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Research Article

CORRELATION OF CREATININE CLEARANCE AND URINE MICROALBUMIN IN TYPE 2 DIABETES MELLITUS

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ABSTRACT
Microalbuminuria and Creatinine Clearance is closely related components of same disease process. This study aims to determined correlation of Microalbuminuria and Creatinine Clearance in Type 2 diabetes in Indian population. A total 100 subjects of age group 31 to 80 years (70 TYPE2DM, 30 controls), diabetic duration six months or more and absence of Albumin in urine, measured by Albustic method were included in the study. Detailed clinical history was taken followed by through physical examination that included in neurological examination in the selected patients. Overall prevalence of microalbuminuria in this study was found 67%, which is the predictor of development of diabetic nephropathy. There is strong correlation between A:C Ratio and Creatinine Clearance. Similarly there is no correlation between HbA1c and Creatinine Clearance. This study concludes in cases without microalbuminuria need yo be monitored for impaired kidney function by measuring serum Creatinine and determining Creatinine clearance.

Keywords: *Creatinine Clearance, Microalbumin, Type 2DM*

INTRODUCTION
Diabetes mellitus is a worldwide public health concern and an important cause of morbidity and mortality. Through lifelong vascular complications, diabetes leads to excessive rates of myocardial infarction, stroke, renal failure, blindness and amputations. The projections of its future impact are alarming. It is associated with reduced life expectancy; significant morbidity due to specific diabetes related macro vascular complications and diminished quality of life. According to the World Health Organization (2004), diabetes effects more than 170 million people worldwide, and this number will rise to 370 million by 2030. About one third of type 2 diabetics will eventually have progressive deterioration of renal function (Remuzzi *et al.,* 2002). Diabetic nephropathy is a public health concern of increasing proportions. It has become the most common single cause of end-stage renal disease all over the world (Molitch *et al.,* 2004). The first clinical sign of renal dysfunction in patients with diabetes generally is microalbuminuria (a sign of endothelial dysfunction that is not necessarily confined to the kidney). Microalbuminuria refers to the excretion of albumin in the urine at a rate that exceeds normal limits but is less than the detection level for traditional dipstick methods (American Diabetes Association, 2003). It is often present at the time of diagnosis, either due to insidious nature and asymptomatic during initial years of type 2 diabetes or its positive association with insulin resistance, even in non diabetic people (Mykkanen *et al.,* 1998). The degree of microalbuminuria determines the progression of diabetic nephropathy. It may reflect the renal manifestation of a global vascular dysfunction (Asselbergs *et al.,* 2004). Increased level of microalbuminuria is an important risk factor for progressive renal impairment leading towards End stage renal disease, and to cardiovascular disease via in type 2 diabetes as well as in non-diabetic population (Haffner *et al.,* 1990; Ritz, 1999). Microalbuminuria develops in 2 to 5 percent of patients of type 2 diabetes per year (Gall *et al.,* 1997; Adler *et al.,* 2003). In type 2 diabetes, unlike type 1 diabetes, microalbuminuria is seldom reversible (Perkins *et al.,* 2003; Parving *et al.,* 2001) but, instead, progresses to overt proteinuria in 20 to 40 percent of patients (Mogensen, 1984; Nelson *et al.,* 1991). In 10 to 50 percent of patients with proteinuria, chronic kidney disease develops that ultimately requires dialysis or transplantation (Nelson *et al.,* 1988). Creatinine clearance (CRCL) is the most widely used marker and provides a more accurate assessment of the GFR in renal diseases. Creatinine clearance

requires a 24 hr urine collection. A blood sample is drawn at some point during the 24 hr period, and creatinine clearance, can then be calculated. Because a small amount of creatinine is released by the renal tubules, creatinine clearance is not exactly the same as the GFR. In fact, creatinine clearance over estimates the GFR, particularly in patients with advanced kidney failure. Normal creatinine clearance values are: male: 97 to 137 ml/min and in females 88 to 128 ml/min (Bazari, 2007). CRCL can be calculated from serum creatinine by a formula without collecting a timed urine specimen (Alkafajei *et al.*, 1980). Formula-derived eGFR results have become widely used in clinical practice. The national service framework for renal services in the U.K recommends the adoption of formula derived eGFR in the annual evaluation of all patients with diabetes (Department of Health Renal Team, 2005). It is anticipated that this process will aid early identification and therefore improve long term outcomes for those with diabetic nephropathy. The American diabetes association recommends estimation of glomerular filtration rate by eGFR (in milliliters per min per 1.73 m2), which is calculated by the Cockcroft-Gault (CG) formula (Cockcroft and Gault, 1976) Elevated levels of HbA1c and microalbuminuria are markers of diabetes and early phase of renal pathology respectively

Cockcroft-Gault formula:-

$$\text{(CRCL) (In Male)} = \frac{\text{(140-Age) X (body weight) in kgs}}{\text{Serum creatinine X 72}}$$

$$\text{(CRCL) (In Female)} = \frac{\text{(140-Age) X (body weight) in kgs}}{\text{Serum creatinine X 72}} \times 0.85$$

MATERIALS AND METHODS

The present study was conducted in the Department of Biochemistry, Ganni Subba Laxmi Medical College and General Hospital, Rajahmundry, Andhra Pradesh from 2011 to 2012, to investigate correlation between Microalbumin and Creatinine Clearance in type 2 DM patients. Study was approved by institutional ethics committee and written informed consent form was taken from all the patients. Hundred subjects with Type 2DM of duration six months or more and negative for albumin in urine by albustic method were included in this study. Subjects with congestive cardiac failure, urinary tract infection, pregnant and patients confined to bed more than two weeks and hypertensions were excluded from this study. Other causes for microalbuminuria like heavy metal poisoning, connective tissue disorders, and chronic NSAIDs use were also ruled out from the study. The selected patients were studied in detail with history and physical examination. Routine investigations including serum creatinine were done in all the selected patients. Creatinine clearance was calculated based on Cockroft-Gault equation.

In the present study, Antigen-antibody reaction by End point method was used for estimation of microalbuminuria. (Quantitative determination of micro albumin is carried out by turbidimetric immunoassay (Mount, 1986; Schmidtz, 1988).

RESULTS

A total of 100 subjects of age group 31 to 80 years, 70 diabetic cases and 30 controls were included in the study. Measurements of Blood Glucose (FBS, PPBS), $HBA_{1c,}$ Serum Creatinine, Creatin Clearance were done in both the groups. Sex percentage in 58.5% male cases and 41.4% were female cases, control group males are 53.3% and 46.6% were females. The sex ratio between male and female was in both groups 1.41:1 (Table 1). Table 2 shows that baseline characteristics of cases and controls. Fasting blood glucose level, post prandial glucose level, HbA1C, Serum Creatinine, Creatinine clearance, micro albumin in cases was highly significant compared to controls. Pearson correlation of A: C Ratio with Creatinine clearance, HbA1C in cases was not significant Table 3. Table 4 shows that correlation of FBS, PPBS, and HbA1c in cases and controls there did not show any significance.

Table 1: Age and sex distribution of diabetic cases and controls

	Cases (70)	Control (30)
Age(range)	31-80	32-73
Mean ±SD	49.79±10.3	47.46±10.54
Sex %	male- 58.5% (41)	male-53.3%(16)
	female- 41.4%(29)	female- 46.6%(14)
sex ratio	1.41	1.14

Table 2: Baseline Characteristics of the Cases and Controls

PARAMETERS		mean + SD	p.value
FBS(mg/dl)	case	178.3±69.27	>0.001
	control	84.2±69.61	
PPBS(mg/dl)	case	270.4±196.81	>0.001
	control	114±110.38	
HBA1C (%)	case	9.18±1.00	>0.001
	control	4.96±0.72	
S.CREATININE(mg/dl)	case	1.16±0.620	>0.001
	control	0.7±0.15	
CRCL(ml/min)	case	69.1±54.6	>0.001
	control	114.8±120.9	
MICROALBUMIN(µg/dl)	case	5886±6134.3	>0.001
	control	1678±817.6	

Table 3: Correlation of A:C Ratio With Creatinine Clearance, Hba_1c In Diabetes Mellitus

VARIABLE	MEAN ± SD	CORR.COEFFICIENT
Creatinine clearance	**1.16± 0.620**	**-0.46**
HBA1C	**9.18± 1.00**	**0.057**

Table 4: Correlation of Fbs, Ppbs And Hba_1c In Cases & Controls

VARIABLE	CASE MEAN ± SD	CONTROL MEAN ± SD	CORR.COEFFICIENT
FBS	**178.3±69.27**	**84.2±69.61**	**0.40**
PPBS	**270.4±196.81**	**114±116.38**	**0.45**
HBA_1C	**9.18±1.00**	**4.96±0.72**	**0.40**

DISCUSSION

This cross sectional study presents data on prevalence and associations of microalbuminuria with various parameters in type-2 diabetes mellitus. Among the 70 patients, 55were only on oral hypoglycemic agents, 4 were on insulin, and 11 were on both insulin and oral hypoglycemic agents. Present study has shown prevalence of microalbuminuria at 65.7%, which is much higher when compared to the studies by Ghai *et al.*, (1994) and Chowtha *et al.*, (2009) where prevalence was reported at 25%, and 37% respectively. The level of glycemic control/ genetic factors may be influencing transition from normoalbuminuria cases to microalbuminuria cases. Earlier studies have shown positive correlation of microalbuminuria with age of diabetic patients. (Ruilope and Segura, 2006; Metcalf *et al.*, 1992) Creatinine clearance has shown negative correlation with microalbuminuria in the present study, which is statistically significant indicating impaired kidney function (diabetic nephropathy)earlier studies has also shown negative correlation with microalbumin in cases (Dinnen and Gerstein, 1997). Hence microalbuminuria is associated with elevated serum creatinine and decrease creatinine clearance reflecting kidney function impairment. Statistically significant correlation was found between the prevalence of microalbuminuria and the fasting blood sugar, post prandial blood sugar and HbA1c. A, Deepa *et al.*, (2001) also reported a

correlation of the prevalence of microalbuminuria with the fasting blood sugar and with HbA1c levels. There are reports of substantially decreased creatinine clearance in a subgroup of the T2D patients who did not have microalbumineexcretion (Kramer *et al.,* 2003; Tsalamandris *et al.,* 1994). However, it is now clear that severe CKD with CrCl (<60 ml/min/1.73 m2) occurs in the absence of increased urine microalbumin excretion in a substantial proportion of adults with T2D, and the screening in T2D for increased urine microalbumin excretion alone will miss a considerable number of CKD cases (Kramer *et al.,* 2003; Tsalamandris *et al.,* 1994). Thus, serum creatinine and CrCL should be measured at least annually in all T2D patients, regardless of the degree of urine microalbumin excretion. Physicians should emphasize that serum creatinine should be not used alone as a marker of kidney function, but rather use creatinine clearance to find out the stage of CKD (Lott and Hayton, 1978; Levey *et al.,* 2003).

Conclusion

Diabetic patients without microalbuminuria need to be monitored for impaired kidney function by measuring serum creatinine and determining creatinine clearance. Old age patients with T2D with or without microalbuminuria were having normal serum creatinine values but showed significantly decreased CrCl indicating impaired renal function.

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