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Microalbuminuria and glycated hemoglobin in children with type 1 diabetes mellitus

Magdy A. Omar [a], **Moustafa M. Rezk** [b], **Ahmed A. El-Kafoury** [a,*], **Marwa S. Kandil** [a]

[a] *Department of Pediatrics, Faculty of Medicine, Alexandria University, Egypt*
[b] *Department of Clinical Pathology, Alexandria University, Faculty of Medicine, Egypt*

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Abstract Diabetic nephropathy (DNP) is a microvascular complication that occurs in 20–40% of patients with type 1 diabetes (T1D). The main modifiable DNP initiation and progression factors in susceptible individuals may be sustained hyperglycemia and hypertension. The aim of the present work was to study glycemic control in children with T1D and the risk of microalbuminuria (MA) expressed as the urinary albumin/creatinine ratio (ACR).

Subjects and methods: Forty children with T1D attending the diabetes clinic at the Alexandria University Children's Hospital with a duration of diabetes of 3 years or more were included in the study and twenty apparently normal children were taken as controls. Clinical examination and blood pressure measurements were performed for all cases. Urine samples were collected within a 3–6 month period. The ACR in 2 of 3 specimens should be >30 mg/g before considering a patient to have microalbuminuria. HbA1c was measured and the mean of the last 4 readings was calculated.

Results: 77.5% of patients had ACR >30 mg/g in two different samples. 88.8% of patients with poor glycemic control had MA compared to 53.8% with accepted glycemic control. The difference was more statistically significant among the adolescent age group ($P = 0.001$). MA was found in 77.2% of children with duration of T1D less than 5 years but the highest proportion was found when the disease duration was more than 10 years. There was no significant difference in systolic and diastolic blood pressure among diabetic children with and without MA ($P = 0.556$ and 0.781).

* Corresponding author. Address: Alexandria University Children's Hospital, Port Said Street, Alexandria, Egypt. Tel.: +20 1222989642; fax: +20 203 4876099.
E-mail address: aaakafouri@hotmail.com (A.A. El-Kafoury).

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Conclusion: Microalbuminuria in children with T1 DM is not limited to those with disease duration of 5 years or more and it may occur earlier. MA is significantly associated with poor glycemic control especially in adolescents. Other factors that may contribute to MA are not yet fully understood, further research is needed to clarify these factors.

1. Introduction

The chronic hyperglycemia of diabetes is mostly associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.[1]

Diabetic microvascular and macrovascular complications may have similar etiologic characteristics. Chronic hyperglycemia plays a major role in the initiation of diabetic vascular complications through many metabolic and structural derangements, including the production of advanced glycation end products (AGE), abnormal activation of signaling cascades such as protein kinase C, elevated production of reactive oxygen species (ROS, oxygen-containing molecules that can interact with other biomolecules and result in damage), and abnormal stimulation of hemodynamic regulation systems, such as the renin-angiotensin system [RAS].[2]

Diabetic nephropathy (DNP) is a microvascular complication that occurs in 20–40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). The main potentially modifiable DNP initiation and progression factors in susceptible individuals may be sustained hyperglycemia and hypertension.[3]

The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels of albumin in the urine (>30 mg/day or 20 μg/min), referred to as microalbuminuria (MA), and patients with MA are referred to as having incipient nephropathy. Without specific interventions, 80% of subjects with type 1 diabetes who develop sustained MA have their urinary albumin excretion increase at a rate of 10–20% per year to the stage of overt nephropathy or clinical albuminuria (300 mg/24 h or 200 μg/min) over a period of 10–15 years, with hypertension also developing along the way. Once overt nephropathy occurs, without specific interventions, the glomerular filtration rate (GFR) gradually falls over a period of several years at a rate that is highly variable from individual to individual (2–20 ml min^{-1} $year^{-1}$). Eventually, ESRD develops in 50% of type 1 diabetic individuals with overt nephropathy within 10 years and in $>75\%$ by 20 years.[3]

The Diabetes Control and Complication Trial (DCCT), a prospective, randomized, controlled trial of intensive versus standard glycemic control in patients with T1D showed that improved glycemic control is associated with significantly decreased rates of microvascular complications (retinopathy, nephropathy and neuropathy).[4]

However, fewer data exist on the relation between HbA1c and risk of MA in children with type 1 DM.[5]

The aim of the present work was to study glycemic control in T1D expressed as the mean of the last 4 readings of glycated hemoglobin (HbA1c) and the risk of MA expressed as the urinary albumin/creatinine ratio (ACR).

2. Subjects and methods

This study was conducted on 40 patients diagnosed with T1D attending the diabetes clinic at the Alexandria University Children's Hospital. The inclusion criteria were: type 1 DM, age: 5–18 years and duration of DM 3 years or more. Patients with evident organ system disease like hemolytic anemia and patients receiving drugs known to affect urinary albumin excretion e.g. corticosteroids, were excluded.

Ethical approval was obtained from the Ethics Committee of the Alexandria Faculty of Medicine and an informed consent was obtained from parents.

All cases were subjected to complete history taking and clinical examination. Arterial blood pressure was measured on the right arm with a standard clinical sphygmomanometer after the patient had been sitting for 10 min. Cases with blood pressure values $\geqslant$90th centile for age were considered prehypertensive while cases $\geqslant$95th centile were considered hypertensive.[6]

Quantitative determination of microalbumin (μALB) was done by urinary microalbumin–turbilatex which is a quantitative turbidimetric test for measurement of μALB in human urine. Urinary creatinine was measured using an automated colorimetric determination based on a modified Jaffe reaction.[7] The albumin/creatinine ratio was obtained by dividing microalbumin (mg/L) by creatinine (g/L). Because of variability in urinary albumin excretion (UAE), two of three specimens collected within a 3–6 month period should be abnormal before considering a patient to have abnormal albumin/creatinine ratio.[8]

HbA1c was measured by Nyco Card and the mean of the last 4 readings was calculated. The age was considered when setting glycemic goals in children and adolescents with type 1 diabetes i.e. for toddlers, 8.5% was considered accepted, school age $<8\%$ and in adolescents $<7.5\%$.[9]

Data were fed to the computer using SPSS software package version 20. Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test. Quantitative data were described using mean and standard deviation. Significance was determined as $P < 0.05$.

3. Results

Table 1 shows that both cases and controls were comparable as regards age and sex but showed a significant difference in family history of DM ($P = <0.001$). The mean duration of DM in the cases was 6.77 ± 3.1 years. It shows also that in 31 out of 40 cases (77.5%) ACR was >30 mg/g in two different samples collected within a 3–6 month period. None of the controls had ACR >30 mg/g.

Table 2 shows the age and duration of T1 DM in patients with accepted glucose control versus poor control. The statistical