Prevalence of Microalbuminuria in Newly Diagnosed Type 2 Diabetes Mellitus

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Abstracts: Background: Studies in the western literature show a linear relationship between degree of microalbuminuria and body mass index (BMI), blood pressure, and duration of diabetes. Aims and Objectives: This study was aimed to determine the prevalence of microalbuminuria in newly diagnosed type 2 diabetes mellitus and its association with age, sex, body mass index, serum creatinine level and development of diabetic retinopathy in Indian population. Materials and Methods: Sixty one (35 males and 26 females) with newly diagnosed type 2 diabetes mellitus of duration of six months and negative for albumin in urine by albustic method were included in study. Detailed clinical history was taken followed by a thorough physical examination that included neurological examination and fundoscopic examination. Micral test was used for estimation of microalbuminuria. Results: Overall prevalence of microalbuminuria in the present study is 54.09%. Among the patients with microalbuminuria, 24 males and 9 were females. Pearson correlation of microalbuminuria with age showed statisestically significant linear relationship. Gender-wise correlation analysis of microalbuminuria show statistical significant high prevalence of microalbuminuria in male. Correlation of microalbuminuria with body mass index was not significant ($p>0.05$). Serum creatinine is also not correlated with microalbuminuria statistically. Incidence of microalbuminuria increases with age as well as with increased duration of diabetes mellitus. There is no effect of body mass index on the prevalence of microalbuminuria. Development of changes of diabetic retinopathy is associated with microalbuminuria and this correlation is statistically significant ($p<0.05$). Conclusion: Microalbuminuria occurs commonly in newly diagnosed type 2 diabetics and it is associated with development of diabetic retinopathy. Screening for this associated factor of diabetic nephropathy is recommended as a routine in all newly diagnosed type 2 diabetic patients to prevent further renal damage. Our finding supports routine screening for microalbuminuria as part of the initial evaluation of these patients. [Thakkar et al NJIRM 2011; 2(4) : 22-25]

Key Words: Microalbuminuria, diabetes mellitus, blood pressure, obesity, retinopathy

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Introduction: The term microalbuminuria is defined by a urinary albumin excretion (UAE) rate higher than normal but lowers than 200 µg/min, the lowest detection limit of proteinuria as measured by standard laboratory methods [1,2] n the absence of urinary tract infection and acute illness including myocardial infarction. [3] Albumin excretion in healthy individuals ranges from 1.5-20 µg/ min. [4] The presence of microalbuminuria precedes the development of overt diabetic nephropathy by 10-14 years. It is at this stage that one can hope to reverse diabetic nephropathy or prevent its progression. Therapeutic interventions which reverse microalbuminuria include intensified glycemic control, use of ACE inhibitors, etc. A diagnosis of microalbuminuria can be made by measuring its excretion rate during 24 hours or in an overnight urine collection, or by measuring albumin/creatinine ratio or albumin concentration in the morning or a random urine sample. Determination of UAE in the morning urine sample constitutes the ideal test for screening, and overnight urine collection might be the best choice for monitoring microalbuminuria. [1] In type-2 diabetes mellitus prevalence of microalbuminuria ranges from 8-47%. [8,9] Microalbuminuria is the strong predictor of diabetic nephropathy, which is the main cause of morbidity and mortality in patients with diabetes mellitus. Microalbuminuria is also characterized by increased prevalence of arterial hypertension, proliferative retinopathy, and peripheral neuropathy. Studies in the Western literature have documented the linear relationship of degree of microalbuminuria with body mass index (BMI), blood pressure, and duration of diabetes. Gender correlation of microalbuminuria was not seen in type-2 diabetes mellitus. [10,11] This study was aimed to determine the prevalence of

microalbuminuria in newly diagnosed type-2 diabetic patients and to evaluate the relation between microalbuminuria and age, sex, body mass index, and Serum creatinine level.

Material and Methods: This cross-sectional prospective observational study was carried out between January 2009 and June 2010, to investigate the correlation between microalbuminuria and assumed risk factors. Study was approved by the institutional ethics committee and written informed consent was taken from all the patients. Patients visiting our outpatient unit were screened for eligibility into the study. Sixty one patients with type-2 diabetes mellitus of recently diagnosed and of duration six months or more and negative for albumin in urine by albustic method were included in the study. Patients with overt albuminuria (>350 mg/day), congestive cardiac failure, urinary tract infection, pregnant patients, patients confined to bed for more than two weeks, and patients on ACE inhibitors for hypertension were excluded from the study. Other causes for microalbuminuria like heavy metal poisoning, connective tissue disorders, and chronic NSAIDs use were also ruled out in the selected patients. The selected patients were studied in detail with history and physical examination, including detailed neurological examination, fundoscopic examination. Body mass index (BMI) was calculated from the height and weight measurements of the patients. Routine investigations including serum creatinine were done in all the selected patients. In the present study, micral test was used for estimation of microalbuminuria (Roche diagnostic India pvt. Ltd., GERMANY). The micral test is a test-strip method in which the colour reaction is mediated by an antibody-bound enzyme. [1] This method has shown good correlations with radioimmunoassay and can be readily used for screening. All patients were afebrile during the collection of urine. Urine was first tested for albumin by Combistix-SG (Siemens health care diagnostic ltd.). Only those patients who were negative for albumin in urine by Combistix-SG method were included in this study. First morning mid-stream urine sample was collected in sterile container. Test strip was immersed in urine such that the fluid level was between two black bars. Strip was withdrawn after five seconds. Strip was placed horizontally across the urine vessel and the colour change in test zone was compared with colour scale after one minute. Sensitivity of the kit is 0.4 ng/ml and the measuring range is 0.8-10 ng/ ml. Microalbuminuria was graded as mild (20 mg/L), moderate (50 mg/L), or severe (100 mg/L) depending on the colour change in the strip. Test was repeated twice for selecting the patients into The study.

Statistical analysis : Data collected were analyzed by student's ' t ' test or chi- square test as appropriate. Pearson correlation test was used to analyze the correlation of microalbuminuria with independent variables like age, sex, BMI, duration of diabetes, and Serum creatinine. Probability (P) value Less than 0.05 was regarded as statistically significant.

Result: A total of 61 patients, 35 males and 26 females, were included in the study. Overall prevalence of microalbuminuria in the present study was 54.09%. Among the patients with microalbuminuria, 24 (68.5%) were males and **9 (34.61%)** were females. Among 33 microalbuminuric patients, 5 patients had mild albuminuria, 23 had moderate albuminuria, and 5 had severe albuminuria. Baseline characteristics of the patients are shown in **(Table 1).**

Table 1: Baseline characteristics of the patients

Variables	All patients	Range	Micro-albuminuric patients (n=33)	Normo-albuminuric patients(n=28)	p-value
Sex (M/F)	35/26		24/9	11/17	
Mean age(at years)	50.80±10.75	39-85	61.91±9.16	48.61±7.6	<0.001
BMI	24.36±4.45	16-33	24.33±4.0	24.39±4.9	0.95
Fasting blood sugar	164.3±51.7	110-459	192.58±55.6	131.00±12.47	<0.001
S. Creatinine (mg/dl)	0.84±0.26	0.5-2.5	0.93±0.32	0.74±0.09	0.61
Retinopathy	23		23	0	<0.001
Neuropathy	8		7	1	<0.001

Age of patients at diagnosis ranged between 39-75 years. Mean age at onset of diabetes mellitus in microalbuminuric patients was 61.9 ± 9.1 years and in normoalbuminuric patients it was 48.6 ± 7.6 years. The difference between the two groups was statistically significant. Gender-wise comparisons of baseline characteristics are shown in **(Table 2)**

Table-2 Gender-wise comparison of baseline characteristics

Variable	Male	Female	P-Value
Mean Age (Yrs)	**59.0**	**51.5**	**0.006**
BMI	**25.03**	**23.46**	**0.176**
S. Creatinine (mg/dl)	**0.88**	**0.79**	**0.09**
Fast. Bl. Glucose (mg/dl)	**170.14**	**156.46**	**0.311**
Retinopathy	**10**	**13**	**0.008**
Neuropathy	**4**	**4**	**0.07**

There was statistically significant difference in Serum creatinine between males and females. 10 patients had BMI ≥30 kg/m^2, among them five had microalbuminuria (15.15%) and five had normoalbuminuric (17.85%). Mean BMI of microalbuminuric patients was 24.33 ± 4.0.9 kg/m^2 and for normoalbuminuric patients it was 24.39 ± 4.9 kg/m^2. The difference between the groups was not statistically significant. Among the 61 patients, 51 were only on oral hypoglycaemic agents, 3 were on insulin, and 7 were on both insulin and oral hypoglycemic agents. Among microalbuminuric patients 17 had severe diabetes, 12 had moderate diabetes, and 4 had mild diabetes. Among the normoalbuminuric patients, 4 had severe diabetes, 18 had moderate diabetes, and 6 had mild diabetes. Average fasting blood sugar was 192.5 ± 55.6 mg/dl in microalbuminuric patients which was higher than normoalbuminuric patients (131.0 ± 12.4 mg/dl). Relationship between severity of diabetes and microalbuminuria was significant. About 69.6% newly diagnosed type II diabetic patients who are microalbuminuric, shows changes of diabetic retinopathy on fundoscopy and this association is statistically significant ($p<0.001$).

Discussion: This cross-sectional study presents data on prevalence and association of microalbuminuria with various parameters in type-2 diabetes mellitus. Present study has shown prevalence of microalbuminuria in newly diagnosed diabetic patient is 54.09**%,** which is much higher when compared to the study by Ghai et al[4] , where prevalence was reported at 25% [5]But another study in nigeria by Unuigbe et al who observed microalbuminuria in 50% of newly diabetic cases.[6]other study from Multan(Pakistan), by Khan et al shows prevalence of 30%.[7] Higher prevalence in the present study may be due to the fact that most of the patients were on irregular treatment with poor glycemic control . Method of estimation of microalbuminuria as well as ethnical differences would have also played a role in giving higher prevalence in the present study. The level of glycemic control seems to be the strongest factor influencing transition from normoalbuminuria to microalbuminuria.

Our study shows gender-wise correlation of microalbuminuria, which is male dominance in the prevalence of microalbuminuria. As reported in many studies, our study failed to show any correlation between BMI and microalbuminuria.[10,11] This may be due to the confounding variables like duration of diabetes and glycemic control that would have played a major role in the occurrence of microalbuminuria.

Serum creatinine was within normal range in all the patients. Diabetic nephropathy can conveniently be categorized into different stages with respect to renal hemodynamic, systemic blood pressure, urinary findings, and susceptibility to therapeutic interventions. In the initial renal hyperperfusion stage, glomerular filtration is elevated with absent albuminuria. In the second stage (clinical latency) glomerular filtration will be high normal with absent albuminuria. Next stage is incipient nephropathy, wherein glomerular filtration will be normal with presence of microalbuminuria. It usually appears 5-15 years after the diagnosis of diabetes mellitus. In the subsequent stage, glomerular filtration decreases with appearance of macroproteinuria and clinical manifestations of nephropathy. Finally ends up in end stage renal disease with massive albuminuria and diminished glomerular filtration. [12] Hence microalbuminuria may not be associated with abnormal serum creatinine, but can be an important warning signal which if ignored can result in irreversible renal damage.

Limitations of the present study must also be considered. As our study was not based on the general population, selection bias might have affected the outcome of the study. Larger sample size in general population may be required to confirm the results of the present study.

our study has found higher prevalence of microalbuminuria (54.09%.) in newly diagnosed type-2 diabetes mellitus, which is the predictor of later development of diabetic nephropathy. Incidence of microalbuminuria increases with age as well as with increased duration of diabetes mellitus. There is no effect of BMI on the prevalence of microalbuminuria in type-2 diabetes mellitus. Results of our study confirm and extend the previous observations in small selected groups of patients with type-2 diabetes mellitus. Serum Creatinine will be within normal range in microalbuminuric patients. But the presence of microalbuminuria alerts the physician to prevent further renal damage by timely administration of ACE inhibitors and correction of risk factors. Urinary excretion of albumin should be monitored routinely in patients with diabetes mellitus.

Conclusion: Microalbuminuria occurs commonly in newly diagnosed diabetics and its development is associated with development of diabetic retinopathy. Screening for this associated factor of diabetic nephropathy is recommended as a routine in all newly diagnosed diabetics. Our finding supports routine screening for microalbuminuria as part of the initial evaluation of these patients.

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