ORIGINAL ARTICLE

PREVALENCE AND DETERMINANTS OF PROTEINURIA IN TYPE 2 DIABETES MELLITUS

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Background: Diabetic nephropathy is a leading cause of end stage kidney disease among type 2 diabetics. Proteinuria has been noted to be the cardinal symptom of progressive loss of renal function. This study examined the impact of duration of diabetes, demography (age, gender) and metabolic factors on the frequency of proteinuria among type 2 diabetic patients. **Methods:** One hundred and forty-four patients suffering from the disease were examined clinically after taking a detailed history and investigated for the study parameters. **Results:** Maximum number of patients (40.3%) were in the age group of 60–69 years followed by 33.3% in age group of 50–59 years with mean age 59.7 years. Duration of diagnosed disease in 46.5% patients was 1–5 years and 36.8% had duration of 6–10 years, 9.8% had duration between 11–15 years, and 6.9% were less than one year. The mean duration was 6.13 years. The numbers of associated complications were high, 40.3% cases were having hypertension, 33.3% had neuropathy and 10.4% had associated ischaemic heart disease. Proteinuria was seen in 36.10% patients; 16.66% had mild proteinuria, and 19.44% had neuropathy. **Conclusion:** Proteinuria is seen in more than one third of diabetic patients, predominantly males, and the risk of nephropathy increases with duration of disease.

Keywords: Proteinuria, type 2 diabetes mellitus (T2DM), nephropathy

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INTRODUCTION

Diabetes Mellitus is one of the oldest metabolic disorders. It is characterised by metabolic abnormalities and by long term complications involving the eyes, kidneys, nerves and blood vessels.

Non Insulin Dependent Diabetes Mellitus (NIDDM) comprises more than 90% diabetics in India.[1] Klein *et al* have also observed that NIDDM is 7–8 times more common than IDDM.[2] The incidence of associated complications is more in NIDDM compared to IDDM group.

One of the complications of type 2 diabetes mellitus (T2DM) is nephropathy characterised by increased excretion of protein in the urine associated with relentless decline in the glomerular filtration rate and raised arterial blood pressure. It is presently the leading attributable cause of chronic kidney disease (CKD).[3] In its typical course, patients thereafter develop micro-albuminuria, the excretion of albumin in the range of 30–300 mg/dl. Normal persons excrete less than 30 mg/dl. When proteinuria is greater than 550 mg/dl this degree of leakage is termed as macroproteinuria.[4] Subsequently with progressive proteinuria, GFR tends to fall in a linear fashion, terminating with end stage renal failure (ESRF) after about 10 years.

In general, patients with nephropathy have a duration of diabetes significantly longer than those without this complication. Characteristically, it takes 10–20 years of known diabetes before the clinical manifestation of nephropathy appears. In addition to the tremendous health care costs of these diabetic patients with end stage renal disease, the incalculable costs of suffering and loss of human productivity demands early diagnosis and alleviation of the debilitating outcome of diabetic renal disease.

SUBJECTS AND METHODS

This study was conducted on 144 diabetic patients admitted in Guru Nanak Dev Hospital attached to Govt. Medical College, Amritsar, India. All the patients of type 2 diabetes mellitus were included in the study irrespective of the duration of disease, age, and gender. The study design was approved by the Ethical Committee of the Institute. Informed consent was obtained from all subjects.

All type 2 diabetics with ages ranging from 50 years and who were on hypoglycaemic agents or on diet therapy, but not on insulin therapy were enrolled into the study. Confirmation of diagnosis was made from patient folders before being recruited into the study. Type 2 diabetics with significant urinary tract infection, congestive heart failure, undergoing any form of dialysis or on insulin therapy were excluded from the study.

Detailed clinical history of all the patients was recorded including age, duration of diabetes, course of illness, associated hypertension and other complaints. All of them had a clinical examination with measurement of blood pressure. The biochemical parameters including Fasting and postprandial blood glucose (FBS), blood urea and serum creatinine, serum

proteins, serum cholesterol, urine protein were recorded. Urine samples were collected for 24 hours from 8.00 AM to 8.00 AM next day. All the samples were mixed and measured and albumin estimation in 24 hrs was done by Esbach's method.[5]

RESULTS

One hundred and forty-four patients of T2DM were included. Out of 144 subjects, 78 (54.2%) were male and 66 (45.8%) were female.

Out of 144 NIDDM patients, 14 (9.7%) were in the age group of 40–49 years, 48 (33.3%) in the age group of 50-59 years, 58 (40.3%) patients were in age group 60–69 years, 24 (16.7%) patients in the age group of more than 70 years. It was seen that maximum patients were in the age group of 60–69 years followed by the age group of 50–59 years. The mean age was found to be 59.7 years.

Maximum number of patients 67/144 (46.5%) were having duration of diabetes 1–5 years followed by 53 (36.8%) having duration of 6–10 years. Only 14 (9.8%) and 10 (6.9%) patients were having duration of 11–15 years and less than 1 year respectively. The mean duration was found to be 6.13 years (Table-1).

Table-1: Duration of diabetes in the patients

Duration (Year)	Patients	%
<1	10	6.9
1–5	67	46.5
6–10	53	36.8
11–15	14	9.8
Total	144	100.0

Fifty-eight (40.28%) patients were having hypertension, 48 (33.33%) were having neuropathy while 15 (10.42%) patients were having associated ischaemic heart disease (Table-2).

Table-2: Associated complications observed in the patients (n=144)

Complication	Patients	%
Hypertension	58	40.28
Neuropathy	48	33.33
Ischaemic heart disease	15	10.42
Total	121	84.03

Out of 144 patients of type 2 diabetes mellitus 24 (16.66%) had proteinuria in the range of 150–500 mg/day, while 28 (19.44%) had proteinuria above 500 mg/day. A total of 52 (36.10%) patients had proteinuria (Table-3).

Table-3: Distribution of proteinuria in the patients (n=144)

Proteinuria (mg/day)	Patients	Percentage
Mild (150–500 mg/day)	24	16.66
Nephropath (>500 mg/day)	28	19.44
Total	52	36.10

Out of 24 patients having mild proteinuria (150–500 mg/day) only 3 (12.5%) had duration of less than 5 years. Six (25%) had duration of diabetes between 5–10 years, and 15 (62.5%) patients had duration of more than 10 years. The prevalence of mild proteinuria was statistically significant in patients with duration of diabetes between 5–10 years as compared to patients with duration less than 5 years ($p<0.05$). Prevalence of mild proteinuria in patients with diabetes of more than 10 years duration was highly significant ($p<0.001$) than the other 2 groups. Out of 28 patients having nephropathy 3 (10.71%) patients had duration of diabetes less than 5 years, 8 (28.57%) had duration between 5–10 years and 17 (60.72%) patients had duration more than 10 years. The prevalence in group 2 (duration between 5–10 years) was statistically significant ($p<0.01$) as compared to group 1 (duration less than 5 years). The prevalence in group 3 (duration >10 years) was statistically very significant ($p<0.001$) as compared to rest of the groups. (Table-4).

Table-4: Distribution of mild proteinuria (150–500 mg/day) and nephropathy (protein excretion >500 mg/day) with duration of diabetes

Duration (years)	Mild Proteinuria		Nephropathy	
	No.	%	No.	%
<5	3	12.5	3	10.71
5–10	6	25.0	8	28.57
>10	15	62.5	17	60.72
Total	24	100.0	28	100.0

Out of 78 male patients with type 2 diabetes, 30 (38.46%) had abnormal proteinuria while out of 66 female patients 22 (33.33%) were having abnormal proteinuria. However the difference was not statistically significant. Out of 78 male patients with T2DM, 16 (20.51%) were having nephropathy and out of 66 female patients, 12 (18.18%) had nephropathy. The difference between the two groups was not significant. (Table-5).

Table-5: Sex distribution in relation to abnormal proteinuria and nephropathy in patients (n=78)

		Proteinuria		Nephropathy	
Sex	Patients	No.	%	No.	%
Male	78	30	38.46	16	20.51
Female	66	22	33.33	12	18.18
Total	144	52	36.11	28	19.44

DISCUSSION

Our study examined the impact of demography, duration of diabetes and associated complications on the frequency of proteinuria and further development of nephropathy among type 2 diabetic patients. There was slight male preponderance in the distribution of the disease. Similar results were noticed by Vijay *et al*[6] and Ballard *et al*[7].

Mean age of the patients in our study was 59.7 years. Similar incidence was noted by Vijay *et al*.[6] They found the mean age of 54±10.5 years in their study. The mean duration was found to be 6.13 years. The mean duration in the present study is less than the earlier study

by Vijay *et al*[6], who found it to be 12.5±7 years. This difference may be due to different design and size of the study.

The total number of complications was found to be 121. The high percentage of hypertension and coronary artery disease in NIDDM patients in the present study is consistent with the study of Miettinen *et al*[8] who found that NIDDM independently increased the risk of atherosclerotic vascular disease events. Rossing *et al*[9], Gall *et al*[10] also found elevated blood pressure to be an independent risk factor for development and progression of proteinuria in T2DM.

A total of 52 (36.10%) patients showed abnormal proteinuria 24 (16.66%) had proteinuria in the range of 150–500 mg/day. This finding is consistent with the findings of Vijay *et al*[6] who found abnormal proteinuria in 35% patients, Klein *et al*[2] in 33% patients, Niskanen *et al*[11] in 33% patients while 28 (19.44%) had proteinuria in the nephropathy range (>500 mg/day) as per Faber *et al*[12] and Vijay *et al*[6]. The prevalence of proteinuria in patients with more than 10 year diabetes was statistically highly significant as compared to other two groups ($p<0.001$).

The prevalence of nephropathy in patients with 5–10 years of diabetes was statistically significant as compared to patients with less than 5 years of diabetes ($p<0.05$), while the prevalence of nephropathy in patients with more than 10 years of diabetes was statistically highly significant as compared to other two groups ($p<0.001$). Stratton *et al*[13], Peterson JC[14] and Ramirez[15] also confirmed the duration of diabetes as an important factor in the development of proteinuria. Prevalence of proteinuria starts increasing with the duration of diabetes and rises dramatically after 10 years of duration of diabetes ($p<0.001$).[16–18]

Men had greater incidence of proteinuria and nephropathy with increased duration. However, the difference in genders was not statistically significant ($p>0.05$). Our study is consistent with the studies of Klein *et al* and Ballard *et al*.[2,7]

CONCLUSION

Factors like age, sex, duration of disease and associated complications individually contribute to kidney damage having direct proportionality ultimately resulting in hyperfilteration and consequently proteinuria, which is a cardinal sign of overt nephropathy.

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