MICROALBUMINURIA AS A MARKER OF CARDIOVASCULAR AND RENAL RISK IN TYPE II DIABETES MELLITUS

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ABSTRACT: AIM OF THE STUDY: With a global increase in the diabetes epidemic, it is inevitable that diabetic complications become a major issue in the future. Diabetic kidney disease is under diagnosed and under treated even now, when detection of early stages is simple. The earliest clinically detectable stage of Diabetic kidney disease is microalbuminuria. Microalbuminuria represents the earliest clinical evidence of diabetic nephropathy and it is a marker of increased cardiovascular morbidity and mortality. **STUDY DESIGN:** A cross sectional study was done during the period of March 2011 to November, 2011. The present study included fifty (50) patients of type 2 DM out of them, 23(46%) had microalbuminuria and 27(54%) are normoalbuminurics. The study also included 50 healthy control subjects who are age matched. The biochemical parameters studied were urine microalbumin, urine creatinine, Serum Total Cholesterol, serum Triglycerides, LDL, VLDL, HDL, Blood Urea, Serum creatinine. All the cases were segregated into 2 groups as cases with microalbuminuria and without microalbuminuria (based on urinary albumin level of 30-300µg/mg of Creatinine) **RESULTS:** As per the results obtained it is found that microalbumin /creatinine ratio is increased in microalbuminurics when compared to normoalbuminurics. In the present study microalbuminurics are overweight; (BMI = 23, overweight) and has increased diastolic blood pressure, Fasting blood glucose, serum creatinine, Triglycerides and VLDL than normoalbuminurics. **CONCLUSIONS:** Early detection of microalbuminuria allows the implementation of individualized and aggressive intervention programs to reduce renal and cardiovascular risk factors.

KEYWORDS: Microalbuminuria, Type 2 Diabetes Mellitus.

INTRODUCTION: Diabetes Mellitus (DM) had long been recognized as rapidly emerging global health problem that threatens to reach pandemic levels by 2030, the number of people with diabetes worldwide is projected to increase from 171 million in 2000 to 366 million by 2030.⁽¹⁾

Diabetes is a chronic illness that requires continuing medical care and on-going patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires many issues, beyond glycaemic control. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes.⁽²⁾ Cardiovascular death rates on the whole are either high or appear to be climbing in countries where diabetes is prevalent. The outlook for cardiovascular disease (CVD) is alarming when one considers the number of people with diabetes worldwide and that this is set to more than double by 2025 ⁽³⁾

In most people with glucose intolerance or type 2 diabetes, there is a multiple set of risk factors that commonly appear together, forming what is now known as the 'Metabolic Syndrome'. This 'clustering' of metabolic abnormalities that occur in the same individual appear to confer a substantial additional cardiovascular risk over and above the sum of the risk associated with each abnormality.^(4,5) However, even before levels of blood glucose are high enough for a person to be

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diagnosed with diabetes, hyperglycemia and related changes in blood lipids (increase in triglycerides and decrease in the 'good' cholesterol HDL-c) increase a person's risk of CVD. The more components of the metabolic syndrome that are evident, the higher is the cardiovascular mortality rate.⁽⁶⁾ Insulin resistance and central obesity are considered significant factors.^(7,8)

Diabetic nephropathy is the leading cause of kidney disease in patients starting renal replacement therapy and affects 40% of type 1 and type 2 diabetic patients. It increases the risk of death, mainly from cardiovascular causes, and is defined by increased urinary albumin excretion (UAE) in the absence of other renal diseases. Diabetic nephropathy is categorized into stages: Microalbuminuria (UAE >30 µg/mg and ≤300 µg/mg) and macro albuminuria (UAE ≥300 µg/mg).

Hyperglycaemia, increased blood pressure levels and genetic predisposition are the main risk factors for the development of diabetic nephropathy. Elevated serum lipids, smoking habits and the amount and origin of dietary protein also seem to play a role as risk factors.

Screening for Microalbuminuria should be performed yearly, starting 5 years after diagnosis in type 1 diabetes or earlier in the presence of puberty or poor metabolic control. In patients with type 2 diabetes, screening should be performed at diagnosis and yearly thereafter. Patients with micro- and macro albuminuria should undergo an evaluation regarding the presence of co morbid associations, especially retinopathy and macro vascular disease.

Achieving the best metabolic control (HbA1c <7%), treating hypertension (<130/80 mmHg or <125/75 mmHg if proteinuria >1.0 g/24 h and increased serum creatinine), using drugs with blockade effect on the rennin angiotensin aldosterone system and treating dyslipidaemia (LDL cholesterol <100 mg/dl) are effective strategies for preventing the development of microalbuminuria, in delaying the progression to more advanced stages of nephropathy and in reducing cardiovascular mortality in patients with type 1 and type 2 diabetes.⁽⁹⁾

MATERIALS AND METHODS: The present study was conducted on fifty (50) patients of type 2 DM in endocrinology department of King George Hospital, at Visakhapatnam during the period of March 2011-Nov 2011. Out of 50 cases, 23 are positive for microalbumin and 27 are negative for microalbumin. With a mean age and S.D of (53.17±11.08 vs. 52.03±9.7), 21 are males and 29 are females. The study also included fifty (50) healthy control subjects who are age matched with patients.

First voided morning urine sample was collected and urine microalbumin is estimated with Microalbumin-turbilatex method. With the same urine sample urinary creatinine was also estimated. Fasting blood sample was collected for lipid profile and blood sugar and in the same sample blood Urea and Serum creatinine were also been estimated. Same parameters (Urine microalbumin, urinary creatinine, serum lipid profile, blood sugar, blood Urea and Serum creatinine) are estimated in control group also. All parameters are analyzed immediately after collection of samples.

A detailed history was taken considering various risk factors for type 2 DM like duration of diabetes, BMI, family history of D. Mellitus, smoking, HTN, renal disease, cardiovascular disease and drug history from study group.

Inclusion Criteria: Patients clinically diagnosed to have type 2 DM were selected for the study.

Exclusion Criteria: Patients those who has already diagnosed to have renal and cardiovascular complications are excluded.

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The following investigations were performed:

1. Estimation of blood sugar (FBS), by GOD – POD Method.
2. Serum Total Cholesterol(TC), Triglycerides(TGs), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), and Very Low Density Lipoprotein (VLDL) cholesterol, by enzymatic methods.
3. Urine Microalbumin was estimated by using Latex Turbidimetry.
4. Urine creatinine, Serum creatinine by modified folin wu tungstic method.
5. Blood urea by Di acetyl monoxime method.
6. Results are expressed as Mean±S.D, data analysis was done using the statistical package for social sciences (SPSS) 16th version epi info 3.32.

RESULTS: The present study comprised 50 cases of type 2 diabetes mellitus. Out of which, 23 are positive for microalbumin and 27 are negative for microalbumin. And 50 healthy age matched controls are included. The Mean, S. D of age of microalbuminurics verses normoalbuminurics verses control groups are 53.17 ± 11.08 vs. 52.03 ± 9.7 vs. 44.10 ± 8.17 .

Sl. No.	Type of cases	No. of persons
1.	Total number of controls	50
2.	Total number of cases	50
3.	Cases with microalbuminuria	23
4.	Cases without microalbuminuria	27

Table 1: Distribution of cases and Controls

STUDY OF CONTROL GROUP (50):

Sl. No.	variable	MEAN	S.D
1.	AGE (yrs)	44.10	8.17
2.	BMI	21.72	1.92
3.	SBP (mm of Hg)	114	10.87
4.	DBP(mm of Hg)	74	7.28
5.	FBS (mg/dl)	83.00	10.20
6.	BLOOD UREA (mg/dl)	30.44	6.13
7.	S.CREATININE (mg/dl)	0.78	0.26
8.	TGS (mg/dl)	118.16	21.42
9.	TC (mg/dl)	181.2	23.72
10.	HDL (mg/dl)	44.8	7.40
11.	VLDL (mg/dl)	23.58	4.27
12.	LDL (mg/dl)	109.34	23.19
13.	M/C Ratio (µg/mg)	14.90	6.96

Table 2: Various Parameter Values Mean, S.D of Control Group

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The Mean, S.D of Age, BMI (body mass index), Blood pressure, Fasting blood sugar, Blood urea, serum creatinine, serum triglycerides, Serum total cholesterol, HDL, VLDL and LDL of control group are represented in table 2: they are within the established normal values.

STUDY OF TEST GROUP: (50)

Sl. No.	Variable	Mean $\pm$ S.D		p-value
		Microalbuminurics	Normoalbuminurics	
1	AGE	53.17 $\pm$ 11.08	52.03 $\pm$ 9.7	0.70;NS
2	BMI	27.47 $\pm$ 2.9	25.22 $\pm$ 4.3	0.04;S
3	SBP(mm of Hg)	133.73 $\pm$ 16.94	126.66 $\pm$ 16.17	0.13;NS
4	DBP(mm of Hg)	92.52 $\pm$ 6.8	78.88 $\pm$ 9.33	0.001;S
5	FBS(mg/dl)	205.47 $\pm$ 78.42	157.92 $\pm$ 63.87	0.02;S
6	BLOOD UREA(mg/dl)	38.56 $\pm$ 18.51	36.07 $\pm$ 16.97	0.62;NS
7	S.CREATININE(mg/dl)	1.2 $\pm$ 0.41	1 $\pm$ 0.39	0.01;S
8	TGS(mg/dl)	133.13 $\pm$ 109.91	85.85 $\pm$ 58.15	0.058;S
9	TC(mg/dl)	174.39 $\pm$ 54.31	170.29 $\pm$ 41.21	0.7;NS
10	HDL(mg/dl)	36.43 $\pm$ 13.56	39.88 $\pm$ 13.49	0.37;NS
11	VLDL(mg/dl)	37.73 $\pm$ 20.10	28.48 $\pm$ 12.07	0.05;S
12	LDL(mg/dl)	104.60 $\pm$ 45.68	102 $\pm$ 38.16	0.8;NS
13	M/C Ratio(μ g/mg)	66.47 $\pm$ 25.39	15.11 $\pm$ 6.9	<0.001;S

Table 3: various parameter values, Mean, S.D and P-values of Microalbuminurics (23) Verses normoalbuminurics (27)

BMI, DBP, FBS, S. Creatinine, T.Gs, VLDL, M/C Ratio are significantly increased in microalbuminurics than normoalbuminurics.

DISCUSSION: The present study was conducted on fifty (50) cases of type 2 DM. Out of them 21 are males and 29 are females. Clinical and biochemical characteristics of the normoalbuminuric and microalbuminurics are discussed below. The microalbuminurics were older and had a longer duration of diabetes compared with the normoalbuminuric group (p=0.03, S). The microalbuminurics had significantly increased diastolic blood pressure compared to normoalbuminurics (p<0.001).

The anthropometric profile included height, weight, Body Mass Index (BMI). Majority of the subjects were overweight or obese as indicated by their BMI (p=0.04, S). The subjects were categorized as overweight and obese on the basis of the Asia Pacific Classification (BMI = 23 overweight and BMI = 25 obese). Similar results were obtained in a similar study conducted by, A. Varghese et al,⁽¹³⁾ Muhammad yakoob et al.⁽¹¹⁾

Medical history information showed that overweight, obesity and hypertension were the most common associated risk factors seen in diabetics.

Microalbumin / creatinine ratio is increased in microalbuminurics when compared to normoalbuminurics, with Mean and S.D, [66.47 $\pm$ 25.39 verses 15.11 $\pm$ 6.9]; P<0.001; S. In the present study we found that 46% of the diabetic patients had microalbuminuria. The high prevalence of

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microalbuminuria observed in, tertiary care hospital of ours is alarming. Benjamin et al⁽¹⁰⁾ in their study, found that 43.1% of the diabetic patients had microalbuminuria.

Fasting plasma glucose concentrations were significantly higher in the microalbuminurics compared with the normoalbuminuric (p=0.02, S). Similar results were obtained in a similar study conducted by, A. Varghese et al.⁽¹³⁾ (p<0.001)

Serum creatinine (p=0.01, S) values were found to be significantly higher in the microalbuminurics group. Similar results were obtained in a similar study conducted by, A. Varghese et al,⁽¹³⁾ Muhammad Baig et al,⁽¹²⁾ Benjamin A. Eghan et al.⁽¹⁰⁾

In the present study there is statistically significant increase in Triglycerides (p-value: 0.058) and VLDL (p-value: 0.05) in microalbuminurics when compared to normoalbuminurics. Results obtained in other studies were, Ramachandran A et al,⁽¹⁵⁾ p-value:0.007, in his study there is statistically significant elevation of Total. Cholesterol; A Varghese et al - p- value Not Significant for Total. Cholesterol, Triglycerides, HDL,⁽¹³⁾ Muhammad Yakoob Ahmedani et al –there is elevation of Total. Cholesterol, Triglycerides, LDL and decreased HDL,⁽¹¹⁾ Benjamin A. Eghan et al –there is increased Triglycerides,⁽¹⁰⁾ M. Afkhami-Ardekani et al- p-value not Significant for Total Cholesterol, Triglycerides.⁽¹⁴⁾

SUMMARY: There is generally a long lag time between the initiation of atherogenesis and the first cardiac event, which provides an opportunity to intervene with preventive therapy in insulin resistance. As insulin resistance and diabetes become more prevalent, its complications loom threateningly on the horizon of these patients.

The pathophysiology of insulin resistance and diabetes related vascular disease likely begins before the diagnosis of type 2 diabetes mellitus. Inflammatory markers begin to increase with the presence of visceral obesity. Microalbuminuria is another marker of endothelial dysfunction, which may occur with early cardiovascular and renal disease. Understanding these issues is critical to prevent mortality from cardiovascular and renal disease in diabetes, especially young adults with type 2 diabetes mellitus.

There is a dire need that microalbuminuria testing should be done in both newly diagnosed as well as already diagnosed type 2 diabetic patients as an early marker of cardiovascular and renal risk factor. Strict glycemic control, having a healthy life style, maintaining standard body weight is especially important for diabetic patients and for those with a family history of diabetes.

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