Evaluation of Microalbuminuria 4 to 6 Years Following Type 1 Diabetes in Children

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Abstract

Objective: Diabetic nephropathy is one of the major complications and a leading cause of mortality and morbidity in diabetes mellitus. Microalbuminuria is the earliest sign of diabetic nephropathy and it is highly related to glycemic control. Progression of diabetic nephropathy is mostly asymptomatic until advanced stages of renal failure. In this study microalbuminuria and its correlation with duration of diabetes and quality of diabetes control (HbA1c level) is evaluated in 50 children with type 1 diabetes mellitus.

Material & Methods: Fifty children 4 to 6 years following the onset of type 1 diabetes, below 20 years of age, were enrolled in this study. Twenty four hrs urine was checked twice within 3 to 6 months period for microalbuminuria by nephelometry method and values >30 mg/24hrs were considered abnormal. Also HbA1c level and FBS level assessed simultaneously. Mean FBS level during the years of diabetes and number of attacks of DKA were

Findings: Fifty children, 4 to 19 years old with mean age of 14.54 ± 3.62 years, 28 (56%) males completed the study. Nineteen (38%), 14 (28%) and 17 (34%) children enrolled in this study 4, 5, 6 years after the onset of their diabetes respectively. At 1st evaluation microalbuminuria was detected in 5 (26.3%), 4 (28.6%) and 6 (35.3%) children, 4, 5, 6 years after diabetes respectively. At 2nd evaluation these values were 4 (21.1%), 6 (42.9%) and 7 (41.2%) respectively. There was no significant correlation between HbA1c level, FBS level, and number of attacks of DKA were

Conclusion: Despite small sample size of this study, microalbuminuria was detected in children even 4 years after the onset of diabetes and its frequency increased in children with 5 and 6 years of diabetes. We recommend earlier than usual recommendations for microalbuminuria screening in diabetic children.

Key Words: Microalbuminuria, Diabetic Nephropathy, Diabetes mellitus, HbA1c,
Introduction

Despite advances in management of diabetes mellitus (DM), it remains one of the major causes of morbidity and mortality, yet. Diabetic nephropathy is one of the main complications of DM and the most common cause of end stage renal disease (ESRD) in most of the dialysis centers [1,2].

Diabetic nephropathy is heralded by progressive proteinuria, hypertension and progressive loss of renal function [3,4]. DM is the fourth cause of mortality in most of the developed countries [5,6]. Generally, 5-15 years following the onset of insulin dependent diabetes mellitus (IDDM) 30-50% of patients suffer from renal complications [4,5].

Microalbuminuria is a beginning to the renal complications of DM. It is a significant index for early detection as well as monitoring the progression of diabetic nephropathy [7]. Every diabetic patient should be monitored for microalbuminuria, for early diagnosis and management [8-10]. Microalbuminuria is defined as 30 to 300 mg/day or 20-200 μg/min of microalbumin in a 24-hour urine collection [1, 11-14]. Onset of microalbuminuria is usually more than 5 years after the beginning of DM [1,2]. Usually there are no specific signs and symptoms for diabetic nephropathy until it reaches advanced stages of renal failure [4,5]. For the first time, Mogensen classified Diabetic nephropathy into 5 steps. The 3rd step was labeled microalbuminuria or incipient nephropathy [1,15].

Regarding the reversible nature of incipient nephropathy, screening for microalbuminuria is routinely suggested in management of DM [1-5,7]. Some disease states or conditions may cause microalbuminuria including: hypertension, urinary tract infection, congestive heart failure, chronic hyperglycemia, fever and intensive exercise and we should consider for these events in our daily practice [4,11,14].

This study was performed as a pilot to see the state of microalbumin excretion in our diabetic children 4 to 6 years after the onset of type 1 diabetes. Also the association between microalbuminuria and metabolic control of DM was assessed.

Material & Methods

This randomized cross sectional study was performed on 50 children with type 1 DM in our center. This study was performed during a 9-month period (April 2006 to December 2006). Inclusion criteria were: age under 20, duration of disease 4 to 6 years, complete hospital and outpatient medical records, regarding previous blood sugar levels and number of admissions, number of attacks of diabetic ketoacidosis (DKA). Exclusion criteria were incomplete previous medical records and circumstances that may effect microalbuminuria including either temporary or permanent such as fever, intensive physical activity, UTI and hypertension.

By referring to diabetic center and hospital records, the name and file number of children who had been diagnosed as IDDM 4 to 6 years ago was obtained and 65 of them were selected randomly out of 128 children in this category. A written consent was obtained from them and/or their parents.

Fasting blood sugar (FBS), 24 hr urine collection for microalbumin and creatinine measurement and hemoglobin A1c (HbA1c) level were evaluated in patients. Creatinine measurements were done for assessing accurate sample collection. A through chart review was done and also we considered some important information including the number of attacks of DKA from the patients or parents. Microalbumin determinations in 24 hr urine collection were repeated once more within a 3 to 6 month period. Microalbuminuria was checked by Nephelometric assay and HbA1c level was checked by cation-exchange chromatography in a reference laboratory by an experienced laboratory technician.

Eventually we categorized the patients into 2 groups, group with microalbuminuria and group without it. We compared the variables such as yearly mean FBS, number of hospitalizations, number of attacks of DKA, HbA1c level, age and gender between the 2 groups.

The data were analyzed by SPSS (version 13) and Chi-square test, Fisher exact test and Mann-Whitney test is used for analyzing of data.
Fifty children completed the study. The age range at enrollment to the study was 4 to 19 years (mean ± SD 14.54 ± 3.62 years). There were 28 (56%) males and 22 (44%) females. The time interval from onset of diabetes was 4 years in 19 (38%), 5 years in 14 (28%) and 6 years in 17 (34%) of the children.

During the first time of laboratory evaluations microalbuminuria (24 hr urine microalbumin> 15 mg/l of urine) was detected in 15 (30%) cases. Microalbuminuria was present in 5 (26.3%), 4 (28.6%) and 6 (35.3%) of the children with 4 years, 5 years and 6 years of diabetes, respectively. In second evaluation, microalbuminuria was present in 4 (21.1%), 6 (42.9%) and 7 (41.2%) of children with 4 years, 5 years and 6 years of diabetes, respectively.

Regarding HbA1c level 26 (52%) of the children had levels >8% at the first evaluation and 28 (56%) at the second time.

There was no correlation between HbA1c level more than 8% and microalbuminuria in each step (first and second) ($P=0.7$, $P=0.9$). There was no correlation between the number of attacks of DKA in patients with and without microalbuminuria in each step (Table 1). In addition, the level of blood sugar didn’t have significant difference in the microalbuminuric and non-microalbuminuric children in each step ($P=0.4$, $P=0.9$).

Mean fasting blood sugar level during the years of diabetes mellitus (1st, 2nd, 3rd, 4th, 5th and 6th years) had no significant differences in children with and without microalbuminuria in each step ($P=0.5$, $P=0.9$) (Table 2).

<table>
<thead>
<tr>
<th>number of attacks of DKA</th>
<th>0</th>
<th>1</th>
<th>≥2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First step of evaluation</td>
<td>Yes</td>
<td>8 (32)</td>
<td>7 (31.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>17 (68)</td>
<td>15 (68.2)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Second step of evaluation</td>
<td>Yes</td>
<td>6 (24)</td>
<td>10 (45.5)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>19 (76)</td>
<td>12 (54.5)</td>
<td>2 (66.7)</td>
</tr>
</tbody>
</table>

Discussion

Diabetic nephropathy and cardiovascular disease are among the most common causes of mortality and morbidity in DM [1,2]. Microalbuminuria is the earliest sign of diabetic nephropathy and the simplest index for early detection of DM-related renal complications [3,4].

Thus a quantitative measurement of albumin in 24 hr urine is both specific and cost-benefit to the diabetic patient and the health system of a country. At our 1st evaluation, there were 15 cases (30%) with microalbuminuria and on 2nd evaluation 17 cases (34%).

In other studies the incidence of microalbuminuria in type 1 diabetes is between 3.7-30.6% and it depends on many factors, including age, duration of DM, race, glycemic control and eventually laboratory method used for urine microalbumin detection [9].

In our study, there was no reasonable relationship between microalbuminuria and lack of glycemic control (HbA1c >8%), this may be related either to a short period of evaluation, small sample size and HbA1c, that can predict only the glycemic control of previous 3 months [1,7].

We couldn’t find any correlation between the recent FBS, 4 PM blood sugar and the mean FBS during the years of diabetes in children with and without microalbuminuria, in our study. This can be related to small sample size, since, as has been clarified in many studies, tight glycemic control (HbA1c <8%) is associated with lower renal complications [5,6,9].

The important finding of this study was that 26.3% of our IDDM children 4 years after the
Table 2- Correlation of mean FBS with microalbuminuria at 1st and 2nd evaluation.

<table>
<thead>
<tr>
<th>FBS Microalbuminuric situation</th>
<th>≤ 160</th>
<th>&gt; 160</th>
<th>P value</th>
</tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (25)</td>
<td>13 (31)</td>
<td>0.5</td>
</tr>
<tr>
<td>No</td>
<td>6 (75)</td>
<td>29 (69)</td>
<td></td>
</tr>
<tr>
<td>Second step of evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (50)</td>
<td>13 (31)</td>
<td>0.9</td>
</tr>
<tr>
<td>No</td>
<td>4 (50)</td>
<td>29 (69)</td>
<td></td>
</tr>
</tbody>
</table>

onset of diabetes had microalbuminuria and this is contrary to the result of other studies that onset of microalbuminuria is usually 5 years after the onset of IDDM.

Screening for microalbuminuria is recommended 3 years after the onset of diabetes or by the onset of puberty and diagnosis is made when 2 of the 3 tests are positive \[1,13-20\].

**Conclusion**

This study could be concerned as a pilot one regarding small sample size; however we can conclude that onset of microalbuminuria is earlier in our population and we should consider its earlier detection and appropriate management.

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**References**


