ORIGINAL ARTICLE

GFR and Cardiovascular Events in Type 2 Diabetes Mellitus

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ABSTRACT

Individual with type 2 diabetes is a high risk group for both adverse cardiac as well as renal events. GFR is an independent predictor of cardiovascular morbidity and mortality. Reduced GFR is associated with a high prevalence of cardiovascular risk factors and higher prevalence of cardiovascular disease. The study was designed to explore the association between reduced GFR and cardiovascular events in diabetic subjects. It was a case-control study. One hundred and twenty nine (129) male subjects with cardiac event or events were selected. Diabetes of them 50 was type 2 and 79 were non diabetic. Modification of diet in renal disease study equation (eGFR) to estimate GFR was used and examined the prevalence of cardiovascular events in both groups. Unpaired t-test and chi square test were done to find out the level of significance. eGFR was compared between the study groups and significant differences were observed (p value <0.01). Reduced GFR (by estimating MDRD equation) is associated with cardiac event or events and should perform as routine assessment of diabetic patients.

Key word: MDRD (Modification of Diet in Renal Disease), eGFR (Estimated Glomerular Filtration Rate), Type 2 Diabetes

Introduction

Diabetes mellitus (DM) is associated with more than three fold increase of cardiovascular disease (CVD)[1]. Reduced glomerular filtration rate (GFR) is associated with an increased risk for the development of cardiovascular events and mortality risk in diabetic patients[2]. In classic diabetic nephropathy, after the phase of microalbuminuria, there is a continued increase in urinary albumin excretion with a declining glomerular filtration rate (GFR)[1].

GFR may be defined as the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule per unit time[3]. The useful measure for approximating the GFR is creatinine clearance rate (Ccr). Ccr is calculated from creatinine concentration in the collected urine sample (Ucr), urine flow rate (v), plasma concentration of creatinine (Pcr)[4]. Besides, the most recently advocated formula for calculating the GFR is one that was developed by the Modification of Diet in Renal Disease (MDRD) study group which estimates GFR using four variables: serum creatinine, age, race and gender[5].

Kidney disease can classified according to estimated GFR (eGFR) as[6].

Stage	Description	GFR(ml/min/ 1.73sq.m)
0	Normal	≥ 90
1	Kidney damage with normal or raised GFR	≥ 90
2	Kidney damage with mild reduce GFR	60-89
3	Moderate reduced GFR	30-59
4	Severe reduced GFR	15-29
5	Kidney failure	< 15 or dialysis

A reduced estimated GFR is common in diabetic patients and was associated with a two fold increase in cardiac events[1]. eGFR <60 ml/min/1.73 sq.m mainly influence the risk of vascular events[2]. The cardiac events defined as major and minor cardiac events. Major cardiac events are: non fatal MI (documented by appropriate cardiac enzyme level changes and ECG evidence of acute MI) and coronary revascularization (either coronary artery bypass graft surgery or percutaneous coronary intervention). Minor events include unstable angina (documented by resting ischemia with evidence of acute MI)[7].

Several pathophysiologic mechanisms have been proposed to explain the association between reduced eGFR and increase cardiovascular risk. First a decrease eGFR is associated with increase oxidative stress[8,9], increase C-reactive protein and homocysteine[8,9], uric acid[8], abnormal level of lipoprotein (a)[8,9,10], decreased insulin sensitivity and hyperinsulinaemia[11] and enhanced coagulability[8,9,10]. All these factors may cause endothelial dysfunction and may contribute to the development of atherosclerosis[12].

Coronary artery disease (CAD) is the most common form of heart disease and the single most important cause of premature death in all regions of the world. As the diabetic patients with reduced GFR are more susceptible to develop cardiac events therefore in clinical practice, during assessment of renal function in patients with type 2 DM, eGFR should be routinely estimated.

Method

It was a case control study carried out in the department of Biochemistry, Anwer Khan Modern Medical College (AKMMC). One hundred and twenty nine (129) male subjects with cardiac event or events were selected purposively from BIRDEM and NICVD. Of them 50 was type 2 DM and 79 were non diabetic. We used the simplified Modification of Diet in Renal Disease Study equation to estimate GFR (eGFR= 186 x s.creat $^{-1.154}$ x Age$^{-0.203}$ x [1.210 if black] x 0.742 if female) and examined the prevalence of cardiovascular events (in the form of non fatal MI, unstable angina and coronary revascularization) in both diabetic and non diabetic subjects. Serum creatinine was measured by standard method. Relevant statistical analysis was done in SPSS 12.0 version (p value <0.05 was taken as a lowest level of significance).

Results

Mean age of the diabetic and non diabetic study subjects was 58.14±7.11 years. and 55.28±12.57 years. respectively which did not differ statistically (p value >0.05).

Table 1 shows comparison of serum creatinine between the study subjects. Un paired t-test was done but no significant difference was found.

Table I: Comparison of serum creatinine between study subjects

Study group	Serum creatinine mean±SD (mg/dl)	t value	p value
Diabetic with vascular events (n=50)	1.30±.46	1.69	>0.05
Non diabetic with vascular events (n=79)	1.15±.53		

***Table II:** shows comparison of eGFR between the two groups. Un paired t-test was done and significant differences (p<0.01) was found between the groups.*

Table II: Comparison of eGFR between the study subjects

Study group	mean±SD (ml/min)	t value	P value
Diabetic with vascular events n=50)	66.16±20.14	3.33	<0.01
Non diabetic with vascular events n=79)	79.51±25.12		

Table III: Comparison of the vascular events in the study subjects

Study group	Diabetic	Non -diabetic	P value
Major cardiac events	44	60	>0.05
Minor cardiac events	6	19	

Table III: shows comparison of vascular events between the two groups. Chi square test was done and no significant differences (p > 0.05) was found between the two groups.

Discussion

In this case control study our attempt was to demonstrate an association between eGFR and cardiovascular events in diabetic subjects.

Our study revealed that serum creatinine did not differ between the diabetic and non diabetic subjects but eGFR differ significantly. Our findings is similar to the findings of Segura et al. 2004 which suggests that serum creatinine is less sensitive than eGFR to detect small differences in level of kidney function.

In our study eGFR differ significantly between two groups. eGFR is lower in diabetic subjects. This finding is similar to the findings of Knobler et al 2004 & Drury et al 2010 which suggests that reduced GFR was common in diabetic patients and was associated with two fold increase in cardiac events[1]. The seventh report of Joint National Committee (JNC-7) recognized eGFR (<60 ml/min) as major cardiovascular risk factors[14]. Several studies across a broad spectrum of population such as the Hope Study, Cardiovascular Health Study (CHS), Hypertension optimal treatment (HOT) study, Atherosclerosis risk in communities (ARIC) study have shown that IHD in diabetic subjects are higher in those with reduced eGFR[14].

In our study we did not find any significant differences in the occurrence of major and minor cardiac events between diabetic and non diabetic group.

Therefore, from our study we can say that eGFR (by MDRD formula) which is not a routine procedure, but less laborious and more or less widely accepted, should perform routinely, in all diabetic subjects to predict the cardiac events.

Conclusion

Reduced eGFR is associated with the highest risk of cardiovascular events in diabetic subjects. Therefore, eGFR should be considered as a routine renal function test to predict cardiovascular abnormality in type 2 diabetes mellitus.

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