Glycaemic control and microvascular complications among paediatric type 2 diabetes mellitus patients in Hong Kong at 2 years after diagnosis

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is becoming increasingly common among children and adolescents worldwide, including those in Hong Kong. This study analysed the characteristics and prevalence of microvascular complications among paediatric T2DM patients in Hong Kong at diagnosis and 2 years after diagnosis.

Methods: All patients aged <18 years who had been diagnosed with DM at public hospitals in Hong Kong were recruited into the Hong Kong Childhood Diabetes Registry. Data collected at diagnosis and 2 years after diagnosis were retrospectively retrieved from the Registry for patients diagnosed from 2014 to 2018.

Results: Median haemoglobin A1c (HbA1c) levels were 7.5% (n=203) at diagnosis and 6.5% (n=135) 2 years after diagnosis; 59.3% of patients achieved optimal glycaemic control (HbA1c level <7%) at 2 years. A higher HbA1c level at diagnosis was associated with worse glycaemic control at 2 years (correlation coefficient=0.39; P<0.001). The presence of dyslipidaemia (adjusted odds ratio [aOR]=3.19; P=0.033) and fatty liver (aOR=2.50; P=0.021) at 2 years were associated with suboptimal glycaemic control. Diabetic neuropathy and retinopathy were rare in our cohort, but 18.6% of patients developed microalbuminuria (MA) within 2 years after diagnosis. Patients with MA had a higher HbA1c level at 2 years (median: 7.2% vs 6.4%; P=0.037). Hypertension was a risk factor for MA at 2 years, independent of glycaemic control (aOR=4.61; P=0.008).

Conclusion: These results highlight the importance of early diagnosis and holistic management (including co-morbidity management) for paediatric T2DM patients.

This article was published on 16 Aug 2024 at www.hkmj.org.

Hong Kong Med J 2024;30:291–9
https://doi.org/10.12809/hkmj2210552

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香港二型糖尿病兒童患者在診斷後兩年的血糖控制與微血管併發症

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引言：二型糖尿病在世界各地（包括香港）的兒童和青少年中日益常見。本研究分析了香港二型糖尿病兒童患者在診斷時和診斷後兩年的血糖控制和微血管併發症的特徵及盛行率。

方法：所有在香港公立醫院被診斷患有糖尿病的18歲以下患者均被邀請納入香港兒童糖尿病登記冊。我們在登記冊回顧2014至2018年期間確診患者在診斷時和診斷後兩年的數據並進行分析。

結果：病童在診斷時的糖化血紅素水平中位數為7.5%（n=203），診斷後兩年為6.5%（n=135）；59.3%患者在兩年內達到理想血糖控制（糖化血紅素水平<7%）。診斷時糖化血紅素水平較高的患者與兩年後血糖控制較差相關（相關系數=0.39；P<0.001）。患有血脂異常（調整後的比值比=3.19；P=0.033）和脂肪肝（調整後的比值比=2.50；P=0.021）的患者在兩年內較大機會達不到理想血糖控制。糖尿病神經病變和視網膜病變在我們的兒童二型糖尿病患者隊列中並不常見，但18.6%患者在診斷後兩年內出現微量白蛋白尿。患有微量白蛋白尿的患者在診斷後兩年的糖化血紅素水平較高（中位數：7.2%與6.4%；P=0.037）。高血壓是微量白蛋白尿的獨立危險因素，與血糖控制無關（調整後的比值比=4.61；P=0.008）。

結論：研究結果強調了二型糖尿病兒童患者早期診斷和整體管理（包括併發症管理）的重要性。

Introduction

Type 2 diabetes mellitus (T2DM) in children and adolescents (hereinafter, youth) is becoming increasingly common worldwide.[1,2] A recent meta-analysis estimated that approximately 41 600 new cases of T2DM were identified among youth in 2021.[3] Type 2 DM in youth exhibits relatively rapid clinical progression with a sharp decline in beta-cell function and high risk of complications.[4] In a study recently published by the TODAY (Type 2 Diabetes in Adolescents and Youth) Study Group, which analysed 500 young adults with youth-onset T2DM, 60.1% of patients developed at least one microvascular complication (diabetic kidney, nerve, or retinal disease) and 28.4% of patients developed at least two complications.[5] In addition to hyperglycaemia, the presence of co-morbidities (eg, hypertension and dyslipidaemia) was associated with an increased risk of complications.[5]

A similar increase in the incidence of T2DM has been observed in Hong Kong. We previously reported that the crude incidence rate increased from 1.27 per 100 000 person-years in 1997-2007 to 3.42 per 100 000 person-years in 2008-2017.[6] However, there have been limited data regarding the outcomes of paediatric T2DM patients in Hong Kong. In this study, we reviewed the glycaemic control findings and microvascular complication rates among recently diagnosed paediatric T2DM patients in Hong Kong, with a focus on outcomes at 2 years after diagnosis; we sought to identify factors associated with poor glycaemic control and the development of microalbuminuria (MA).

Methods

Setting

Data analysed in this study were retrieved from the Hong Kong Childhood Diabetes Registry, a database established in 2016. The Registry was approved by the Research Ethics Committee of the Hospital Authority of Hong Kong, which includes 11 public hospitals. Investigators retrieved information from medical records and entered relevant data into the Registry. Standardised data entry forms for recording baseline clinical characteristics and annual entry forms were provided for investigators to enter data into the Registry at diagnosis and annually thereafter. Data were cross-checked by at least two investigators.

Inclusion and exclusion criteria

All patients aged <18 years who had been diagnosed with DM at public hospitals in Hong Kong were recruited. All recruited patients met the diagnostic criteria for DM according to the International Society for Paediatric and Adolescent Diabetes

New knowledge added by this study

- A total of 59.3% of paediatric type 2 diabetes mellitus patients in Hong Kong had achieved satisfactory glycaemic control at 2 years after diagnosis.
- Factors associated with suboptimal glycaemic control at 2 years after diagnosis were higher haemoglobin A1c level at diagnosis, fatty liver at 2 years, and dyslipidaemia at 2 years.
- Overall, 18.6% of patients had microalbuminuria at 2 years and exhibited hypertension as a risk factor, independent of glycaemic control.

Implications for clinical practice or policy

- Early diagnosis of diabetes mellitus is important because initial disease severity predicts the risk of suboptimal glycaemic control at 2 years.
- Management of co-morbidities, including fatty liver, dyslipidaemia, and hypertension, is important for the maintenance of glycaemic control and prevention of microalbuminuria.

Clinical Practice Consensus Guidelines: patients were symptomatic and had either fasting blood glucose level ≥7 mmol/L, 2-hour blood glucose level ≥11.1 mmol/L during an oral glucose tolerance test, random blood glucose level ≥11.1 mmol/L, or haemoglobin A1c (HbA1c) level ≥6.5%.[4] Asymptomatic patients underwent repeat testing with a different test, as suggested in the Guidelines.[4] The classification of DM was based on the attending clinician's assessment of clinical symptoms and laboratory findings, including obesity status, family history, autoimmunity, and clinical course. Patients diagnosed with T2DM from 2014 to 2018 were included in the analysis, including those who had an initial diagnosis of type 1 DM that was subsequently revised to T2DM. Patients who refused Registry recruitment and patients whose diagnosis was revised to type 1 DM or maturity-onset DM of the young were not included in the analysis.

Data collection and definitions

The following data were retrieved from the Registry: patient age, sex, family history of T2DM (in first- or second-degree relatives), symptoms at presentation, anti-islet cell antibody test results, body mass index (BMI), HbA1c level, presence of co-morbidities (non-alcoholic fatty liver disease, dyslipidaemia, hypertension, and obstructive sleep apnoea), presence of complications (MA, retinopathy, and neuropathy), treatments received, and frequency of blood glucose self-monitoring. Overweight and obesity were defined using age- and sex-specific cut-offs established by the International Obesity Task Force, which predicted BMI values at 18 years (25, 30, and 35 kg/m^2) by the respective standard deviations to define overweight, obesity and morbid obesity, respectively; standard deviations of BMI were calculated according to age- and sex-specific reference data provided by the International Obesity Task Force.[7] In this study, weight loss was defined as any decrease in BMI z-score, and improvement in HbA1c level was defined as any decrease in HbA1c level. Non-alcoholic fatty liver disease was defined as an elevated alanine transferase level (based on age- and sex-specific reference data) or compatible ultrasound findings. Dyslipidaemia was defined as an elevated low-density lipoprotein level of ≥2.6 mmol/L, a triglyceride level ≥1.7 mmol/L, or the receipt of lipid-lowering agents. Hypertension was defined as an elevated systolic blood pressure ≥95th percentile for age, height, and sex—on at least two occasions—or the receipt of anti-hypertensive medication. Obstructive sleep apnoea was defined as the presence of clinical symptoms indicating sleep-disordered breathing, along with polysomnography findings of obstructive apnoeas/hypopneas. Microalbuminuria was defined as an elevated spot urine albumin-creatinine ratio >2.5 mg/mmol for boys and >3.5 mg/mmol for girls in at least two of three samples within a 6-month period, or as the receipt of any treatment for MA. Retinopathy (eg, non-proliferative and proliferative diabetic retinopathy, as well as macula oedema) was identified by digital fundus photography and confirmed via referral to an ophthalmologist. Neuropathy was clinically identified by the presence of symptoms (numbness and paraesthesia) and through clinical examinations including the 10-g monofilament test, vibration sense assessment, and ankle reflex evaluation. Suboptimal glycaemic control was defined as HbA1c level ≥7%, as suggested by the International Society for Paediatric and Adolescent Diabetes Clinical Practice Consensus Guidelines.[4]

Data analysis

Statistical analyses were performed using SPSS software (Windows version 23; IBM Corp, Armonk [NY], United States). All available data were included in the statistical analysis, and the numbers of available values are listed in the tables. Continuous variables, including age, HbA1c level, and BMI z-score, were tested for normality using the Shapiro–Wilk test. Data with skewed distributions were expressed as medians and interquartile ranges (IQRs), and comparisons were made using the Mann-Whitney *U* test. Analyses of relationships between two continuous variables were assessed by Spearman rank correlation and expressed using the Spearman correlation coefficient (ρ). Categorical variables were expressed as exact numbers of patients with percentages. Binary logistic regression analysis was used to assess risk factors for suboptimal glycaemic control at 2 years and MA at 2 years. Univariate analyses were performed to determine unadjusted odds ratios and 95% confidence intervals. Multivariate analyses of factors associated with suboptimal glycaemic control at 2 years were performed while including HbA1c level at diagnosis to adjust for initial disease severity. Multivariate analyses of factors associated with MA at 2 years were performed while including HbA1c level at 2 years to eliminate the effect of glycaemic control at 2 years; this approach was intended to independently assess the effects of co-morbidities. Missing data were not included in regression analyses. Statistical tests were two-sided and were performed with a 5% significance threshold (ie, alpha=0.05). The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist for cohort studies was used when reporting the study findings.

Results

Study population

In total, 212 patients diagnosed with T2DM between 2014 and 2018 were recruited into the Registry. Their

baseline demographics are summarised in Tables 1 and 2. Of these patients, 71.3% had a family history of T2DM, and 21.7% were symptomatic at diagnosis (Table 1). At 2 years after the diagnosis of DM, 143 patients (67.5%) continued attending follow-up visits. There were no significant differences in baseline characteristics between the groups with and without follow-up at 2 years, except for a higher age at diagnosis in the loss to follow-up group (online supplementary Table).

Glycaemic control

Haemoglobin A1c levels at diagnosis, 1 year after diagnosis, and 2 years after diagnosis were available for 203, 176, and 135 patients, respectively. The median HbA1c levels at diagnosis, 1 year after diagnosis, and 2 years after diagnosis were 7.5% (IQR=6.5%-10.6%), 6.3% (IQR=5.8%-7.4%), and 6.5% (IQR=5.8%-8.0%), respectively; at these times, 65.5%, 29.0%, and 40.7% of patients had suboptimal glycaemic control (ie, HbA1c level ≥7%), respectively [Table 2].

Co-morbidities

There was an overall improvement in BMI z-score at 2 years after diagnosis (median BMI z-score decreased from 2.5 at diagnosis to 2.3 at 2 years). Overall, 146 of 191 patients (76.4%) had dyslipidaemia at diagnosis, whereas 62 of 95 patients (65.3%) had dyslipidaemia at 2 years. However, more patients had hypertension at 2 years—the number increased from 45 of 212 patients (21.2%) at diagnosis to 55 of 143 patients (38.5%) at 2 years (Table 2).

TABLE 1. Baseline patient demographics*

	No.	At diagnosis
Median age (IQR), y	212	14.8 (13.2-16.4)
Male sex	212	115 (54.2%)
Ethnicity (Chinese)	211	203 (96.2%)
Family history of T2DM	188	134 (71.3%)
Symptomatic at diagnosis	212	46 (21.7%)
Polyuria	46	33 (71.7%)
Polydipsia	46	43 (93.5%)
Nocturia	46	19 (41.3%)
Weight loss	46	28 (60.9%)
Lethargy	46	8 (17.4%)
Vomiting	46	7 (15.2%)
Ketosis or ketoacidosis at diagnosis	212	21 (9.9%)
Anti-islet cell antibody positivity	100	4 (4.0%)
Initially diagnosed with T1DM	212	3 (1.4%)

Abbreviations: IQR = interquartile range; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

* Data are shown as No. or No. (%), unless otherwise specified

Microvascular complications

Overall, 21 of 113 (18.6%) patients screened at 2 years after diagnosis developed MA, compared with 9.0% at diagnosis. Two patients (1.8%) developed retinopathy, whereas one patient (0.9%) developed neuropathy, at 2 years after diagnosis (Table 2).

Treatments received and monitoring

At diagnosis, 24.1% of patients were not receiving any pharmacological treatment, 58.0% were receiving anti-diabetic drugs, and 18% required insulin. At 2 years, only 12.6% of patients were not receiving any medications. The proportions of patients requiring insulin were similar at diagnosis and 2 years (2.1%). In total, 64.9% of patients did not perform daily blood glucose self-monitoring (Table 2).

Factors affecting glycaemic control at 2 years

A higher initial HbA1c level was associated with suboptimal glycaemic level at 2 years (correlation coefficient=0.39, P<0.001; n=130). There were no significant correlations of HbA1c level at 2 years with age at diagnosis (correlation coefficient=0.02, P=0.852; n=135), BMI z-score at diagnosis (correlation coefficient=-0.10, P=0.277; n=133), or BMI z-score at 2 years (correlation coefficient=0.04, P=0.638; n=131). Greater decline in BMI z-score was associated with a lower HbA1c level at 2 years (correlation coefficient=-0.22, P=0.011; n=129). However, there was no correlation between the change in BMI z-score and the change in HbA1c level (correlation coefficient <0.01, P=0.973; n=126).

Table 3 shows factors associated with suboptimal glycaemic control at 2 years. The effect of a family history of T2DM was not statistically significant after adjustment for initial HbA1c level (adjusted odds ratio [aOR]=2.29; P=0.075). A similar result was observed regarding the effect of symptomatic disease at diagnosis (aOR=2.01; P=0.174) and weight loss (aOR=0.53; P=0.128). The presence of fatty liver (aOR=2.50; P=0.021) and dyslipidaemia (aOR=3.19; P=0.033) at 2 years were associated with suboptimal glycaemic control at 2 years, even after adjustment for initial HbA1c level.

Factors associated with the development of microalbuminuria at 2 years

Patients with MA had higher HbA1c levels at 2 years compared with patients who did not exhibit MA (median HbA1c level: 7.2% vs 6.4%; P=0.037) [Table 4]. Dyslipidaemia at 2 years was associated with MA at 2 years in the univariate analysis (unadjusted odds ratio=5.51; P=0.030), but the effect did not

TABLE 2. Glycaemic control, co-morbidities and microvascular complications, and treatment received*

	No.	At diagnosis	No.	At 1 year	No.	At 2 years
HbA1c level						
Median (IQR)	203	7.5% (6.5%-10.6%)	176	6.3% (5.8%-7.4%)	135	6.5% (5.8%-8.0%)
≥7%	203	133 (65.5%)	176	51 (29.0%)	135	55 (40.7%)
Change at 2 years					131	-0.9%
(-0.1% to -2.95%)						
Improvement at 2 years					131	99 (75.6%)
			No.	**At diagnosis**	**No.**	**At 2 years**
Body weight						
Median BMI z-score (IQR)			205	2.5 (2.1-2.9)	138	2.3 (1.7-2.7)
BMI†			205		138	
Normal or underweight				21 (10.2%)		33 (23.9%)
Overweight				42 (20.5%)		35 (25.4%)
Obesity				89 (43.4%)		49 (35.5%)
Morbid obesity				53 (25.9%)		41 (29.7%)
Achieved weight loss at 2 years‡					129	91 (70.5%)
Co-morbidities						
Fatty liver			212	78 (36.8%)	143	52 (36.4%)
Dyslipidaemia			191	146 (76.4%)	95	62 (65.3%)
Hypertension			212	45 (21.2%)	143	55 (38.5%)
Obstructive sleep apnoea			212	14 (6.6%)	143	10 (7.0%)
Microvascular complications						
Microalbuminuria			212	19 (9.0%)	113	21 (18.6%)
Retinopathy			212	1 (0.5%)	113	2 (1.8%)
Neuropathy			212	0	113	1 (0.9%)
Treatment received			212		143	
Diet only				51 (24.1%)		18 (12.6%)
Anti-diabetic drugs§ only				123 (58.0%)		96 (67.1%)
Metformin only				123/123 (100%)		89/96 (92.7%)¶
Insulin only				8 (3.8%)		3 (2.1%)
Insulin plus anti-diabetic drugs				30 (14.2%)		26 (18.2%)
Insulin plus metformin only				30/30 (100%)		24/26 (92.3%)**
Frequency of blood glucose self-monitoring, times per day					77	
Not performed						50 (64.9%)
1-3						19 (24.7%)
≥4 or regular CGMS user						8 (10.4%)

Abbreviations: BMI = body mass index; CGMS = continuous glucose monitoring system; HbA1c = haemoglobin A1c; IQR = interquartile range

* Data are shown as No. (%), unless otherwise specified

† Definitions of overweight, obesity, and morbid obesity were based on the predicted corresponding adult BMIs of 25, 30, and 35 kg/m^2, respectively

‡ Any decrease in BMI z-score at 2 years

§ Included metformin, sulphonylureas, thiazolidinediones, dipeptidyl peptidase (DPP)–4 inhibitors, glucagon-like peptide-1 analogues, and sodium-glucose cotransporter-2 (SGLT2) inhibitors

¶ Three patients on metformin and sulphonylurea; one patient on metformin and DPP-4 inhibitor; two patients on metformin, sulphonylurea, and DPP-4 inhibitor; one patient on metformin and SGLT2 inhibitor

** One patient on insulin, metformin and sulphonylurea; one patient on insulin, metformin, and sulphonylurea

TABLE 3. Factors associated with suboptimal glycaemic control (haemoglobin A1c level ≥7%) at 2 years*

	Patients with HbA1c level ≥7% at 2 years	Patients with HbA1c level <7% at 2 years	Unadjusted odds ratio (95% CI)	P value	Adjusted odds ratio† (95% CI)	P value
Baseline demographics						
Male sex	31/55 (56.4%)	42/80 (52.5%)	1.17 (0.59-2.33)	0.658	0.84 (0.40-1.78)	0.649
Ethnicity (Chinese)	52/55 (94.5%)	78/80 (97.5%)	0.44 (0.07-2.75)	0.383	0.86 (0.13-5.96)	0.881
Family history of T2DM	40/49 (81.6%)	48/74 (64.9%)	2.41 (1.01-5.73)	0.047	2.29 (0.92-5.71)	0.075
Symptomatic at diagnosis	20/55 (36.4%)	11/80 (13.8%)	3.58 (1.55-8.31)	0.003	2.01 (0.71-5.51)	0.174
Weight loss at 2 years	30/51 (58.8%)	61/78 (78.2%)	0.40 (0.18-0.86)	0.020	0.53 (0.23-1.21)	0.128
Improvement in HbA1c level at 2 years	30/52 (57.7%)	68/78 (87.2%)	0.20 (0.08-0.47)	<0.001	0.06 (0.02-0.18)	<0.001
Blood glucose monitoring at least daily	8/26 (30.8%)	18/46 (39.1%)	1.11 (0.54-2.29)	0.784	0.95 (0.44-2.08)	0.906
Fatty liver						
At diagnosis	23/55 (41.8%)	27/80 (33.8%)	1.41 (0.70-2.87)	0.341	1.57 (0.73-3.38)	0.246
At 2 years	26/55 (47.3%)	24/80 (30.0%)	2.09 (1.03-4.27)	0.043	2.50 (1.15-5.45)	0.021
Dyslipidaemia						
At diagnosis	38/46 (82.6%)	60/78 (76.9%)	1.43 (0.56-3.60)	0.454	1.11 (0.42-2.97)	0.832
At 2 years	27/33 (81.8%)	32/59 (54.2%)	3.80 (1.37-10.55)	0.011	3.19 (1.10-9.29)	0.033
Hypertension						
At diagnosis	12/55 (21.8%)	17/80 (21.3%)	1.03 (0.45-2.38)	0.937	1.06 (0.43-2.60)	0.897
At 2 years	21/55 (38.2%)	31/80 (38.8%)	0.98 (0.48-1.98)	0.947	0.81 (0.38-1.74)	0.590
Obstructive sleep apnoea						
At diagnosis	3/55 (5.5%)	5/80 (6.3%)	0.87 (0.20-3.78)	0.848	0.83 (0.17-4.01)	0.818
At 2 years	4/55 (7.3%)	6/80 (7.5%)	0.97 (0.26-3.60)	0.960	1.01 (0.25-4.08)	0.991

Abbreviations: 95% CI = 95% confidence interval; HbA1c = haemoglobin A1c; T2DM = type 2 diabetes mellitus
* Data are shown as No. (%), unless otherwise specified
† Adjusted for the effect of HbA1c at diagnosis

TABLE 4. Univariate analysis of factors associated with the development of microalbuminuria at 2 years*

	No.	With MA at 2 years	No.	Without MA at 2 years	P value
HbA1c level					
At diagnosis	20	8.1% (6.7%-10.9%)	88	7.9% (6.5%-11.2%)	0.695
At 2 years	19	7.2% (6.3%-9.8%)	91	6.4% (5.7%-7.9%)	0.037
Change in HbA1c	18	-0.7% (-0.98% to 0.1%)	87	-1.1% (-3.15% to -0.1%)	0.174
BMI z-score					
At diagnosis	20	2.51 (2.14-2.81)	90	2.52 (2.16-2.93)	0.843
At 2 years	20	2.27 (1.93-2.74)	89	2.34 (1.75-2.73)	0.739
Age at diagnosis, y	21	14.7 (13.2-15.8)	92	14.4 (13.2-15.8)	0.283

Abbreviations: BMI = body mass index; HbA1c = haemoglobin A1c; MA = microalbuminuria
* Data are shown as No. or median (interquartile range), unless otherwise specified

remain statistically significant after adjusting for glycaemic control at 2 years (Table 5). The presence of hypertension at 2 years was a risk factor for MA at 2 years, independent of glycaemic control at 2 years (aOR=4.61; P=0.008) [Table 5].

Discussion

Glycaemic control

The results of this study provide insights into the early post-diagnosis clinical course of T2DM among

TABLE 5. Multivariate analysis of factors associated with the development of microalbuminuria at 2 years*

	Patients with MA at 2 years	Patients without MA at 2 years	Unadjusted odds ratio (95% CI)	P value	Adjusted odds ratio† (95% CI)	P value
Baseline demographics						
Male sex	9/21 (42.9%)	52/92 (56.5%)	0.58 (0.22-1.50)	0.260		
Ethnicity (Chinese)	21/21 (100%)	88/92 (95.7%)	N/A			
Family history of T2DM	15/19 (78.9%)	57/86 (66.3%)	1.91 (0.58-6.27)	0.287		
Symptomatic at diagnosis	5/21 (23.8%)	19/92 (20.7%)	1.20 (0.39-3.69)	0.750		
Weight loss at 2 years	12/19 (63.2%)	62/87 (71.3%)	0.69 (0.24-1.96)	0.487	0.84 (0.28-2.60)	0.762
Improvement in HbA1c level at 2 years	13/18 (72.2%)	66/87 (75.9%)	0.83 (0.26-2.59)	0.745	1.47 (0.41-5.27)	0.552
Blood glucose monitoring at least daily	2/7 (28.6%)	19/55 (34.5%)	0.49 (0.16-1.44)	0.194	1.92 (0.61-6.08)	0.264
Fatty liver						
At diagnosis	7/21 (33.3%)	34/92 (37.0%)	0.86 (0.31-2.32)	0.756		
At 2 years	11/21 (52.4%)	32/92 (34.8%)	2.06 (0.79-5.38)	0.139	2.09 (0.74-5.90)	0.160
Dyslipidaemia						
At diagnosis	18/21 (85.7%)	67/85 (78.8%)	1.61 (0.43-6.09)	0.481		
At 2 years	16/18 (88.9%)	45/76 (59.2%)	5.51 (1.18-25.70)	0.030	3.87 (0.79-18.97)	0.096
Hypertension						
At diagnosis	8/21 (38.1%)	19/92 (20.7%)	2.36 (0.86-6.53)	0.097		
At 2 years	15/21 (71.4%)	33/92 (35.9%)	4.47 (1.58-12.62)	0.005	4.61 (1.48-14.35)	0.008
Obstructive sleep apnoea						
At diagnosis	2/21 (9.5%)	6/92 (6.5%)	1.51 (0.28-8.06)	0.630		
At 2 years	1/21 (4.8%)	8/92 (8.7%)	0.53 (0.06-4.44)	0.554	0.69 (0.08-6.01)	0.733

Abbreviations: 95% CI = 95% confidence interval; HbA1c = haemoglobin A1c; MA = microalbuminuria; N/A = not available; T2DM = type 2 diabetes mellitus

* Data are shown as No. (%), unless otherwise specified

† Adjusted for the effect of HbA1c at 2 years

youth in Hong Kong. Nearly 60% of patients (59.3%) in our cohort had optimal glycaemic control with HbA1c level <7% at 2 years after diagnosis. Previous studies regarding glycaemic control among youth with T2DM showed variable results, presumably due to heterogeneity in the study populations, follow-up periods, and glycaemic targets.[8-11] A clinical trial by the TODAY Study Group[8] followed up 234 youth with DM, who were put on metformin and lifestyle modifications and with initial HbA1c level <8%, for 3.86 years on average. It showed that 46.6% of youth with DM exhibited loss of glycaemic control, defined by HbA1c level >8%.[8] In a study of 301 paediatric T2DM patients with initial HbA1c level ≥7% in the United States, Barr et al[9] found that after 1 year, 37% of patients achieved optimal control (HbA1c level ≤6.5%) and 58% achieved durable glycaemic control (HbA1c level ≤8%). However, at 3 years, only 26% of patients achieved HbA1c level ≤6.5%, whereas 59% exhibited HbA1c level ≤8%.[9] Candler et al[10] followed 100 paediatric T2DM patients in the United Kingdom; the median HbA1c level was 7% after 1 year, and 38.8% of patients exhibited HbA1c level <6.5%. Notably, no data regarding HbA1c levels at diagnosis were provided in the study.[10] In a study of 96 patients in Israel, Meyerovitch et al[11] found that the median HbA1c level was 7.97% after an average follow-up period of 3.11 years, compared with 7.8% at diagnosis. Additionally, >50% of patients required insulin at the end of the follow-up period.[11] Although our cohort appeared to have better glycaemic control compared with the previous studies, our patients might have had lower initial HbA1c levels at diagnosis, considering that most of them were asymptomatic (78.3%). Our study also showed that patients with a higher initial HbA1c level tended to have a persistently high HbA1c level at 2 years. These findings emphasise the importance of early diagnosis and treatment before patients develop clinically significant hyperglycaemia, which makes DM more difficult to control. Most of our patients were overweight or obese (89.8%); many of them also had co-morbidities including hypertension, dyslipidaemia, and fatty liver (Table 2). Previous studies in Hong Kong showed a high risk of metabolic syndrome (OR up to 32.2) in overweight and obese children.[12,13] Active screening for metabolic syndrome would enable early diagnosis

and treatment of DM and its co-morbidities.

Co-morbidities

Factors associated with suboptimal glycaemic control were dyslipidaemia and fatty liver at 2 years after diagnosis. A recent study showed that each 1% increase in HbA1c level was associated with 13% and 20% increases in the risks of abnormal triglyceride and low-density lipoprotein levels, respectively.[14] The importance of weight loss has been emphasised in various guidelines, for example, The American Diabetes Association recommends weight loss of at least 5% in adult overweight or obese DM patients.[15] However, a specific weight loss target cannot be established in growing children. The study by Candler et al[10] regarding youth with T2DM showed that each one-unit increase in BMI z-score was associated with a 34.9% increase in HbA1c level. Although the present study indicated that a greater drop in BMI z-score was associated with lower HbA1c level at 2 years, the association between weight loss and prevention of suboptimal glycaemic control at 2 years was not significant after adjustment for initial HbA1c level.

Microvascular complications

Diabetic retinopathy and neuropathy were rare among youth with T2DM. However, the proportion of patients with MA increased from 9.0% at diagnosis to 18.6% at 2 years (Table 2). Previous studies regarding the prevalence of diabetic complications in youth have shown mixed results, probably due to genetic variation and differences in DM duration. High prevalences have been observed in cohorts with long DM durations.[16] The MA prevalence has been approximately 20% to 30% in most studies of youth with a short duration of T2DM. In the SEARCH for Diabetes in Youth study, the MA prevalence in youth with T2DM was 22.2%, and the average duration of disease was 1.9 years.[17] In an Australian population, Eppens et al[18] found that 28% of patients had MA, with a median disease duration of 1.3 years. Candler et al[10] showed that the MA prevalence increased from 4.2% to 16.4% within 1 year after diagnosis. Our cohort showed a similar prevalence compared with other cohorts. Nevertheless, the increasing trend is concerning, particularly because MA has been identified as an independent predictor of mortality risk in adults.[19] Thus, we conducted further analysis of risk factors for MA, revealing the associations of higher HbA1c level and hypertension at 2 years, consistent with the SEARCH for Diabetes in Youth study.[17] The deleterious effects of hypertension on the kidneys explain the additional increase in MA risk, independent of glycaemic control.

Strengths and limitations

Strengths of this study included its provision of insights regarding the early outcomes of youth with T2DM in Hong Kong, particularly concerning glycaemic control and associated factors. First, our findings supported the implementation of active screening in overweight and obese individuals to allow early diagnosis of DM, considering the high prevalence of overweight or obesity and the relationship of lower initial HbA1c level with better glycaemic control at 2 years. Second, our findings indicated that the presence of co-morbidities at 2 years, rather than baseline, was associated with suboptimal glycaemic control and MA, demonstrating the reversibility of the risk factors and highlighting the importance of co-morbidity management. Third, our study identified challenges in managing youth with T2DM, including a high loss to follow-up rate (n=69, 23.5%) [online supplementary Table], suboptimal glycaemic control in >40% of patients at 2 years, infrequent blood glucose self-monitoring by the patients, and increasing trends in MA and hypertension.

Indeed, the high loss to follow-up rate was a major limitation of our study. Many patients did not return for clinical assessment or were transferred to an adult endocrinology clinic. Although the loss to follow-up group had a higher age at diagnosis (online supplementary Table), this presumably did not have a substantial impact on the results because age was not a significant risk factor for poor glycaemic control or the likelihood of MA onset. Although a high loss to follow-up rate is a common phenomenon in studies of children with T2DM,[20] this obstacle hindered the achievement of good glycaemic control and prevention of complications. It also created difficulty in acquiring long-term follow-up data. Another limitation was that our patients were managed by different doctors in different hospitals; there remains no standardised protocol for the management of paediatric T2DM patients in Hong Kong, which may be a confounding factor for multicentre studies such as ours.

Conclusion

Approximately 60% of youth with T2DM in Hong Kong achieved HbA1c level <7% at 2 years after diagnosis. A higher HbA1c level at diagnosis was associated with worse glycaemic control at 2 years. The presence of dyslipidaemia and fatty liver at 2 years were factors associated with suboptimal glycaemic control. Overall, 18.6% of patients developed MA at 2 years; other microvascular complications were rare. These results highlight the importance of early diagnosis and holistic management, including co-morbidity management. The high loss to follow-up rate, high proportion of patients with suboptimal glycaemic control, and increasing number of patients with MA and hypertension are ongoing challenges in the management of youth with DM.

The establishment of a standardised protocol may improve outcomes in our patient population. Future research could include studies regarding the effects of insulin resistance and beta-cell function on metabolic outcomes in youth with DM.

Author contributions

Concept or design: All authors.
Acquisition of data: All authors.
Analysis or interpretation of data: WI Yam, SMY Wong.
Drafting of the manuscript: WI Yam.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The research was conducted as a part of the Hong Kong Childhood Diabetes Registry, which was approved by the Kowloon Central / Kowloon East Cluster Research Ethics Committee of Hospital Authority, Hong Kong (Ref No.: KC/KE-16-0087/ER-3). Written informed consent was obtained from parents for patients aged <16 years and from both parents and patients for patients aged between ≥16 and <18 years.

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj2210552).

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