

Evaluation of glomerular function in patients with type 2 diabetes mellitus

Asmabi M^{1,*}, Netravathi Basappa Sajjan², Tousif Devale³, Shivaleela M Birasar⁴, Shireen Quadri⁵

^{1,2}Assistant Professor, Al Ameen Medical College, Vijaypur, ³PG Student, HCG Hospital, Bangalore, ⁴Assistant Professor, BLDE Medical College, Vijaypur, ⁵Assistant Professor, Shivamoga Medical College, Shivamoga

***Corresponding Author:**

Email: asma.m444@gmail.com

Abstract

Background: The leading cause of chronic renal disease and end stage renal disease is diabetic nephropathy, so early recognition is very important. The important biochemical test for diagnosis of renal function is estimation of glomerular filtration rate (GFR). The accurate methods of GFR estimation are Inulin clearance and 24h urine collection, which are expensive and time consuming and require experts to perform. Hence some formulas have been developed for the GFR measurement.

Objective: To find out the prevalence of renal dysfunction based on the levels of serum creatinine and estimated GFR, calculated using Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations in type 2 diabetic patients.

Materials and Methods: A case control study was carried out on 50 type 2 diabetic patients and 50 healthy controls. Renal function was analyzed through serum creatinine and GFR estimated using the CG and MDRD equations.

Results: Among the 50 diabetic patients, 34% show high level of serum creatinine i.e. > 1.4 mg/dl, while the low eGFR that is < 90ml/min is seen in 58% of diabetic patients by MDRD equation and 64% of patients by CG equation. The mean serum Creatinine level is significantly high p value (<0.001) in diabetic patients when compared with controls. The eGFR is significantly low p value (< 0.001) in diabetic patients when compared with controls.

Conclusion: The prevalence of renal dysfunction based on serum creatinine level is low when compared with eGFR by MDRD and CG equation, indicating the significance of these equations in estimating GFR. Hence for the better assessment of renal function these equations can be used as compliment to the levels of serum creatinine alone.

Keywords: Diabetes mellitus, Diabetic nephropathy, Glomerular filtration rate, Modification of Diet in Renal Disease, Cockcroft-Gault.

Introduction

One of leading cause for increasing morbidity and mortality in the world and as well as in Indian subcontinent is Diabetes mellitus and its related complications.⁽¹⁾ It is well known fact that macrovascular and microvascular complications causes pathophysiologic changes in multiple organ systems.⁽²⁾ Diabetic nephropathy is the major cause of end-stage renal disease (ESRD) worldwide, and it is estimated that 20% of type 2 diabetic patients reach ESRD during their lifetime.⁽³⁾

Prolonged hyperglycemia leads to production of advanced glycosylated end product (AGE), which in turn leads to increase in the activity of protein kinase and TGF- β . This is responsible for glomerular dysfunction causing increased glomerular permeability.^(4,5,6) The stages of development of DN are glomerular hyperfiltration, noralbuminuric phase, proteinuria-macroalbuminuria phase and chronic kidney disease. Early recognition of diabetic nephropathy is important because in the first three phase kidney damage could be prevented and improve long term outcomes and retard progression to ESRD.⁽⁷⁾

Early identification and appropriate management of chronic kidney diseases are important measure of its slow progression. In clinical practice, measurement of plasma creatinine has been the method most often used to assess renal function. However, it has been demonstrated that "apparently normal" serum creatinine

levels may be accompanied by loss of renal function, making this a relatively late parameter for lesion detection.⁽⁸⁾ Nevertheless, serum creatinine has many limitations because it is affected by factors other than renal function, such as age, gender, race, muscle weight, diet and certain medications.⁽⁹⁾

GFR is the best determinant of kidney function.^(10,11) At present, National Kidney foundation has advised GFR as a useful tool in defining, screening, staging and evaluation of chronic kidney disease progression.⁽¹²⁾ The most common method for GFR measurement is creatinine clearance in 24- hour urine collection.⁽¹³⁾ Urine collection for 24 hours is not often favorable for patients and this step can be a major source of errors in GFR estimation.⁽¹⁴⁾ Periodic monitoring of GFR in diabetic patients regularly is recommended by National Kidney Foundation and the American Diabetes Association.^(15,16) The MDRD and CG equation, which are creatinine-based formulas are recommended.⁽¹⁷⁾ We aimed to use CG and MDRD equations for GFR estimation for better assessment of renal function when compared to serum creatinine alone in diabetic patients and controls.

Materials and Methods

Source of Data: This study was carried out in Al Ameen Medical College and Hospital, Vijaypur.

Inclusion criteria: This study includes 100 subjects which are divided into 2 groups.

- a. Cases:** 50 type 2 diabetic patients who were confirmed diabetes by measuring RSG > 200 mg detected on more than 2 occasion based on the American Diabetes Association (ADA) 2010 criteria for diagnosis of DM.⁽¹⁸⁾
- b. Controls:** 50 age and sex matched healthy volunteers without a history of diabetes and with normal RSG were considered to be control subjects.

Exclusion criteria: We excluded patients with kidney diseases, patients with history of DN and very ill patients.

Data collection: After taking the informed consent, the study subjects both including cases and controls were subjected to medical examination and blood investigations. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were investigated by a self-administered questionnaire.

Biochemical investigation: A random blood sample of about 3 ml was drawn from all the study subjects. Serum was separated by centrifugation and used for the estimation of RSG, serum creatinine and blood urea.

Methods of estimation:

- a. RSG was measured by Glucose oxidase (GOD-POD) method.⁽¹⁹⁾
- b. Serum creatinine was analyzed by kit based on Jaffe's method.
- c. Blood urea by modified berthelot's method.⁽²⁰⁾

The entire tests were carried out on ERBA Diagnostics Mannheim EM-200 autoanalyzer.

Estimated GFR was calculated using CG and MDRD formulas.

As per CG formula creatinine clearance = $\{140 - \text{age} \times \text{body weight (kg)}\} / \{72 \times \text{serum creatinine (mg/dl)}\}$. The final value should be multiplied by 0.85 for females.⁽²¹⁾

MDRD GFR (ml/min/1.73 m²) equation= $186.3 \times (\text{creatinine (mg/dl)})^{-1.154} \times \text{age(years)}^{-0.203} \times 0.742$ (if female)⁽²²⁾

Renal function was analyzed from the result of serum creatinine, obtained from biochemical test, and GFR estimated using CG and MDRD equations, calculated using the formulas provided in the SBN and NKF websites. Values above 1.4 mg/dl for serum creatinine and below 60 mL/min/1.73m² for GFR estimated by CG and MDRD,^(19,20) were regarded as impaired renal function, since glomerular filtration rate below 90 ml/ min/1.73m² represents a decrease of approximately 50% in normal renal function.⁽²³⁾

Statistical Analysis: Descriptive data are presented as mean ± SD. Students 't' test was used for comparing different biochemical parameters between cases and controls. Relationship between the parameters was assessed by Pearson's correlation coefficient. The statistical software SPSS 17.0 version was used for

analysis of the data. For all the tests, the probability value (p-value) of less than 0.05 was considered statistically significant.

Results

Study design: A case control study was carried out on 50 diabetic patients and 50 healthy controls to find out the prevalence of renal dysfunction based on levels of serum creatinine and eGFR using CG and MDRD equation.

Table 1: Comparison of study Parameters between controls and Cases

Parameters	Controls (Mean±S.D.)	Cases (Mean±S.D.)	P value of unpaired student's t test
Mean Age (years)	50.74 ± 7.45	52.72 ± 10.73	0.28
Weight (kg)	61.3± 3.54	64.56±5.51	<0.001
Randon serum glucose (mg/dL)	97.44 ± 15.40	239.41 ± 116.74	< 0.001
Blood Urea (mg/dL)	25.37 ± 8.64	56.65 ± 43.46	< 0.001
Serum creatinine (mg/dL)	0.75 ± 0.16	1.39 ± 0.829	< 0.001

Table 1 shows that the mean age of the patients and controls did not differ significantly (p > 0.05). The mean level of weight, RSG, urea and creatinine of the cases are increased significantly (p < 0.001) compared to the controls.

Table 2: Comparison between the mean levels of eGFR by MDRD and CG equation

	GFR (MDRD)	GFR (CG)	P value
Controls	103.34± 14.6	94.97±12.36	0.002
Cases	70.9± 36.4	68.19±	0.678
P value	< 0.0001	< 0.0001	

Table 2 the mean level of the GFR estimated by MDRD and CG equation is reduced significantly (p < 0.001) in cases compared with controls. The mean level of GFR estimated by MDRD and CG equation did not differ significantly in cases (p value >0.5).

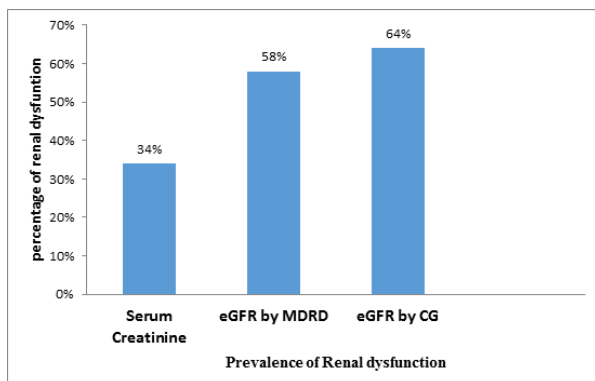


Fig. 1: Prevalence of renal dysfunction

Fig. 1 shows the prevalence of renal dysfunction based on values of serum creatinine (34%) is very low as compared to the levels of eGFR by MDRD equation (58%) and eGFR by CG equation (64%).

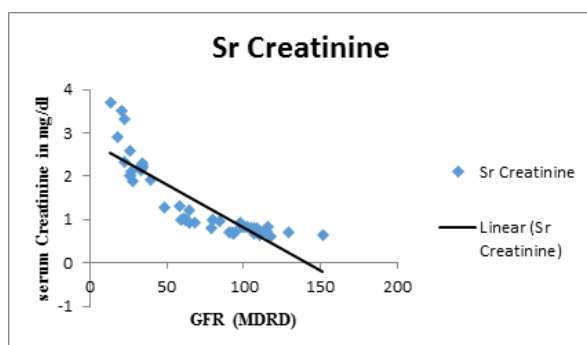


Fig. 2: Correlation between serum creatinine and eGFR (MDRD)

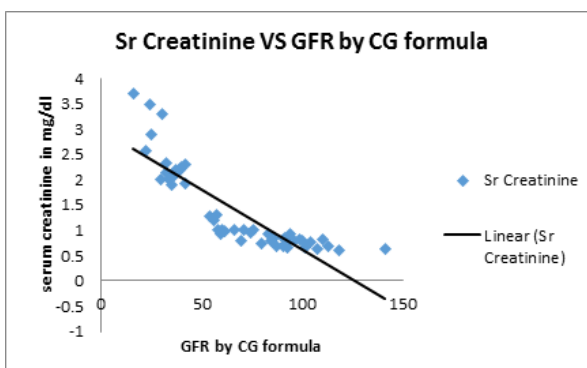


Fig. 3: Correlation between serum creatinine and eGFR (CG)

Fig. 2 and 3 shows that the serum creatinine levels have significant negative correlation with GFR estimated by MDRD ($r = -0.86813$) and CG ($r = -0.8655$) equation.

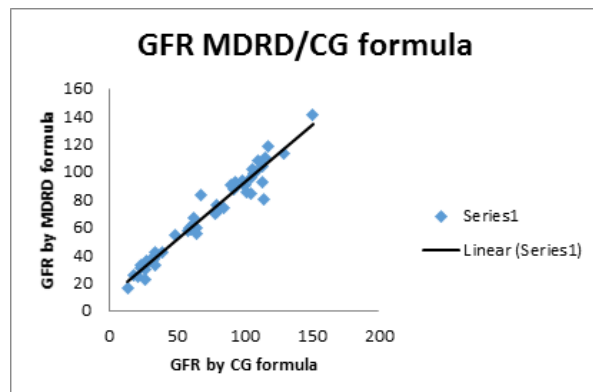


Fig. 4: Correlation between GFR estimated by MDRD and CG equation

Fig. 4 the GFR estimated by MDRD and CG equation in case of diabetic patients have the significant positive ($r = 0.9785$) correlation.

Discussion

One of the major complications of diabetes mellitus is nephropathy. Hence periodic assessment of the kidney function is an important aspect in early detection and management of diabetic nephropathy.⁽¹²⁾

This study was conducted to find out the prevalence of renal dysfunction based on the serum creatinine level and eGFR. Age is the one of major factor affecting GFR,⁽²⁴⁾ therefore age matched cases and controls are selected to remove the bias.

In our study among the 50 diabetic patients 34% have increased serum creatinine level $> 1.4\text{mg/dl}$, while low eGFR i.e. $< 90\text{ml/min}$ is seen in 58% of patients by MDRD equation and in 64% of the patients by CG equation. The mean level of random serum glucose and serum creatinine are significantly higher ($p < 0.001$) when compared with controls. The mean eGFR level is significantly low ($p < 0.001$) in diabetic patients as compared to the controls. Several studies have been carried out to find out accuracy CG and MDRD equations by comparing it with other standard methods of estimation of GFR. Our results are supported by a similar study conducted by Fontela PC et al.⁽⁸⁾

Dehghani H et al. found that GFR estimated by CG and MDRD correlate well with creatinine clearance in 24-hour urine collection, while MDRD is more accurate in diabetes patients with stage 3 or 4 CKD.,⁽¹²⁾ Cat H et al conducted a study on patients with metabolic syndrome. They found that MDRD equation is accurate in estimating GFR and can be used in clinical practice.⁽²⁵⁾ In patients with myocardial infarction MDRD formula was significantly more accurate in predicting the severity of CAD and two year CV risk in patients admitted to the ICU when compared with CG formula.⁽²⁶⁾

However Fontsero N et al, found that GFR levels estimated by MDRD equation are inaccurate in patients with hyperfiltration and in subjects with normal renal

function, MDRD equation can be used for monitoring of diabetic nephropathy patients.⁽⁹⁾ Kumaresan R and Giri reported that the CG formula is useful to estimate the GFR in normal or mild renal disease patients only. The extent of disease in the patients with moderate and severe kidney disease is ideally estimated by MDRD equation. But both formulae are not reliable to estimate the GFR especially with end stage kidney disease.⁽¹⁴⁾

Conclusion

The prevalence of renal dysfunction based on serum creatinine level is low (34%), while with MDRD equation it is 58%, and with CG equation it is 64%, indicating the significance of these equation in estimating GFR. The equations can be used in compliment with the serum creatinine level for the better assessment of renal function.

Our study recommend that GFR estimated by CG and MDRD is better indicator of renal function than serum creatinine alone, though it may not be accurate when compared with GFR of 24h urinary creatinine clearance and Labeled EDTA which are laborious, time consuming and expensive. Limitations of our study are small sample size, did not compare the levels of eGFR with any standard method of estimation of GFR.

References

- Pasupathi P, Bakthavathsalam G, Saravanan G and Sundaramoorthi R. Screening for thyroid dysfunction in the diabetic / non-diabetic population. *Thyroid Science* 2008;3(8):CLSI-6.
- American Diabetes Association, Diagnosis and classification of diabetes mellitus. *Diab Care* 2005;28:37-42.
- Unnikrishnan R, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, et al. Prevalence and risk factors of diabetic Nephropathy in an urban south Indian Population. *Diabetes Care*. 2007;30:2019–2024.
- Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care* 2005;28:164-76.
- Makita Z, Radoff S, Rayfield EJ, Yang Z, Skolnik E, Delaney V, et al. Advanced glycosylation end products in patients with diabetic nephropathy. *N Engl J Med* 1991;325:836-42.
- Shahbazian H, Rezaei I. Diabetic kidney disease; review of the current knowledge. *J Renal Inj Prev* 2013;2(2):73-80.
- Risovic I and Popovic-Pejicic S. Renal function in diabetes mellitus. *Curr Top Neurol Psychiatr Relat Discip*. 2011;19(2):24-28.
- Fontela PC, Winkelmann ER, Ott JN and Uggeri DP. Estimated glomerular filtration rate in patients with type 2 diabetes mellitus. *Rev Assoc Med Bras* 2014;60(6):531-537.
- Fontseré NS, Salinas I, Bonal J, Baye´s B, Riba J, Torres F, et al. Are prediction equations for glomerular filtration rate useful for the long-term monitoring of type 2 diabetic patients?. *Nephrol Dial Transplant*.2006;21:2152–2158.
- Prigent A, editor. Monitoring renal function and limitations of renal function tests. *Seminars in nuclear medicine*; 2008: Elsevier.
- Diamandopoulos A, Goudas P, Arvanitis A. Comparison of estimated creatinine clearance among five formulae (Cockcroft–Gault, Jelliffe, Sanaka, simplified 4-variable MDRD and DAF) and the 24hours-urine-collection creatinine clearance. *Hippokratia*. 2010;14(2):98.
- Dehghani H, Heidari F, Mozaffari-Khosravi H, Nouri-Majelan N, Rahmani M, Dehghani A. Evaluation of Glomerular Filtration Rate Estimating Formulas in Diabetic Patients with Chronic Kidney Disease. *Iranian Journal Of Diabetes And Obesity*.2013;5(2):47-53.
- Johnson, C.A., Levey, A.S., Coresh, J. (2004). Clinical practice guidelines for chronic kidney disease in adults: part-II. Glomerular filtration rate, Proteinuria, and other markers..70:1091-97.
- Kumaresan R and Giri. A Comparison of Modification of Diet in Renal Disease and Cockcroft-Gault Equations for estimating Glomerular Filtration Rate in Chronic Kidney Disease Patients. *Asian J Exp Biol Sci*.2011;2(3):537-540.
- KDOQI. Clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. *Am J Kidney Dis* 2007;49(2): S12–S154.
- American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 2008;31:S12–S54.
- Leung T, Luk AO, SO W, LO MK and Chan JC. Development and validation of equations estimating glomerular filtration rates in Chinese patients with type 2 diabetes. *Kidney International*. 2010;77:729–735.
- Mahajan RD, and Mishra B. Using Glycated Hemoglobin HbA1c for diagnosis of diabetes mellitus: An Indian perspective. *Int J Biol Med Res*. 2011;2(2):508-512.
- Kricka L. Principles of immunochemical techniques. In: Burtis CA, Ashwood ER and Bruns DA, eds. *Teitz Textbook of clinical chemistry and Molecular diagnostics*, 4th edn. New Delhi: Elsevier; 2006:219-244.
- Lamb E, Path F, Price C. Creatinine, Urea and Uric acid. In: Burtis C, Ashwood E, Bruns D, editors. *Teitz fundamentals of clinical chemistry*. 6th ed. USA: Elsevier, 2008: p.363-6.
- Cockcroft D, Gault M. Prediction of creatinine clearance from serum creatinine. *Nephron*, 1976;16:31-41.
- Poggio E, Wang X, Greene T, Van Lente F, Hall P. Performance of the Modification of Diet in Renal Disease and Cockcroft-Gault Equations in the Estimation of GFR in Health and in Chronic Kidney Disease. *J Am Soc Nephrol*, 2005;16:459-66.
- Sonagra AD, Makandar A, Chandrakar S, Sonagra J and Dattatreya K. Evaluation of glomerular function in women with preeclampsia. *European Journal of Pharmaceutical and Medical Research*. 2015;2(2):288-295.
- Çat H, Öztürk AO, Karadağ B, Altuntaş Y. Comparison of Modification of Diet in the Renal Disease (MDRD) and Cockcroft-Gault (CG) Formulas for Estimating Glomerular Filtration Rate (GFR) in Patients Metabolic Syndrome. *Turk Neph Dial Transpl* 2015;24(1):55-60
- Barra S, Providência R, Silva J, Lourenc P, Gomes O, Seca L et al. Glomerular filtration rate: Which formula should be used in patients with myocardial infarction? *Rev Port Cardiol*. 2012;31(7-8):493-502.

