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Original Research Article

Correlation of HbA1c with urinary ACR, serum creatinine and eGFR in type-2 diabetes mellitus at Puducherry, South India

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ABSTRACT

Background: Diabetes Mellitus (DM) is a major emerging clinical health problem in this world. Anemia is a common problem in diabetes. Type 2 DM comprises about 90% of diabetic population of any country.
Methods: A cross-sectional study carried out among 125 type 2 diabetic mellitus patients' area at Department of Medicine Aarupadai Veedu Medical college (AVMC) and hospital, Puducherry during the period from May 2018 to October 2018.The objectives of the study were to evaluate the association of HbA1c with urinary ACR, eGFR and serum creatinine in Type 2 diabetes mellitus. Data was analyzed using the SPSS version 20.0 software.
Results: The randomly selected study group comprised 100 type 2 DM patients and 25 control peoples of 35-70 years of age. Type 2 DM patients were evaluated of HbA1c, normotensives or hypertensives. FBS, serum creatinine, urinary albumin and creatinine were estimated. Urinary ACR and eGFR and were calculated. The data result was expressed as mean and standard deviation. A probability value is less than 0.05 and it was considered statistically significant.
Conclusions: Type 2 diabetes mellitus patients, HbA1c and duration of diabetes were the strongest predictors of micro albuminuria and age was the strongest predictors of a low eGFR. The diabetes was poorly controlled, making the progression to end stage renal failure in concern patients. They measure the prevention of urinary albumin excretion, development of renal abrasion, smoking termination, strict glycaemic control and initiating lipid lowering therapy.

Keywords: eGFR, HbA1c, Type 2 diabetes mellitus, Urinary ACR

INTRODUCTION

Diabetes mellitus (DM) is a major emerging clinical health problem in this world. Anemia is a common problem in diabetes.[1] It is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin.[2] Type 2 DM comprises about 90% of diabetic population of any country. Diabetic nephropathy is a chronic micro vascular complication of poorly controlled diabetes mellitus (DM), leading to end stage renal disease (ESRD).[3] The diabetic nephropathy is estimated to turn into the most frequent cause of ESRD in the developing world. About 20% to 30% of people with either type 1 or type 2 diabetes develop nephropathy, whose incidence increases with the duration of diabetes.[4-6] Micro albuminuria significantly increases the relative risk of development of diabetic nephropathy and is a risk factor for adverse cardiovascular outcomes.[7] In diabetic patients, glycemic control i.e. maintaining the normal blood sugar levels plays a very significant role in averting the risk of developing both acute and chronic complications.

Diabetes is a major cause of morbidity and mortality throughout the world especially more alarming in developing countries. Diabetes is among the leading causes of kidney failure and screening for early signs of diabetes related to kidney disease is a cost saving intervention and feasible for developing countries. Microvascular complications including nephropathy, retinopathy and neuropathy are initiated by chronic hyperglycemia.[8]

In India, the prevalence of diabetic nephropathy ranges from 32% to 57% and overt proteinuria is found in 5% to 28% of diabetic patients.[9] Diabetes mellitus contributes to a third of all patients in dialysis units in India. Diabetic nephropathy is a major public health concern, because dialysis and kidney transplantation therapy are almost completely inaccessible to most diabetic patients in India.[10,11] According to international diabetes federation (IDF) in 2013, 382 million people had diabetes worldwide of which type 2 makes up about 90% of the cases. This is equivalent to 8.3% of the adult people with equal rates in both men and women. More than 80% of diabetic patient's deaths obtain in little and middle-income countries. The number of groups with diabetes is estimated to rise to 592 million by 2035.[12,13]

Diabetic nephropathy is the leading cause of chronic kidney disease (CKD) in United States and other Western Societies. Diabetes is responsible for 30-40% of all ESRD cases in United States.[13] The estimated overall incidence rate of CKD and end-stage renal disease (ESRD) in India is currently 800 per million population (pmp) and 150-200 pmp, respectively. It has made observation that DM as the cause of CKD found in 31.2% of patients. The estimation of microalbumin levels in urine has been the gold standard for monitoring the diabetic nephropathy progression and is also predictive of high HbA1C levels.[14] Microalbuminuria (MAU) is a preliminary manifestation of diabetic nephropathy which initiates as a result of microvascular changes. Long term control of diabetes is monitored by estimation of glycated hemoglobin (HbA1c). There are two important markers to asses renal impairment-glomerular filtration rate (GFR) and microalbuminuria. Microalbuminria is better reflected by spot urine albumin-creatinine ratio (urinary ACR). There are some formula-based calculations of GFR, called estimated GFR or eGFR cockroft-Gault (C-G) formula and modification of diet in renal disease Study (MDRD). In the present study, to evaluation of HbA1c with urinary ACR, serum creatinine and eGFR in type-2 diabetes mellitus were measured.

METHODS

A cross-sectional study carried out the evaluation of HbA1c with urinary ACR, serum creatinine and eGFR among 125 type 2 diabetic mellitus patients in around Puducherry. The study was analyzed in type 2 diabetic mellitus patients of 35-70 years of age in practice area at Department of Medicine, AVMC and H, Puducherry and South India. This study was carried out from six month in the duration of May 2018 to October 2018. 10 ml of fasting venous blood was collected from the antecubital vein of each patient/study subject 5 ml dispensed in clotted vial for estimation of serum creatinine, 2ml in ethylene diamine tetraacetic acid (EDTA) vial for estimation of HbA1c by high performance liquid chromatography (HPLC); 3 ml in fluride vial for estimation of fasting plasma glucose (FPG).Written consent taken from each patient before the procedure and each patient was counseled separately about the procedure and purpose of the study. 20 ml morning urine sample was collected from each study subject for the estimation of spot urine ACR. Fasting plasma glucose (FPG) was estimated by glucose oxidase-peroxidase method.[16] Glycated hemoglobin or HbA1c was estimated by using HPLC technique and the obtained value is expressed as percentage (%).[17] Urinary microalbumin (Immunotubidimetric method) and urinary creatinine (Modified Jaff method) were estimated by Mindray autoanalyzer using supplied respective reagent kit and their ratio i.e., urinary ACR was calculated and expressed in mg/gm (µg/mg) unit.[18,19] Serum creatinine (mg/dl) is measured by Modified Jaff Method.[20] eGFR is calculated by using MDRD formula.[21]

MDRD formula = eGFR (mL/min/1.73 m^2) = 186 × (Scr)-1.154 × (Age)-0.203 × (0.742 if female) × (1.212 if black).

Statistical analysis

The data were analyzed using SPSS software program, version 20.0. The mean and standard deviation were measured. Analyzed and interpreted using descriptive and inferential statistics. The correlations of HbA1c with urinary ACR, eGFR and serum creatinine were calculated by Pearson's correlation test and relevant 'p' value was calculated as level of significance. The probability value is less than 0.05 ($p < 0.05$) and it was considered as statistically significant.

RESULTS

The result of the study samples was included 125 type 2 DM patients. The age of the participants ranges from 35 to 70 years (mean age 54.25±6.92). A total of 125 patients in which majority of 85 (68%) patients were male and 40 (32%) were females. The clinical parameter of diabetic patients is shown in (Table 1).

Out of 125 patients 87 are residing in rural area and 38 are residing in urban area. The distribution of the Type 2 DM patients based on education and there are 74 patients with high education levels and 51 patients with Low education levels. It reveals the distribution of the patients based on economic status.

Out of 125 patients 44 are good, 33 patients medium and 48 are low. The mean duration of diabetes is 9.27±2.34 in

years. Most patients (60%) had never smoked, 12% were current smokers and 35% were smoking stopped at the time of data collection. The majority of patients (64%) were classified as overweight and 24% were in normal weights. The most of these patients (74%) were found as hypertension.

Table 1: Clinical parameters of diabetic patients (N=125).

Parameters		Mean value ± SD	'P' value
Age (range 35-70 years)		54.25±6.92	0.965
Gender	Male (85)	42.5±38.89	0.825
	Female (40)	20±16.97	
Residence	Rural (87)	43.5±44.54	0.486
	Urban (38)	19±11.31	
Education	High education level (74)	37±46.66	0.739
	Low education level (51)	25.5±9.19	
Economic status	Good (44)	22±25.45	0.650
	Medium (33)	16.5±10.60	
	Low (48)	24±19.79	
DOD (Duration of diabetes in years)		9.27±2.34	0.967
Smoking status	Present	15	12 %
	Never	75	60 %
	Stopped	35	28 %
BMI	Underweight	13	10 %
	Normal	32	26 %
	Overweight	80	64 %
Hypertension		115	74 %
Unknown		10	26 %
FPG (mg/dl)		110.25±18.50	0.007
HbA1c (%)		8.24±1.18	0.215
Serum creatinine (mg/dl)		1.12±0.29	0.426
eGFR (ml/min/1.73sq. m)		74.65±22.55	0.324
Urinary ACR (mg/gm)		52.24±82.15	0.050

The evaluation of HbA1c was assessed with serum creatinine, urinary ACR and eGFR among total study subjects (N=125), group I with HbA1c < 8% (N=80) and group II with HbA1c ≥ 8% (N=45) were presented in (Table 2).

There is significant positive correlation of HbA1c with urinary ACR and serum creatinine in 125 type 2 DM patients (r value= 0.654 and 0.825 respectively. The probability value both is less than 0.001 at level of significance and only with serum creatinine in group I, HbA1c <8% ('p' value =0.001). The significant positive correlation of HbA1c remained with serum creatinine and ACR in group II, HbA1c ≥8% (p value is <0.001). There is also significant negative correlation is found between HbA1c and eGFR in all type 2 DM patients in group I and II (p values are 0.042, 0.005 and <0.001 respectively. The p value is less than 0.05 is the level of significance.

Table 2: Correlation of HbA1c with and S. creatinine, ACR and eGFR.

Diabetic patients	Parameters		R value	P value
N=125	HbA1c	Serum creatinine	0.825	0.001^S
		Urinary ACR	0.654	0.001^S
		eGFR	-0.742	0.042^S
Group I HbA1c <8%, N= 80	HbA1c	Serum creatinine	0.420	0.001^S
		Urinary ACR	0.335	0.050^S
		eGFR	-0.402	0.005^S
Group II HbA1c ≥8%; N = 45	HbA1c	Serum creatinine	0.744	0.001^S
		Urinary ACR	0.632	0.001^S
		eGFR	-0.708	0.001^S

P<0.05 level of significant.

DISCUSSION

In cross-sectional study, out of 125 type 2 DM patients of age range between 35-70 years (54.25±6.92) and p value 0.965. The mean duration of diabetes is 9.27±2.34 in years with p value is 0.967. Venugopal S et al, and Layer UM et al, have reported that the significant correlation of HbA1c with microalbuminuria type 2 diabetes mellitus patients.[22] Haque N et al, has also reported significant positive correlation of HbA1c with S. creatinine and urinary ACR in type 2 diabetic patients (p values are 0.008 and <0.001 respectively.[23] The similar studies were reported by Sheik et al.[24] They have found significant positive correlation of HbA1c with microalbuminuria (p <0.05) and S. creatinine (p <0.001) in type 2 DM patients. These positive correlations remained significant when HbA1c ≥8% (p values are 0.04 and <0.001) and when HbA1c <8%, they found only significant positive correlation between HbA1c and ACR (p value 0.005) but not between HbA1c and S. Creatinine where p value is 0.614. Haque N et al.[23] have found that the positive correlation of HbA1c with eGFR although this positive correlation is not statistically significant (p value=0.158). In this study, negative correlation is statistically significant between HbA1c with eGFR (p value=0.036). They have also found that the mean years of duration of diabetes was 6.36±1.65 in their study, whereas in present study the mean years of duration of diabetes are 9.27±2.34. Glomerular hyperperfusion and renal hypertrophy occur in the first years after the onset of type-2 diabetes mellitus and are associated with an increase of the GFR. During the first 5 years of type-2 diabetes mellitus, thickening of the glomerular basement membrane, glomerular hypertrophy and mesangial

volume expansion occurs as the GFR returns to normal. Diabetic nephropathy is a chronic microvascular complication in uncontrolled type 2 diabetes mellitus. There is a spectrum of changes in chronic kidney disease, with well-defined functional progression from hyperfiltration to micro to macro albuminuria to renal failure.[25] In early renal impairment, classical markers (serum urea and serum creatinine) may be normal, but there are early glomerular changes like thickening of basement membrane, accumulation of matrix materials in the mesangium, subsequently nodular deposits with consequent microalbuminuria. At this stage, glomerular pathological changes can be reversed by pharmacological intervention. So, newly detected or known type 2 DM patients need monitoring for glycemic control, with simultaneous monitoring for early reversible nephropathy and microalbuminuria.[23]

CONCLUSION

It concluded that the significant correlation of HbA1c with Urinary ACR, eGFR and S. creatinine were measured. The finding and treatment of nephropathy in type-2 diabetes mellitus patients both eGFR and urinary ACR should be measured along with tight glycaemic control so that progression to ESRD can be prevented. Type 2 diabetes mellitus patients, HbA1c and duration of diabetes were the strongest predictors of microalbuminuria and age was the strongest predictors of a low eGFR. The diabetes was poorly controlled, making the progression to end stage renal failure in concern patients. They measure the prevention of urinary albumin excretion, development of renal abrasion, smoking termination, strict glycaemic control and initiating lipid lowering therapy.

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