



## STUDY OF MICROALBUMIN IN TYPE 2 DIABETES MELLITUS WITH LESS THAN AND MORE THAN FIVE YEARS OF DURATION.

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### ABSTRACT

Presence of microalbumin in type 2 diabetes mellitus patients is early sign of onset of microvascular complications which can damage various organs like heart, kidneys, eyes and nervous system. The principal aim of the study is to compare the microalbumin levels with duration of diabetes. The study was conducted in 30 diabetic subjects with less than 5 years of duration and more than 5 years of duration as controls and subjects respectively. Microalbuminuria was considered to be positive when 24 hrs urine sample contains 30 to 300mg /g of creatinine. Biochemical analysis was done using commercially available kit for plasma glucose (GOD-POD method), lipid profile - cholesterol by enzymatic method, triglycerides by glycerol kinase method, HDL by enzymatic method, VLDL and LDL by Friedwalds calculated method and Serum creatinine by Jaffes method. Microalbumin was measured using commercially available kit by immunoturbidimetric method. The mean fasting blood sugar, cholesterol, triglycerides and microalbumin levels are high in subjects compared to controls ( $p < 0.001$ ). Systolic blood pressure was also high in subjects compared to controls. The duration of diabetes also showed significant association with microalbumin levels ( $p < 0.001$ ).

**KEY WORDS:** Type 2 diabetes mellitus, microalbuminuria, lipid profile, diabetic nephropathy.



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## INTRODUCTION

Diabetic Nephropathy is the leading cause of end stage renal disease worldwide (1). One of the earliest markers of Diabetic Nephropathy is microalbuminuria (2). Microalbuminuria is considered to be a predictor of cardiovascular disease both among diabetic and non diabetic subjects (3, 4, 5). Studies on microalbumin levels are helpful to prevent early onset of nephropathy. Microalbuminuria, an early marker of diabetic nephropathy, is an independent risk factor for cardiovascular diseases. Microalbuminuria is defined as urinary albumin excretion rate of 30 to 300mg/d in a 24 hr urinary collection or urinary protein excretion rate of 30 to 300 mg/g of creatinine which predicts future development of overt nephropathy (6). Presence of microalbuminuria is the most important early signal heralding the onset of systemic vasculopathy and associated organ damage. Microalbuminuria also identifies patients who need more rigorous cardiovascular risk management, especially more intensive blood pressure control and strict attention to glycemic control and lipid levels (7). The causal risk factors for microalbuminuria are raised blood pressure and poor glycemic control resulting in hyperperfusion of glomerulus and glomerular filtration (8). Hyperglycemia, arterial hypertension and dyslipidemia causes disorders of the albumin excretion rate by damaging the podocytes and slit diaphragm protein scaffold with overproduction and extracellular release of oxygen radical species at the glomerular level (9). Male gender, old age, longer duration of diabetes, poor glycemic control and raised blood pressure are risk factors of microalbuminuria (10). Levels of HbA1C are also associated with microalbuminuria (11). Vijay et al reported duration of diabetes, systolic and diastolic blood pressure, age of the patient, serum creatinine are also associated with proteinuria (12). There are 3 major histological changes in glomeruli in diabetic nephropathy, includes: (1) Mesangial expansion (2) glomerular basement thickening and (3) glomerular sclerosis (13). Alterations in the molecular structure of components of

glomerulus and its basement membrane have also been suggested as primary pathogenic mechanism (14). The pathophysiologic mechanism of diabetic nephropathy includes glycosylation of circulating and intrarenal proteins, hypertension and abnormal intra-renal hemodynamics. The earliest demonstrable abnormalities include intra renal hypertension, hyperfiltration increased GFR and microalbuminuria (15). A reduction in negative charge of basement membrane secondary to decrease in sialic acid and sulphated proteoglycans has been suggested as the basis for proteinuria. The repulsive electrostatic interaction with negatively charged plasma proteins, such as albumin is reduced and so increased filtration of albumin may occur (16). Another possible causative mechanism is that alteration in glomerular filtration barrier at the podocyte level will cause leakage of albumin. Arterial hypertension and abnormalities of blood lipid concentrations are important complications of diabetes mellitus (17).

## METHODS

### *Patients*

Study group comprised of 30 T2DM patients with less than 5 years of duration as controls and 30 T2DM patients with more than 5yrs of duration as subjects. Study was conducted at Government Medical College, Tirupati. Informed consent was obtained from subjects after and controls who has participated in the study. Serum creatinine concentration within the normal range i.e 1.1 mg/dl in women and 1.2 mg/dl in men were selected for the study and patients with incomplete records, presence of urinary tract infection and presence of proteinuria were excluded from study. A fasting blood sample was drawn after an overnight fasting and analysis of plasma glucose, lipid profile and serum creatinine was done. 24hrs urine sample was collected to estimate urine microalbumin levels. Blood pressure was recorded in right upper arm in sitting posture. After five minutes of rest, patients blood

pressure was recorded and categorized as normotensives (120mm of Hg systolic and 80 mm of Hg of diastolic blood pressure) and hypertensives (>140mm of Hg systolic and >90 mm of Hg diastolic blood pressure). Biochemical analysis was done using commercially available kit for plasma glucose (GOD-POD) method, lipid profile - cholesterol by enzymatic method, triglycerides by glycerol kinase method, HDL by enzymatic method, VLDL and LDL by Friedwalds calculated method and Serum creatinine by Jaffes method. Microalbumin was measured using commercially available kit by immunoturbidimetric method (18). Data was expressed as mean±SD. Students 't' test (p value<0.05) was used to know the statistical significance.

## RESULTS

The study group comprised of 30T2DM patients with less than 5 yrs of duration as controls and 30T2DM with more than 5yrs of duration as subjects. Table 1 shows the biochemical characteristics of normo albuminuric and microalbuminuric patients. The subjects had a longer duration of diabetes compared with control group (p<0.001). Systolic blood pressure was significantly high in subjects when compared with the controls. Fasting plasma glucose was high in subjects compared with controls. Serum triglycerides and serum cholesterol were significantly high in subjects compared to controls. The level of microalbuminuria increased with increase in duration of diabetes (p<0.001). Systolic blood pressure, (p<0.001), fasting plasma glucose (p<0.01) and duration of diabetes (p<0.001) showed a significant association with microalbuminuria.

**Table 1**

***Shows comparison of biochemical characteristics of subjects and control group. Duration of diabetes, lipid profile and microalbuminuria were significantly higher in subjects when compared to control.***

Microalbumin	Mean S.D	subjects	controls	p value
Microalbumin	Mean S.D	39.4±15.6	27.7±9.85	<0.0001
FBS	Mean S.D	143±36	121±27.2	<0.01
TC	Mean S.D	231±27.4	199±25.9	<0.0001
TGL	Mean S.D	134±23.5	108±20.4	<0.0001
HDL	Mean S.D	33.1±5.76	35.3±4.15	0.1 NS
LDL	Mean S.D	137±35.5	125±30.8	0.1 NS
S.Creatinine	Mean S.D	1.31±0.434	1.17±0.424	0.19 NS
Years duration of	Mean S.D	8.43±2.87	2.23±1.39	<0.0001
S.B.P	Mean S.D	144±15.3	128±13.1	<0.0001
D.B.P	Mean S.D	88.2±9.73	81.1±7.66	<0.002

*p<0.001 is considered as statistically significant*

## DISCUSSION

Diabetic nephropathy is characterized by proteinuria and is the leading cause of end stage renal disease (18A). Microalbuminuria is the first clinical detectable sign of involvement of the kidney. Microalbuminuria is considered to be an early stage of diabetic nephropathy (19). In our study there was a significant association between duration of diabetes and microalbuminuria that was similar with the other studies (20, 21, 22, 22A). Poor glycemic control has been shown to be an independent risk factor for microalbuminuria. The association of glycemic control with microalbuminuria has been well established by various studies. A correlation of prevalence of microalbuminuria with the fasting blood sugar and with HbA1C levels were reported (23). In our study there was a rise in fasting blood sugar levels when compared to controls. Our study shows an increase in systolic blood pressure in subjects compared to controls. Both systolic and diastolic blood pressure were found to be increased in accordance to microalbuminuria (23). Huraib et al reported correlation between the prevalence of microalbuminuria and hypertension in his studies (24). Svensson et al showed that high blood pressure increased the risk of developing signs of nephropathy ( $p=0.003$ ). Hypertension in turn causes hypertensive nephropathy that can speed up progression of diabetic nephropathy (25). The microalbuminuria positive group (subjects) had more deranged lipid profile with higher serum

total cholesterol and triglycerides compared to controls. Several studies have shown that there are significant lipid abnormalities including high VLDL, LDL and triglycerides and low levels of HDL. Mather et al also reported a statistical significance between the presence of microalbuminuria and serum triglycerides (26). Smulders et al. reported that diabetic dyslipidemia (high serum triglycerides and low HDL) is a predictor of rapid progression of microalbuminuria in patients with well controlled blood pressure (27).

## CONCLUSION

Since there is high prevalence of diabetes in Indians with over 20 million diabetics already and expected to increase further in coming years, this will increase further morbidity and cost effectiveness in management of diabetes. Several factors contribute to diabetic nephropathy; most important among those are hyperglycemia and hypertension in diabetic population. Patients with microalbuminuria can revert back to normal with intensive blood glucose and Blood pressure control strategies, such as glycated hemoglobin below 7%, B.P 115/70mm of Hg and a strict lipid profile control. Screening should be done regularly to prevent microalbuminuria and thereby diabetic nephropathy.

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