PREVALENCE OF MICROALBUMINURIA IN NON-INSULIN-DEPENDENT DIABETES MELLITUS

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ABSTRACT

The prevalence of microalbuminuria was assessed in 50 patients of non-insulin dependent diabetes mellitus. The mean age of patients was 52.1 ± 11.6 years and the duration of diabetes was 8.3 ± 6.8 years. Twenty (40%) patients had microalbuminuria. Microalbuminuria was more common in patients with a longer duration of diabetes (more than 5 years), a poor glycaemic control, and higher systolic blood pressure.

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KEY WORDS : Microalbuminuria; Diabetes mellitus; Diabetic nephropathy; Chronic renal failure.

Introduction

Until recently non-insulin-dependent diabetes mellitus (NIDDM) was considered to have a relatively benign prognosis and a variable incidence of renal involvement in contrast to insulin dependent diabetes (IDDM) [1]. In IDDM a stage of incipient nephropathy characterized by microproteinuria, supernormal glomerular filtration rate (GFR), rising blood pressure (BP) and a high risk of subsequently developing proliferative retinopathy have been well described [2]. The natural history of nephropathy in NIDDM however remains uncertain.

The purpose of this study was to assess the prevalence of incipient nephropathy in patients with NIDDM by assessing the occurrence of microalbuminuria and to describe its associations.

Material and Methods

This was a cross-sectional study in which 50 randomly chosen patients with NIDDM attending the endocrine outpatient department of Army Hospital Referral and Research, Delhi Cantt, were assessed. None of these patients had dip-stick positive proteinuria. Care was taken to exclude those patients with pre-existing renal insufficiency, congestive cardiac failure, urinary tract infections, uncontrolled hypertension (all conditions likely to

produce microalbuminuria), and those in their first visit after the diagnosis of diabetes mellitus was established.

Microalbuminuria was assessed by the Micral test strips (Boehringer Mannheim, India) which is based on the principle of immunochemical reactions for specific detection of human albumin. The test was repeated thrice in each patient at weekly intervals before being considered as positive [2]. Hypertension was diagnosed as per the criteria of World Health Organization [3]. Basal blood pressures (after 30 minutes of rest) were recorded with the same sphygmomanometer on at least two occasions. The average of all the readings was taken as the final reading. Diabetic retinopathy was detected by fluorescein angiography and it was classified either as simple background or as proliferative retinopathy.

The glycaemic control was assessed by estimating fasting blood glucose (FBG) levels (modified Folin and Wu method) and by measuring the glycosylated haemoglobin percentages (GHB%) (ion exchange resin method; Stangen Immunodiagnosics Ltd). The glycaemic control was graded as good (FBG less than 130 mg/dL and/or GHB% 8%-9%), fair (FBG 130-150 mg/dL and/or GHB% 9%-10%), or poor (FBG more than 150 mg/dL and/or GHB% more than 10%).

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The values of GFR were derived from calculation of creatinine clearance (CCr) by using the Cockcroft and Gault formula [4].

$$CCr \text{ (mL/min)} : \frac{(140 - \text{age in year} \times \text{Weight in kg})}{72 \times \text{plasma creatinine (mg/dL)}}$$

For a uniform comparison all these values were corrected to 1.73 m^2 body surface area.

The kidney size was measured ultrasonographically (Siemens Sonoline; real time, grey image, 3.5 MHz linear transducer). The normal kidney length was considered to range from 90 mm - 120 mm. Any value more than 120 mm, corrected for 1.73 m^2 body surface area, was taken as abnormal.

Results

Fifty patients of NIDDM were studied. Fourteen (28%) were males and 36 (72%) were females. The mean age was 52.1 ± 11.6 years; range 30-75 years. The average duration of diabetes was 8.3 ± 6.8 years; range 2 weeks - 24 years. Twenty (40%) patients were detected to have microalbuminuria.

Of the 50 patients studied, 20 (40%) patients had a history of diabetes for less than 5 years.

Only 3 (15%) of these 20 patients had microalbuminuria in contrast to 17 (56.6%) out of the 30 patients who had NIDDM for more than 5 years ($p < 0.05$). The relationship of the degree of glycaemic control with the prevalence of microalbuminuria is shown in Tables 1 and 2.

Amongst 28 patients with good glycaemic control only 6 (24%) had microalbuminuria in comparison to 10 (62.5%) out of 16 patients with poor glycaemic control ($p = 0.05$). Amongst the 25 patients who had a good control based on GHB% a significantly greater number of patients had no microalbuminuria (Table 2).

Of the 32 patients with a systolic BP up to 140 mmHg only 10 (31.2%) had microalbuminuria while 10 (55.5%) patients with higher blood pressures were detected to have microalbuminuria (Table 3). Amongst the 36 patients with a diastolic BP less than 90 mmHg, 13 (36.2%) had microalbuminuria as against 7 (50%) out of 14 patients with higher diastolic pressures (difference not significant) (Table 4). Based on the presence or absence of microalbuminuria the patients were divided into two groups for comparison (Table 5).

TABLE 1

Relationship of fasting blood glucose and microalbuminuria

Control	Total	Without microalbuminuria		With microalbuminuria	
		Blood glucose (mg/dL)		Blood glucose (mg/dL)	
		No.	Mean $\pm$ SD	No.	Mean $\pm$ SD
Good	28	22 *	95.95 $\pm$ 15.6	6	90.5 $\pm$ 16.57
Fair	6	2	133.5 $\pm$ 1.41	4	137 $\pm$ 10.3
Poor	16	6	215.66 $\pm$ 41	10	187 $\pm$ 32.57

*Significant ($p < 0.05$)

TABLE 2

Relationship of glycosylated haemoglobin with microalbuminuria

Control	Total	Without microalbuminuria			With microalbuminuria		
		No.	GHB%	Mean $\pm$ SD	No.	GHB%	Mean $\pm$ SD
Good	25	19 *	6.74 $\pm$	0.87	6	7.92 $\pm$	0.55
Fair	8	3	9.33 $\pm$	0.33	5	9.52 $\pm$	0.3
Poor	17	8	13.2 $\pm$	1.2	9	13.4 $\pm$	1.7

*Significant ($p < 0.05$); GHB - Glycosylated haemoglobin

TABLE 3
Relationship between microalbuminuria and systolic blood pressure

Systolic BP (mmHg)	Total No	Without microalbuminuria		With microalbuminuria	
		No	BP (mmHg) Mean $\pm$ SD	No.	BP (mmHg) Mean $\pm$ SD
< 140	32	22 *	122 $\pm$ 10.5	10	118 $\pm$ 11.5
140 - 160	14	7	148.7 $\pm$ 7.2	7	152.4 $\pm$ 6.4
> 160	4	1	167	3	179 $\pm$ 15.7

*Significant ($p < 0.05$)

TABLE 4
Relationship between microalbuminuria with diastolic blood pressure

Diastolic BP (mmHg)	Total No	Without microalbuminuria		With microalbuminuria	
		No	BP (mmHg) Mean $\pm$ SD	No.	BP (mmHg) Mean $\pm$ SD
< 90	36	23	77.9 $\pm$ 8.99	13	77.38 $\pm$ 6.1
90 - 95	9	4	90 $\pm$ 0	5	91 $\pm$ 2
> 95	5	3	103.7 $\pm$ 4	2	98 $\pm$ 0

TABLE 5
Characteristics of microalbuminuria in non insulin dependent diabetes mellitus

	With microalbuminuria (n=20)	Without microalbuminuria (n=30)
Age	54.6 $\pm$ 11.6	49.9 $\pm$ 11.6
Sex		
Male	5 (25%)	9 (30%)
Female	15 (75%)	21 (70%)
Duration of diabetes (> 5 years)	17 (85%)*	13 (43.3%)
Fasting blood sugar (> 150 mg%)	10 (50%)*	6 (20%)
Diastolic blood pressure (> 95 mmHg)	2 (10%)	3 (10%)
Systolic blood pressure (> 160 mmHg)	3 (15%)*	1 (3.3%)
Kidney size (mm/1.73m ²)	110 $\pm$ 11.85	106 $\pm$ 8.6
GFR/1.73 m ² (mL/min)	98.7 $\pm$ 25	100.06 $\pm$ 0.8
Diabetic retinopathy		
Background	7 (35%)	
Proliferative	1 (5%)	

*Significant ($p < 0.05$)

Discussion

Diabetic nephropathy contributes to a large pro-

portion of patients on renal replacement therapy and in the West it is estimated to be the third most common cause of end-stage renal disease. In NIDDM persistent proteinuria, a clinical hallmark of nephropathy, is associated with a significantly higher morbidity and mortality [6,7]. The cumulative risk for developing chronic renal failure by 15 years in NIDDM with proteinuria is reported to be 11.6 per cent when compared to 0.5 per cent in non-proteinuric patients [6]. Moreover an excess incidence of cardiovascular mortality has been observed in these patients, with a 10-year survival rate of 30 per cent as compared to 55 per cent in non-proteinuric patients [7]. Therefore early detection of proteinuria is necessary for intervention trials.

Microalbuminuria was detected in 40 per cent of out NIDDM patients. However a wide variation in its prevalence (8-46 per cent) has been reported [8]. This may be related to the different ethnic groups studied, the duration of diabetes, the degree of glycaemic control and the presence of hypertension. There is controversy on the effect of the duration of diabetes mellitus on the occurrence of microproteinuria. Some workers have noticed the prevalence of microproteinuria to increase with the

duration of diabetes while others have failed to notice any association [7,9,10]. This may partly be attributed to the difficulty in timing the onset of diabetes. Analysis of our data shows that there was a higher prevalence of microalbuminuria in patients with a history of more than 5 years of diabetes.

That renal involvement of NIDDM occurs as part of a generalized vasculopathy is borne out by the fact that 60 per cent of our patients had associated diabetic retinopathy. This is consistent with the incidence of 47-63 per cent reported by other worker [11]. The discordance in the incidence of renal and retinal involvement may be related to an earlier observation that 30 per cent of proteinuria in NIDDM was of non-diabetic origin [11].

In our study we demonstrated that patients with microalbuminuria had a higher prevalence of hypertension despite maintained glomerular function. This argues in favour of a more complex relationship between hypertension and renal involvement rather than the assumption that raised blood pressure is a consequence of renal dysfunction. Based on the observation that hypertension is present even at the early stage of microalbuminuria it has been postulated that hypertension may contribute to the progression of the renal disease. Long term longitudinal studies have shown that tight glycaemic control and lowering of blood pressure even below normal during the microalbuminuric stage may prevent or at least retard the onset of clinically overt disease [8].

The higher prevalence of microalbuminuria in our patients with poor glycaemic control suggests a positive relationship between the abnormal glycaemic milieu of diabetes and microvascular complications. However the occurrence of microalbuminuria in patients with good glycaemic control and its absence in some of our patients with poor control suggest that other environmental factors are needed for the manifestation of the syndrome [11].

In discordance with the hyperfiltration hypothesis we were not able to demonstrate a significant increase in the glomerular filtration rate or the renal size in these NIDDM patients. This suggests

that other factors like defects in barrier size selectivity, glomerular hypertrophy and genetic susceptibility may play a part in the genesis of incipient nephropathy [11].

We conclude that microalbuminuria is present in a significant number of patients with NIDDM and analysis shows a correlation with the duration of diabetes, poor glycaemic control and higher systolic blood pressures. Hence long term intervention trials should aim at blood pressure control and normal glycaemic levels.

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