PREVALENCE OF MICROALBUMINURIA AND ASSOCIATED COMORBIDITIES IN DIABETIC PATIENTS- A HOSPITAL BASED STUDY FROM KERALA

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ABSTRACT

BACKGROUND

Microalbuminuria is more prevalent in Asians. There are not many published data on the prevalence of microalbuminuria and its associations in Indians, especially South Indians. Diabetic nephropathy is a common consequence of long-standing diabetes mellitus; microalbuminuria (MA) is considered an early change of diabetic nephropathy.

The objectives of the study is to study the prevalence of microalbuminuria and associated comorbidities in diabetic patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Medicine Department of a tertiary care hospital. Type 2 diabetes patients between the ages of 20-70 years who attended the clinic in 2014 were included in this study. Data was collected by reviewing medical records for demographic and disease-related variables. MA was detected by measuring the albumin to creatinine ratio, and MA was diagnosed if this ratio was between 30 and 300 mg/g on two occasions.

RESULTS

37.3% had MA in the study and the rate was higher among females ($p < 0.024$). There was a positive correlation between MA and duration of diabetes ($p < 0.001$), the presence of hypertension ($p < 0.001$), body mass index (BMI) ($p < 0.002$), fasting plasma glucose ($p < 0.001$), and low-density lipoprotein (LDL) ($p < 0.039$). A HbA1c >7 was associated with higher incidence of microalbuminuria ($p < 0.001$). Age, creatinine level, high-density lipoprotein, and triglyceride did not show any significant correlation with the presence of MA.

CONCLUSION

There is a high prevalence of MA in patients with diabetes in this study. Early detection of MA, and the active management of modifiable risk factors, in particular, hyperglycaemia, hypertension, dyslipidaemia and obesity, can delay the onset of complications.

KEYWORDS

Microalbuminuria, Diabetes, Kerala.

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BACKGROUND

Type 2 DM is an endocrine disorder characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production.[1] It is one of the leading causes of morbidity and mortality and is a major risk factor for cardiovascular events.[2] Ageing of the population and an increasing prevalence of obesity and sedentary life habits lead to a greater prevalence of diabetes, particularly in Asia.[3] It is estimated by WHO that by 2025, the number of patients with the disease worldwide will increase to 300 million. Half of them will be from the Asian countries.[4]

Micro vascular complications like retinopathy and nephropathy, are frequent and contribute to the total disease burden. Microalbuminuria is defined as the excretion of 30-300 mg of albumin per 24 hours (or 20-200 mcg/min or 30-300 mcg/mg creatinine) on 2 of 3 urine collections.[5] It occurs in 30-40% of patients with type 2 diabetes and the presence of kidney disease enhances the mortality from cardiovascular disease.[6]

Microalbuminuria, which arises very early in the disease is one of the first markers for diabetic nephropathy and is an independent risk factor for cardiovascular disease. The increased levels of urinary albumin secretion may represent a more generalized vascular damage than renal microvascular injury alone.[7] It is reported that during the past decade, due to increase in the incidence of diabetics, the end-stage renal disease has risen dramatically.[5] Glomerular hyper perfusion and renal hypertrophy occurs in the initial phase after the onset of

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diabetes mellitus and are reflected by an increased glomerular filtration rate. Microalbuminuria occurs 5 to 10 years before macroalbuminuria in patients who progress to overt nephropathy.[8]

Diabetic nephropathy is the leading cause of end-stage renal disease[9,10,11] which may require dialysis and cause financial burden on the family. Patients with diabetes on dialysis and transplant recipients also have higher morbidity and mortality rates.[12] MA is considered an early stage of diabetic nephropathy. The prevalence of MA in patients with type II diabetes has been reported from 20% to 61%.[13,14,15]

A significant positive correlation between MA and the duration of diabetes is seen in many studies.[13,14] However the relationship between MA and fasting blood sugar (FBS), age, and gender is not that certain.[13,14,15]

Until complications become develop most patients are asymptomatic. Both micro and macrovascular complications increase the morbidity, and these can be slowed with early interventions. Screening for MA is a relatively cheap and convenient procedure. Early detection helps to reduce cardiovascular risks and the rate of progression of diabetes-related nephropathy. Early intervention to control BP and hyperglycaemia reverses MA and delays subsequent development.[16,17] The objective of our study was to study the prevalence of microalbuminuria in diabetic patients and its associations.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Medicine Department of the WIMS Hospital. Type 2 DM patients between 20 and 70 years who visited the centre in 2014 were included in this study. Patients having albuminuria >300 mg/day, congestive cardiac failure, urinary tract infection and pregnant women were excluded from the study. The initial study population had 2998 patients with type II diabetes attending the Medicine Department of WIMS Hospital, during the year 2014. Using a simple random sampling technique, 512 patients were selected from the study population. A questionnaire of demographic data and disease-related variables was designed. Data were collected by reviewing medical records for demographic and disease-related variables.

Definitions

Body mass index (BMI) of <25 was considered normal, 25.0-29.9 as overweight range, 30-39.9 as obese, and more than 40 was considered morbidly obese.

Patients were categorized as hypertensive if the systolic blood pressure was >140 mmHg and/or the diastolic blood pressure was >90 mmHg.

MA was defined as an albumin-to-creatinine ratio between 30-300 µg/mg in 2 of 3 urine samples collected over a 3-month period.

Glycated haemoglobin (HbA1c) <7% was considered normal, and fasting glucose < 130 was taken as normal.

Cardiovascular Disease

As documented in the medical record is the presence or absence of stable and unstable angina, myocardial infarction.

Neuropathy

As documented in the medical record is the presence or absence of weakness or diminished sensation, loss of ankle jerks and vibratory sensation, wasting of the small muscles of hands and feet.

Retinopathy

As documented in the medical record as the presence or absence of a sign of non-proliferative or proliferative retinopathy as documented by an Ophthalmologist.

Statistical Analysis

Statistical analysis was performed using SPSS software. Descriptive analysis results were presented as mean ± standard deviation for all quantitative variables, whereas, categorical variables were presented as frequencies and percentages. Chi-square test or Fisher's Exact test, as appropriate, were used to compare all the demographics and clinical characteristics of the patients with microalbuminuric versus those not having MA; P<0.05 was considered statistically significant."

RESULTS

50.7% of the study population were males while 49.21% were females. The mean age of the patients was 54.32 years with standard deviation of 12.57; majority were between 40-60 (58.2%) followed by 60 years or older (34.17). Hypertension was present in majority of the patients (68.75%). The mean duration of diabetes was 9.98 ± 6.7 years. 25.78% had had diabetes for 1-5 years, 27.73% had had it for 6-10 years, 19.33% for 11-15 years, and 27.14% for more than 15 years. Nearly 31.83% of the patients were obese and 27.73% were morbidly obese. The mean BMI was 31.98 ± 7.37 kg/m^2 Complications such as CAD, neuropathy, and retinopathy were absent in 93.94%, 90.23%, and 96.28%, respectively.(Table 1).

Variable	N (%)
Gender	
Male	260 (50.7)
Female	252 (49.21)
Age in Years	
20 - 40	39 (7.61)
40 - 60	298 (58.20)
>60	175 (34.17)
Mean ± SD	53.04 ± 11.8
Duration of Diabetes (in Years)	
1 - 5	132 (25.78)
6 - 10	142 (27.73)
11 - 15	99 (19.33)
> 15	139 (27.14)
Mean ± SD	9.98 ± 6.7

Hypertension	
Yes	352 (68.75)
No	160 (31.25)
Body Mass Index	
< 25	54 (10.54)
25 – 29.9	153 (29.88)
30 – 39.9	163 (31.83)
> 40	142 (27.73)
Mean ± SD	32.66 ± 6.5
Cardiovascular Disease	
Present	31 (6.05)
Absent	481 (93.94)
Retinopathy	
Present	19 (3.71)
Absent	493 (96.28)
Neuropathy	
Present	50 (9.76)
Absent	462 (90.23)

Table 1. Sociodemographic Features and Disease-Related Variables of Diabetic Patients in Medicine Department, WIMS (n=512)

The overall prevalence of MA was 37.3%. High HbA1c (80.46%) and high fasting sugar (82.61%) was present in most patients. The different percentages of abnormal laboratory parameters in the study subjects were as follows: creatinine 24.21%, low-density lipoprotein (LDL) 53.13%, high-density lipoprotein (HDL) 88.08%, and triglyceride 40.82%. The mean FBS, HbA1c, and creatinine levels were 149.2 ± 6.7 mg/dL, 8.54 ± 2.1, and 1.33 ± 0.6, respectively. The mean serum triglyceride, LDL, and HDL levels were 142.5 ± 31.2, 121 ± 31, and 34.8 ± 9.2 mg/dL, respectively (Table 2).

Variable	N (%)
Albumin to Creatinine Ratio	
<30	321 (62.69)
30 - 300	191 (37.30)
Mean ± SD	38.11 ± 32.6
HbA1c	
< 7	100 (19.53)
> 7	412 (80.46)
Mean ± SD	8.54 ± 2.1
Fasting Blood Glucose (mg/dl)	
< 130	89 (17.38)
> 130	423 (82.61)
Mean ± SD	149.2 ± 6.7
Serum Creatinine	
< 1.3	388 (75.78)
> 1.3	124 (24.21)
Mean ± SD	1.33 ± 0.6
LDL	
< 100	240 (46.87)
> 100	262 (53.13)
Mean ± SD	121 ± 31
HDL	
>40	61 (11.92)
< 40	451 (88.08)
Mean ± SD	34.8 ± 9.2
Triglyceride	
< 150	303 (59.18)
> 150	209 (40.82)
Mean ± SD	142.5 ± 31.2

Table 2

Females (42.86%) had a higher prevalence of MA than males (31.93%) (P = 0.024). The prevalence of MA was not statistically different between the various age groups (P = 0.101). There was statistically significantly correlation between MA and the presence of diabetic retinopathy (63.16%) (P = 0.016) and diabetic neuropathy (48%) (P = 0.004). However, there was no significant associations with cardiovascular disease. MA was more in patients with hypertension (44.32) than in those with normal blood pressure (P < 0.001). The prevalence of MA was significantly higher in the overweight, obese, and morbidly obese compared to individuals of normal weight (P < 0.002). Duration of diabetes of 15 years or more (66.91%) had a strong association with MA (P < 0.001) (Table 3).

	Microalbuminuria		
Variable	**Absent N (%)**	**Present N (%)**	**P value**
Gender			
Male	177 (68.07)	83 (31.93)	0.024
Female	144 (57.14)	108 (42.86)	
Age in Years			
20 - 40	31 (79.49)	8 (20.51)	0.101
40 - 60	182 (61.07)	116 (38.93)	
>60	108 (61.71)	67 (38.29)	
Duration of Diabetes (in years)			
1 - 5	108 (81.81)	24 (18.19)	<0.001
6 - 10	104 (73.24)	38 (26.76)	
11 - 15	63 (63.64)	36 (36.36)	
> 15	46 (33.09)	93 (66.91)	
Hypertension			
Yes	196 (55.68)	156 (44.32)	<0.001
No	25 (41.66)	35 (58.34)	
Body Mass Index			
< 25	44 (81.48)	10 (18.52)	0.002
25 – 29.9	98 (64.05)	55 (35.95)	
30 – 39.9	106 (65.03)	57 (34.97)	
> 40	73 (51.41)	69 (48.59)	
Cardiovascular Disease			
Present	16 (51.61)	15 (48.39)	0.121
Absent	305 (63.41)	176 (36.59)	
Retinopathy			
Present	7 (36.84)	12 (63.16)	0.016
Absent	314 (63.69)	179 (36.31)	
Neuropathy			
Present	21 (42)	29 (48)	0.004
Absent	300 (64.93)	162 (35.17)	

Table 3

The prevalence of MA in patients with abnormal HbA1c was 43.69% with a statistically significant correlation (P <0.001). Abnormal fasting glucose was in 80.46% of patients with statistically significant correlation (P <0.001). A significant correlation was noted with abnormal LDL (42.75%) and MA (P = 0.039). There was no statistically significant correlation between MA and variables like creatinine, HDL, and triglycerides (Table 4)

Variable	Microalbuminuria		P Value
	Absent N (%)	Present N (%)	
HbA1c			
< 7	89 (89)	11 (11)	<0.001
> 7	232 (56.31)	180 (43.69)	
Fasting Blood Glucose (mg/dl)			
< 130	78 (87.64)	11 (12.36)	<0.001
> 130	243 (57.45)	180 (42.55)	
Serum Creatinine			
< 1.3	256 (65.98)	132 (34.02)	0.003
> 1.3	65 (52.42)	59 (47.58)	
LDL			
< 100	161 (67.08)	79 (32.92)	0.039
> 100	150 (57.25)	112 (42.75)	
HDL			
> 40	49 (80.33)	12 (19.67)	0.069
<40	272 (60.31)	179 (39.69)	
Triglyceride			
< 150	200 (66.01)	103 (33.99)	0.113
> 150	121 (57.89)	88 (42.11)	

Table 4

DISCUSSION

We studied 512 patients with type II diabetes and the overall prevalence of MA found was 37.3%. Various studies have reported varying incidence of microalbuminuria in diabetes. In India, Vijay et al. reported and incidence of 15.7% in Chennai,[18] while in another study in Chennai by Verghese et al., 36.3% of prevalence was reported. From North India, Gupta et al. reported an incidence of 26.5% microalbuminuria in type 2 diabetic patients.[19]

A statistically significant correlation was found between the prevalence of MA and modifiable risk factors like HbA1c, FBG, Hypertension, BMI, LDL as well as non-modifiable risk factors like female sex and the duration of diabetes. Several epidemiological studies have reported the prevalence rates of MA as ranging between 20% and 61% in patients with type II diabetes.[14,15,17,20,21,22] This variation in the prevalence of MA can be attributed to several factors such as differences in populations, the definition of MA, the methods of measurement and urine collection.

Some studies have found a statistical correlation between age of patients and MA[15] where as some other studies[11,23] finds no co relation. Our study did not find any statistically significant co relation between age of patients and microalbuminuria. These variations are probably related to the varied distribution of patients' ages in the different studies.

The prevalence of MA shows a female dominance in our study similar to a study in. Middle East[11] but another study reported increased prevalence of MA in men compared to women.[24] The differences in results may be because of the selection of samples or certain differences in population.

A statistically significant correlation was found in our study between the prevalence of MA and the duration of diabetes similar to the findings in earlier studies.[13,14,21,25] Another study reported no significant correlation between MA and the duration of diabetes.[15] This conflicting observation may be the result of the discrepancy in recording the exact period of onset of diabetes. Diabetes often goes undetected for a long period, and newly detected patients with diabetes sometimes present with well-established complications.

The present study found a significant correlation between MA and BMI, similar to a study reported in 2012 study.[15] However, a study from Africa showed no relation of MA to BMI[26] The American Diabetes Association recommends screening adults ≥45 years of age and especially those with BMI ≥25 kg/m^2 since weight gain was significantly associated with diabetes.

In our study, most patients with MA also had hypertension which was similar to that observed in another study.[13] This is probably because the high blood pressure, particularly the systolic component damages the glomerular filtration membrane leading to microalbuminuria.[27]

In the present study, a statistically significant correlation was found between the prevalence of MA and HbA1c, which was similar to findings reported by other studies.[14,15,20,28,29] However, in another study, there was no significant association of MA with HbA1c[13] but there was a strong association with fasting glucose, which is similar to an earlier study.[13,30]

The result of the present study showed an association of MA with LDL but not with HDL and triglyceride. Previous studies have suggested a correlation between an adverse lipid profile and nephropathy in patients with type II diabetes through certain mechanisms including mesangial cell proliferation, recruitment of macrophages, altered cytokine responses, and increased matrix deposition.[31]

The present study found a statistical correlation between the prevalence of MA and presence of diabetic retinopathy and neuropathy, similar to other reported studies.[11,14,21,32,] but no statistical correlation was found with presence of coronary artery disease. However, some studies have found a statistical correlation between cardiovascular disease and MA.[14,33,34] This difference may be due to poor documentation in medical records.

The present study failed to show any correlation between MA and creatinine, a result which is similar to an earlier study.[13] Other studies, however, showed higher serum creatinine levels, which can be an important warning sign of possible irreversible renal damage if ignored.[15]

Our study showed poor glycaemic control, high systolic blood pressure, duration of diabetes, HbA1C and high BMI to be important risk factors for microalbuminuria. Many studies have reported the duration of diabetes, male sex as the major risk factors. Vijay et al have reported duration of diabetes, systolic and diastolic BP age and serum creatinine levels to be associated with proteinuria,[18] while HbA1c was reported to be the risk factor by Gupta et al.[19] In a study by John et al, male sex, age, longer duration of diabetes, poor glycaemic control and raised blood pressure was associated with microalbuminuria.[35] Yet in another study by Verghese et al, age, duration of diabetes, diastolic blood pressure, HbA1c, and fasting plasma glucose were reported to be the risk factors. Other factors that have been reported are alcohol intake, foot ulcers and smoking.[36,37,38]

The strength of this study was a good sample size of high-risk individuals but since the study is not population based and only included patients who presented at our centre, there might be some limitations while extending it to cover the general population of diabetes patients.

CONCLUSION

There is a high prevalence of microalbuminuria in patients with type 2 diabetes. The risk factors associated with this condition are hypertension, high HbA1c levels, high fasting sugar levels and obesity.

There is evidence that early therapeutic intervention in diabetic patients can delay onset of complications and improve outcomes. The control of modifiable risk factors, especially hyperglycaemia, obesity and hypertension, as well as timely detection of albuminuria needs focus.

The early identification of patients at greatest risk, and the subsequent initiation of renal and cardiovascular protective measures, are of utmost importance.

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