycemia may lead to secondary hyperglycemia, which will further causes thirst. Secondly, it may be due to sugar-containing drinks. Especially younger patients, who were found to be associated with IDWG in our study, may be more proned to consume glucose-containing drinks due to their social environment. Drinking sugar-containing fluids resolve hypoglycemia quickly, while it causes an increase in blood glucose as a consequence. Besides, drinking fluids also enhances IDWG. In this study IDWG was also found to be correlated with HbA1c. Ifudu et al.[17] showed for the first time that IDWG was correlated with HbA1c in DHD patients, while it was a small group of 33 patients. Davenport,[19] on 175 DHD patients, revealed a correlation of IDWG with HbA1c. Similarly, Creme et al.[18] found a significant correlation between HbA1c and IDWG in a study including 412 DHD patients. All these studies are consistent with our results.

In this study, GV was found to be correlated well with both HbA1c and MPG. Fang et al.[20] revealed that GV was associated with HbA1c in a study including 291 diabetic patients. In a study on 93 DHD patients, Khan et al.[21] found that GV was associated with HbA1c levels, which was consistent with our study. This finding shows that decreasing GV may also improve HbA1c. Also, a well correlation of HbA1c and MPG was shown in this study, likewise put forth previously.[2]

Age was negatively correlated with IDWG, HbA1c and MPG in this study. Ipema et al.[23] revealed that younger HD patients have higher IDWG. In a study with 300 HD patients, Jalalzadeh et al.[24] showed that younger HD patients were significantly proned to higher IDWG. They concluded that higher fluid intake was a consequence of increased social and physical activity. This conclusion may be also true for poor glycemic control in young patients. On 649 diabetic patients, Shamshirgaran et al.[25] found that glycemic control was better in the elderly group, which is consistent with the current study.

GV, MPG and HbA1c were found to be negatively correlated with PSNa levels. Hyperglycemia is known to reduce serum sodium levels by increasing the osmolality, thus causing translocational hyponatremia. Furthermore, hyperglycemia leads to excessive water consumption, which further causes a dilutional decrease in sodium levels, especially in anuric HD patients. In the study of Davenport[19] on 175 DHD patients, a negative correlation of HbA1c and PSNa was found. On 1549 HD patients, Waikar et al.[26] showed that serum sodium levels were lower in DHD patients and were negatively correlated with HbA1c. Similarly, in a study including 697 HD patients, Sahin et al.[27] also found that PSNa were lower in DHD patients and were negatively correlated with HbA1c in DHD patients. These results too, are concordant with our study.

Our study has a few limitations. Despite it was a two-center study, our case number was relatively low. Increased patient numbers may reveal a stronger and independent correlation. Even so, high GV group was found to have increased IDWG. Besides, the number of patients below 40 years of age was only 3. Increased number of young patients could show a better relation of age with IDWG and glycemic indices. Finally, we had only one measurement of serum sodium. However, serum sodium tends to be stable over time in HD patients, so this may be overlooked as a real limitation.[28] Indeed, to our knowledge, this study was the first to investigate and show the correlation of GV with IDWG in DHD patients.

CONCLUSION

GV, HbA1c and age are associated with IDWG in DHD patients. Therefore, not only long-term markers of glycemic control, but also the variability of glucose should be taken into account to improve IDWG in HD units.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the KTO Karatay University Medical Faculty Clinical Researches Ethics Committee (Date: 21.09.2022, Decision No: E-41901325-200-43559-024).

Informed Consent: Written informed consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

REFERENCES

1. Collins AJ, Foley RN, Chavers B, et al. US Renal Data System. 2013 annual data report. *Am J Kidney Dis.* 2014;63(1 Suppl):A7.
2. Kalantar-Zadeh K, Kopple JD, Regidor DL, et al. A1C and survival in maintenance hemodialysis patients. *Diabetes Care.* 2007;30(5):1049-1055.
3. Zhou Z, Sun B, Huang S, Zhu C, Bian M. Glycemic variability: adverse clinical outcomes and how to improve it? *Cardiovasc Diabetol.* 2020;19(1):102.
4. Gorst C, Kwok CS, Aslam S,et al. Long-term glycemic variability and risk of adverse outcomes:a systematic review and meta-analysis. *Diabetes Care.* 2015;38(12):2354-2369.
5. Bancks MP, Carson AP, Lewis CE, et al. Fasting glucose variability in young adulthood and incident diabetes, cardiovascular disease and all-cause mortality. *Diabetologia.* 2019;62(8):1366-1374.
6. Echouffo-Tcheugui JB, Zhao S, Brock G, Matsouaka RA, Kline D, Joseph JJ. Visit-to-visit glycemic variability and risks of cardiovascular events and all-cause mortality: the ALLHAT study. *Diabetes Care.* 2019;42(3):486-493.
7. Williams ME, Garg R, Wang W, Lacson R, Maddux F, Lacson E Jr. High hemoglobin A1c levels and glycemic variability increase risk of severe hypoglycemia in diabetic hemodialysis patients. *Hemodial Int.* 2014;18(2):423-432.
8. Shi C, Liu S, Yu HF, Han B. Glycemic variability and all-cause mortality in patients with diabetes receiving hemodialysis: a prospective cohort study. *J Diabetes Complications.* 2020;34(4):107549.
9. Afghahi H, Nasic S, Peters B, Rydell H, Hadimeri H, Svensson J. Long-term glycemic variability and the risk of mortality in diabetic patients receiving peritoneal dialysis. *PLoS One.* 2022;17(1):e0262880.
10. Fouque D, Vennegoor M, ter Wee P, et al. EBPG guideline on nutrition. *Nephrol Dial Transplant.* 2007;22 Suppl 2:ii45-87.
11. Stefánsson BV, Brunelli SM, Cabrera C, et al. Intradialytic hypotension and risk of cardiovascular disease. *Clin J Am Soc Nephrol.* 2014;9(12):2124-2132.
12. Davenport A, Cox C, Thuraisingham R. Blood pressure control and symptomatic intradialytic hypotension in diabetic haemodialysis patients: a cross-sectional survey. *Nephron Clin Pract*. 2008;109(2):65-71.
13. Al Maimani Y, Elias F, Al Salmi I, Aboshakra A, Allan MA, Hannawi S. Interdialytic weight gain in hemodialysis patients: worse hospital admissions and intradialytic hypotension. *Open J Nephrol.* 2021;11(2):156-170.
14. Kimmel PL, Varela MP, Peterson RA, et al. Interdialytic weight gain and survival in hemodialysis patients:effects of duration of ESRD and diabetes mellitus. *Kidney Int.* 2000;57(3):1141-1151.
15. Dantas LGG, de Seixas Rocha M, Junior JAM, Paschoalin EL, Paschoalin SRKP, Sampaio Cruz CM. Non-adherence to Haemodialysis, Interdialytic weight gain and cardiovascular mortality:a cohort study. *BMC Nephrol.* 2019;20(1):402.
16. Goto J, Forsberg U, Jonsson P, et al. Interdialytic weight gain of less than 2.5% seems to limit cardiac damage during hemodialysis. *Int J Artif Organs.* 2021;44(8):539-550.
17. Ifudu O, Dulin AL, Friedman EA. Interdialytic weight gain correlates with glycosylated hemoglobin in diabetic hemodialysis patients. *Am J Kidney Dis.* 1994;23(5):686-691.
18. Creme D, McCafferty K. Glycaemic control impact on renal endpoints in diabetic patients on haemodialysis. *Int J Nephrol.* 2015;2015:523521.
19. Davenport A. Interdialytic weight gain in diabetic haemodialysis patients and diabetic control as assessed by glycated haemoglobin. *Nephron Clin Pract.* 2009;113(1):33-37.
20. Fang FS, Li ZB, Li CL, Tian H, Li J, Cheng XL. Influence of glycemic variability on the HbA1c level in elderly male patients with type 2 diabetes. *Intern Med.* 2012;51(22):3109-3113.
21. Yusof Khan AHK, Zakaria NF, Zainal Abidin MA, Kamaruddin NA. Prevalence of glycemic variability and factors associated with the glycemic arrays among end-stage kidney disease patients on chronic hemodialysis. *Medicine (Baltimore).* 2021;100(30):e26729.
22. Topal M, Ozkan Kurtgoz P. The use of predialysis glucose as long term glycemic marker in hemodialysis patients. *J Health Sci Med.* 2022;5(2):487-490.
23. Ipema KJ, Kuipers J, Westerhuis R, et al. Causes and Consequences of Interdialytic weight gain. *Kidney Blood Press Res.* 2016;41(5):710-720.
24. Jalalzadeh M, Mousavinasab S, Villavicencio C, Aameish M, Chaudhari S, Baumstein D. Consequences of interdialytic weight gain among hemodialysis patients. *Cureus.* 2021;13(5):e15013.
25. Shamshirgaran SM, Mamaghanian A, Aliasgarzadeh A, Aiminisani N, Iranparvar-Alamdari M, Ataie J. Age differences in diabetes-related complications and glycemic control. *BMC Endocr Disord.* 2017;17(1):25.
26. Waikar SS, Curhan GC, Brunelli SM. Mortality associated with low serum sodium concentration in maintenance hemodialysis. *Am J Med.* 2011;124(1):77-84.
27. Sahin OZ, Asci G, Kircelli F, et al. The impact of low serum sodium level on mortality depends on glycemic control. *Eur J Clin Invest.* 2012;;42(5):534-540.
28. Peixoto AJ, Gowda N, Parikh CR, Santos SF. Long-term stability of serum sodium in hemodialysis patients. *Blood Purif.* 2010;29(3):264-267.