



## MICROALBUMIURIA AND SERUM CREATININE LEVELS IN DIABETIC AND NON-DIABETIC SUBJECTS

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### ABSTRACT

Diabetes mellitus (DM) is one of the commonest endocrine disorders encountered in clinical practice. It is characterized by hyperglycaemia due to an absolute or relative lack of insulin and/or insulin resistance. DM is the major cause of renal morbidity and mortality and diabetic nephropathy is one of chronic kidney failure. The most common lesions involve the glomeruli and are associated clinically with three glomerular syndromes, including non nephritic proteinuria, nephrotic syndrome and chronic renal failure. The present study design included 64 subjects between age group of 55- 68 years admitted in Government Wenlock hospital, Mangalore. The study subjects included 3 groups. Group 1: senile cataract patients without diabetes, Group 2: diabetic subjects with cataract, Group 3: diabetic subjects with cataract and nephropathy. The measurement of the urinary albumin, serum creatinine and creatinine clearance was done. Results were subjected to statistical analysis by Analysis of variance (ANOVA) and the values expressed as mean  $\pm$  SD. There was no significant difference in the age and weight of the subjects. The UACR levels were significantly increased in group 2 & 3 as compared to control subjects. However there was no significant change in the serum creatinine levels. So in conclusion, we would like to say the measurement of serum creatinine and creatinine clearance may falsely indicate the renal function and newer markers has to be found other than microalbuminuria for early detection of nephropathy.

**Keywords:** Diabetes mellitus, chronic kidney failure, urinary albumin, serum creatinine, creatinine clearance.

### INTRODUCTION

Diabetes mellitus (DM) is one of the commonest endocrine disorders encountered in clinical practice. It is characterized by hyperglycaemia due to an absolute or relative lack of insulin and/or insulin resistance. Type 2 diabetes mellitus occurs at any age, but is more common between 40–80 years of age and also has a strong genetic component<sup>1</sup>. DM is the major cause of renal morbidity and mortality and diabetic nephropathy is one of chronic kidney failure<sup>2</sup>. The most common lesions involve the glomeruli and are associated clinically with three glomerular syndromes, including non nephritic proteinuria, nephrotic syndrome and chronic renal failure<sup>3</sup>. After many years of diabetes the delicate filtering system in the kidney becomes destroyed, initially becoming leaky to larger blood proteins such as albumin which are then lost in urine. This is more likely to occur if the blood sugar is poorly controlled<sup>4</sup>. Type 2 diabetes mellitus has quickly become a global health problem due to rapidly increasing population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity. There is, therefore, an urgent need to prevent diabetes and its complications. In a study on Type 2 diabetic subjects having poor metabolic control a prevalence of microalbuminuria approximates 20% and is associated with components of the metabolic syndrome<sup>5</sup>. Microalbuminuria is related to hyperglycaemia and control of blood glucose level has been shown to prevent

the development of nephropathy in Type 1 & 2 diabetes<sup>6</sup>. Measurement of the urinary albumin, serum creatinine and creatinine clearance is widely regarded as a test of renal function.

The aim of our study is to measure urinary albumin and serum creatinine levels in diabetes and non-diabetic subjects.

### MATERIALS AND METHODS

The present study design included 64 subjects between age group of 55- 68 years admitted in Government Wenlock hospital, Mangalore. The study subjects included 3 groups. Group 1: senile cataract patients without diabetes, Group 2: diabetic subjects with cataract, Group 3: diabetic subjects with cataract and nephropathy.

Inclusion criteria: Hospitalized diabetic subjects with cataract or h/o cataract and nephropathy.

Exclusion criteria: Subjects with type 1 diabetes, pregnant with type 2 diabetes and patients with urinary tract infection were excluded from the study. The study was approved by the Institutional Time Bound Research committee. A written informed consent was taken from the subjects.

**Sample collection:** Blood samples were collected during preoperative period from both senile and diabetic cataract patients. 4 ml of venous blood and early morning



mid stream urine was collected under aseptic precautions. The blood was analyzed for creatinine and plasma glucose. Assessment of microalbuminuria was done by UACR.

**Biochemical estimations:** Plasma glucose was estimated by GOD – POD method<sup>7</sup>. Estimation of creatinine was done by the modified Jaffe's method<sup>8-10</sup>. Albumin in urine was estimated by Turbidimetric method<sup>11</sup> and creatinine was determined by alkaline picrate method<sup>12</sup>.

The presence of MA in early morning mid stream urine samples was defined as urinary albumin excretion in the range of 30-300 mg/G creatinine.

**Statistical analysis:** Results were subjected to statistical analysis by Analysis of variance (ANOVA) (Kruskal wallis

test) and the values expressed as mean  $\pm$  SD. Since the data showed a skewed distribution median & inter quartile range were given. Wherever the Kruskal wallis test was significant pair wise comparison was done using mann whitney test adjusting for type 1 error.

## RESULTS

The results of the study are shown in table 1 and 2. There was no significant difference in the age and weight of the subjects. The UACR levels were significantly increased in group 2 & 3 as compared to control subjects. However there was no significant change in the serum creatinine levels and there was no statistical significance of creatinine clearance between the groups.

**Table 1: Age and weight of subjects**

	GROUP 1 (n=27)	GROUP 2 (n=20)	GROUP 3 (n=12)	SIGNIFICANCE
Age (Yrs)	58.52 $\pm$ 13.61	61.90 $\pm$ 10.54	67.25 $\pm$ 7.15	ns
Weight (Kgs)	49.89 $\pm$ 9.48	49.00 $\pm$ 16.20	49.38 $\pm$ 11.22	ns

**Table 2: Blood parameters of subjects**

	GROUP1 (n=27)	GROUP 2 (n=20)	GROUP 3 (n=12)	SIGNIFICANCE
Glucose (mg/dl)	91.50 (79.59-99.48)	142.17 (103.2-168.6)	174.53 (168.55-197.51)	vhs
Creatinine (mg/dl)	0.78 (0.7-0.9)	1.02 (0.68-1.39)	0.87 (0.63-1.37)	ns
UACR (mg/g)	51.61 (36.38-72.10)	86.76 (58.11-186.90)	249.72 (180.49-418.62)	vhs
Creatinine clearance (ml/min)	65.44 (54.23-96.82)	54.47 (39.35-80.75)	47.14 (35.4-67.04)	ns

ns = Not significant; vhs = Very Highly Significant ( $p < 0.001$ )

## DISCUSSION

Several epidemiological studies have indicated that the presence of microalbuminuria is an independent predictor of cardio vascular morbidity & mortality in patients with essential hypertension<sup>13,14</sup>. Also, other studies have shown that the presence of microalbuminuria in type 1 & type 2 diabetic patients is an important predictor of progressive renal failure<sup>15</sup>. Ophthalmic complication i.e. retinopathy is present in 47 % to 63 % of NIDDM patients with persistent proteinuria and diabetic retinopathy occurs much earlier than diabetic nephropathy<sup>16</sup>. In patients with nephropathy, the absence of retinopathy should lead to the consideration of other non-diabetic causes for proteinuria & renal disease<sup>17</sup>.

Albumin to creatinine ratio (UACR) in the morning urine sample is a reliable estimate of the 24hrs AER and better than albumin concentration alone<sup>18-20</sup>, as noted in the study by Ravijit et al<sup>21</sup> in diabetic subjects and in the study by Sheth et al<sup>22</sup> in hypertensive subjects.

In this study, a statistically significant increase was found in UACR of 1.6 fold and 5 fold in diabetic cataract & diabetic nephropathy patients respectively, when compared with normal subjects. There was no significant

difference in the serum creatinine levels. However this does not rule out the renal changes in diabetic patients, because studies have shown that estimation of serum creatinine may falsely indicate that the renal function is normal<sup>23,24</sup>. Also individuals can lose upto 50% of their creatinine clearance before the serum creatinine rises to an abnormal range<sup>25</sup>.

The laboratory marker that has long served as the mainstay for detecting impaired kidney function is serum creatinine. Unfortunately, serum creatinine is an insensitive marker of kidney injury. Two factors underlie this insensitivity. The first factor is that the reference interval is relatively wide because it must encompass a large range of creatinine production, which is related to muscle mass.

The second factor is that the inverse relationship between GFR and serum creatinine predicts that large reductions in GFR from normal produce only small absolute increases in serum creatinine. Indeed, for small or elderly people with small muscle mass, serum creatinine will remain within the usual reference limits despite substantial kidney damage<sup>26</sup>.

We also found no significant difference in the creatinine clearance values. The possible reason for this could be



due to the decrease in BMI of subjects. And other reason may be, direct measurements of creatinine clearance are not an ideal solution to the shortcomings of serum creatinine because these results often are made inaccurate by tubular creatinine secretion and by errors in specimen collection. Measurement of creatinine clearance can be useful in patients on a vegetarian diet or with low muscle mass attributable to amputation or severe malnutrition. Measurement of the renal clearance of infused tracers such as inulin, iothalamate, or iohexol can provide accurate measurements of GFR, but they are too costly and cumbersome for routine clinical use.

So in conclusion, we would like to say the measurement of serum creatinine and creatinine clearance may falsely indicate the renal function and newer markers has to be found other than microalbuminuria for early detection of nephropathy.

### REFERENCES

1. Powers A C. Diabetes Mellitus. In: Jameson JL. (editor) Harrison's Endocrinology. 1st ed. New York: McGraw-Hill; 2006. p 303–4.
2. Olimpia Ortega, Isabel Rodriguez, Alvaro Molina, Ana Hernandez. Chronic renal failure – complications, cardiovascular morbidity/ mortality 2005;73-4.
3. Schrier RW, Gottschalk CW, Disease of the Kidney, (5th ed.). Boston, little, Brown, 1993; 2153-89.
4. Saweirs Walaa. Diabetic nephropathy, Edren Juny 2006; 25. Kassab A, Ajmi T, Issaoui M, Chaeib L, Miled A, Hammami M. Homocysteine enhances LDL fatty acid peroxidation, promoting microalbuminuria in Type 2 diabetes. Ann Clin Biochem, 45; 2008:476–80.
5. S, Barit D, Cooper ME. Mechanism of diabetic nephropathy. Role of hypertension Hypertension, 48;2006: 519–26.
6. Trinder P. Quantitative determination of glucose using GOD-PAP method. Ann Clin Biochem, 6;1969:24-27.
7. Bowers L D. Kinetic serum creatinine assays. The role of various factors in determining specificity. Clin Chem, 26;1980: 551-554.
8. Bartel H, Bohmer M etal. Serum Creatinine determination without protein precipitation. Clin Chem Acta,37;1972: 193-197.
9. Slot C. Plasma creatinine determination. A new and specific jaffe reaction method. J .Clin lab.Invest, 17; 1965: 381-387.
10. Schmidt A et al.Microalbuminuria : a major risk factor in non insulin dependent diabetes. A 10 year follow up study of 503 patients. Diabetic Medicine, 5; 1988: 126.
11. Bonsnes RW and Taussky HH. The colorimetric determination of creatinine by the Jaffe's reaction. J.Biol.Chem, 158;1945: 581.
12. Lewin A, Blaufox D, Castle H, Entwisle G & Langford H. Apparent prevalence of curable hypertension in the hypertension detection and follow up program. Arch Intern Med. 145;1985: 424-427.
13. Samuelsson O, Wilhelmsen L et al. Predictors of cardiovascular morbidity in treated hypertension: Results from the primary preventive trial in Goteborg, Sweden. J Hypertens. 3;1985:167-176.
14. Viberti GC, Hill RD, Jarret RD et al. Microalbuminuria as a predictor of clinical nephropathy in insulin dependent diabetes mellitus. Lancet. 1;1982: 1430-1432.
15. West KM, Erdreich LJ and Stober JA. A detailed study of risk factors for retinopathy and nephropathy in diabetes.Diabetes.29; 501-508.
16. Bilous RW, Viberti GC, Parving HH et al.Dissociation of diabetic complications in insulin-dependent diabetes: A clinical report. Diabetic Nephropathy. 4; 73-76.
17. Rodby RA, Rohde RD, Sharon Z, Pohl MA, Bain RP, Lewis EJ. The urine protein to creatinine ratio as a predictor of 24-hour urine protein excretion in type 1 diabetic patients with nephropathy. The Collaborative Study Group. Am J Kidney Dis. 26(6);1995: 904-9.
18. Eshoj O, Feldt-Rasmussen B, Larsen ML, Mogensen EF. Comparison of overnight, morning and 24-hour urine collections in the assessment of diabetic microalbuminuria. Diabet Med. 4(6); 1987: 531-3.
19. Goldschmid MG, Domin WS, Ziemer DC, Gallina DL, Phillips LS. Diabetes in urban African-Americans. II. High prevalence of microalbuminuria and nephropathy in African-Americans with diabetes. Diabetes Care. 18(7); 1995: 955-61.
20. Ravjit Kaur Sabharwal, Parduman Singh, M M Arora, B L Somani and Vivek Ambade. Incidence of microalbuminuria in hypertension patients. Indian Journal of Clinical Biochemistry. 23 (1); 2008 : 71-75.
21. Sheth J, Trivedi L, Shah and Sheth VS. Prevalence of microalbuminuria in diabetic subjects. JAPI. 41;1993:562-564.
22. Gault MH, Longerich LL, Harnett JD, et al. Predicting glomerular function from adjusted serum creatinine. Nephron. 62;1992: 249-256.
23. Bending JJ, Keen H and Viberti GC. Creatinine is a poor marker of renal failure. Diabet Med. 2;1985: 65-66.
24. Shemesh O, Golbetz H, Kriss JP et al. Limitations of creatinine as a filtration marker in glomerulopathic patients. Kidney Int. 28;1985: 830-838.
25. Robert Star, Thomas Hostetter, Glen L. Hortin. New Markers for Kidney Disease. Clinical Chemistry 48, No. 9, 2002
26. National Kidney Foundation K/DOQI Clinical Practice Guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis,39;2002:S1–200.

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