Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India

A Varghese, R Deepa, M Rema, V Mohan

Abstract

Objective—The aim of this study was to determine the prevalence and risk factors for microalbuminuria among south Indian type 2 diabetic patients attending a diabetes centre.

Methods—One thousand four hundred and twenty five type 2 diabetic patients attending a diabetes centre in south India were recruited for the study. Urinary albumin concentration was measured by immunoturbodimetric assay. Microalbuminuria was diagnosed if the urinary albumin excretion was >30 mg/g of creatinine.

Results—Overall prevalence of microalbuminuria was 36.3% (95% confidence interval 33.8 to 38.9). The prevalence of microalbuminuria increased with the increase in duration of diabetes. Multivariate regression analysis revealed age, diastolic blood pressure, glycated haemoglobin, fasting plasma glucose, and duration of diabetes to be associated with microalbuminuria.

Conclusion—The overall prevalence of microalbuminuria in this south Indian clinic population and its risk factors are similar to that reported in Europeans.

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Diabetic nephropathy is the leading cause of end stage renal disease world wide.[1 2] Microalbuminuria is considered to be an early stage of diabetic nephropathy.[3–6] Microalbuminuria is also considered to be a predictor for cardiovascular disease both among diabetic and non-diabetic subjects,[7–9] and is one of the components of the metabolic syndrome (insulin resistance syndrome).[10 11] Recent statistics from the World Health Organisation (WHO) project an increase in the prevalence of diabetes world wide particularly in developing countries.[12] Currently, India leads the world with the largest number of diabetic subjects and this is expected to further rise in the coming years.[12 13] Hence studies on diabetes related complications are essential to assess the burden of diabetes. In this study we report on the prevalence of microalbuminuria in south Indian type 2 diabetic patients attending a diabetes centre in southern India.

Patients and methods

The study group comprised of 1620 consecutive type 2 diabetic patients attending the M V Diabetes Specialities Centre, a large diabetes

centre at Chennai in southern India, during the period from 1 January 1998 to 31 March 1998. Type 2 diabetes was diagnosed based on the WHO study group report criteria.[14] Patients with incomplete records, presence of urinary tract infection, or heart failure were excluded (n = 90). Of the remaining 1530 patients, 105 (6.9%) subjects had proteinuria ≥500 mg/day, and these patients were also excluded from the study as we have separately reported on the prevalence of proteinuria.[15] Thus a total of 1425 individuals were included in the study.

In all study patients, a complete clinical work up was done including height, weight, and body mass index. The body mass index was calculated and expressed as kg/m^2. The blood pressure was recorded in the right upper arm in the sitting posture, after a five minute rest. Patients were categorised as being hypertensive if they were on antihypertensive treatment or if they had a systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg.[16] A fasting sample of blood was drawn after an overnight fast of 10 hours and the following investigations were done: plasma glucose, serum cholesterol, serum triglycerides, high density lipoprotein-cholesterol, and serum creatinine.

Biochemical analysis were done on Ciba Corning Express Plus Auto Analyser (Corning, Medfield, MA, USA) using kits supplied by Boehringer Mannheim, (Mannheim, Germany). Fasting and postprandial plasma glucose (glucose oxidase method), serum cholesterol (CHOD-PAP method), serum triglycerides (GPO-PAP method), and serum creatinine (modified kinetic method of Jaffe) were estimated in all patients. Glycated haemoglobin (HbA1c) was estimated by high pressure liquid chromatography using the Variant machine (Bio Rad, Hercules, CA, USA).

Urine samples were collected in the early morning after an overnight fast. Urine creatinine was measured using Jaffe's method. Urine microalbumin concentration was measured using commercially available immunoturbidometric assay kits from Randox (Randox, UK) on Opera Technicon Auto Analyser (Bayer Diagnostics, USA). The urine sample was added to a buffer containing antibody specific for human serum albumin. The absorbance of the resulting turbid solution is proportional to the concentration of albumin in the sample solution. By constructing a standard curve from the absorbances of the standards, the albumin concentration in the sample can be determined. The mean interassay and intra-assay coefficient of variation were 3.4% and 2.4% respectively.

Madras Diabetes Research Foundation and MV Diabetes Specialities Centre (P) Ltd, Gopalapuram, Chennai, India
A Varghese
R Deepa
M Rema
V Mohan

Correspondence to: Professor V Mohan, M V Diabetes Specialities Centre & Madras Diabetes Research Foundation, 35 Conran Smith Road, Gopalapuram, Chennai 600 086, India
mvdsc@.vsnl.com

Table 1   Clinical and biochemical characteristics of the study subjects

Parameters	Normoalbuminuric group (n=907)	Microalbuminuric group (n=518)	p Value
Age (years)	51 (10)	54 (11)	<0.001
Male (%)	577 (63.6%)	299 (57.7%)	0.03
Age at diagnosis (years)	45 (10)	46 (11)	NS
Duration of diabetes (years)	6 (6)	8 (7)	<0.001
Body mass index (kg/m^2)	25.2 (4.2)	24.8 (4.1)	NS
Systolic BP (mm Hg)	133 (16)	138 (17)	<0.001
Diastolic BP (mm Hg)	83 (7)	84 (8)	0.013
Fasting blood glucose (mmol/l)	9.9 (3.6)	11.5 (4.8)	<0.001
HbA1c (%)	9.1 (2.2)	9.7 (2.3)	<0.001
Serum creatinine (μmol/l)	80.4 (29.2)	84.1 (19.4)	0.010
Serum cholesterol (mmol/l)	5.0 (1.0)	5.0 (1.1)	NS
Serum triglycerides (mmol/l)	2.2 (1.6)	2.2 (2.0)	NS
High density lipoprotein-cholesterol (mmol/l)	1.0 (0.26)	1.0 (0.34)	NS
No (%) with ischaemic heart disease			
Ischaemia	45 (5)	47 (9)	0.002
Infarction	18 (2)	15 (3)	NS
No (%) with retinopathy			
NPDR	72 (8)	83 (16)	<0.001
NPDR with maculopathy	45 (5)	62 (12)	<0.001
Proliferative retinopathy	7 (0.8)	14 (3)	<0.001
Peripheral vascular disease	6 (0.7)	7 (3.3)	<0.001
Neuropathy	45 (5.0)	64 (12.4)	<0.001

Data are No(%) or mean (SD). NPDR = non-proliferative diabetic retinopathy; BP = blood pressure; HbA1c = glycated haemoglobin.

DEFINITIONS

Microalbuminuria was diagnosed if the albumin creatinine ratio exceeded 30 mg/g of creatinine.

The ocular fundi were examined by a retinal specialist both by direct and indirect ophthalmoscopy, after complete mydriasis. Retinopathy when present was classified as *non-proliferative diabetic retinopathy* (NPDR) and *proliferative diabetic retinopathy* (PDR). NPDR was diagnosed when there was evidence of microaneurysms, dot haemorrhages, exudates, or cotton wool spots in the absence of any new vessels or advanced diabetic eye disease. PDR was diagnosed when any new vessels were present or if there was evidence of fibrous retinitis proliferans, vitreous haemorrhage, retinal detachment, or other features of advanced diabetic eye disease.

Ischaemic heart disease was considered to be present when either myocardial ischaemia or infarction was present.

Myocardial ischaemia was diagnosed if there was a history of exertional chest pain (angina) with unequivocal T wave changes in the electrocardiogram (ECG), but no evidence of infarction.

Myocardial infarction was diagnosed if there was a classical history of chest pain documented by hospital records along with ST or Q wave changes on ECG suggestive of recent or past myocardial infarction.

Neuropathy was diagnosed if the vibratory threshold in the great toe documented by Biothesiometer (Bio Medical Instrument Co, Newbury, Ohio, USA) exceeded 25.

Peripheral vascular disease was diagnosed using Doppler recording of pressure tracings using a KODY vaslab machine (Kody Labs, Madras). An ankle brachial pressure index of less than 0.9 was considered as evidence of peripheral vascular disease.

STATISTICS

Statistical analysis were done using SPSS PC + 4.0.1. version. Student's *t* test was used to compare the means of continuous variables

Table 2   Prevalence of microalbuminuria in relation to duration of diabetes

Duration of diabetes (years)	Prevalence No (%)	Odds ratio (95% CI)	p Value
≤5	237/776 (30.4)	—	—
6–10	133/349 (38.1)	1.4 (1.06 to 1.8)	0.02
11–15	85/171 (49.7)	2.3 (1.6 to 3.9)	<0.00001
16–20	42/84 (50.0)	2.3 (1.4 to 3.7)	0.0005
>20	21/45 (46.7)	2.0 (1.04 to 3.8)	0.04

CI = confidence interval.

and χ^2 test was used to compare proportions. Multiple logistic regression analysis was done using microalbuminuria as the dependent variable and age, body mass index, duration of diabetes, fasting plasma glucose, HbA1c, serum cholesterol, serum triglycerides, serum creatinine, systolic and diastolic blood pressure as independent variables.

Results

The 1425 patients studied included 876 males and 549 females. Overall 518 had microalbuminuria (36.3%, 95% confidence interval (CI) 33.8 to 38.9). Prevalence of microalbuminuria among males was 32.1% (95% CI 31.0 to 37.4) and among females, 39.9% (95% CI 35.7 to 44.1).

Table 1 presents the clinical and biochemical characteristics of the normoalbuminuric and microalbuminuric patients. The microalbuminuric patients were older and had a longer duration of diabetes compared with the normoalbuminuric group (p<0.001). The microalbuminuric patients had significantly increased systolic and diastolic blood pressure compared to normoalbuminuric subjects (p<0.01). Fasting plasma glucose and HbA1c concentrations were significantly higher in the microalbuminuric group compared with the normoalbuminuric subjects (p<0.001). Serum creatinine (p<0.001) values were found to be significantly higher in the microalbuminuric group. Serum triglycerides and cholesterol values were not significantly different in both groups. Prevalence of all complications were higher among the patients with microalbuminuria compared to the normoalbuminuric subjects (p<0.001).

Table 2 presents the prevalence of microalbuminuria in relation to duration of diabetes. Altogether 27.5% of the newly diagnosed diabetic subjects had microalbuminuria. The prevalence of microalbuminuria increased with increase in duration of diabetes. Taking duration ≤5 years as the reference, the odds ratios for duration of diabetes 6–10,11–15,16–20, and >20 years respectively were calculated. The odds ratio for microalbuminuria showed a statistically significant increase with increase in duration of diabetes.

Figure 1 shows the cumulative prevalence of microalbuminuria in relation to duration of diabetes. It can be seen that the prevalence increased with increase in duration of diabetes until 10 years and thereafter remained unchanged.

Table 3 shows the results of the multiple logistic regression analyses using microalbuminuria as the dependent variable. Age,
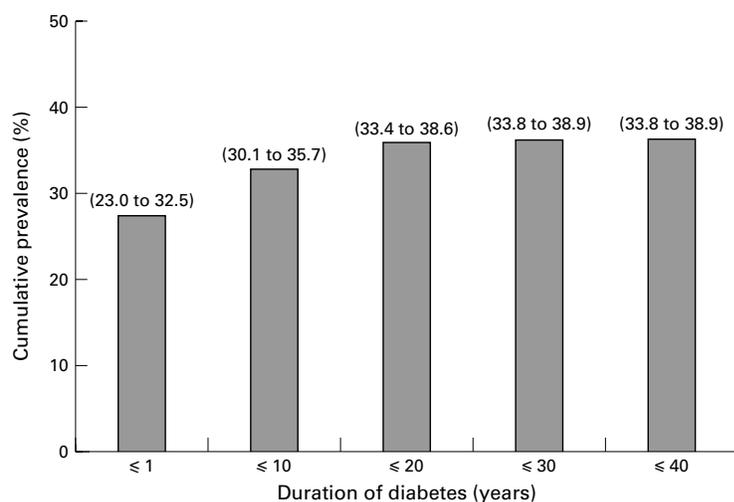
Figure 1 Cumulative prevalence of microalbuminuria in relation to duration of diabetes; figures in parentheses are 95% confidence intervals.

Table 3 Multiple logistic regression analysis using microalbuminuria as a dependent variable

Varible	β	SE β	p Value	Odds ratio (95% CI)
Age (years)	0.25	0.06	<0.0001	1.3 (1.1 to 1.4)
Diastolic BP (mm Hg)	0.43	0.08	<0.0001	1.5 (1.3 to 1.8)
HbA1c (%)	0.29	0.068	<0.0001	1.3 (1.2 to 1.5)
Fasting plasma glucose (mg/dl)	0.23	0.074	0.002	1.3 (1.1 to 1.5)
Duration of diabetes (years)	0.18	0.052	0.005	1.2 (1.1 to 1.3)

CI = confidence interval.
Microalbuminuria was taken as the dependent variable. The following categories were taken as independent variables; sex was a discrete variable, other variables like age, body mass index, systolic blood pressure (BP), diastolic BP, fasting plasma glucose, glycated haemoglobin (HbA1c), duration of diabetes, serum cholesterol, serum triglycerides and creatinine were continuous variables.

diastolic blood pressure, HbA1c, fasting plasma glucose, and duretion of diabetes showed a significant association with microalbuminuria.

Discussion

Various epidemiological and cross sectional studies have reported marked variation in the prevalence of microalbuminuria.[17–21] Earlier studies on Asian immigrant Indians and native Indians have suggested a high prevalence of microalbuminuria.[19–21] Gupta *et al* reported a prevalence of 26.6% in 65 type 2 north Indian non-proteinuric patients,[19] while John *et al* reported a prevalence of 19.7% from a tertiary hospital in Vellore, south India,[22] and Vijay *et al* reported that 15.7% had proteinuria among 600 type 2 diabetic patients studied at a diabetic centre in Chennai city.[23] Studies in the white UK population revealed a prevalence of microalbuminuria of 7%–9%,[24 25] while in Mexican Americans, it was 31%,[26] Pima Indians 26%,[27] Nauruans 42%,[18] and Hispanic Americans 35%.[28]

This variation in prevalence can be attributed to factors such as differences in populations, in the definitions of microalbuminuria, method of urine collection, etc. However this could also reflect true differences in the ethnic susceptibility to nephropathy. Earlier studies by Vijay *et al* from Madras (Chennai)[29] have demonstrated a familial clustering of diabetic nephropathy among south Indian type 2 diabetic subjects. Genetic susceptibility linked to angiotensin encoding gene as shown in Oji-Kree Indians could also be an important determinant for development of diabetes renal disease.[30]

In the present study the prevalence of microalbuminuria across the genders were not statistically different. Earlier studies have reported an increased prevalence of microalbuminuria in men compared with women.[31] Because women have a lower creatinine excretion than men there is, however, a problem about using the albumin creatinine ratio when comparing prevalence across genders. Thus some authors use a lower threshold for men than women.[32]

The causal risk factors for microalbuminuria are raised blood pressure and poor glycaemic control. Some studies have revealed duration of diabetes, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria.[20 26] In our study, multiple logistic regression analysis revealed age, duration of diabetes, diastolic blood pressure, HbA1c, and fasting plasma glucose as the risk factors for microalbuminuria. Gupta *et al* reported HbA1c to be associated with microalbuminuria,[19] John *et al* reported male sex, older age, longer duration of diabetes, poor glycaemic control, and raised blood pressure as risk factors of microalbuminuria,[22] while Vijay *et al* reported duration of diabetes, systolic and diastolic blood pressure, age of the patient, and serum creatinine to be associated with proteinuria.[23] Age was reported as one of the risk factors in the Wisconsin study,[20] in a Danish population study,[33] and in the Pima Indians.[27] The association of glycaemic control with microalbuminuria has been well established by various studies.[20 26 27 33] Other factors which are reported to be associated with microalbuminuria are alcohol intake,[20] foot ulcers,[34] and smoking.[35]

Microalbuminuria has also been reported to be associated with generalised vascular disease.[36] In our study we observed that the microalbuminuric patients had a significantly higher prevalence of ischaemic heart disease compared with normoalbuminuric patients. Retinopathy was also common among the microalbuminuric group. Similar associations have been reported in the Danish population[33] and in the UK.[25]

One of the limitations of this study is that it is a clinic based study. This could have introduced some degree of referral bias. However the prevalence of microalbuminuria is similar to that reported in other studies.[37]

In conclusion, the prevalence of microalbuminuria in this clinic based south Indian type 2 diabetic study is 36.7% and the risk factors are similar to that reported among Europeans. Given the high prevalence of diabetes in Indians with over 20 million diabetics already and the numbers expected to increase to 57 million diabetics by the year 2025, this could place considerable burden on the health budgets of this country. This calls for early detection and good control of diabetes to reduce the burden of diabetic kidney disease in the future.

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