Original Article

A Comparative Study of Glomerular Filtration Rate in Normal Healthy Controls and Type 2 Diabetes Mellitus Patients in South India

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Abstract

Background and Aim: Diabetes mellitus (DM) is one of the most common metabolic diseases, which is characterized by increased blood glucose levels. DM is the leading cause for chronic kidney disease (CKD) and end-stage renal disease. To estimate the glomerular filtration rate (GFR) of normal healthy controls and type II DM (T2DM) patients using Cockcroft–Gault (CG) formula and to compare the GFR values of normal subjects and T2DM patients (with respect to glycated hemoglobin [HbA1c]). **Methods:** The total sample size of the study was 60, among which 30 were healthy individuals (controls) and 30 were T2DM patients (subjects with both controlled and uncontrolled HbA1c). A detailed history was taken from the subjects and controls followed by a thorough clinical examination. Blood and urine samples were collected from all the subjects for the estimation of serum creatinine, HbA1c, and urine routine analysis. The GFR is calculated for all the study participants using CG formula, and the results were expressed in the form of graphs and charts. **Results:** The overall GFR value was well within the normal limits in controls than the subjects. In the present study, the values of GFR were 106.87 + 8.29 and 100.03 + 12.42 in normal healthy controls (Group A) and diabetic subjects (Group B), respectively. In this study, value of HbA1c in healthy control males and females was 6.74 ± 0.39 and6.76 ± 1.04, respectively. Similarly, the value of HbA1c in diabetic subject males and females was 7.32 ± 0.69 and 7.06 ± 1.45, respectively. There was a significant positive correlation between GFR with the degree glycemic control in T2DM of the study population. **Conclusion:** The present study indicates that the degree of glycemic control in T2DM reflects the ongoing kidney damage by change in GFR of the kidney. The GFR of diabetic subjects is comparatively lower when compared with GFR of normal healthy controls. Our study also shows that there is a higher risk of developing CKD in diabetics with poor glycemic index than diabetics with good glycemic index.

Keywords: Chronic kidney disease, glomerular filtration rate, type 2 diabetes mellitus

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Introduction

Diabetes mellitus (DM) is one of the most common metabolic diseases characterized by increased blood glucose level either due to insufficiency/absence of insulin or due to decrease in the insulin sensitivity at cellular receptor level. Depending on the etiology, factors contributing to hyperglycemia may include reduced insulin secretion, insulin resistance, decreased peripheral glucose utilization, and increased glucose production.[1]

The global prevalence of type 2 DM (T2DM) is increasing day by day and has reached epidemic proportions in many countries. The number of adults suffering from T2DM is estimated as 366 million in 2011, and it is expected that by 2030, the prevalence may increase to 552 million globally.[2]

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India has one of the largest numbers of diabetic subjects compared to total world diabetic population. At present, China tops the world among diabetes affected countries having a total of around 90 million T2DM patients and India follows China with a prevalence of 61.3 million. The number of diabetic subjects in India was 40.9 million in 2007, and now, it is expected to rise to 101.2 million by 2030.[3]

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DM is classified on the basis of pathogenic processes that lead to hyperglycemia, into T1DM and T2DM. T1DM is characterized by insulin deficiency either due to autoimmune related β-cell damage or by unknown mechanisms. T2DM is a heterogeneous group of disorders characterized by variable degree of insulin resistance, impaired insulin secretion, and increased glucose production.[1]

Recent studies have shown that patients with history of DM are more prone to other noncommunicable diseases such as hypertension, cardiovascular diseases, chronic renal disease, micro- and macro-vascular disease, and diabetes is the leading cause of chronic renal disease (chronic kidney disease [CKD]) and end-stage renal disease in most of the countries.

Around 25%–40% of the diabetic patients suffer from diabetic nephropathy during the disease.[4] Hence, measurement of renal function test becomes very vital and crucial in patients with DM.[3]

Estimation of glomerular filtration rate (GFR) is the best measure of overall kidney function in health and disease; this is due to the fact that filtration capacity of the kidney correlates with the various functions of nephron.[5] Therefore, GFR is usually accepted as the best overall estimate of kidney function in evaluating the onset and progression of kidney disease.[6]

Serum creatinine concentration is widely used as an indirect marker of GFR.[4] However, serum creatinine alone is not a strong marker in estimating GFR as it is influenced by muscle mass and diet; hence, the National Kidney Foundation For The Diagnosis and Stratification of Chronic Kidney Diseases recommends the use of prediction equations to estimate the GFR from serum creatinine and other variables such as age, sex, race, and body weight.[4]

There are many tests conducted in calculating GFR in diabetic and nondiabetic individuals; however, there are minimal studies done in comparing the GFR values in diabetic and nondiabetic individuals. Hence, the study aims to compare the GFR values in normal subjects and diabetic patients. The study also aims to correlate between glycated hemoglobin (HbA1c) values and the GFR values in both controls and subjects.

Therefore, in the present study, we have planned to estimate the GFR of normal subjects and T2DM patients using Cockcroft–Gault (CG) formula and to compare the GFR values of normal subjects with T2DM patients (with respect to HbA1c <8% and >8%).

Materials and Methods

The present study was carried out in Rajarajeswari Medical College and Hospital (RRMCH), Kengeri, Bangalore, Karnataka. It was a type of case–control study and ethical clearance was obtained from the Institutional Ethical Committee of RRMCH, Kumbalgodu, Kengeri, Bangalore. The proposed study was conducted over a period of 1 year from January 2013 to January 2014.

Cases were selected as diagnosed T2DM patients from the Department of Medicine, RRMCH, who were willing to participate in the study. Age- and sex-matched controls without T2DM were selected randomly from the general population.

Sample size

The study was discussed with an institutional statistician from the Department of Community Medicine, and the sample size is finalized under the guidance of the statistician. The sample size of the present study is 60, among which 30 subjects were healthy controls and other 30 were T2DM patients.

- Group A: Normal healthy controls ($n = 30$)
- Group B: T2DM patients ($n = 30$)
  - Group B1: Diabetics with better glycemic control – HbA1c <8, $n = 27$
  - Group B2: Diabetics with poor glycemic control – HbA1c >8, $n = 3$.

Inclusion criteria

1. Diagnosed T2DM patients belonging to the age group of 30 years and above
2. Those who are willing to give written consent for the study.

Exclusion criteria

1. Patients with any history of micro- or macro-vascular complications of DM
2. Patients suffering from hypertension, hypothyroidism, or any other chronic illness
3. Patients having preexisting renal disorders or on dialysis
4. T1DM patients
5. Pregnant women
6. Patients who are not willing to give the written informed consent for the study.

Method of collection of data

Subjects were enrolled in the study based on the inclusion and exclusion criteria. The selected subjects were briefed about the nature of the study, and written informed consent was obtained before the subject was enrolled in this study. Demographic data such as gender and age were collected along with relevant history and recorded on predesigned form. A thorough clinical examination was conducted and findings were recorded. Anthropometry including height and weight was measured. The patient was then instructed to come the next day under 8 h fasting state for the blood investigations (serum creatinine, HbA1c, urine routine).

Height of all the subjects was measured using height meter. Weight was measured in kilogram using standardized weighing machine, and the body mass index (BMI) was calculated from the available data using the following formula:

$$BMI = \text{weight (kg)}/\text{height (m)}^2$$

The patient's blood was collected the next day of clinical examination for laboratory investigations. The laboratory investigations included serum creatinine, HbA1c, and urine routine. Serum creatinine is measured by Jaffe kinetic

method (automated technique) in the laboratory. Under aseptic precautions, morning (mid-stream) urine sample is collected up to the three-fourth of the container and urine analysis is done by chemical strip reagent method and cell counts done under compound microscope. Venous blood sample collected in fluorides ethylenediaminetetraacetic acid, vacuum evacuated tubes under aseptic precautions, and ion exchange high-performance liquid chromatography technique were used to measure HbA1c.

Estimation of glomerular filtration rate

GFR of the study population is calculated by CG formula, a multiequational formula, which depends on age, sex, body weight, and serum creatinine of the subject to be calculated, i.e.,

$$\text{GFR (ml/min)} = \frac{(140 - \text{age in years}) \times \text{body weight in kg}}{\text{Plasma creatinine (mg/dl)} \times 72} \times 0.85 \text{ (if female)}$$

The GFR values thus obtained from CG formula are tabulated in Table 1 and analyzed as a predictor of chronic kidney damage based on the classification of CKD given by the National Kidney Foundation.

Statistical analysis

The data collected were analyzed and expressed as mean ± standard deviation. One-way analysis of variance was used to compare the levels GFR, serum creatinine, and HbA1c levels in both groups. Statistical software namely SPSS 20 (SPSS Software Inc., Chicago, IL, USA) was used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables. Level of significance: $P < 0.05$

Results

Thirty diabetic subjects were divided into two groups based on HbA1c levels, based on better glycemic control group (<8) and poor glycemic control group (8 or > 8). These two groups were compared with the normal healthy controls and the results are tabulated and analyzed as shown in Tables 2 and 3; the composition of each group is shown below.

- Group A: Healthy controls, $n = 30$
- Group B: DM subjects, $n = 30$.

Subjects from Group B were further subdivided into two more groups based on their HbA1c levels [Figures 1 and 2].

- Group B1: Diabetics with better glycemic control – HbA1c <8, $n = 27$
- Group B2: Diabetics with poor glycemic control – HbA1c >8, $n = 3$.

The results are expressed in the form of charts and graphs and are summarized in Tables 2 and 3.

Discussion

It is observed from the study that the GFR value among the healthy controls is 106.87 ± 8.29 which is well within the normal limit, but the GFR value of diabetic subjects is 100.03 ± 12.42 which is also normal but lower than the GFR values of controls, which is statistically significant.

For the better interpretation of the result, 30 diabetic subjects were again classified into two groups based on the glycemic index, i.e., diabetics with HbA1c of <8 was considered as poor glycemic control and diabetics with HbA1c of >8 was considered

Table 1: Levels of GFR in different stages of kidney function

Stage	Description	GFR (mL/min)
At increased risk	Risk factors for kidney disease DM, HTN, family history, old age	>90
1	Kidney damage (proteinuria) and normal or increase in GFR	>90
2	Kidney damage and mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15

DM: Diabetes mellitus, HTN: Hypertension, GFR: Glomerular filtration rate

Table 2: Comparison of glomerular filtration rate between the groups

Variable	Group A	Group B	Unpaired *t*	*P*
GFR (mL/min)	106.87±8.29*	100.03±12.42	2.506	0.015

Values are mean±SD. *GFR significantly differs over Group A versus Group B at $P<0.05$. SD: Standard deviation, GFR: Glomerular filtration rate

Table 3: Comparison of glycated hemoglobin between the groups

Variable	Group A	Group B	Unpaired *t*	*P*
HbA1C	6.75±0.41	7.19±0.57*	3.450	001

Values are mean±SD. *HbA1C significantly differs over Group B versus Group A at $P<0.05$. HbA1C: Glycated hemoglobin, SD: Standard deviation

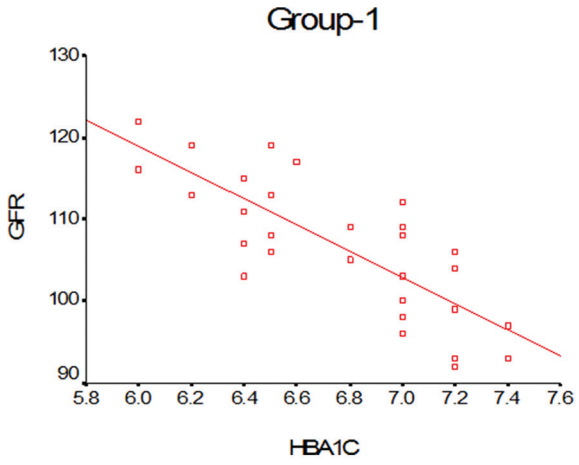

Figure 1: Scatter graph for correlation between glomerular filtration rate and glycated hemoglobin in Group A

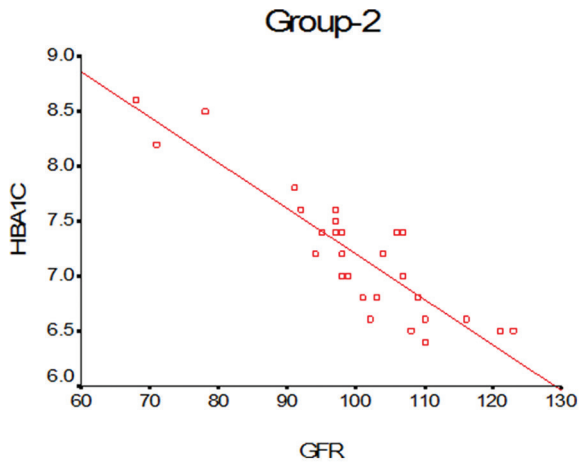

Figure 2: Scatter graph for correlation between glomerular filtration rate and glycated hemoglobin in Group B

as good glycemic control. In this study, among 30 diabetic subjects, 27 were considered to be with good glycemic control and 3 diabetics were considered to be poor glycemic control with HbA1c >8. The mean values of HbA1c among controls were 6.75 ± 0.41 and 7.19 ± 0.57 in diabetics, respectively.

When the GFR of diabetics were compared with their glycemic index, it was noted that the GFR is positively correlated with the degree of glycemic control in T2DM patients.[7-10]

Here, HbA1c acting as independent variable factor and the GFR as dependent variable factor. Though the study was age- and sex-matched case–control study, there was no significant correlation between the sex and GFR of the subjects/controls.

The present study was conducted to correlate the GFR values of the kidney among controls and diabetics and to assess whether the GFR is related to the degree of glycemic control in type 2 diabetic south Indian patients in Karnataka.

On the basis of our results, it can be concluded that that GFR is positively correlated with the degree of glycemic control in T2DM. The GFR values were well within the normal range in controls whereas the GFR value was relatively lower in T2DM patients when compared to that of the normal controls. It was also observed that increase in HbA1c value in diabetics tend to decrease the GFR value of the kidney with or without proteinuria.[11-14] The GFR value was normal in diabetics with good control of HbA1c, relatively lower in diabetics with progressively increasing HbA1c and lowest in diabetics with poor glycemic control. This indicates that the degree of glycemic control in T2DM reflects onto the GFR values of the kidney *in vivo*.[15-20]

This study also showed that there is no statistically significant effect of sex on GFR values of the cases and controls.

Conclusion

The GFR value is positively correlated with the degree of glycemic control in T2DM. It is the HbA1c which acts as an independent variable and the GFR as a dependent variable in the study; hence, it is of utmost importance to achieve good glycemic control in T2DM, to improve longevity and the quality of life in terms of kidney health and disease.

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Conflicts of interest

There are no conflicts of interest.

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