

Risk Factors Associated with Microalbuminuria in Children and Adolescents with Diabetes in Bangladesh

Bedowra Zabeen^{1,2}, Jebun Nahar¹, Nasreen Islam¹, Kishwar Azad^{1,2,3}, Kim Donaghue⁴

^{1,2}Department of Paediatrics and Changing Diabetes in Children Program, BIRDEM, ³Perinatal Care Project, BIRDEM, Dhaka 1000, Bangladesh, ⁴Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead Sydney, Westmead, NSW, Australia

Abstract

Introduction: Diabetic nephropathy is leading cause of morbidity and mortality of type 1 diabetes mellitus (DM). Microalbuminuria is the first clinical sign of nephropathy. **Methods:** This was a cross-section study with longitudinal evaluation of urinary albumin excretion in 199 children with type 1 diabetes attending CDiC Clinic in BIRDEM over a period of two years. The aim of the study was to assess the frequency of microalbuminuria and to determine other risk factors. We collected blood and early morning spot urinary sample and analyzed for HbA1c by Clover A1c and urinary microalbumin by a DCA analyzer. Children had urinary microalbumin 30-300 mg/L on at least two occasions were categorized as having persistent microalbuminuria. Demographic and clinical data were recorded including age at onset of diabetes, age during registration, gender and duration of diabetes which were compared between patients without microalbuminuria and with microalbuminuria. **Result:** Microalbuminuria developed in forty nine children and adolescents (25%). Among them 24% were Type 1, 27% were with Fibrocalculous pancreatic diabetes (FCPD) and 68% were Type 2 diabetes. Median HbA1c was higher 10.8 [9.4-12.4] vs 9.5 [8.0-11.2] ($P=0.006$) in adolescents with microalbuminuria. On logistic regression univariate analysis independent predictors of microalbuminuria were older age, systolic blood pressure, BMI SDS and mean HbA1c which remained significant in multivariate analysis as predictors of microalbuminuria. **Conclusion:** We found high prevalence of microalbuminuria which was associated with higher age, systolic blood pressure, BMI SDS and HbA1c.

Keywords: Adolescents, children, microalbuminuria, type 1 diabetes, type 2 diabetes

BACKGROUND

Diabetic nephropathy is the most common microvascular complication of type 1 diabetes which affects around 15%–40% patients, with a peak incidence after 15–20-year diabetes duration.^[1] Microalbuminuria is the earliest clinical stage of clinical nephropathy, and its persistence is highly predictive of progression to overt proteinuria and of risk for cardiovascular diseases.^[1] Several studies suggest that at these early stages, progression of diabetic nephropathy can be prevented.^[2-4] In people with childhood-onset type 1 diabetes, the cumulative prevalence of microalbuminuria is around 12%–25% after 5 to 10 years of diabetes.^[5-10] Within 2 decades of diabetes onset, a single episode of microalbuminuria is found in 2%–18% of children and adolescents with type 1 diabetes^[11-13] but may be transient in up to half of cases.^[10,14] Established risk factors for microalbuminuria in adolescents and adults include duration of diabetes,^[14,15] suboptimal glycemic control,^[16,17] and hypertension. In this study of 199 adolescents with diabetes,

we examined the frequency of microalbuminuria in different types of diabetes and we specifically focused on the association between microalbuminuria and recognized risk factors – age, diabetes duration, body mass index (BMI), insulin dose, blood pressure, and hemoglobin A1c (HbA1c).

RESEARCH DESIGN AND METHODS

Children and adolescents with diabetes who were regularly attending the Changing Diabetes in Children (CDiC) clinic, a paediatric diabetes multidisciplinary clinic in BIRDEM, over 2-year period from February 2012 to February 2014 were included in this study. BIRDEM (Bangladesh Institute of Research and Rehabilitation of Diabetes Endocrine and

Address for correspondence: Dr. Bedowra Zabeen,
Department of Paediatrics and CDiC BIRDEM Dhaka 1000, Bangladesh.
E-mail: bzabeen@hotmail.com

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Table 1: Characteristics in normoalbuminuric versus microalbuminuric patients

Parameter	Normoalbuminuria	Microalbuminuria	P
Age at assessment (years)	16.4 (13.7-18)	17 (15-18.3)	0.086
Age at diagnosis (years)	11.7±3.7	12.1±3.1	0.491
Sex (female %)	91 (60.7)	34 (69.4)	0.273
Duration of diabetes (years)	3.1 (IQR:1.8-5.2)	3.8 (IQR:2.4-5.4)	0.073
HbA1c	9.5 (IQR:8.0-11.2)	10.8 (IQR:9.4-12.4)	0.006
SBP SDS	-0.56 (IQR:0.91-0.19)	0.22 (IQR:0.66-1.61)	0.000
Height SDS	149.50 (141.75-157.0)	150.50 (144.0-159.50)	0.478
Diastolic blood pressure SDS	0.81 (IQR:0.34-1.64)	1.64 (IQR:0.76-2.03)	0.001
BMI SDS	-0.47±1.30	0.10±1.35	0.010
Waist/height ratio	0.43 (IQR:0.40-0.48)	0.45 (0.43-0.56)	0.031
Waist circumference	66.0 (60.0-71.0)	75.0 (65.0-92.5)	0.024
Insulin dose (U/kg/day)	1.16±0.59	1.15±0.58	0.937

SDS: Standard deviation score, BMI: Body mass index, IQR: Interquartile range, HbA1c: Hemoglobin A1c, SBP: Systolic blood pressure

Metabolic disorders) is a tertiary care diabetic hospital where patients are referred from all over Bangladesh. Clinical assessment including anthropometry and blood pressure measurement was done by pediatric endocrinologist during complications assessment. Diabetes mellitus was diagnosed according to WHO, ISPAD, and Mohan's criteria.^[18-20] and all patients underwent abdominal X-Ray. Pancreatic autoantibodies were not available in our clinic. Patients were classified clinically as T1D with abrupt onset of typical symptoms of diabetes, usually who were nonobese, absence of signs of insulin resistance, severe diabetes with markedly elevated HbA1c, presenting with diabetic ketoacidosis (DKA), requiring insulin from time of onset. Patients were classified as fibrocalculus pancreatic diabetes (FCPD) if they had pancreatic calcification on X-ray or ultrasonography reported by radiologist and absence of alcohol intake hypercalcemia or biliary duct stones. Patients presenting with overweight (BMI more than 85th centile) or obesity (BMI more than 95th centile), at pubertal age, with signs of insulin resistance-acanthosis nigricans, hypertension, dyslipidemia, polycystic ovaries, and positive family history in 1st or 2nd degree relatives were classified as type 2 diabetes.

Screening for microalbuminuria was done during the visit. Children with febrile illness, DKA, urinary tract infection, and preexistent renal disease were excluded from the study. Patients were included in this study if albumin concentration had been measured two or more times within 6 months. Spot early morning urinary albumin concentration was measured by DCA analyzer. Normoalbuminuria was defined as urinary albumin concentration <30 mg/L in all urine samples collected. Microalbuminuria was defined as urinary albumin concentration 30–300 mg/L on at least two of three samples. Macroalbuminuria was defined if it was >300 mg/L in at least two samples. Height was measured using a Harpenden stadiometer and weight using the bathroom scales. Obesity was defined as a BMI standard deviation [SD] score ≥ 2 .^[21] Blood pressure was measured by auscultation after 5 min of rest, and percentiles and SD score were calculated based on age and gender.^[22] HbA1c was assessed by Clover A1c using

photoelectric method. HbA1c done during the screening was taken for analysis. Patients and their families gave informed consent for the results of the complications' assessment to be analyzed. The project was approved by local Diabetic Association of Bangladesh.

Statistical analysis

Descriptive statistics is presented as mean (\pm SD) score for normally distributed data and median (interquartile range or range) for skewed data. Continuous data were compared using parametric test ANOVA and skewed data using the nonparametric test Kruskal–Wallis test.

Risk factors for the development of microalbuminuria from the last complication assessment were examined using logistic regression. Potential variables from the last complication assessment used in the regression model were age during the examination, BMI, HbA1c, and blood pressure.

RESULTS

Majority of the patients (88%) were type 1, 10.6% FCPD, and 1.5% were type 2 diabetes. Microalbuminuria was found in forty-nine children and adolescents (25%). Among them, seven patients (3.5%) had macroalbuminuria (≥ 300 mg/L). Considering the prevalence in different types of diabetes, microalbuminuria was found in 24% of type 1 diabetes, 27% of FCPD, and 68% of type 2 diabetes patients. We also analyzed the duration of diabetes among different types of diabetes in microalbuminuric patients. The median duration was longer in FCPD patients, i.e., 4.4 [3.1–5.60] compared to type 1 3.8 [2.4–5.7] and type 2 patients 3.4 [1.8–5.0] years ($P = 0.139$). Seven patients (14%) developed microalbuminuria within 2 years of diagnosis. Among them, six (13%) were type 1 and one (50%) was type 2 diabetes. The shortest diabetes duration to development of microalbuminuria was 7 months. Compared with the patients with normoalbuminuria, microalbuminuric patients had significantly higher BMI SD score -0.47 ± 1.30 versus 0.10 ± 1.35 ($P = 0.010$) and waist height ratio 0.45 [IQR: 0.43–0.56] versus 0.43 [IQR: 0.40–0.48] ($P = 0.031$)

[Table 1]. Systolic and diastolic blood pressure was significantly higher in patients with microalbuminuria.

Median HbA1c was higher 10.8 (9.4–12.4) v rsus 9.5 (8.0–11.2) ($P = 0.006$) in adolescents with microalbuminuria. More than 81% patients had high HbA1c $>9\%$ and only 8% patients had $<7.5\%$ in microalbuminuric group ($P < 0.014$) [Figure 1]. On logistic regression, univariate analysis-independent predictors of microalbuminuria were older age, systolic blood pressure, BMI SDS, and mean HbA1c which remained significant in multivariate analysis as predictors of microalbuminuria [Table 2].

DISCUSSION

In this cohort of 199 youth with diabetes, the prevalence of microalbuminuria was 25%, and among them, seven patients (3.5%) had macroalbuminuria (≥ 300 mg/L).

The prevalence of microalbuminuria in children with type 1 diabetes varies between 3%–30%.^[23-26] The wide range of prevalence in various studies may be due to multiple genetic factors in different ethnic groups. The prevalence of microalbuminuria was highest in type 2 diabetes in our population. Higher prevalence was found in adolescents with type 2 diabetes in comparison with type 1 diabetes in different reports. Microalbuminuria was found in 28% of youth with type 2 diabetes after a relatively short duration of diabetes in a study done in Australia.^[27] Similarly, the incidence of nephropathy among type 2 diabetic patients is as twice as high than in type 1 diabetic patients in a study done in Japan.^[28] Microalbuminuria

was observed in 18% of Korean patients with type 2 diabetes compared with 11% with type 1 diabetes.^[29] Increasing age in our population increased the risk of microalbuminuria and all patients were at pubertal age. Older age and puberty were determined as risk factors for complications in previous reports.^[30-33] Although longer duration of diabetes, older age, and puberty were determined as risk factors for complications in previous reports,^[31-33] seven patients in our population developed microalbuminuria within 2 years of diagnosis of diabetes. Among them, two developed earliest within 1 year. One study done in India has demonstrated urine microalbuminuria in five children with <2 years of diabetes duration.^[34] Screening from age 11 years with 2 years diabetes duration and from 9 years with 5 years duration are recommended according to ISPAD 2009 guideline.^[35] Seven children in our study would have not been diagnosed with microalbuminuria based on the current ISPAD criteria for screening. Obesity at the first complications assessment was associated with the development of persistent microalbuminuria in one study.^[36] BMI SDS was significantly ($p. 018$) higher and waist/height ratio was also higher ($p. 035$) in our microalbuminuric children. An increase in blood pressure is associated with increase in urinary albumin excretion in both adults and children.^[17,33] Though there is controversy as to whether an increase in blood pressure precedes or is a result of the development of microalbuminuria. In our population, we found that systolic blood pressure was associated with development of microalbuminuria. Our data indicate that the modifiable predictors for the development of microalbuminuria were poor glycemic control, high blood pressure, and high BMI which are consistent with findings in different studies.^[33-36] Both baseline and more recent lack of glycemic control predict risk of microalbuminuria, 5–16, and follow-up data from the diabetes control, and complications trial showed that previous intensive treatment of patients with diabetes and near normal glycemia has an extended benefit in delaying progression of diabetic nephropathy.^[17]

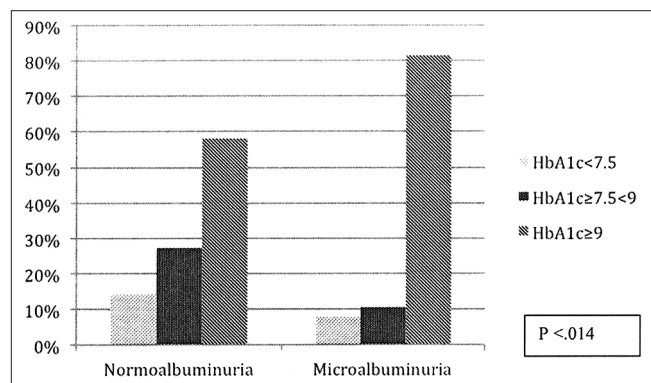


Figure 1: Frequency of hemoglobin A1c in two groups

Table 2: Factors associated with microalbuminuria in adolescents with diabetes

Factors	Univariate model		Multivariate model	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.15 (1.01-1.30)	0.024	1.27 (1.04-1.56)	0.019
SBP SDS	2.03 (1.46-2.84)	0.0001	2.11 (1.31-3.40)	0.002
BMI SDS	1.43 (1.08-1.89)	0.011	1.49 (1.01-2.22)	0.04
HbA1c	1.26 (1.06-1.49)	0.007	1.31 (1.07-1.60)	0.007

SBP: Systolic blood pressure, OR: Odds ratio, CI: Confidence interval, HbA1c: Hemoglobin A1c, BMI: Body mass index, SDS: Standard deviation score

CONCLUSION

We found there is high prevalence of microalbuminuria which was associated with higher age, systolic blood pressure, BMI SDS, and HbA1c. The earlier, after 2–5-year diabetes duration evaluation microalbuminuria in childhood diabetes much earlier than the current recommendations. Evaluation of risk factors and early screening for microvascular complications in children and adolescents are imperative to assist in preventive strategies.

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Conflicts of interest

There are no conflicts of interest.

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