

ASSOCIATION OF MICROALBUMINURIA IN TYPE 2 DIABETES MELLITUS WITH DURATION OF DISEASE AND GLYCEMIC CONTROLSuma K. R¹, Srinath S², Ganesh Shetty³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND AND OBJECTIVES: Diabetic nephropathy is a dreaded complication of type 2 diabetes mellitus. However in the early stages, also known as incipient nephropathy, it can be detected by the presence of microalbuminuria. The aim of our study was to know the occurrence of microalbuminuria in patients with type 2 diabetes mellitus and to note its associations with duration of diabetes since diagnosis and its association with glycemic control. **METHODOLOGY:** This study was undertaken in our institution from October 2010 to April 2012. A total of 100 type 2 diabetes mellitus patients satisfying the inclusion criteria were selected by systematic random sampling for the study. All patients were evaluated in detail along with the testing of microalbuminuria by calculating albumin-creatinine ratio of spot urine sample. **RESULTS:** The overall occurrence of microalbuminuria was 31%. The occurrence of microalbuminuria showed a direct relationship with increasing duration of diabetes since diagnosis ($p=0.001$). Patients with HbA1C value above 7% is associated with 42.2% of microalbuminuria ($p=0.001$). **INTERPRETATION AND CONCLUSIONS:** The occurrence of microalbuminuria in type 2 diabetic patients in this study was quite high. During the initial evaluation of patients with type 2 diabetes, and also during follow up visits, estimation of microalbuminuria should be routinely done, as it will help in early diagnosis and treatment of diabetic nephropathy.

KEYWORDS: Type 2 diabetes mellitus, microalbuminuria, diabetic nephropathy, HbA1c.

INTRODUCTION: Diabetes has emerged as the major public health problem in India. Genetic predisposition combined with changes in lifestyle, associated with urbanization and globalization contributes to this rapid rise of diabetes in India. Moreover type 2 diabetes in India occurs a decade earlier than the western population, thus affecting the productive youth of this country.^{1,2,3}

The real burden of the disease is due to its micro and macro vascular complications which lead to increased mortality and morbidity.⁴ Type 2 diabetes mellitus is the leading cause of end stage renal disease (ESRD). Asian Indians have shown an increased tendency towards development of end stage diabetic nephropathy. The early marker for diabetic nephropathy is microalbuminuria, which is also a risk factor for cardio vascular disease.⁴ Microalbuminuria is also associated with an increased prevalence of arterial hypertension, proliferative retinopathy and peripheral neuropathy.⁵ The development of microalbuminuria precedes the development of overt diabetic nephropathy by 10 to 15 years. It is at this stage that one can hope to reverse diabetic renal disease or prevent its progression. Thus it is an important warning sign for both the physician and the patient, which if ignored can lead to irreversible renal damage.⁵

So the aim of this study was to assess the occurrence of microalbuminuria in patients with type 2 diabetes mellitus and find out its association with the duration of the disease and HbA1c.

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METHODOLOGY: The study was conducted at Sri Siddhartha medical college hospital from October 2010 to April 2012. 100 patients over the age of 40 years, diagnosed of type 2 diabetes according to ADA criteria,⁶ were selected by systematic random sampling. Type 1 diabetes patients with macroalbuminuria or overt nephropathy, congestive cardiac failure, urinary tract infection, hematuria, patients confined to bed for more than 2 weeks, pregnant patients and patients with hypertension of more than 160/100 mm hg were excluded from study. A detailed history regarding onset and duration of diabetes, modality of treatment and the drugs and dosage, and also regularity of treatment was noted. A detailed clinical examination was done to note the presence of other complications of diabetes. Apart from the routine investigations, fasting and post prandial blood sugar, blood urea, serum creatinine, HbA1c, urine routine/ culture, ophthalmological evaluation for diabetic retinopathy, electrocardiogram were done.

Estimation of Microalbuminuria: Spot urine sample was collected from the patients and was tested for albuminuria by Microalbumin-turbidatex technique and the same sample was used to estimate urine creatinine by semi auto analyzer calorimetry. The diagnosis of microalbuminuria was done by calculating albumin creatinine ratio (ACR) of the spot urine sample. An albumin creatinine ratio of 30-300mcg/mg of creatinine from a spot urine collection was taken as presence of microalbuminuria,⁷ which has been shown to have a sensitivity of 83% and specificity of 100%.⁸

RESULTS: Out of the 100 patients in the study, 56 were males, and 44 were females. 29 patients were in the age group of 40-50years, 30 in 51-60years, 27 in 61-70years, 14 in >70years age group. The mean age of the patients was 59.01+/-11.62 years. 65 patients had diabetes of less than 5 years duration, 20 patients had diabetes for 6-10 years, 11 patients had 11-15 years of diabetes, and 4 patients had more than 15 years of diabetes. The mean duration of the disease was 5.88+/-4.56 years. Total number of patients who were on treatment with oral hypoglycemic agents (OHAs) were 79, 13 were on insulin, and 8 were on both OHAs and insulin. A total of 31 patients tested positive for microalbuminuria, and 69 tested negative. Out of these 31 patients, 18 were male and 13 were female. The age distribution is shown in table 1.

The association of duration of diabetes with occurrence of microalbuminuria is shown in table 2. Among the patients with less than 5 years of diabetes, 9 were positive for microalbuminuria, in 5 to 10 years group, 10 were positive, and in patients with 11-15 years of diabetes, 10 were positive, and in patients of > 15 years diabetes 3 were positive for microalbuminuria. This study showed that as the duration of diabetes increased, the percentage of patients with microalbuminuria also increased, and it was statistically significant ($p<0.001$).

The association of HbA1c with occurrence of microalbuminuria is shown in table 3. Among the 29 patients in whom HbA1c was <7%, only 3.4% was positive for microalbuminuria. In 55 patients with HbA1c between 7% and 8%, 30.9% were positive for microalbuminuria. And among 16 patients with HbA1c values >8%, 81.25% of patients had microalbuminuria. So with increasing values of HbA1c, or poor glycemic control, the percentage of patients with microalbuminuria also significantly increased ($p<0.001$).

The mean pattern of other laboratory parameters is shown in table 4.

DISCUSSION: The percentage of patients with microalbuminuria in the present study was 31%, which is similar to the previous studies. A study by Gupta et al showed 26.6% of patients with

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microalbuminuria, and another study by Patel et al had 28.65 % of the patients with microalbuminuria. The slightly higher percentage in this study is probably due to the fact that most patients were on irregular treatment.^{9,10}

Michael Siebels et al and Viberti GC et al showed that there was no association between albumin excretion rate and age and sex in type 2 diabetes mellitus patients^{11,12}. Present study also showed no statistical significance with age and sex. The reason for lower occurrence of microalbuminuria in patients with age >70 yrs could be that, there were few patients in this group, possibly because many were excluded due to the presence of comorbid conditions, or they had already developed macroalbuminuria. And most of these patients in our study group had duration of diabetes less than 5 years, and the 2 patients who were positive for microalbuminuria had > 15 years of disease.

Naz s et al, Patel et al showed that the frequency of microalbuminuria increased with the increase in duration of diabetes.^{10,13} The present study also showed that as the duration since diagnosis of diabetes increased, the percentage of patients with microalbuminuria increased, which was statistically significant.

As in previous studies, the frequency of occurrence of microalbuminuria was strongly associated with the rising HbA1c values. In this study, only 3.4% of the patients with HbA1c<7% had microalbuminuria, whereas, 81.25% of the patients with HbA1c >8% had microalbuminuria. Studies by Gupta et al and John et al also reported that incidence of microalbuminuria increased with increasing HbA1c values.^{9,14} suggesting that poor glycemic control is directly associated with the development of microalbuminuria which heralds the onset of diabetic nephropathy.

Finally 2 recent reports have shown further insight into the significance of microalbuminuria in type 2 diabetes mellitus. Haffner et al in a cross sectional study, and Mykannen et al in a prospective study have reported that microalbuminuria in non-diabetic individuals may precede or even predict the onset of type 2 diabetes mellitus.^{15,16} So microalbuminuria may be regarded as a prominent feature of prediabetic state and also a risk factor for cardiovascular disease. (Rutter et al, Hertzal et al, Wendy et al).^{17,18,19}

Therefore it can be concluded that microalbuminuria is an important early sign of diabetic nephropathy and its recognition helps in retarding the progression to overt nephropathy and good glycemic control is associated with lesser occurrence of microalbuminuria and therefore nephropathy.

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Clinical variables	Microalbuminuria		P value
	Absent (n=69)	Present (n=31)	
Age in years			
• 40-50 (n=29)	22(75.86%)	7(24.13%)	0.117
• 51-60 (n=30)	21(70%)	9(30%)	
• 61-70 (n=27)	14(51.8%)	13(48.1%)	
• >70 (n=14)	12(85.7%)	2(14.3%)	

Table 1: Age distribution of patients with microalbuminuria

Duration of DM in years	Absent (n=69)	Present (n=31)	P value
• 0-5 (n=65)	56(86.15%)	9(13.8%)	<0.001**
• 6-10 (n=20)	10(50%)	10(50%)	
• 11-15 (n=11)	1(9.09%)	10(90.9%)	
• >15 (n=4)	1(25%)	3(75%)	

Table 2: Showing Association of Duration of diabetes since diagnosis with the occurrence of microalbuminuria

HbA1c	Microalbuminuria			P value
	Absent(n=69)	Present(n=31)	Total	
• <7	28(96.5%)	1(3.5%)	29	<0.001**
• 7-8	38(69.1%)	17(30.9%)	55	
• >8	3(18.75%)	13(81.25%)	16	
Total			100	

Table 3: The association of HbA1c with occurrence of microalbuminuria

Variables	Microalbuminuria (Mean \pm SD)		P value
	Absent(n=69)	Present(n=31)	
Glucose parameter			
• FBS (mg/dl)	174.32 \pm 36.95	188.90 \pm 52.04	0.113
• PPBS (mg/dl)	249.33 \pm 50.06	270.97 \pm 63.67	0.070+
• HbA1C	7.12 \pm 0.46	7.87 \pm 0.57	<0.001**
Lipid parameters			
• Cholesterol (mg/dl)	178.48 \pm 34.12	177.67 \pm 22.34	0.789
• TGL(mg/dl)	151.48 \pm 57.57	156.90 \pm 51.59	0.654
• LDL(mg/dl)	121.29 \pm 21.31	117.77 \pm 14.99	0.408
• HDL (mg/dl)	32.74 \pm 4.69	34.67 \pm 19.19	0.430

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Renal Parameters			
• Blood urea(mg/dl)	24.98±4.80	29.73±10.07	0.784
• S Creatinine (mg/dl)	1.09±0.15	1.10±0.19	0.764

Table 4 : Mean pattern of other laboratory parameters of patients

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