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MICROALBUMINURIA IN TYPE 2 DIABETES MELLITUS: ASSOCIATION WITH AGE, SEX, BMI, HBA1C, LIPID PROFILE AND COMPLICATIONS

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ABSTRACT

Microalbuminuria predicts overt renal disease in diabetes mellitusand it is also associated with increased morbidity and mortality. In non-insulin-dependent diabetes mellitus, microalbuminuria is quite common (20 to 40 percent of patients) in both newly diagnosed patients and patients with established diabetes. This study was aimed to correlate cases of microalbuminuria with glycosylated haemoglobin (HbA_{1C}), lipid profile, and duration since diagnosis, age, sex, and associated complications like Ischaemic heart disease, Hypertension, Retinopathy, Neuropathy among proven Type2 Diabetes Mellitus cases in Indian population.
We concluded that there was significant correlation of microalbuminuria with duration since diagnosis i.e, first 0-5 yrs of Type 2 Diabetes Mellitus, Body mass index ≥ 25, HbA1 smaller than 7%, total cholesterol >200mg/dl, serum triglycerides >150mg/dl, LDL >100 mg/dl, hypertension, Ischaemic heart diseases and retinopathy thus proving the association of microalbuminuria with early onset inType2 Diabetes Mellitus population, with poor glycemic control, with retinopathy, cardiovascular risk factors like dyslipidemia, obesity and hypertension.

Keywords: Microalbuminuria, Type2 Diabetes Mellitus, Albuminuria, NIDDM,

INTRODUCTION

Type 2 diabetes mellitus is a worldwide public health concern and an important cause of morbidity and mortality. Through lifelong vascular complications, diabetes leads to excessive rates of myocardial infarction, stroke, renal failure, blindness and amputations. The projections of its future impact are alarming. According to the World Health Organization, diabetes affects more than 170 million people worldwide, and this number will rise to 370 million by 2030 [1].

Microalbuminuria refers to the excretion of albumin in the urine at a rate that exceeds normal limits but is less than the detection level for traditional dipstick methods [2]. The normal rate of albumin excretion is less than 30 mg/day (20µg/min); persistent albumin excretion between 30 and 300 mg/day (20 to 200 µg/min) is called microalbuminuria. Values above 300 mg/day (200 µg/min) are considered to represent overt proteinuria. Although the 24-hours urine collection was previously the gold standard for the detection of microalbuminuria [3]. The effect of volume can be avoided entirely by calculation of the albumin-to-creatinine ratio in an untimed urine specimen. A value above 30 mg/g (or 0.03 mg/mg) suggests that albumin excretion is above 30 mg/day and therefore that microalbuminuria is probably present [4]

Type 2 Diabetes known as Non-Insulin Dependent Diabetes (NIDDM) accounts for 85 to 95% of patients with Diabetes in various populations of the world. Diabetic nephropathy is the leading cause of End Stage Renal Disease [5]. The earliest manifestation of diabetic nephropathy is the appearance of microalbuminuria [6]. The progression of the disease culminates in renal changes with microalbuminuria (incipient nephropathy) and macroalbuminuria (overt nephropathy). Albumin excretion rate is elevated years before reduction in Glomerular Filtration Rate [7].Prompt recognition and intervention can delay the progression of the disease.

METHODS

This cross-sectional prospective studywas carried out in 2015, toinvestigate the correlation between cases of microalbuminuria with glycosylated haemoglobin (HbA_{1C}), lipid profile, duration since diagnosis, age, sex, and associated complications like Ischaemic heart disease, Hypertension, Retinopathy, Neuropathy among proven Type2 Diabetes Mellitus cases. Study was approved by theinstitutional ethics committee and informedconsent was taken from all the patients. Patients admitted inour Indoordepartment were screened for eligibility into thestudy. Hundred patients with proven type-2 diabetes mellituswere included inthe study.

Patients with Renal glycosuria, Alimentary glycosuria, congestive cardiac failure, urinary tract infection, hematuria, intake of Vitamin B-complex, Jaundice, urinary antiseptic, Hypertensive with taking angiotensin converting enzyme (ACE) inhibitors or Angiotensin receptor blockers (ARBs) drugs were excluded from study to minimize effect on microalbuminuria. Theselected patients were studied in detail with history andphysical examination, including detailed neurologicalexamination. Body mass index (BMI) was calculated fromthe height and weight measurements of the patients.Routine investing ations including serum urea and creatinine weredone in all the selected patients.In the present study, DxUrilyzer was used for estimationof microalbuminuria (Piramal HealthcareLtd.) forscreening.For other tests(like serum glucose, lipid profile, Urine creatinine, microabumin) Miura 200 fully automated clinical chemistery analyzer was used.
First morning mid-stream urine sample wascollected in sterile container. Urine was first tested for albumin by Dx urine test 11. Test strip was immersed inurine for five seconds. Strip wasplaced horizontally across the urine vessel and the colorchange in test zone was compared with color scale afterone minute. The strip was read between 1-2 minutes after dipping on a automated urine analyzer (Dxurilyzer) and results were noted.

Urine albumin / creatinine ratio was calculated by dividing urine albumin in milligram through urine creatinine in gram. Then albuminuria were further group edinto three broad categories as Normoalbuminurics (<30mg/g of creatinine),Microalbuminurics(30-299 mg/g of creatinine)and Macroalbuminurics(>300 mg/g of creatinine).

Statistical analysis

Results were subjected for appropriate statistical analysis. Levels of albuminuria were correlated with age, gender, duration since diagnosis, Lipid profile and associated complications.. Univariate analysis was done for Categorical data using chi-square test. Multivariate analysis was done continuous variable for with unpairedstudent t test to know effect of different variables on microalbuminuria with microalbuminuria as a dependent variable. Probability (P) value less than 0.05 was regarded as statisticallysignificant.

RESULTS

A total of 100 patients were included in the study in which 56 males and 44 females. Overall prevalence ofmicroalbuminuria in the present study was 32%. Amongthe patients with microalbuminuria, 17 (53.1%) were males and 15 (46.9%) were females. Among Normo albuminuria (54.3%), microalbuminuria (53.1%) and Macro albuminuria (63.6%), male patients were higher than female patients.Gender-wise correlation analysis of microalbuminuria was not significant (*P = 0.762*).

Age of patient's atdiagnosis ranged between 30–80 years. Mean age atonset of diabetes mellitus in microalbuminuric patients was 60.2± 12.1 years and in normoalbuminuric patient sit was 58.5 ±12.6 years. The age group from 61-70 years showed maximum percentage of microalbuminuria (37.5%) and 51-60 years group showed maximum number of macro albuminuria cases (36.4%). The difference between the two groups was statistically not significant (*P value 0.358*).

Maximum number of patients (57%) had duration since diagnosis of diabetes between 0-5 years. Among the microalbuminuria cases 20 (62.5%) of cases are presented in the 0-5 years duration since diagnosis of diabetes followed by 8 in the 6-10 years, 3 in the 11-15 years and 1 in the >15 years since diagnosis of type 2 diabetes mellitus. Among microalbuminuria cases, 45.5% of cases were presented in the 0-5 years since diagnosis followed by 36.4% in the 6-10 year's duration. Mean duration of diabetes in microalbuminuric patients was 5.02+4.85 years while in normoalbuminuric patients it was 4.10± 3.17years. Most of the patients were detected with microalbuminuria in the first few years of the disease i.e 0-5y period. There was significant correlation of microalbuminuria with first 5years since diagnosis.

Maximum (42% cases) were in the category of obese (BMI≥ 30 kg/m2) followed by 37% cases were normal BMI (25.0–29.9 kg/m2) and then 21% cases were overweight (25.0–29.9 kg/m2) BMI category. The percentage of microalbuminuria is more in the obese and the overweight BMI categories (total 75%) when compared to microalbuminuria in normal BMI category (only 25% cases). The difference between the groups was statistically significant (P value 0.017).

Based on the glycemic control they were divided into those with HbA1c less than 7 and those with HbA1c equal to or more than7%. In the present study, there was significant correlation of microalbuminuria withHbA1c >7% group (p=0.0005). (Table 1)

Lipid Profile (Serum Total cholesterol, Serum Triglyceride, LDL) showed positive correlation with microalbuminuria but not with high Serum VLDL and low serum HDL levels. (Table 1)

Table 1: Association between different variables and albuminuria in Type2 Diabetes Mellitus

Variable	Normo-albuminuria		Micro-albuminuria		Macro-albuminuria		P Value
	% cases	Mean	% cases	Mean	% cases	Mean mg/dl	
HbA1c>7%	52.2	7.2±1.2	84.4	8.2 ±1.2	81.2	8.7 ±1.8	*0.0005*
Cholesterol (>200 mg/dl)	23.9	187±21.8 mg/dl	58.1	200.7±23.2 mg/dl	54.5	197±18.5 mg/dl	*0.0095*
Triglyceride (>150 mg/dl)	21.7	139.3 ±19.7 mg/dl	65.6	152.1±27.1 mg/dl	59.1	152.5±37.8 mg/dl	*0.0181*
HDL(<35 mg/dl)	15.2	41.7 ±4.5 mg/dl	15.6	40.3±4.3 mg/dl	22.7	40±5.2 mg/dl	*0.1728*
LDL(>100mg/dl)	56.5	109 ±22.5 mg/dl	87.5	119.6±20.5 mg/dl	90.9	118.9±19.5 mg/dl	*0.0371*
VLDL(>50mg/dl)	4.3	29.8 ±8.2 mg/dl	15.6	31.2±10.8 mg/dl	9.1	28.6±10.4 mg/dl	*0.5173*

Among100 cases 23 cases had neuropathy. The cases with neuropathy had more percentage of microalbuminuria (39.2%) when compared the cases of microalbuminuria withoutneuropathy (29.9%). The difference between the groups was statistically not significant (*P value 0. 0.0895*)

Among 100 cases15 cases had IHD, 46.7% of the cases with IHD were microalbuminuria cases and only 29.4% of the cases were microalbuminuric in those without IHD. The difference between the groups was statistically significant (*P value 0. 0.0285*)

Among total 100 cases 39 cases had retinopathy. Microalbuminuria cases were 46.2% among those with retinopathy as compared to only 23.0% of the cases in those without retinopathy. The difference between the groups was statistically significant (*P value <0.0001*)

Among 100 cases, hypertension was present in 42 cases and 42.5% of the cases with hypertension had microalbuminuria while only 25% of the cases without hypertension were microalbuminuric. The difference between the groups was statistically significant (*P value 0. 0.033*).

Among 100 cases, dermatopathy was present in 18 cases and 44.5 of the cases with dermatopathy had microalbuminuria while only 29.3% of the cases without dermatopathy were microalbuminuric. The difference between the groups was not statistically significant (*P value 0. 0.238*).

Urine analysis: physical analysis: Colour-In 76 cases the samples showed colorless urine, 19 cases showed yellow urine, 4 cases showed cloudy urine, 1 case showed yellow orange urine. dour- In 98 cases the samples had ammonicalodour and in 2 cases the samples had fruity odour.

Chemical analysis

Urine analysis by using 11 parameter chemical reagent strips- Multistiks (Dx Urine analyzer 11) showed the following results (Table 2) :

Table 2: Results of urine analysis by using 11 parameter chemical reagent strips

PARAMETER	NO.OFPOSITIVE CASES
Urobilinogen	0
Bilirubin	0
Blood	0
Ketones	7
Protein	56
Microalbumin	35
Nitrite	0
Leucocytes	0
Glucose	61
Specificgravity	100 (mean=1.0165±0.003)
pH 7	3
AcidicpH	87
AlkalinepH	10

Among 88 Protein positive cases, 30 cases had 1+ (0.3g/l) positivity, 22 cases had 2+ (1g/l) positivity and 4 cases had 3+ (3g/l) positivity. Among 109 Glucose positive cases 33 cases had 1+ (0.1g%) positivity, 19 cases had 2+ (0.25g%) positivity, 8 cases had3 + (0.5g%) positivity and 1 case had 4 + (1.0g%) positivity. Urine microscopy revealed 18 cases with hyaline casts, 3 cases with fatty cast, 3 cases with granular cast and 2 cases had both hyaline and granular casts. 6caseswithcholesterolcrystals, 5 cases with triple phosphate crystals, 6 cases with calcium oxalate crystals and4 cases with uric acid.

DISCUSSION

This cross-sectional study presents data on prevalenceand associations of microalbuminuria with variousparameters in type-2 diabetes mellitus. Present study hasshown prevalence of microalbuminuria at 32%, whichis comparable to the various studies like Schmitz et al [8] (30%), Gall et al [9] (27%), Olivarius et al [10] (30%), Ghai et al [11] (25%), Alazid et al [12] (36%), Dasmahapatra et al [13] 31%. Some variation in prevalence may be due to irregular treatment, ethnical differences, method of estimation of microalbuminuria and variablesample size.

Our study has not shown relationship of degree of albuminuria with age and gender-wise correlation of microalbuminuria, which is in contrast to the Earlier studies have also shown positive correlation of microalbuminuria with age of the patients [14,15] and have reported male

dominance in the prevalence of microalbuminuria. However male patient have higher prevalence of microalbuminuria but it was not statically significant. As reported in many studies [9,12], our study showed correlation between BMI and microalbuminuria.

The level of glycemic control seems to be the strongestfactor influencing transition from normo albuminuria to microalbuminuria. Like other studies [8,9]have showed associations between poor glycemic control and microalbuminuria, our study also showed significant correlation of microalbuminuria withHbA1c > 7%.

A higher proportion of individuals with type 2 diabetes are found to have microalbuminuria and overt nephropathy shortly after the diagnosis of their diabetes because diabetes is actually present for many years before the diagnosis is made and also because the presence of albuminuria may be less specific for the presence of diabetic nephropathy as shown by the biopsy studies.[16]In our study most of the patients were detected with microalbuminuria in the first few years of the disease i.e 0-5 yr period. Our study was showed significant correlation of microalbuminuria with first 5 years since diagnosis.

Like other study [17], our study also showed significant more prevalence of dyslipidemia NIDDM cases. Our study also showed significant correlation of microalbuminuria with High serum cholesterol, Triglyceride, LDL. A study [18, 19] showed significant correlation High serum cholesterol and microalbuminuria but no correlation found with factors. A study [19] also found correlation of microalbuminuria with Cholesterol, LDL and triglyceride. These variations may be due to small study population and other confounding factors like hypertension, obesity.

Patient of NIDDM may be associated many acute and long term complications. We studied association of microalbuminuria in NIDDM with complications. As in other study [20]has confirmed the strong association between microalbuminuria and cardiovascular mortality in NIDDM. Our study also showed significant correlation between microalbuminuria and cardiovascular mortality in NIDDM. Our study also showed significant correlation between Microalbuminuria and hypertension like other studies [8,9]and Retinopathy like other studies [8-10,21]

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 thestudy. Larger sample size in general population may berequired to confirm the results of the present study.

CONCLUSION

we concluded that there was significant correlation of microalbuminuria with durations nice diagnosis i.e, first 0-5yrs of NIDDM, BMI ≥ 25, HbA1c values more than 7%, total cholesterol >200mg/dl, serum triglycerides >150mg/dl, LDL >100 mg/dl, hypertension, IHD and retinopathy thus proving the association of microalbuminuria with early onset in NIDDM population, with poor glycemic control, with cardiovascular risk factors like dyslipidemia, obesity and hypertension. 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.

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