Research Article

Glycemic control affects progression of kidney disease in patients with type 2 diabetes mellitus

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Abstract

Background: Improvement in glycemic control, particularly early in the treatment, is associated with reductions in the incidence of microvascular complications, including chronic kidney disease (CKD).

Objective: To study the effect of glycemic control on diabetic nephropathy (DN) in patients with type 2 diabetes.

Materials and Methods: We investigated progression of DN by measuring glycosylated hemoglobin (HbA1c), serum creatinine, and glomerular filtration rate (GFR) level in 70 (37 men and 33 women) patients with type 2 diabetes mellitus (DM) on antihypertensive treatment.

Result: The survey was done for 6 months during which 40 patients with DM (group 1) with serum creatinine <1.2 mg/dL were compared with 30 patients with DM (group 2) with serum creatinine ≥1.2 mg/dL who had mean HbA1c of 9.0%. In group 2, the mean level of serum creatinine (1.71 ± 0.46 mg/dL) was significantly higher and the mean GFR (54.57 ± 35.26 mL/min) was significantly lower than group 1 ($P < 0.05$).

Conclusion: Uncontrolled glycemic control leads to progression of DN with an earlier decline in GFR in patients with type 2 diabetes.

KEY WORDS: Glycemic control, GFR, serum creatinine, type 2 diabetes mellitus (DM)

Introduction

The prevalence of diabetes has reached epidemic proportions. The World Health Organization predicts that developing countries will bear the brunt of this epidemic in the 21st century. Although the global prevalence of diabetes is 6.4%, India has the world's largest population with diabetes with an estimated 50.8 million people, followed by China with 43.2 million. Diabetic nephropathy (DN) is a clinical syndrome characterized by persistent albuminuria, arterial blood pressure elevation, progressive decline in glomerular filtration rate (GFR), and a high risk of cardiovascular morbidity and mortality.[1] Approximately 40% of people with diabetes will develop nephropathy. DN is a leading cause of end-stage renal disease. However, the decline in GFR is highly variable, ranging from 2 to 20 mL/min/year.[2–5] Chronic kidney disease (CKD) can be quantitatively defined as a GFR <60 mL/min/1.73 m^2 and the rate of rise in serum creatinine, a well-accepted marker for the progression of DN, (creatinine value 1.4 to 3.0 mg/dL is the indicator for impaired renal function).[6,7]

The Diabetes Control and Complications Trial showed a significant relationship between reduction in glycosylated hemoglobin (HbA1c) levels and the risk of microvascular complications including CKD.[8] In patients with diabetes, poor glycemic control is a risk factor for the development of nephropathy. Similarly, the incidence of a decline in renal function over 5 years was greater among the older patients with hypertension.[9] DN is characterized histologically by the

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thickening of the glomerular basement membrane, increased fraction of mesangial volume, and podocyte abnormalities. Consistent with the findings in clinical studies that hyperglycemia per se plays a key role in the development of diabetic kidney disease; studies on both kidney cells and isolated glomeruli have confirmed that high glucose concentrations lead to extracellular matrix deposition. The purpose of this study was to examine the relationship between fluctuations in glycemic control (HbA1c) over time and changes in GFR and estimated stage of CKD.

Materials and Methods

An observational cross-sectional study was conducted in 2011 at GG Hospital, Jamnagar District, Gujarat, India comprising 70 patients with type 2 diabetes mellitus (DM) under antidiabetic and antihypertensive treatment, of which 37 were men and 33 were women in the age group of 40–70 years. Individuals who had already been treated for diabetes and hypertension were included in the study. The research protocol was approved by institutional ethical committee and informed consent was obtained from each subject before inclusion in the study. Personal history and medical history were collected in predesigned pro forma.

Fasting blood sample was collected for HbA1c, which was measured by liquid chromatography. For glycemic control, HbA1c target value of ≤7%was used, as recommended by the American Diabetes Association.[10] Blood samples were drawn for the measurement of serum concentrations of creatinine. Serum creatinine was estimated by modified Jaffe's kinetic reaction with initial rate colorimetry and single reagent density by using picric acid.[11–13]

GFR was calculated by Cockcroft–Gault equation: Estimated creatinine clearance (mL/min) = (140 - age) × weight (kg)/ 72 × serum creatinine (mg/dL). Values for women were estimated after multiplying 0.85 to the above formula.[14] Patients were grouped according to the level of serum creatinine as the following:

1. Group 1 (N = 40): patients with type 2 DM having serum creatinine <1.2 mg/dL
2. Group 2 (N = 30): patients with type 2 DM having serum creatinine ≥1.2 mg/dL

Result

Table 1 shows the comparison of general characteristics of group 1 and group 2. The mean age of group 1 was 57.41 years and group 2 was 60.08 years; the mean BMI of group 1 and group 2 was 24.68 kg/m^2 and 24.69 kg/m^2, respectively; and the mean duration of type 2 DM of group 1 and group 2 was 8.62 years and 9.69 years, respectively. All the above parameters in group 1 and group 2 were not significantly different.

Table 2 shows mean HbA1c in group 1 was 7.97% whereas in group 2 it was 9.00%, which was significantly higher ($P < 0.05$). Mean serum creatinine was significantly lower in group 1 (1.14 mg/dL) compared with group 2 (1.71 mg/dL) and the mean GFR in group 1 was 103.92 mL/min, which was significantly higher than 54.57 mL/min in group 2.

Discussion

Our study shows that the mean HbA1c was significantly higher in group 2 patients with diabetes with serum creatinine ≥1.2 mg/dL and GFR was significantly lower as well as suggestive of poor prognosis of DN. A retrospective cohort, follow-up study by Cummings et al.[8] in which HbA1c was evaluated in patients with diabetes shows mean GFR declined during follow-up in African–American population, which shows that stronger prediction change in GFR was proportion of HbA1c values >7%. A retrospective analytic study by Wijesuriya et al.,[15] conducted by reviewing the clinical records of the patients with type 2 diabetes who attended the National Diabetes Centre of Sri Lanka from January 2005 to December 2010 observed that nephropathy was significantly associated with poor glycemic control, high HbA1c, high fasting blood glucose, and high systolic blood pressure. Rossing et al.[16] in a follow-up study of patients with type 2 DM with nehropathy, evaluated renal functions where it was found that the rate of decline in mean GFR was 5.2 mL/min/year with mean HbA1c of 8.9% suggesting that elevated mean HbA1c was significantly associated with increased decline in GFR during follow-up.

This study tunes with all the abovementioned studies suggesting that in persistent hyperglycemia that is associated by HbA1c, poor glycemic control is the independent factor that affects renal function outcome in patients with type 2 DM.

This study has a number of limitations. Assumptions inherent in extrapolating HbA1c data from a single time point; the lack of measurement of HbA1c at similar time points among all participants; the lack of available data on other important risk factors such as microalbuminuria/proteinuria, diet, and medication adherence; and the observational nature of the study in routine primary care practice limit the interpretation of these results. Measurement of serum creatinine has a ±10% measurement error. Likewise, the Cockcroft–Gault equation may be less precise as an estimate of GFR in patients with relatively preserved renal function. However, given the profound discussions in the literature in recent years about the importance of tight glycemic control, we contend that additional research is needed to better understand potential associations between the magnitude, frequency, and the overall time course of fluctuations in HbA1c in routine primary care and the development of CKD and other microvascular complications of diabetes.

Table 1: General characteristics of patients in two groups (values in mean ± SD)

	Group 1	Group 2
No of patients	40	30
Age (years)	57.41 ± 12.5	60.08 ± 11.37
BMI (kg/m^2)	24.68 ± 2.57	24.69 ± 2.00
Duration of type 2 DM	8.62 ± 2.90	9.69 ± 3.11

BMI, body mass index; DM, diabetes mellitus; SD, standard deviation.

Table 2: Comparison of HbA1c, serum creatinine, and GFR in group 1 and group 2 (values in mean ± SD)

	HbA1c (%)	Serum creatinine (mg/dL)	GFR (mL/min)
Group 1 (*N* = 40)	7.97 ± 1.00	1.14 ± 0.50	103.92 ± 50.53
Group 2 (*N* = 30)	9.00 ± 0.98	1.71 ± 0.46	54.57 ± 35.26
	<0.05	<0.05	<0.05

GFR, glomerular filtration rate; HbA1c, glycosylated hemoglobin; SD, standard deviation.

Conclusion

In our study, it was found that the poor glycemic control with lower GFR in group 2 patients as compare to group 1. Glycemic control (HbA1c) is one of the risk factors leading to the progression of DN with earlier decline in GFR. This study may allow one to gain deeper insight into the various differences that may exist between the treatments suggested by previous studies and, hence, further guide the management of type 2 DN.

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