

FREQUENCY OF NEPHROPATHY AND ITS RELATION TO METABOLIC CONTROL IN PATIENTS WITH DIABETES MELLITUS

Maryam Razzaghy Azar⁽¹⁾, Zahra Farahnak⁽²⁾

Abstract

INTRODUCTION: Diabetic nephropathy is a serious complication of both type 1 and type 2 diabetes, and unless arrested, leads to end-stage renal disease. The aim of this study was to find the prevalence of kidney dysfunction in patients with diabetes mellitus and to determine its correlation with metabolic control.

METHODS: We randomly selected 1203 cases with diabetes mellitus presenting to the Institute of Endocrinology and Metabolism. Urinary protein and creatinine were determined in a sample of 24-hour urine collection by the enzymatic methods and spot urine dipstick blood urea nitrogen, serum creatinine, HbA1c and fasting blood glucose were assessed.

RESULTS: In this study, 1203 patients (438 patients with type 1 diabetes mellitus [T1DM] and 777 with type 2 diabetes mellitus [T2DM]) were randomly selected. They consisted of 512 females and 721 males. Mean \pm SD (standard deviation) of HbA1c was 7.9 ± 3.4 in T1DM and 7.4 ± 3.5 in T2DM. Based on HbA1c levels, good control was detected in 50.2% of patients, fair control in 20.4% and bad control in 29.4%. Of 1022 patients who were evaluated for proteinuria, 201 (19.7%) had albuminuria or clinical proteinuria. Of 931 patients, 19% had high levels of blood urea nitrogen and serum creatinine. End-stage renal disease (ESRD) was seen in 10 (0.8%) of all the cases. A statistically significant positive correlation was found between duration of DM, serum creatinine and 24-hour urinary protein ($P < 0.001$).

CONCLUSION: We found a high prevalence of clinical proteinuria in diabetic patients. Duration of diabetes and poor metabolic control were identified as a strong predictors of kidney damage in patients with diabetes.

Keywords: Diabetic nephropathy, albuminuria, end-stage renal disease.

ARYA Atherosclerosis Journal 2008, 3(4): 219-222

Date of submission: 11 Oct 2007, *Date of acceptance:* 15 Feb 2008

Introduction

It has been estimated that by the year 2030, 366 million people will have diabetes worldwide. Over 5% of newly diagnosed patients with type 2 diabetes will already have diabetic kidney disease and a further 30-40% will develop diabetic nephropathy, mostly within 10 years of diagnosis. In patients with type 1 diabetes, 25-40% will develop diabetic nephropathy.¹

Diabetic nephropathy is a serious complication of both type 1 and type 2 diabetes, and unless arrested, leads to end-stage renal disease.² Diabetic nephropathy is clinically defined by persistent proteinuria

greater than 500 mg/24 hours in a person with diabetic retinopathy (or defined as UAE [urine albumin excretion]=30 mg/24h) without other renal disease.³ The urinary albumin excretion rate (AER) is the standard method of diagnosis and grading loss of glomerular permselectivity in diabetic patients.⁴

Many studies in the Western world have demonstrated that diabetic patients with microalbuminuria have an increased risk of progression to overt proteinuria, and after some time, renal failure. The progression of diabetic nephropathy from the

1) M.D. Professor of Pediatric Endocrinology and Metabolism, Ali-Asghar Hospital, Iran University of Medical Sciences, Tehran, Iran. Tel: 0098-21-22255208

2) MSc. Department of Nutrition and Biochemistry, School of Public Health and Institute of Public Health Research, Tehran University of Medical Science. Tehran, Iran.

Corresponding author: Maryam Razzaghy Azar

appearance of clinical proteinuria to end-stage renal failure is usually irreversible. Without any intervention, approximately 80% of type 1 diabetic patients with persistent microalbuminuria develop overt nephropathy after 10-15 years. Eventually 50% of these develop end-stage renal failure within 10 years and 75% by 20 years. In type 2 diabetic patients, 20-40% with microalbuminuria progress to overt nephropathy and 20 years later, approximately 20% develop end-stage renal failure.⁵

The aim of this study was to find the prevalence of kidney dysfunction in patients with diabetes mellitus and assess its correlation with different factors.

Materials and Methods

This was a cross-sectional study of patients with diabetes mellitus, who presented to the Institute of Endocrinology and Metabolism for metabolic control. Among 6000 patients, 1203 cases were randomly recalled for physical examination, laboratory tests and filling out the questionnaires. Their diagnosis was established according to ADA (American Diabetic Association) criteria and classifications.⁶ All subjects gave informed consent.

Plasma glucose level was determined by using the enzymatic method. Glycosylated hemoglobin (HbA1c) was determined by electrophoresis. We considered HbA1c < 7 as good control, 7 ≤ HbA1c < 9 as fair control and HbA1c ≥ 9 as bad control. Urinary protein and creatinine were determined in 24-hour urine collection and spot urine dipstick. Albuminuria

or clinical proteinuria was defined as urinary protein more than 300 mg/24 hour or spot urine dipstick > 30 mg/dl (Table 1).⁷ Serum Creatinine > 115 μmol/l in males and > 97 μmol/l in females and blood urea nitrogen > 20 mg/dl were considered high.

Urine specimens for creatinine and protein measurements were frozen at -20 °C until analysis. Creatinine concentration (mg/dl) was determined with the Jaffe method. 24-hour urinary protein concentration was determined with turbidimetry assay. Blood urea nitrogen (BUN) was determined with the urease method. For those with previously diagnosed diabetes, the duration of diabetes was determined by self report.

SPSS (statistical package for social sciences) version 13 was used for data analysis. Pearson test and Student's t-test were used to assess the correlations between the variables and to compare mean values. P values less than 0.05 were considered significant.

Results

In the sample of 1203 patients with diabetes mellitus, 43 (3.6%) were newly diagnosed, and 1160 (96.4%) were known cases of diabetes. There were 438 patients (36%) with type 1 diabetes mellitus (T1DM) and 777 (64%) with type 2 diabetes mellitus (T2DM). They consisted of 512 females and 721 males. Mean ± SD of HbA1c was 7.9 ± 3.4 in T1DM and 7.4 ± 3.5 in T2DM. HbA1c showing good control was detected in 50.2% of patients, fair control in 20.4%, and bad control in 29.4%. Of 1022 patients evaluated

TABLE 1. Definitions of Albuminuria and Proteinuria

	Urine collection method	Normal	Microalbuminuria	Albuminuria or clinical proteinuria
Total protein	24-hour excretion (varies with method)	<300 mg/day	NA	>300 mg/day
	Spot urine dipstick	<30 mg/day	NA	>30 mg/day
	Spot urine protein-to-creatinine ratio (varies with method)	<200 mg/day	NA	>200 mg/day
Albumin	24-hour excretion	<30 mg/day	30-300 mg/day	>300 mg/day
	Spot urine albumin-specific dipstick	<3 mg/day	>3 mg/day	NA
	Spot urine Albumin-to-creatinine ratio (varies by gender*)	<17 mg/g (men) <25 mg/g (women)	17-250 mg/g (men) 25-355 mg/g (women)	>250 mg/g (men) >355 mg/g (women)

*Gender-specific cut-off values are from a single study. Use of the same cut-off value for men and women leads to higher values of prevalence for women than men. Current recommendations from the American Diabetes Association define cut-off values for spot urine albumin-to-creatinine ratio for microalbuminuria and albuminuria as 30 and 300 mg/g respectively, regardless of gender.

for proteinuria, 201 (19.7%) had albuminuria or clinical proteinuria. Of 931 patients, 19% had high levels of blood urea nitrogen and serum creatinine (Table 2).

End-stage renal disease (ESRD) was seen in 10 (0.8%) of all of the cases. A statistically significant positive correlation was found between duration of DM and serum creatinine ($P < 0.001$) and 24-hour urinary protein ($P < 0.001$).

TABEL 2. Characteristics of Study Groups

Variable	Diabetes (type 1)	Diabetes (type 2)
Duration (year)	6.46±6.9	12.1±7.5
Age (year)	19.49±11.6	53.47±10.9
BUN (mg/dL)	14.95±8.9	18.47±9.8
Urea amount	27.71±9.2	34.87±15.2
Serum creatinine (mg/dL)	0.82±0.4	1±0.7
24-hour urinary protein (mg/day)	174.96±463.0	319.12±833.1

All data are expressed as mean ± SD

Discussion

As reported recently, undiagnosed chronic kidney disease is common in diabetes. It is of importance because almost a half of the patients die before reaching end-stage renal failure and diabetic nephropathy has now become the single most common cause of end-stage renal disease. Early identification of kidney disease may allow for timely treatments that could arrest or delay the progression of renal damage.¹ We measured protein in 24-hour urine. As in some recent studies, proteinuria and high creatinine levels in T2DM were more prevalent than in T1DM.⁸ In other words, today many patients with type 2 diabetes live long enough to experience end-stage renal disease. Important factors contributing to the high prevalence of diabetic nephropathy in the population of patients with type 2 diabetes are delayed diagnosis of diabetes and poor glycemic control.⁷ In our study, 20.4% and 29.4% of the patients had fair and bad HbA1c control, respectively. Hyperglycemia appears to be an important underlying cause of proteinuria in patients with type 2 diabetes,⁹ but in our study patients with type 1 diabetes had higher HbA1c. The greater duration of T2DM may be related to higher proteinuria and creatinine levels in patients. Furthermore, recent studies have demonstrated that insulin resistance precedes the onset of microalbuminuria in type 2 diabetes.^{10,11}

By correlation analysis, we found direct significant relationships between duration of diabetes and 24-hour proteinuria, and creatinine excretion. In several

studies, the duration of diabetes has been recognized as the strongest predictor of microalbuminuria, but even when the diagnosis of T2DM has only recently been made, a sizeable proportion of patients (15-20%) already have an elevated rate of urinary albumin excretion.^{4,12,13}

As indicated by Aryal and Jha, these findings suggest that control of diabetes should decrease the risk of proteinuria, thus decreasing ESRD and its associated mortality.¹⁴ The American Diabetic Association (ADA) recommends annual testing for microalbuminuria in patients with type 1 diabetes at 5 years of onset and in all patients with type 2 diabetes after the time of diagnosis.¹⁵ Detection of microalbuminuria is now possible in some laboratories in Iran, enabling early diagnosis of kidney damage. Evaluation of renal function is important in order to select the appropriate strategy to reduce the progression of renal damage. There is a need for early diagnosis and optimal management of diabetic patients with renal dysfunction.

References

- Gajewska HB, Malyszko J, Malyszko JS, Musial W, Dobrzycki S. Undiagnosed renal impairment in patients with and without diabetes with normal serum creatinine undergoing percutaneous coronary intervention. *Nephrology*. 2006;11:549-554.
- Rao PV, Lu X, Standley M, Pattee P, Neelima G, Girish G, Dakshinamurthy V, Roberts CT Jr, Nagalla SR. Proteomic identification of urinary biomarkers of diabetic nephropathy. *Diabetes Care* 2007;Mar30(3):629-37.
- Williams textbook of endocrinology 2002.
- Jensen JS, Clausen P, Borch-johnsen K, Jensen G, Feldt-rasmussen B. Detecting microalbuminuria by urinary albumin/creatinine concentration ratio. *Nephrology Dialysis Transplantation*. 1997;12(2):6-9.
- Janet Joy Kachuchuru Lutale, Hrafnkell Thordarson, Zulficarali Gulam Abbas, Kare Vetvik. Microalbuminuria among Type 1 and Type 2 diabetic patients of African origin in Dar Es Salaam, Tanzania. *BMC Nephrology*. 2007;8:2.
- The American Diabetes Association: Standards of medical care in diabetes—2006. *Diabetes Care*. 2006;29(1):S4.
- Ritz E. Nephropathy in type 2 diabetes. *Journal of Internal Medicine*. 1999;245: 111-126.
- Hasslacher C, Ritz E, Wahl P, Michael C. Similar risks of nephropathy in patients type 1 or type 2 diabetes mellitus. *Nephrol Dial Transplant*. 1989;4:859-863.
- Ballard DJ, Humphrey LL, Melton LJ, Frohnert PD, Chu PC, O' Fallon WM .Epidemiology of persistent proteinuria in type 2 diabetes mellitus. Population based study in Rochester, Minnesota. *Diabetes*. 1988;37:405-412.
- Nosadini R, Solini A, Velussi M, Muollo B, Frigato F, Sambataro M et al. Impaired insulin-induced glucose uptake by extrahepatic tissue is hallmark of NIDDM patients who have or will develop hypertension and microalbuminuria. *Diabetes*. 1994;43:491-494.
- Mykkanen L, Haffner SM, Kuusisto J, Pyorala K, Laakso M. Microalbuminuria precedes the development of NIDDM. *Diabetes*. 1994;43:552-557.

12. Keller CK, Bergis KG, Flkiser D, Ritz E. Renal findings in patients with short term type 2 diabetes. JASN 1996;7:2627-2635.
13. Standle E, Stiegler H. Microalbuminuria is a random cohort of recently diagnosed type 2 diabetic patients living in the greater Munich area. Diabetologia.1993;36: 1017-1020.
14. Aryal M and Jha B. Assessment of proteinuria as a marker of nephropathy in type 2 diabetes mellitus. Nepal Med Coll J. 2006;8(4):250-253.
15. The American Diabetes Association: Standards of medical care in diabetes. Diabetes Care 2006;29(1):S4.

Archive of SID