Study of glycaemic control and microalbuminuria in children with type 1 diabetes mellitus

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Abstract

Background: There is a lacuna in the literature concerning children with type 1 diabetes mellitus (TIDM) and glycaemic control and the occurrence of microalbuminuria in the Indian sub-continent.

Objectives: To study the glycaemic control based on glycated haemoglobin level (HbA1C) and the risk and occurrence of microalbuminuria in children with TIDM.

Study design: Prospective observational study.

Participants: Children between the ages of 1-18 years with diabetes of six or more months.

Outcome: Glycaemic control based on HbA1C, occurrence and relation of microalbuminuria to age, sex, HbA1C, hypertension and body mass index (BMI) were studied.

Results: Fifty two (M: F=1.25:1) children were included in the study with 48 children completing their second visit (6 months after the 1st visit). Ideal glycaemic control (HbA1C<7.5%) was observed only in 6 (12.5%) children in the study group. No significant relationship was observed between the duration of diabetes and HbA1C levels (p=0.64). Nineteen (36.5%) children had microalbuminuria. No significant differences were found in the sex, age groups, HbA1C and insulin dosage per day between children with and without microalbuminuria. Median BMI was 15.7 kg/m^2 and 13.5 kg/m^2 in the groups with and without microalbuminuria respectively (p=0.003).

Conclusions: Ideal glycaemic control was observed only in 12.5% children in the study group. No statistically significant relationship was observed between the duration of diabetes, sex or age and HbA1C levels in the present study. No significant differences were found in the sex, age groups, HbA1C and insulin dosage per day between children with and without microalbuminuria. However, median BMI had a significant positive association with urinary albumin excretion.

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(Keywords: Diabetes mellitus type 1, child, insulin, albuminuria, glycated haemoglobin A)

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Introduction

Onset of type 1 diabetes mellitus (TIDM) is mainly in the 7-15 year age group, but it can present at any age[1]. Microalbuminuria precedes proteinuria and is a potentially reversible stage of diabetic nephropathy[2-4]. Earlier detection and necessary intervention could change the progression of the disease. This study is conducted to fill the lacunae in the literature concerning children with T1DM and glycaemic control and occurrence of microalbuminuria in the Indian sub-continent.

Objectives

1. To study glycaemic control in children with TIDM based on glycated haemoglobin level (HbA1C).

2. To study the risk and occurrence of microalbuminuria in children with TIDM.

Method

Study design: Prospective observational

Study period: Case recruitment from 1st October 2016 to 31st December 2017. Follow-up till 30th June 2018.

Study population: Children between the ages of 1 - 18 years, attending the paediatric outpatient department (OPD)/medicine OPD or admitted in the department of Paediatrics with a duration of diabetes of 6 months or more.

Inclusion criteria: Age: 1-18 years, TIDM, duration of diabetes: 6 months or more

Exclusion criteria: Children with evident organ system diseases such as connective tissue disorders,

pre-existing renal diseases and haemolytic anaemias.

Data were collected and history and examination was recorded in a pre-designed proforma. Height, weight, body mass index (BMI), blood pressure, and type, frequency and dosage of insulin received were noted during the hospital visits. Blood samples were collected in plain and fluoride-containing vacutainers for glycated haemoglobin (analysed using turbidometric inhibitory immunoassay) and blood sugar (RBS/FBS) estimation (Hexokinase method), respectively. Two random, midstream urine samples six months apart, were collected from the children included in the study. Quantitative determination of urine microalbumin was done using a quantitative turbidometric test and creatinine was measured using an automated colorimetric determination based on a modified Jaffe reaction. Urine microalbumin was measured as mcg/mg of creatinine; ≥30mcg/mg creatinine was considered as a cut-off for microalbuminuria[3,5]. In individuals with diabetes mellitus, HbA1C values ≤7.5% indicated good metabolic control, whilst values >7.5 % indicated poor metabolic control.

Ethical issues: Ethical approval was obtained from the Institutional Ethics Committee of Kasturba Hospital, Manipal (IEC 937/2016) on 13 December 2016. Written informed consent was obtained from the parents of the participating children.

Statistical analysis: Data were analysed using SPSS 20 software. Mean, and standard deviation were used for data with a normal distribution. Median and IQR (75, 25) were used for data with skewed distribution. For categorical data Chi-squared test and Fischer's exact test were used. For continuous data Mann Whitney's test was used. $p< 0.05$ was considered statistically significant.

Results

A total of 54 children satisfied the inclusion criteria, and of them, two were excluded (One had systemic lupus erythematosus and the other had Wolcott-Rallison syndrome). Thus, 52 children were included in the study group at the first visit. Forty-eight children completed their second visit, 6 months after the 1st visit. Four children were lost to follow up. No mortality was observed in the study group.

The male: female ratio was 1.25: 1 in the study group. The median age of onset of TIDM was 10.7 years (IQR -13.3, 8). The youngest child at the time of diagnosis was one year five months and the oldest child at diagnosis was 17 years. Thirty two (66.7%) and 16 (33.3%) children were <13years and ≥13 of age respectively, at the time of recruitment. The median duration of diabetes at the time of recruitment was 24 months (IQR - 48, 12), 69% of them being less than 3 years old.

The most common presenting symptoms were polyphagia and polydipsia, observed in 49 (94.2%) children followed by polyuria in 47 (90.3%) children. Weight loss was observed in 29 (55.7%) children. Among the group, 19 (36.6%) children presented with diabetic ketoacidosis (DKA) at initial diagnosis. Median HbA1C level in the study population was 10.4% (IQR -12.6, 8.8). Range of HbA1C was 6-19.3%. Median urine microalbuminuria (mcg/mg creatinine) was 12.0 (IQR -34.2, 3.8).

Forty (76.9%) of the children were on combined short-acting and intermediate-acting insulin, 8 (15.3%) were on ultra-short acting and long-acting insulin, and 4 (7.8%) were on intermediate insulin only. No significant difference (p=0.39) was observed in HbA1C levels among males and females. No correlation was observed between the age and HbA1C levels in the present study. Ideal glycaemic control was observed only in 6 (12.5%) children in the study group. No significant relationship was observed between the duration of diabetes and HbA1C levels in the present study (p=0.64). In the present study, 19 (36.5%) children were found to have microalbuminuria. No significant differences were found in the sex, age groups, HbA1C and insulin dosage per day between children with and without microalbuminuria (Table 1). Median BMI was 15.7 kg/m^2 and 13.5 kg/m^2 in the groups with and without microalbuminuria respectively (p=0.003).

Majority (93.8%) of the children had poor glycaemic control, HbA1C >7.5%, at the second visit in the present study. Improved glycaemic control was noted in 22 out of 48 children at follow up. However, only 3 out of 48 children had good glycaemic control (HbA1C ≤7.5%) at follow up. No significant relationship was observed between HbA1C and urine albumin excretion at the second visit (Table 2).

Median BMI was significantly higher in children with microalbuminuria, with a p-value of 0.04 (Table 2).

Table 1: ***Clinical & biochemical characteristics in children with no microalbuminuria and microalbuminuria***

Characteristic	No microalbuminuria *(n=31)*	Microalbuminuria *(n=17)*	p value
BMI (kg/m²) Median (IQR75, 25)	13.5 (14.5,12.4)	15.7(19.2,14.1)	0.003
Hypertension <90th centile ≥90th centile	23 06	14 05	0.52
Insulin dose (U/kg) Median (IQR75, 25)	1.06 (1.17, 0.69)	1.08 (1.32, 0.78)	0.65
HbA1C (%) Median (IQR75, 25)	10.8 (12.6, 8.7)	10.1 (12.05, 8.8)	0.69
HbA1C ≤7.5% >7.5%	03 28	03 14	0.47
Urinary albumin excretion (mcg/mg) creatinine Median (IQR75, 25)	4 (11.05, 2.39)	52.8 (178.8,31.2)	

Table 2: ***Clinical & biochemical characteristics in children with no microalbuminuria and microalbuminuria at second visit***

Characteristic	No microalbuminuria *(n=31)*	Microalbuminuria *(n=17)*	p value
BMI (kg/m²) Median (IQR75, 25)	14.9 (16.3,13.6)	16.5 (20.2,14.1)	0.04
HbA1C (%) Median (IQR75, 25)	10 (13.05,8.95)	11 (12,10.1)	0.65
HbA1C ≤7.5% >7.5%	02 27	01 18	
Urinary albumin excretion (mcg/mg) creatinine Median (IQR75, 25)	4.5 (9.65,2.25)	66.5 (90,53.3)	

Discussion

The male-female ratio was 1.25: 1 in the study group and this is similar to other studies[2,6,7]. The median age of onset of TIDM in the current study was 10.69 years (IQR -13.32, 8.00). In a study by Alleyn, *et al*[2] (n= 471, aged 8-18 years) mean age was 12.9 ± 2.3 years. Omar, *et al*[8] (n= 40, aged 2-16 years) reported a mean age of 11.78 ± 3.83 years. In the current study, median duration of diabetes at the time of recruitment was 24 months (IQR 48, 12). The duration of diabetes in other studies was higher[2,6,8].

In our study common presenting symptoms were polyphagia and polydipsia (94.2%), polyuria (90.3%), weight loss (55.7%) and DKA (36.6%). In studies conducted by Amritanshu, *et al*[9] and Ibekwe, *et al*[10], polyuria and polydipsia were seen in all the patients while polyphagia was seen less frequently. DKA was seen in 20 out of 43 children (46.5%) who had microalbuminuria, in the study done by Amritanshu *et al.*[9] Median HbA1C level in the study population was 10.4% (IQR -12.57, 8.75). Various studies reported mean HbA1C values ranging 8.4-10.3%[2,6,11,12]. No statistically significant difference was observed in HbA1C levels among males and females in the present study and this was similar to other studies[6,13,14]. No correlation was observed between the age and HbA1C levels in the present study. Archinkova *et al*[6] and Mohammad, *et al*.[7] reported an increase in the HbA1C levels with age of patient.

Ideal glycaemic control was observed only in 6 (12.5%) children in the study group. Good glycaemic control was reported in 39% by Archinkova *et al.*[6] Poor glycaemic control (HbA1C >7.5%), was reported in 61%[6] and 45%[7] in other studies. There was no statistically significant relationship between the duration of diabetes and HbA1C levels in present study. In studies by Mohammad, *et al*[7] and Niba, *et al*[12], children with poor control had a significantly longer duration of diabetes than those with good control. In a study by Mohammad, *et al*[7] it was found that children with 5 or more years of diabetes were thrice more likely to have poor glycaemic control than those with shorter duration.

In the present study, 19 (36.5%) children had microalbuminuria. However, no significant differences were found in the sex, age groups, HbA1C and insulin dosage per day between children with and without microalbuminuria. In a study conducted by Alleyn, *et al*[2] 23% had microalbuminuria and HbA1C was significantly higher in those having microalbuminuria than in those without microalbuminuria (p=0.03). A greater proportion of females among those having persistent microalbuminuria compared to those without microalbuminuria was reported by various studies[2,9,15]. In a study conducted by Patel *et al*[16], males had a higher incidence of microalbuminuria. Hypertension, which modulates progression of vascular complications in diabetes, was found to have varied results on microalbuminuria[17-19]. In our study, median BMI was 15.7 kg/m^2 and 13.5 kg/m^2 in the groups with and without microalbuminuria respectively (p=0.003). In a study conducted by Alleyn, *et al*[2], there were no statistically significant differences between those with and without microalbuminuria for age, duration of diabetes and BMI.

The authors believe that the sample size in the current study is small and a study with larger sample size is required to draw more firm conclusions. This is a limitation of the study.

Conclusions

Ideal glycaemic control was observed only in 12.5% children in the study group. No statistically significant relationship was observed between the duration of diabetes, sex or age and HbA1C levels in the present study. No significant differences were found in the sex, age groups, HbA1C and insulin dosage per day between children with and without microalbuminuria. However, median BMI had significant positive association with microalbuminuria.

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