Original Article

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Frequency of Microalbuminuria in Type 1 Diabetic Children

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Abstract

Objective: Diabetic nephropathy is a serious complication of type 1 diabetes which involves one third of the patients. The aim of this study was to estimate the frequency of microalbuminuria in type 1 diabetic patients visited in Pediatric Endocrine Clinic in Hamedan, west province of Iran, in 2007.

Methods: Diabetic patients visited in Pediatric Diabetes Clinic were enrolled in the study. Variable data such as age, sex, duration of the disease, stage of puberty, dose of insulin/kg/day, and blood pressure of the patients were obtained according to history and physical examination. 24h urine samples were collected for protein, creatinine, and microalbumine. Data analysis was assessed using independent *t*-test and chi-square test**.**

Findings: One-hundred five patients (56 females and 49 males) with a mean age of 13.3±5.5 years, were evaluated. Fifteen (14.3%) cases had microalbuminuria. Mean age in microalbuminuric group was 16.2±2.8, and in non-microalbuminuric group was 12.7±5.6 years (*P*=0.024). Mean duration of diabetes was 9.1±3.2 yr in microalbuminuric and 4.5± 3.9 in non-microalbuminuric group. There was a significant correlation between duration of diabetes and microalbuminuria (*P*<0.001). Blood pressure was normal in 95.5% of the patients while in patients with microalbuminuria 73.3% had hypertension (*P*<0.001). Frequency of micro-albuminuria was higher in patients taking lower doses of insulin corrected to their body weight (*P*=0.008).

Conclusion: Frequency of microalbuminuria was significant, so regular screening is highly recommended for early detection and timely treatment of diabetic nephropathy in order to prevent progression to end stage renal disease.

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Key Words: Diabetes type 1; Frequency; Microalbuminuria; Children

Introduction

The increasingly prolonged survival of the diabetic child is associated with an increasing prevalence of complications affecting microcirculation including nephropathy[1].

Patients with type 1 diabetes face a 20–50% risk of developing end-stage renal disease

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(ESRD) requiring dialysis or renal transplantation[2]. Albumin excretion rate (AER) remains the best available noninvasive predictor for diabetic nephropathy[3]. Because it is the earliest clinically detectable stage of diabetic kidney disease at which appropriate interventions can retard or reverse the progress of the disease, it should be measured regularly according to established guidelines[4,5].

Screening for microalbuminuria should be performed yearly, starting 5 years after diagnosis in type 1 diabetes or earlier in the presence of puberty or poor metabolic control [6].

Microalbuminuria confers a 60 to 85 percent risk of the development of overt proteinuria within 6 to 14 years [7]. Without any intervention, approximately 80% of type 1 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[7,8]. Although microalbuminuria is well recognized as a risk factor for the development of diabetic nephropathy in adults, its natural history is less clear in children and adolescents [9].

The incidence of micro- or macroalbuminuria in type 1 and type 2 diabetic individuals varies greatly among different populations. There is a racial difference in prevalence of diabetic nephropathy and end stage renal failure.

Diabetic nephropathy is more prevalent among African Americans, Asians, and Native Americans than in Caucasians[6,10-13]. The frequency and risk factors of microalbuminuria are not fully described among children and adolescents with type 1 diabetes in our region. The aim of this study was to determine frequency of microalbuminuria among children with type 1 diabetes mellitus in Hamedan, a west province of Iran.

Subjects and Methods

One hundred five patients with type 1 diabetes who had been treated with insulin before 20 years of age were enrolled in this study. They were visited in outpatient clinic for diabetics regularly. Patients were screened according to established guidelines, which recommend annual assessment beginning 5 years after diagnosis in prepubertal children and 2 years after diagnosis in pubertal children [14]. Patients attending the outpatient diabetes clinic for their regular visits who accepted to participate in the study were included. The study lasted from October 2005 to September 2007. After receiving informed consent from all patients they were interviewed using a standardized questionnaire.

The history including age, gender and disease duration was obtained. Clinical assessment was done during a visit by the pediatric endocrinologist. Blood was collected for chemistry and HbA_{1C} level and urine for microalbuminuria. Assessment of complications was undertaken during a 2h visit. Blood pressure was measured with an aneroid sphyngomanometer (Reichter Co.) in the supine position with a cuff of appropriate size twice at 10 minutes interval in two separate visits. Hypertension was defined as over 95 percentile of blood pressure according to standardized table of age, gender and height.

Estimation of microalbuminuria was performed by the following method: 24h urine collection with measurement of creatinine and microalbumin concentration by a immunoturbidometric assay (Hitachi 902 autoanalyser; Roche Diagnostics.). Microalbuminuria was defined as albumin excretion ≥20 μg/min and <200μg/min, and macroalbuminuria as over 200μg/min.

Glycemic control was assessed as average HbA_{1C} level during 1-year period. It was measured using Bayer DCA 2000+ analyzer and a value of less than 7% was regarded as good glycemic control. Patients with short course hyperglycemia, exercise, urinary tract infection, hypertension crisis, cardiac disease, renal disease, diabetic ketoacidosis and acute febrile disease at the time of 24h urine collection were excluded from the study.

Statistical analysis: Data analysis was assessed by independent *t*-test and chi-square test. Analysis was done using Windows-based SPSS statistical package version 15. Mean values were reported with standard deviations. $P<0.05$ was considered statistically significant.

Ethical consideration: The study was conducted in accordance with The National Ethical Committee at the Ministry of Health and Medical Education in Iran. The Committee of Ethics in Research of Hamedan University of Medical Sciences approved the study in 2004.

Findings

In this study 105 patients (56 females and 49 males) were evaluated. Mean age of patients was 13.3±5.5 years and mean duration of disease 5.2±4.1 years. 15 patients (14.3%) had microalbuminuria and one patient (1%) had overt proteinuria. In microalbuminuric group 8 (53.3%) were females, and in non-microalbuminuric group 47 (52.8%) were females. Sex distribution was not statistically different between microalbumiuric and non-microalbuminuric group (P=0.9). Mean age of patients with microalbuminuria was significantly different from non–microalbuminuric group (16.2±2.85 vs 12.7±5, P=0.024). Mean duration of disease was longer in microalbuminuric patients with significant difference (9.1±3.2 vs 4.5±3.2, P<0.001). Microalbuminuria increased with increasing age and disease duration.

Eleven (73.3%) patients in microalbuminuric group and 4 (4.5%) without microalbuminuria had hypertension. Microalbuminuria was significantly associated with hypertension (P<0.001). Microalbuminuria was more common in patients who received lower doses of insulin corrected to their body weight. There was also a significant association between microalbuminuria and low insulin administration (unit/kg/day) (P=0.008).

Average Level of HbA_{1c} was higher than 10.5% in 60% of patients with microalbumnuria and in 17.9% of nonmicroalbuminuric group. Significant difference was found between the level of HbA_{1c} and microalbuminuria (P<0.001). Mean GFR was 111.2±22.6 in microalbuminuric group.

Discussion

The presence of proteinuria is a sign of early diabetic nephropathy. The incidence of micro- or macro-albuminuria in type 1 and type 2 diabetic individuals varies greatly among different populations. Despite that, little is known about microalbuminuria in our region.

In our study frequency of microalbuminuria among diabetic patients was 14.3% and rate of overt proteinuria 1%. This is consistent with data from Lutale et al, who found microalbuminuria in 12% and macroalbumiuria in 1% of their patients[7]. The cumulative incidence of microalbuminuria in patients with type 1 diabetes was 12.6% over 7.3 years according to the European Diabetes Prospective Complications Study Group (EURODIAB)[15,16], ~33% in an 18-year follow-up study in Denmark[16], and 19% in Bramlage study[17]. In African Americans with type 1 diabetes, incidence of proteinuria was significant, particularly among young patients and those with a relatively short duration of diabetes according to Roy's study[11,12,13.18].

There was no sex predilection in microalbuminuric patients in this study but Patel and Raile showed that microalbuminuria was more common in their male patients [19,20].

Mean duration of disease was longer in microalbumiuric group. This finding was similar to the results of Patel and Lutale studies[7,19] and indicates higher risk of microalbuminuria in diabetic patients with longer duration of the disease. Risk factor for microalbuminuria was length of diabetes duration in Raile's study [20].

In the present study microalbuminuria was significantly associated with hypertension. Lutale, Roy and Patel found similar results in their studies [7,11,19].

In agreement with other studies we also found meaningful correlation between HbA_{1C} level (glycemic control index) and microalbumiuria in present study. For instance, Patel, Roy and Klein also showed correlation between higher rate of microalbuminuria and poor glycemic control (high level of HbA_{1C}) [11,19]. In contrast to this study Lutale did not find any significant difference in glycemic control levels among

diabetic patients without microalbuminuria compared to those with elevated albumin excretion rate[7]. Some authors suppose that it is the interaction of hyperglycemia with hypertension that may be the main factor in the development of diabetic nephropathy[21], but previously published studies have shown that poor glycemic control is the risk factor for proteinuria[11,19,21,22,23]; for instance, in the Diabetes Control and Complications Trial, intensive glycemic control reduced the 9-year incidence of microalbuminuria by 37%[22].

In our patients there was no case of microalbuminuria before puberty and 9 of microalbuminuric patients were in stages 4-5 of puberty. Donaghue et al reported that risk for retinopathy and microalbuminuria increases as the child approaches the clinical onset of gonadarche[24]. Frequency of microalbuminuria was higher in patients who received lower doses of insulin corrected to their body weight in our study. This led the authors to suggest that one of the reasons for poor glycemic control is low insulin administration.

Finally, normal or high normal GFR in our microalbuminuric patients was consistent with known data in the literature. Overt diabetic nephropathy is characterized by an initial period of transient rise in GFR, associated with progressively increasing proteinuria, and followed by a gradual decline in glomerular filtration rate resulting in ESRD [25,26].

However, we realize that there are inherent limitations in our study. The sample size was relatively small. It is therefore possible that multicenter study in different parts of Iran show different results. In addition, study was done in a relatively short period, so that further studies with longer period of follow up may show different results.

Conclusion

Frequency of microalbuminuria was significant in children and adolescents with diabetes type 1 in our region. So annual screening of diabetic patients for microalbuminuria particularly after puberty is highly recommended for early diagnosis and management of diabetic nephropathy.

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