Assessment of Proteinuria as a marker of nephropathy in type 2 Diabetes Mellitus

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ABSTRACT

This is a cross sectional hospital based study carried out at Om Hospital and Research Center Kathmandu, Nepal. In the study, 200 diabetic patients attending the hospital were taken as the subjects and we evaluated the urinary albumin excretion and other biochemical parameters (such as creatinine, total cholesterol, HDL cholesterol, LDL cholesterol), blood pressure and body mass index (BMI). Among these 200 patients with type 2 diabetes mellitus (DM), 52.0% were having high blood pressure. The proteinuria was present in 23.0% of the overall subjects but when it is categorized in hypertensive and non-hypertensive group, 30.7% of the diabetic patients with hypertension were having proteinuria. It has been found that males were having higher prevalence of proteinuria (53.8%) than female (17.6%). There was significant difference in systolic blood pressure, diastolic blood pressure in nephropathy and without nephropathy group. Thus the nephropathy or the incidence of proteinuria was associated with obesity, high diastolic blood pressure and male sex. These data suggest that control of diabetes; hypertension should decrease the risk for proteinuria thus decreasing end stage renal disease (ESRD) and mortality from ESRD.

Keywords: Diabetes mellitus, proteinuria, diabetic nephropathy.

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative insufficiency of insulin in the body. According to World Health Organization, diabetes affects more than 170 million people worldwide and the number will rise to 370 million people by 2030.[1] About one third of those affected, will eventually have progressive deterioration of renal function.[2]

The prevalence of diabetes kidney diseases among the Asians is one of the highest in the world. Based on a survey involving 6000 people 39.0% of people with diabetes were found to have microalbuminuria and another 19.0% had critical proteinuria.[3] The mechanism by which chronic hyperglycemia leads to end stage renal disease (ESRD) though incompletely defined involves the following: interaction of soluble factors (growth factors, angiotensin II, endothelin), hemodynamic alteration in the renal microcirculation (glomerular hyperfiltration, increased glomerular capillary pressure) and structural changes in glomerulus (increased extracellular matrix, basement membrane thickening, messengial expansion fibrosis).

Proteinuria is the hallmark of diabetic nephropathy. Clinically evident proteinuria is considered after a phase of microalbuminuria where the albumin concentration is too low to be detected by dipstick method but can be measured by radioimmunoassay or immuno-turbidimetric method. When urinary albumin excretion exceeds >300 mg/day it is considered as overt proteinuria.[4]

The prevalence of overt proteinuria or diabetic nephropathy in Nepalese patients has not been adequately studied. We undertook this study to determine the prevalence of overt proteinuria in patients with type 2 DM attending Om Hospital and Research Center to determine the contribution of factors such as hypertension, hyperlipidemia, obesity and duration of diabetes.

MATERIALS AND METHODS

The subjects were above 29 years of age having a known history of type 2 DM not exceeding 25 years. Arterial hypertension was considered as an untreated systolic blood pressure of more than 139 mm Hg or a diastolic blood pressure of 90 mm Hg or more or as the need for anti-hypertensive therapy to attain a systolic or diastolic blood pressure under these levelas.[5] Type 2 diabetes was diagnosed according to the criteria of the American Diabetes Association.[6] Patients with infectious diseases and other conditions such as pregnancy were excluded from the study.

We evaluated 200 subjects (80 males and 120 females). Patients attending Om hospital and Research Center, Chabahil, Kathmandu from June 2004 to September 2004 participated in this cross-sectional study. All the patients were interviewed and ask to bring 24 hrs urine specimens.

Duration of diabetes, weight, height, blood pressure and body mass index (BMI) were noted. Urine specimen collected were used for the measurement of urinary protein and creatinine. Blood samples were examined for the measurement of serum creatinine, total cholesterol, HDL cholesterol and triglycerides (TGs) by using standard kits. The total: HDL cholesterol ratio was calculated.

Patients were categorized into two groups; one group, without nephropathy showing no proteinuria and the other having diabetic nephropathy showing proteinuria. The above mentioned parameters were compared in these two groups.

The frequency of nephropathy in hypertensive and normotensive subjects was compared using 2X2 contingency Chi-square test. A one-way Fischer least significant difference was performed to compare data between the two groups with proteinuria and without proteinuria. Significance of all test were indicated by $p< 0.05$. Data are presented as mean ±SD.

RESULTS

The overall prevalence of nephropathy (proteinuria) in type 2 subjects was 23%. The trend of more prevalent hypertension with nephropathy was statistically significant ($P<0.001$, χ^2 test) as in Table-1. Table-2 shows the gender wise distribution of proteinuria in type 2 DM. There was high prevalence of proteinuria in males than female, which was statistically significant.

Table-3 demonstrates the clinical characteristics of subjects in nephropathy group. Systolic blood pressure (SBP) was significantly higher in nephropathy group when compared with other group. Diastolic blood pressure (DBP) was significantly higher in nephropathy group. Patients with diabetic nephropathy had a significantly longer duration of diabetes than subjects without nephropathy. Subjects with nephropathy had significantly higher BMI than other group.

The data for males and females are presented in table-5 and 6 respectively. Men with nephropathy showed less duration of diabetes i.e. male showed early onset of diabetic nephropathy compared to the females (Table-6). There was significantly high DBP in women with nephropathy when compared without nephropathy. Women subjects with nephropathy have higher BMI than without nephropathy, which was statistically significant.

DISCUSSION

This study demonstrated a high prevalence of both nephropathy and hypertension among type -2 diabetics. Among 200 patients, 23.0% of diabetic patients were having proteinuria similar result to the study suggesting 19.0% of the Asian individual have critical proteinuria,[3] which is the highest in the world. In another study regardless of the diabetic type nearly half of the patients have microalbuminuria and patients with type-2 diabetes are more likely to have peripheral vascular disease, neuropathy, retinopathy and proteinuria. The presence of symptoms may be often associated with duration of diabetes; poor glycemic control as were complication but complication is often associated with dyslipidemia and elevated mean arterial pressure.

In a similar study, it has been shown that the prevalence of hypertension in older onset DM was found to be 58.0%[8] but in our study it has been found 52.0% of hypertension was having proteinuria. Subtle differences were noted between men and women although the distribution of nephropathy was similar to overall group. In women however age of onset of diabetes was a significant determinant of albumin excretion. Blood pressure was significant factor for both men and women. According to Klien *et al,*

proteinuria is associated with increased duration of diabetes, high blood pressure and the males are more prone to it.[9]

High blood pressure accelerated the progressive increase in albumin level in patient with type-2 DM who had initially normal albumin and accelerated the loss of renal function in those with overt nephropathy.[10] The diabetes sub study of heart outcome prevention evaluation (HOPE) study showed that at similar blood pressure an angiotensin converting enzyme (ACE) inhibitor resulted in 24.0% greater decrease in rate of progression to overt nephropathy than did placebo patient with type-2 DM and normoalbuminuria or microalbuminuria.[11] The creatinine clearance was found to be significantly different between without nephropathy and nephropathy group and had associated with proteinuria. Once even microalbuminuria is present, creatinine clearance declines at the rate that widely vary from patients to patients, the average reduction is 10-12 ml/min.[12]

Numerous epidemiological and clinical studies presented evidence that several metabolic, cardiovascular, and anthropometric factors consistently cluster together. These factors includes: insulin resistance, hyperinsulinemia, glucose intolerance, central obesity, hypertension, a unique dyslipidemia (high plasma triglycerides, low plasma HDL-cholesterol, and an increase in the proportion of small dense LDL particles in the plasma), increased plasma plasminogen activator inhibitor 1, and an increased risk of atherosclerotic disease.[13] But in our studies no significant difference were seen in the biochemical parameters. Insulin resistance, hyperinsulinemia, dyslipidemia, and obesity in 75.0–85.0% of the patients precede type 2 DM. The dyslipidemia and the development of type 2 diabetes are highly correlated with insulin resistance and hyperinsulinemia in almost all studies. The relationship between hypertension and insulin resistance is more controversial. Although some studies have shown a close association, others, particularly those who are of African origin or obese individuals, show little or no relationship.[14]

The presence of increased urinary albumin excretion indicates the increased transcapillary escape rate of albumin and is therefore a marker of microvascular disease. It is independent predictor of progressive renal disease, atherosclerotic disease, cardiovascular mortality and a valuable marker for the management of type 2 diabetes patients.

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Table-1: Prevalence of nephropathy in Type 2 subjects

	Without Nephropathy (Without proteinuria)	**Nephropathy (Proteinuria)**
Hypertension	72	32
Normotension	82	14

(P>0.001, Chi-Square test)

Table-2: Sex wise distribution of Nephropathy

Gender	**Without Nephropathy (Without proteinuria)**	**Nephropathy (Proteinuria)**
Male	52	28
Female	102	18

(P>0.001, Chi-Square test)

Table-3: Clinical Characteristics of type 2 diabetes subjects

	Without Nephropathy (Without proteinuria)	**Nephropathy (Proteinuria)**
Age	56.5±12.4	56.8±10.08
Duration of Diabetes(Years)	10.1±8.2	15.4±7.14*
sBP (mmHg)	136.6±54.04	148.2±21.0*
dBP (mmHg)	74.8±11.0	87.6±11.76*
BMI	24.2±6.27	29.5±8.96*

Data were mean±SD
*Significantly different from no nephropathy group ($p<0.05$)

Table-4: Comparison of Biochemical Parameters in nephropathy with type 2 DM

	Without Nephropathy (Without proteinuria)	**Nephropathy (Proteinuria)**
Total Cholesterol (mg/dl)	190±61.04	220.3±37.0
LDL	138.3±22.26	145.0±21.5
HDL	42.0±19.04	39±22.68
TG	158.9±67.2	162±56
Total: HDL cholesterol	4.8±3.4	4.3±2.3*
Creatinine Clearance(mg/min)	83.8±32.06	73.3±44.60

Data were mean±SD
*Significantly different from no nephropathy group ($p<0.05$)

Table-5: Clinical Characteristics in Males with type 2 DM

	Without Nephropathy (Without proteinuria)	**Nephropathy (Proteinuria)**
Age (Years)	54.9±12.6	53±16.8
Duration (Years)	8.0±9.1	12.4±8.3
sBP (mmHg)	126.6±15.68	152.7±19.6
dBP (mmHg)	80±8.26	93±5.8*
BMI	25.8±8.4	29.2±5.32

Data were mean±SD

*Significantly different from no nephropathy group ($p<0.05$)

Table-6: Clinical Characteristics in Females with type 2 DM

	Without Nephropathy (Without proteinuria)	**Nephropathy (Proteinuria)**
Age (Years)	56.5±12.04	57.0±8.12
Duration (Years)	10.6±7.7	15.9±6.58*
sBP (mmHg)	133±19.18	146±22.4
dBP (mmHg)	81±8.38	86.2±13.3
BMI	24.4±6.72	28.8±6.44*

Data were mean±SD,

*Significantly different from no nephropathy group ($p<0.05$)