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Prevalence of Diabetic Nephropathy in Turkish Children with Insulin-Dependent Diabetes Mellitus

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Abstract: This study was involved with determining the prevalence of diabetic nephropathy in 72 Turkish children with insulin-Dependent diabetes mellitus. Diabetic nephropathy was diagnosed with blood pressure levels, glomerular filtration rate, albumin excretion rate, β-2 microglobulinuria and kidney length. There wereo significant differences between laboratory data for boys and girls, but adolescent patients had significantly higher albumin excretion rates than preadolescent patients ($p<0.05$). The mean kidney length of the diabetic patients was 1-2 cm longer than in health children.

It was found that the prevalence of clinical diabetic nephropathy in pediatric patients with insulin-dependent diabetes mellitus was 5.5%. Four patients who were diagnosed as having diabetic nephropathy were given ACE inhibitors and were put under strict metabolic control. The progression of the disease reversed in two patients. However, in the other two end stage renal failure developed. This may be due to some unexplained genetic factor as well as the patients' ages.

In order to prevent diabetic nephropathy the conventional two dose insulin regimen was abandoned and a new intensive insulin regimen was adopted.

Key Words: İnsulin-dependent diabetes mellitus, diabetic nephropathy, prevalence.

Introduction

Although the long-term complications of insulin-dependent diabetes mellitus (IDDM) have long been recognized (1, 2), the population-based epidemiologic data of complications have not yet been determined in the Turkish pediatric population. The major cause of morbidity and mortality of IDDM is diabetic nephropathy in young patients (1, 2). Owing to advances in the diagnosis and treatment of diabetic nephropathy, its management has become more effective and is now initiated earlier after the presence of microalbuminuria has been established.

This paper focuses on determining the prevalence of nephropathy in diabetic patients who were followed up in our pediatric endocrinology clinics. The preliminary data obtained forced us to change our conventional protocol for improving metabolic control in order to prevent nephropathy.

Material and Methods

This cross-sectional study involved a total of 72 diabetic patients, 31 girls and 41 boys, who were followed up at the pediatric endocrinology clinic, aged between 5 and 16 (mean 12.7±6.8). All received conventional therapy of mixed-split insulin by two daily injections of insulin. Their glucose was monitored and they received education for nutritional planning and exercise.

Blood pressure was measured in the sitting position on each visit after a 5-minute rest, with an ordinary mercury sphygmonometer with appropriately sized cuffs.

Blood samples were taken for serum glucose, glycosylated hemoglobin (HbA1c), serum creatinine, BUN, albumin, electrolytes. The 24-hour urine samples were collected for creatinine clearance, albumin excretion rate (AER) and β-2 microglobulinuria. The glomerular filtration rate (GFR) was calculated and

Table 1. The Clinical and Laboratory Data of the 72 Diabetic Subjects.

	Total diabetic (n:72)	Girls (n:31)	Boys (n:41)	Preadolescent patients (n:30)	Adolescent patients (n:42)
Mean age (year)	12.7±6.8	12.9±4.1	11.9±7.4	8.3±2.9	14.7±2.5
Mean duration of diabetes (year)	4.5±3.1	4.4±2.2	3.8±2.3	3.4±1.7	5.0±2.5
HbA1c(%)	9.5±4.3	9.4±3.9	9.8±4.4	9.1±4.6	9.8±3.6
Insulin dosage (U/kg)	0.7±0.2	0.8±0.3	0.6±0.2	0.6±0.2	0.8±0.3
Glomerular filtration rate (ml/min/1.73)	121±32.4	120.5±21.7	122±41.8	136.5±43.3	115.0±12.7
Blood pressure (mm/Hg): systolic	110.1±10.5	110.5±11.6	109.9±9.5	104.3±13.4	122.2±7.5*
diastolic	64.7±11.5	63.6±11.0	65.6±11	62.5±6.9	74.3±113
Albumin excretion rate (μg/min)	120±118.4	125±114.4	116±120.3	94.4±114.4	154.4±110*
β-2 microglobulin (mg/L)	0.6±0.5	0.7±0.2	0.6±0.5	0.9±2.5	0.3±0.2
Kidney length (cm)	93.7±3.0	-	-	92.5±5.8	95.6±1.9
Kidney length of healthy childen (cm)	92.1±2.9	-	-	91.5±4.6	94.5±2.7

Adolescent patients have significantly higher blood pressure and AER than preadolescent patients (*p<0.05).

Table 2. The Initial Clinical and Laboratory Data of the 4 Nephropathic Diabetic Patients.

	Case 1	Case 2	Case 3	Case 4
Duration of diabetes (year)	9	12	1.5	2
Age (year)	14	16	16	15
Sex	M	F	F	F
Systolic blood pressure (mmHg)	130	135	130	135
Diastolic blood pressure (mmHg)	90	95	85	90
Glomerular filtration rate (mm/min/1.73)	58	65	40	48
Albumin excretion rate (μg/min)	250	245	260	310

corrected for 1.73 m^2 body surface area. The baseline AER was calculated from the mean of the three 24-hour urine samples.

HbA1c was measured with latex agglutination methods (Bayer Diagnostic). Urinary albumin and β-2 migroglobulin were measured by double antibody radioimmunoassay (Pharmacia).

Kidney ultrasonography was performed with a renal time scanner with a 3.5 MHZ transducer. Kidney lengths were measured bilaterally and mean kidney lengths were calculated for each subject. As a control, two sex-age matched healthy children's kidney length was measured for each diabetic patient.

The statistical analyses were performed with the Mann Whitney-U test.

Results

The study involved 72 patients with IDDM. The demographic and laboratory data of the subjects are

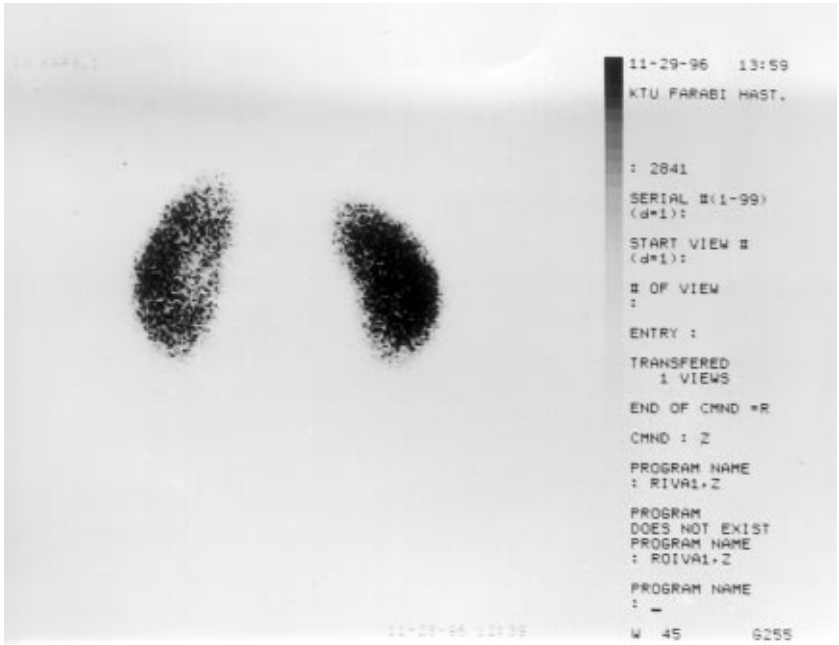

Figure. Renal scintignophy shows marked cortical uptake defects.

shown in Table 1.

There were no significant differences between the demographic and laboratory data for boys and girls, although girls had a slightly higher albumin exretion rate ($p>0.05$). Preadolescent patients had higher GFR and urinary β-2 microglobulin levels than adolescent patients, but this was not statistically significnat ($p>0.05$). Adolescent patients had significantly higher blood pressure and AER than preadolescent patients ($p<0.05$). Although there were no significant differences between the kidney lengths of diabetic and healthy subjects ($p>0.05$), the mean kidey length of the diabetic patients was 1-2 cm longer even if sex and age was taken into consideration.

Of the 72, 4 patients were considered as having diabetic nephropathy. Their laboratory data is shown in table 2. The prevalence of diabetic nephropathy was found to be 5.5% in our population.

Discussion

Nephropathy is a diabetes-specific complication associated with the highest mortality. Nephropathy develops in 35-45% of cases of IDDM. The natural history of clinically detectable diabetic nephropathy in IDDM begins with the development of microalbuminuria (30-300 mg albumin per 24 hours) which may occur as early as five years after the onset of diabetes. This stage of incipient nephropathy may be more likely in patients with glomerular hyperfiltration (glomerular filtration rate >150 ml per minute). Overt proteinuria (>500 mg of protein per liter, equivalent to 300 mg of albumin per 24 hours) develops in patients after another 5 to 10 years of diabetes. Hypertension invariably develops during this period. The appearance of persistent proteinuria and hypertension is considered clinically overt nephropathy. Although the prevalence of diabetic nephropathy in IDDM patients has been studied with large series in the world, population-based studies in Turkey have not been carried out (1-5).

Several studies showed elevated GFR in IDDM similar to our findings. Elevation of GFR is a phenomenon that occurs with hyperglycemia, but appears to be multifactorial (6). GFR was found to decline with long duration of diabetes in our series. This might not be considered clinical nephropathy because the levels of GFR were still within the normal range except in four patients.

We studied the excretion of albumin as a marker of the glomerular dysfunction and excretion of β-2 microglobulin as a parameter of the dysfunction of renal tubules. The levels of urinary β-2 microglobulin were found to be higher in newly diagnosed patients. Several studies have demonstrated renal tubular parameters to be abnormal during the early course of IDDM (7, 8).

High mean AER in total diabetic phatients in our series may be explained by the poor metabolic control (9, 10). Slightly higher mean AER in girls and significantly higher AER in adolescent patients were found. In healthy

subjects the reference value of AER changes according to age and sex; the values of AER increase with age and the normal values for females are significantly higher than for males. This should be taken into consideration in the assessment of diabetic nephropathy in IDDM (11).

The occurrence of microalbuminuria and its relation to puberty has also been reported in the course of diabetic nephropathy (12). The higher values of AER for adolescent patients found in our study may be an indication of diabetic nephropathy.

Over the pats two decades there has been increasing interest in hypertension as a risk factor for diabetic renal disease (13, 14). Higher blood pressure levels in our adolescent patients were not thought to be related with the progression of nephropathy because their blood pressure levels were within the physiological limits for their chronoloical age.

Kidney hypertrophy is a well known manifestation of diabetic nephropathy, and it involves both glomerular and tubular elements, due to progressive accumulation of extracellular matrix components in the glomerular and tubular basement membrane (15, 16). Although there were no significant differences between diabetic and healthy subjects, we found the kidneys of the diabetic patients to be slightly longer.

Only four patients with persistent proteinuria with mild hypertension and decreasing GFR were diagnosed as having clinical nephropathy. Two patients with clinical nephropathy had had DM for more than five years but the other two patients had had overt nephropathy in the very early stage of their disease. The prevalence found in this study was 5.5%. ACE inhibitors were used in all four patients, and in two, AER decreased in microalbuminuric levels. However the other two showed a rapid progression of renal failure. The progression of diabetic renal disease depends on genetic factors and shows ethnic variations (17, 19). Such early occurrence of renal failure in our two patients may be due to an unexplained genetic factor as well as the patients' pubertal ages.

The incidence of diabetic nephropathy has been

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