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ALBUMIN/CREATININE RATIO, AS PREDICTOR OF MICROALBUMINURIA, A RISK FACTOR FOR NEPHROPATHY IN TYPE 2 DIABETES MELLITUS PATIENTS.

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ABSTRAT

Diabetic nephropathy is characterized by proteinuria and is the leading cause of end-stage renal disease worldwide. A case control study was designed to determine the prevalence of microalbuminuria in type 2 diabetic subjects. 50 subjects with type 2 diabetes and 50 normal healthy controls were screened for albumin and creatinine. The urinary albumin was calculated in terms of ratio with respect to urinary creatinine and expressed as albumin/creatinine ratio (mg/g). Albumin/Creatinine ratio in controls was found to be 11.05 ± 4.52 mg/g. The mean ± SD of Albumin/Creatinine ratio in total 50 patients was 38.77 ± 23.13 mg/g. The value of urinary albumin between 30 and 300 mg/g of creatinine was considered to be positive for microalbuminuria. Out of total 50 diabetic subjects, 31 patients were found to have albumin excretion of more than 30 mg/g of creatinine in random morning samples and therefore positive for microalbuminuria. The prevalence of microalbuminuria in type 2 diabetic subjects in this study was 62%. Use of the albumin-to-creatinine ratio in an untimed urinary sample should be recommended as the preferred screening strategy for all diabetic patients.

Key words: Microalbuminuria, albumin, creatinine, urine albumin creatinine ratio, type 2 diabetes.

INTRODUCTION

Microalbuminuria is a marker of an increased risk of diabetic nephropathy in patients with Type 1 as well as with Type 2 diabetes. It is common in Type 2 diabetic patients, especially those of non-European origin. Poor long-term control, hypertension, dyslipidemia and cigarette smoking facilitate the development of diabetic nephropathy.**(1)** Albumin, a protein having molecular weight of 50,000 is not easily filtered and is not excreted into urine. This makes albumin excretion into the urine a useful indicator of early glomerular disease.**(2)**

Increase in urine albumin seen with diabetic nephropathy can be attributed to degradation of the glomerular basement membranes & hypertension both characteristics of Diabetic Nephropathy.[3] Use of the albumin-to-creatinine ratio in an untimed urinary sample is now recommended as the preferred screening strategy for all diabetic patients.[4,5,6] The effect of volume can be avoided entirely by calculation of the albumin-to-creatinine ratio in an untimed urine specimen. A ratio above 30 mg/g (or 0.03 mg/mg) suggests that albumin excretion is above 30 mg/day and therefore that microalbuminuria is probably present.[7]

Microalbumin has been reported in several studies to predict development of diabetic nephropathy and its mortality risk in diabetic patients. Early detection and aggressive intervention should be given to retard the progression of diabetic nephropathy to end stage renal failure.[8]

MATERIALS AND METHODS

The case control study was performed at Department of Medicine, S.P. Medical college, Bikaner, Rajasthan, India. The study was approved by institutional ethical committee. Total 50 patient samples between age group 40-60 years with Diabetes mellitus, diagnosed according to WHO criteria, from department of medicine. The patients were without any history of cardiovascular complications, hypertension or renal diseases, and written informed consent was taken. The study group was compared with group of age and sex matched 50 control samples. The routine samples in the central clinical laboratory were taken as control samples, the control samples were without any history of diabetes mellitus, nephropathy, cardiovascular diseases and hypertension.The early morning urine samples were collected for the determination of albumin & creatinine and sample for blood glucose in fluoride bulb with potassium oxalate as an anticoagulant. Each urine sample was assayed for creatinine and albumin. The albumin was measured by latex turbidimetry method.[9,10] Urine creatinine was measured by Jaffe's kinetic method[11, 12] and blood glucose by enzymatic GOD-POD method.[13]

RESULTS

The age, blood glucose level, urine albumin, urine creatinine and urine albumin/creatinine ratio were calculated and expressed as mean ± SD, the results are depicted in Table: 1. The mean age of the patients was 52.6 ± 7.92 years and to that of healthy controls 47.21 ± 9.45 years. The blood glucose level in study group was 298± 47.05 mg/dl and highly significant (<0.01) increase is observed as compared to healthy controls i.e. 107 ± 27.39 mg/dl. The urinary albumin level was 62.80 ± 5.31 mg/l in patients and 15.24 ± 0.85 mg/l in controls. Compared to controls the increase in the albumin level in patients was found to be highly significant (<0.01). The difference in urine creatinine level was not found to be significant (>0.05) between patient group (1.62 ± 0.23 g/l) and healthy controls (1.38± 0.19 g/l).

The urinary albumin was calculated in terms of ratio with respect to urinary creatinine and expressed as albumin/creatinine ratio (mg/g). Albumin/Creatinine ratio in patients was 38.77 ± 23.13 mg/g, and to that of in controls was 11.05 ± 4.52 mg/g, and this increase in the ratio was found to be highly significant ($p<0.01$). The ratio of urinary albumin to creatinine between

30 and 300 mg/g is considered to be positive for microalbuminuria. 31 patients were found to have albumin excretion of >30 mg/g of creatinine in random morning samples and therefore positive for microalbuminuria, and confirmed by measurement of microalbumin in 24 hour urine sample.

DISCUSSION

Prevalence of nephropathy in type 2 Diabetes mellitus varies in different population groups i.e., fairly low incidence in Caucasians and a very high incidence in Pima Indians.[14] Microalbuminuria is a marker for diabetic nephropathy in type 2 diabetes mellitus.[2,15] Using a specific assay for albumin is a more sensitive technique to confirm nephropathy. Persistent albumin excretion between 30 and 300 mg/day is called microalbuminuria. Fever, exercise, heart failure, hypertension, obesity and poor glycemic control are among the factors that can cause transient microalbuminuria.[5]

Although the 24-hour urine collection was previously the gold standard for the detection of microalbuminuria, it has been suggested that screening can be more simply achieved by a timed urine collection or an early morning specimen to minimize changes in urine volume that occur during the day.[4, 16]

A value above 30 mg of albumin /gm of creatinine (or 0.03 mg/mg) suggests that albumin excretion is above 30 mg/day and therefore that microalbuminuria is probably present.[7] In one report by Gross JL[5] 24- hour urine collections and random, single- void urine specimens for albumin and creatinine were obtained in 14 normal subjects, 13 with type 1 diabetes, and 12 with type 2 diabetes. A close correlation was noted between the two measurements with small variability within patient.

Use of the albumin/creatinine ratio in an untimed urinary sample is now recommended as the preferred screening strategy for all diabetic patients.[4,5,6] Earlier reports have shown good correlation between urinary albumin/creatinine ratio and 24-h urinary excretion in screening for microalbuminuria[17,18] and guidelines[19,20] suggest that using albumin/creatinine ratio is valid for screening in the diabetic patient.

In the present study the blood sugar level was higher in the study group than healthy controls which was found to be significant ($p<0.01$). Urine albumin level in patients was significantly ($p<0.01$) increased as compared to healthy controls, where as difference of urine creatinine level between study group and healthy controls was not significant. Urine albumin/creatinine ratio was increased in patients as compared to controls, and it is found highly significant ($p<0.01$).

In a study by Zelmanovitz T, [16] 95 patients with type 2 diabetes found an equally high correlation between 24-hour urine albumin excretion and the albumin/creatinine ratio in the first morning urine.[21] Mattix[22] et al used albumin/creatinine ratio to calculate microalbuminuria among men and women, the prevalence of microalbuminuria was significantly

lower among the men compared with women Waugh[23]et al studied urinary microalbumin/creatinine ratios reference range in uncomplicated pregnancy. Significant increase ($p<0.016$) in the albumin/creatinine ratio in the third trimester was found by them.

In a cohort study conducted by Cirillo[24] et al consisted of 1623 men and women, ages between 45 & 64. They found high albumin/creatinine ratio prevalence, it was 8.5%. The effectiveness of albumin/creatinine ratio was studied by Tazeen[25] et al they found, the sensitivity was 46 and specificity was 95%, in women and 60 and 97%, respectively, in men.

This test has the following advantages: it does not require early morning or timed collections, it gives a quantitative result that correlates with the 24-hour urine values over a wide range of protein excretion, it is cheap to perform, and repeat values can be easily obtained to ascertain that microalbuminuria, if present, is persistent.

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Table: 1- The levels of biochemical parameters in study and control group.

Parameter	Patients	Controls	'p' Value
Blood glucose (mg/dl)	298 ± 47.05	107 ± 27.39	p<0.01
Urine albumin (mg/l)	62.80 ± 5.31	15.24 ± 0.85	p<0.01
Urine creatinine (g/l)	1.62 ± 0.23	1.38 ± 0.19	p>0.05
Albumin/creatinine ratio (mg/g)	38.77 ± 23.13	11.05 ± 4.52	p<0.01