

## Changes in Microalbuminuria in Relation to Glycosylated Haemoglobin(HbA1c) and Duration in Type 2 Diabetes Mellitus

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### Abstract

**Introduction :** Diabetes Mellitus is a widely prevalent endocrine disease in the world and Nephropathy is one of the major complications that could lead to severe morbidity and mortality. Persistent microalbuminuria is the best predictor of development of macroalbuminuria and further development of end-stage renal disease as well as cardiovascular complications. The relation between microalbuminuria and glycosylated haemoglobin(HbA1c) as well as duration of diabetes are not clear and studies relating these parameters are few in our country. This study aims to understand this aspect. **Aims & Objectives :** Our objective is to observe the changes in microalbuminuria level in relation to various parameters of patients of type 2 Diabetes mellitus and to

correlate the changes in microalbuminuria levels to HbA1c and duration of diabetes. **Materials and Methods :** The study was conducted in Medical College & Hospital, Kolkata. 40 patients of type 2 Diabetes mellitus fulfilling inclusion and exclusion criteria were included in this study. Results were analysed by SPSS software. **Results :** Microalbuminuria had positive correlation with BMI and Waist circumference (WC). No correlation was found between age and microalbuminuria. There was a significant and positive correlation found between microalbuminuria and duration of diabetes as well as microalbuminuria and HbA1c.

### Keywords

*type 2 diabetes mellitus, duration of type 2 diabetes mellitus, hba1c, microalbuminuria*

### Introduction

Diabetic Nephropathy has been divided into five distinct functional stages: the earliest being a stage of hyperfiltration and renomegaly and the most advanced being the end stage renal disease. The intervening stages are characterised by increasing urinary albumin excretion and decreasing glomerular filtration rate (GFR)<sup>1</sup>. Microalbuminuria is defined as detection of 30-300 mg of albumin in 24 hr urine collection or 30-300 mcg of albumin/mg creatinine in spot collection<sup>2</sup>. Persistent microalbuminuria is an independent predictor for progression of diabetic nephropathy<sup>3</sup> as well as an independent risk factor for cardiovascular disease<sup>4,5</sup>.

Diabetic Nephropathy remains a major cause of morbidity and mortality of persons with either type 1 or type 2 diabetes mellitus. It is estimated that 25% to 40% patients with type 1 diabetes mellitus and 5-40% patients with type 2 diabetes mellitus ultimately develop diabetic kidney disease. In cross sectional studies prevalence of microalbuminuria in type 2 diabetes mellitus is 10-42%, depending on population studied. In patients with type 2 diabetes mellitus microalbuminuria is associated with 2-4 fold increased risk of death<sup>8</sup>. Early diagnosis and treatment of microalbuminuria is an effective strategy for reduction of diabetic mortality and morbidity.

The natural history of diabetic nephropathy in patients with type 2 diabetes mellitus is less well understood than type 1 diabetes mellitus. The appearance of microalbuminuria in type 1 diabetes mellitus is a very important predictor of progression to overt proteinuria, when overt proteinuria is presented, 50% of these cases reach end-stage renal disease in 7-10 yrs. Although in type 2 diabetes mellitus persistent microalbuminuria or overt nephropathy may be present at the time of diagnosis of diabetes, in that cases it has been stated that the actual hyperglycemia was there for some time before diagnosis<sup>10</sup>.

It has been suggested that chronic hyperglycemia causes disorders of albumin excretion rate by inducing podocyte dysfunction and subsequent apoptosis ultimately leading to depletion of podocytes at the glomerular level<sup>11</sup>.

While epidemiological studies have evaluated factors (like hyperglycemia, duration of diabetes, age, sex, BMI) associated with the microalbuminuria in type 2 diabetes mellitus, the extent to which the interaction between these

factors and the likelihood of microalbuminuria occurs has not been widely explored<sup>12</sup>.

So, our aim is to study the changes in microalbuminuria level in relation to various parameters of diabetes with special reference to glycosylated haemoglobin and duration of diabetes and to determine correlation between microalbuminuria and glycosylated haemoglobin as well as between microalbuminuria and duration of diabetes.

### Materials and Methods

The study was carried out on 40 patients of type 2 diabetes mellitus who attended the Endocrine OPD from March 2010 to Feb 2011 in Medical College & Hospital, Kolkata, fulfilling inclusion and exclusion criteria. The patients aged between 30 and 60 years were included in this study and those with hypertension, urinary tract infection, congestive cardiac failure, severe anemia, renal failure and those on ACE inhibitor/ARB and Statin were excluded from the study.

**Methods :** Patients were evaluated by detailed history and thorough clinical examination. Informed consents were taken from the patients. 5ml of venous blood was collected from each of the subjects. The samples were centrifuged, separated and stored at 2-8°C until analysis. The blood samples were analysed for HbA1c, FPG, PPPG, serum urea and creatinine. HbA1c was measured by Affinity Chromatography method, plasma glucose by GOD-POD method. 24hr Urine samples were analysed for microalbumin by Immunoturbidometric method.

### Observations

The present study was carried out to see the changes in microalbuminuria level with special reference to glycemia and duration of diabetes in type 2 diabetes mellitus. 40 cases of type 2 diabetes mellitus fulfilling inclusion and exclusion criteria were included in the study.

The number of males were more in this study with a M:F of 1.3:1. The baseline characteristics of the patients were shown in **Table 1**. It showed that patients were mostly overweight-obese (mean BMI-28kg/m<sup>2</sup>) and they did not have good glycemic control (mean HbA1c-7.6%).

The correlation between microalbuminuria and various parameters were shown in the **Table 2**. It was evident from the table that microalbuminuria was positively correlated

**Table1**  
Baseline characteristics of the patients

	N	Minimum	Maximum	Mean	Std. Deviation
Age(yrs)	40	34.00	58.00	45.67	6.62
Duration(yrs)	40	.50	6.70	2.92	1.87
BMI(kg/m <sup>2</sup> )	40	23.40	32.60	28.18	1.98
Waist circum(cm)	40	86.00	110.00	94.62	5.95
W/H ratio	40	0.86	1.10	0.946	0.059
FPG(mg/dl)	40	87.00	223.00	140.42	39.06
PPPG(mg/dl)	40	112.00	334.00	204.48	70.20
Urea(mg/dl)	40	19.00	40.00	29.07	5.69
Creatinine(mg/dl)	40	.60	1.20	.88	.15
HbA1c(%)	40	5.80	11.90	7.64	1.30
Microalbuminuria(mg/24hr urine vol)	40	31.00	680.00	177.05	132.76

**Table 2**  
Correlation between microalbuminuria and various parameters

		Age	BMI	Waist circum	Duration	HbA1c
Microalbuminuria	Pearson Correlation	0.417**	0.808**	0.854**	0.638**	0.651**
	Sig. (2-tailed)	0.007	0.000	0.000	0.000	0.000
	N	40	40	40	40	40

with age, BMI and waist circumference. Also a good correlation was observed between microalbuminuria and glycosylated haemoglobin as well as microalbuminuria and duration of diabetes.

However, microalbuminuria was correlated with glycosylated haemoglobin level in a non-linear fashion and there was a sharp rise in 24hr urinary microalbumin excretion above the glycosylated haemoglobin level of 8% as it was evident from the **Graph 1**.

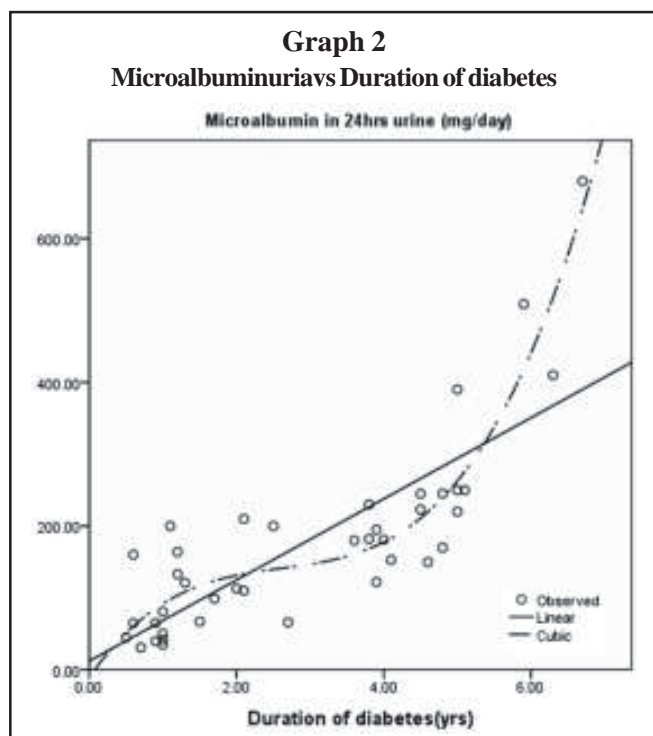
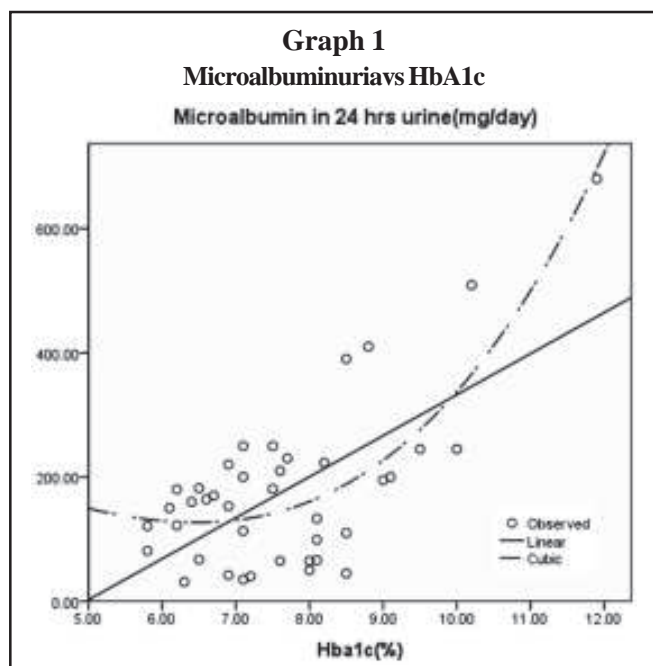
The present study showed that increased level of microalbuminuria was found with increased duration of diabetes. It has also been shown that above the duration of

4yrs, 24hr urinary albumin excretion rises sharply **Graph 2**.

### Discussion

In this study the mean value of urinary microalbumin was more in males compared with females as shown in other studies<sup>13</sup>, which may be because of more male patients were included in our study.

Significant correlation was found between microalbuminuria and age of the patients as compared to other studies<sup>14,15</sup> which show no correlation between the two. This may be because of more numbers of older patients were enrolled in our study.



It is evident that hyperglycemia is necessary for the initiation of renal injury, however intensive therapy designed to achieve improved glycemic control does not fully prevent urinary albumin excretion<sup>16</sup>. There are some evidences which showed that improved glucose control delays progression of microalbuminuria.

In the UKPDS (United Kingdom Prospective Diabetes Study), in the intensively managed group (HbA1c-7.1%) as opposed to conventionally treated group(HbA1c-7.9%) there was a reduction in the relative risk of developing microalbuminuria and proteinuria of approx. 30% after 9-12yrs<sup>17</sup>. For a 1% reduction in HbA1c,there was a 37% reduction in the risk of microvascular complications<sup>18</sup>. In the ADVANCE(Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation ) study intensive group (6.5%) compared to conventional group(HbA1c-7.3%) was associated with a 9% relative risk reduction in new onset microalbuminuria<sup>19</sup>.

In a small study of Japanese patients with type 2 diabetes mellitus, with normal urinary albumin excretion or microalbuminuria at baseline, the proportion of patients with worsening of nephropathy was significantly lower after 6-8 years of intensive glucose management<sup>20</sup>.

The present study also showed that patients with poor glycemic control as evidenced by higher HbA1c (particularly HbA1c>8%) had higher microalbumin excretion in urine. There was a significant positive correlation found between HbA1c and microalbuminuria<sup>17-20</sup>.

Diabetes duration is one of the strongest risk factor for nephropathy along with glycemic control, blood pressure and blood lipid levels<sup>21</sup>.

Incidence of proteinuria has doubled in Pima Indians in last 4 yrs despite good glycemic control and blood pressure (BP) control, probably because of increased survival and therefore duration of diabetes<sup>22</sup>.

The relationship of microalbuminuria to duration in type 2 diabetes mellitus is not as strong as in type 1. The rate of progression from normal urinary albumin excretion to microalbuminuria is 3-4% per annum<sup>23,24</sup>.

In the present study, a statistically significant positive correlation was found between the prevalence of microalbuminuria and duration of diabetes, which was consistent with the findings of past studies<sup>25,26</sup>. However, it has been shown in this study that above the duration of 4 years the correlation curve is more stiff indicating large change in microalbuminuria to a small change in the duration of diabetes. No such studies are available which showsuch an apparent duration cut off. This may be because of small number of patients having values of microalbuminuria

distributed over an wide area. But, it can be strongly said that more is the duration of diabetes more is the chance of increase in microalbumin excretion in urine. Studies have shown that duration of diabetes is a strong predictor for development of abnormal albuminuria in type 2 diabetes mellitus<sup>21</sup>. The present study also showed that duration of diabetes is a strong predictor of microalbuminuria.

### Conclusion

Increasing evidence points to an association between increased microalbumin excretion in urine and various parameters of cases of type 2 diabetes mellitus.

Though the studies relating microalbuminuria to HbA1c and duration of diabetes are there in other parts of world, but they are few in this country.

The present study shows significant positive correlation found between 24 hr urinary microalbumin levels and HbA1c in type 2 diabetes mellitus in our study, strengthening further the already observed association in some studies<sup>17-20</sup>.

Furthermore, it was found that with increasing duration of diabetes there was an increase in urinary microalbumin levels.

So, there are some modifiable factors like HbA1c, BMI, Waist Circumference, which can affect microalbuminuria in a significant way and if taken care early may prevent or reduce increased urinary albumin excretion and thereby further complications, morbidity and mortality.

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