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Original Research Article

Correlation of estimated glomerular filtration rate with ejection fraction among type 2 diabetes mellitus patients: results of a cross sectional study from Southern India

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ABSTRACT

Background: There is paucity of data regarding the relationship between the severity of left ventricular dysfunction and renal function impairment in diabetic patients. Aims and objectives was to study the relation between eGFR and ejection fraction in type 2 diabetes mellitus of more than 5 years duration.
Methods: This cross sectional was carried out from May 2017 to May 2018 at Yenepoya Medical college a tertiary care center in the southern Indian state of Karnataka. The data on 220 diabetic patients were studied. A detailed clinical history physical examination was carried out on the study population as per the approved proforma. Apart from base line investigations, eGFR was calculated using serum creatinine levels. 2D echocardiography was done for the assessment of ventricular function.
Results: Out of 220 patients, 138 were men (63%) and 82 were women (37%) and the mean age of the patients was 59.60±11.145 years. The mean duration of diabetes was 10.08±5.28 years. We found a progressive reduction in ejection fraction from 57.74±9.97% to 50.64±14.7 as the eGFR declined from <90 mL/min/1.73m^2 to 30 mL/min/1.73m^2. There was significant correlation between eGFR and RWMA (p value 0.001) and LVDD (p value 0.029) in this study cohort. Micro/macroalbuminuria was found to be in 55% of patients. Proteinuria had significant correlation with longer duration of diabetes, blood urea, serum creatinine and eGFR.
Conclusions: This study found positive clinical correlation between LVEF and eGFR. However, it did not reach significant levels statistically. Further studies may be carried out to confirm the association.

Keywords: Creatinine, Diabetes mellitus, Estimated glomerular filtration rate, Ejection fraction

INTRODUCTION

The metabolic dys-regulation associated with DM causes secondary pathophysiologic changes in multiple organ systems imposing a tremendous burden on the patient with diabetes and correspondingly to the health care system.[1] There is a progressive rise in diabetic population all over the world including India. In a study it was observed that there were over 72,946,400 cases (8.8% of total population) of diabetes in India in 2017and the number is steadily on rise.[2] Indian Council of Medical Research estimated that the overall prevalence of diabetes in Karnataka was 7.7%.

World over, the data from South East Asia showed that there were 82 million people with diabetes in 2017, and were expected to steep up to 151 million by 2045.[3]

While diabetic population are prone to get myriad complications of the disease, the cardiovascular disease

(CVD) is a major cause of morbidity and mortality in this population.[4] CVD includes stroke, coronary artery disease and peripheral artery disease. As the number of people with diabetes is predicted to increase hence the outlook for CVD is expected to become more alarming. It was estimated that 21.1% of patients with type 2 diabetes mellitus (T2DM) in India develop renal dysfunction during their life span.[5] The spectrum of renal impairment in diabetes ranges from a decrease in the estimated glomerular filtration rate (eGFR), to the progression of microalbuminuria, macroalbuminuria , gross proteinuria and finally end stage renal disease.[6]

The dynamic inter-relationship between heart and kidney malfunction have been defined in the recent consensus process by the Acute Dialysis Quality Initiative (ADQI) suggesting a synergistic relationship between the two.[7] Keeping in view the rising trend of diabetes mellitus and hence chronic complications of the disease in the southern Indian state of Karnataka we were prompted to undertake this study. This study aimed to explore the association between eGFR and ejection fraction in type 2 diabetes mellitus of more than 5 years from diagnosis at our tertiary care hospital.

METHODS

This cross sectional study was conducted between May 2017 to May 2018 at Yenepoya medical college Hospital, a tertiary care centre in the southern Indian state of Karnataka. The sample size was calculated on the assumption that 21.1% of Indian diabetic patients develop a moderate to severe renal function impairment during their life span.[5] Assuming nephropathy for hospitalised patients with type 2 diabetes of more than 5 year duration is 20%, a sample size of 220 was calculated with 95% Confidence Interval. The study was approved by ethical committee of our University.

The study was conducted on 220 type 2 diabetic patients of more than 5 years duration from diagnosis. Informed written consent was obtained from all study participants. Detailed history regarding age, gender, place, duration of diabetes, anti-diabetic medications, history of hypertension, coronary artery disease, cerebrovascular disease, peripheral vascular disease, smoking and alcoholism were noted. Physical examination with respect to body mass index, blood pressure and fundus examination were done.

Investigations done for each patient included complete blood count, fasting and post prandial blood glucose, HbA1c, serum creatinine, eGFR, serum total cholesterol, triglyceride, HDL, LDL, urine routine examination, urine dipstick test for proteinuria, morning spot urinary albumin-creatinine ratio,24 hour urine protein when indicated, ECG, 2-dimensional echocardiography.

Estimated glomerular filtration rate (eGFR) was calculated from the serum creatinine using the Modification of Diet in Renal Disease equation formula: eGFR = [186.3 × (serum creatinine [mg/dL]$^{-1.154}$) ×(age$^{-0.203}$) × (0.742 if female)].

Conventional 2 D Echocardiography was used to assess the left ventricular function.

Inclusion criteria

Patients with diagnosed with type 2 diabetes mellitus by ADA guidelines, of more than 5 years from diagnosis were included.

Exclusion criteria

Patients with diabetes of <5 years from diagnosis and those with type 1 Diabetes Mellitus were excluded. Patients with valvular heart disease, obvious renal disease like chronic kidney disease on dialysis, glomerulonephritis, polycystic kidney disease and obstructive uropathy, overt pulmonary disease, pregnancy were excluded.

Statistical analysis

The data was entered in Microsoft Excel. Continuous variables were expressed in terms of mean and standard deviation and categorical variables presented in frequency and percentages.

Independent t-test was used to compare all the continuous variables between the groups. Chi square test was used to evaluate whether there is any association between two categorical variables. A p-value <0.05 was considered significant. All the analysis is done using SPSS version 22 software and Microsoft excel

RESULTS

Of 220 type 2 diabetic patients studied, 138 were men (63%) and 82 were women (37%). Table 1 represents the baseline characteristics of patients in this study. The mean age of the patients was 59.60±11.145 years and the mean duration of diabetes was 10.08±5.38 years. The mean body mass index was 25.46±5.53 kg/m^2. The mean systolic blood pressure and diastolic blood pressure were 126.86±22.57 and 79.05±13.84 mm Hg, respectively. The mean fasting blood sugar and HbA1c levels were 182.57±80.65 mg/dL and 9.545±2.60%, respectively. The mean serum creatinine and blood urea were 1.32±1.08 and 36.61±22.70 respectively. The mean eGFR level was 74.10±33.56mL/min/1.73m^2 and the mean ejection fraction was 54.31±12.73 %. In the study population 51.4 % had systemic hypertension, 20.5% had past history of CAD, 6.4% patients had past history of CVA and 4.5% had history of PVD.

Majority of the study population were on OHA (61.4%), 24.5% takes both insulin and OHA, 10% of the study cohort were on insulin and 4.09% were on diet control.

Table 1: Baseline characteristics of study population.

Characteristics	Mean±SD
Age (years)	59.60±11.14
Duration of diabetes (years)	10.08±5.38
Body mass index (kg/m^2)	25.46±5.53
Systolic blood pressure (mmHg)	126.86±22.57
Diastolic blood pressure (mmHg)	79.05±13.84
Fasting blood sugar (mg/dl)	182.57±80.65
Post prandial blood sugar (mg/dl)	231.01±91.08
HbA1C (%)	9.545±2.60
Total cholesterol (mg/dl)	153.22±41.26
Triglyceride (mg/dl)	143.11±71.03
HDL cholesterol (mg/dl)	31.71±10.41
LDL cholesterol (mg/dl)	94.05±38.00
VLDL (mg/dl)	27.23±12.2
Serum creatinine (mg/dl)	1.32±1.08
Blood urea (mg/dl)	36.61±22.70
eGFR (mL/min/1.73m^2)	74.10±33.56
Ejection fraction (%)	54.31±12.73

In our study population, 143 patients (65%) had eGFR below 90 and 77 patients (35%) had eGFR above 90.

In this study population among diabetics, majority had ejection fraction ≥60% (69.5%). Nearly one third of diabetics (30.5%) had significant cardiac dysfunction, that is ejection fraction less than 60%.

In this study population, those with eGFR ≥90mL/min/1.73m^2 had an ejection fraction of 57.74±9.972% and those with <15mL/min/1.73m^2 eGFR had mean EF of 50±18.84% (Table 2). The ejection fraction was lowest in the group with lowest eGFR and highest in the group with eGFR>90 ml/min/1.73m^2. The corresponding decline in ejection fraction to eGFR using ANOVA was clinically significant, however it didn't reach statistically significant levels (p=0.168).

Further, eGFR was not normally distributed (p value0.037, Shapiro-Wilk test) hence nonparametric tests were used to find the associations. By using Spearman's correlation coefficient it was seen that there is a positive clinical correlation between eGFR and ejection fraction but this was not statistically significant. (Spearman's correlation coefficient =0.097, p value 0.162) Table 3.

Table 2: Correlation of eGFR with echo findings.

Parameters	eGFR (Mean ± SD)		p value
	No	Yes	
RWMA*	77.25±34.77	61.95±25.24	0.001
LVDD**	79.74±33.82	69.78±32.85	0.029
LVH***	75.76±32.78	66.71±36.36	0.123

*RWMA: Regional wall motion abnormality, **LVDD: Left ventricular diastolic dysfunction,
***LVH: Left ventricular hypertrophy

Table 3: Correlation of ejection fraction with echo findings.

Parameters	Ejection fraction (Mean±SD)		p value
	No	Yes	
RWMA*	57.75±10.61	40.91±11.40	<0.0001
LVDD**	58.01±8.39	51.44±14.66	<0.0001
LVH***	54.47±12.45	53.60±14.08	0.698

*RWMA: Regional wall motion abnormality, **LVDD: Left ventricular diastolic dysfunction,
***LVH: Left ventricular hypertrophy

Independent t- test was used to find the correlation of ejection fraction with echo findings. A significant association of ejection fraction with RWMA and LVDD (p value <0.0001) was observed. In the subgroup analysis the independent t- test was used to find the association between <45% and >45%. We observed statistically significant correlation of duration of diabetes (p value 0.014), VLDL (p value 0.04), blood urea (p value 0.007) and eGFR (p value 0.016) with ejection fraction of <45% and >45%. Using Independent test, we observed a statistically significant association of eGFR (p value 0.001) with RWMA Table 4.

Table 4: Factors correlating with ejection fraction.

Parameters (Mean±SD)	Ejection fraction		p value
	<45%	>45%	
Duration of diabetes	11.66±5.49	9.58±5.26	0.014
VLDL	24.24±9.95	28.18±12.71	0.040
Blood urea	43.85±24.02	34.32±21.84	0.007
eGFR	64.46±29.24	77.18±34.34	0.016

Chi square test to find association between the type of diabetic treatment and diabetic nephropathy it was observed that the group of people taking insulin or insulin+OHA had statistically significant correlation with incidence of diabetic nephropathy (p value 0.001).

DISCUSSION

In this study positive relationship between eGFR and ejection fraction was observed among type II diabetics of more than 5 years duration. As eGFR declined from <90 mL/min/1.73m^2 to 30 mL/min/1.73m^2 there was progressive reduction in ejection fraction from 57.74±9.97 to 50.64±14.27. However, this relationship was lost for the group of eGFR 15-29 mL/min/1.73m^2. There was no linear association between eGFR and ejection fraction as seen by correlation coefficient of 0.097 which was not statistically significant. Our results are in cognizance to Szu-Chia Chen et al, who reported a linear relationship between LVEF and stage of CKD.[8]

In another study by Jingmin Zhou et al, the data on 1166 elderly diabetic population it was observed that the

prevalence of left ventricular diastolic dysfunction increased in proportion to serum urea, urea to creatinine ratio and urine albumin creatinine ratio.[9] Further, the association between GFR and LVEF in two community based cohort of elderly patients without clinical heart failure (LVEF more than 40%,) a positive association between eGFR and echocardiographic indices of left ventricular dysfunction were found.[10] Various pathogenic mechanisms attributed to heart failure in CKD could be due to bidirectional injury and dysfunction via a final common pathway of cell-to-cell death and accelerated apoptosis mediated by oxidative stress, endothelial dysfunction. It is quite possible that, accelerated atherosclerosis, volume overload, acid base imbalances, anemia etc may be contributing as well. In this study while correlating eGFR with echocardiographic abnormalities of regional wall motion abnormality (left ventricular diastolic dysfunction, left ventricular hypertrophy) a significant association was found with lower eGFR. This indicates that myocardial damage due to ischemic heart disease could lead to renal impairment due to decrease in left ventricular systolic and diastolic dysfunction of the heart leading to impaired eGFR. In a study by Jiji I et al, the data on 120 patients with Type 2 diabetes showed that as the duration of diabetes mellitus increases, there is corresponding impairment of kidney function (increase in microalbuminuria followed by increase in blood urea, serum creatinine).[11] The data was supported by other researchers as well.[12-14] This study had some limitation as it excluded diabetics of lesser than 5 years duration and included only Type 2 Diabetes mellitus. Nevertheless, the study showed a positive clinical correlation between e GFR and echocardiography.

CONCLUSION

Based on discussed results we conclude that there is a positive clinical correlation between LVEF and eGFR. We recommend that patients with diabetes mellitus of more than 5 years with eGFR less than 60 should undergo a routine echocardiography, however, further studies may be carried out to establish the co relation.

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