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Original article

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Factors associated with glycemic control in children and adolescents with type 1 diabetes mellitus at a tertiary-care center in Thailand: a retrospective observational study

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Abstract

Background: Children and adolescents with type 1 diabetes mellitus (T1D), even those with intensive insulin treatment regimens, often have higher glycated hemoglobin (HbA_{1c}) levels than adults.

Objective: To delineate the medical and psychosocial factors associated with glycemic control in an unselected pediatric population with T1D.

Methods: We included a cross-section of 58 adolescents (28 boys and 30 girls) aged 13.6 ± 4.0 years with T1D ≥1 year attending a well-established pediatric diabetes clinic in Thailand. Median diabetes duration was 4.1 years (range 1–18 years). Participants were divided into 2 subgroups according to their average HbA_{1c} level over the past year. Those with good control (HbA_{1c} <8%) (n = 13) were compared with those with poor control (HbA_{1c} ≥8%) (n = 45). Data collected from self-report standardized questionnaires and medical records were used to compare variables between groups.

Results: Adolescents with good control used significantly less daily insulin and had higher family income, higher scores for family support, and quality of life (QoL) than those in the group with poor control ($P < 0.05$). Age, sex, puberty, duration of diabetes, insulin regimen, frequency of blood glucose monitoring, and self-report adherence did not differ between groups. By univariate logistic regression, the only factor associated significantly with poor glycemic control was a QoL score <25.

Conclusion: Adolescents with T1D may be at a higher risk of poor glycemic control if they have poor QoL, impaired family functioning, poor coping skills, and lower socioeconomic status, suggesting that psychosocial interventions could potentially improve glycemic control in this population.

Keywords: adherence, adolescents, children, glycemic control type 1 diabetes mellitus (DM)

Type 1 diabetes mellitus (T1D) is a chronic disease caused by an immune-mediated destruction of β-cells, resulting in lifelong dependence on exogenous insulin [1]. The incidence of newly diagnosed T1D in children and adolescents has been increasing rapidly worldwide [2]. In 1993, the Diabetes Control and Complications Trial (DCCT) study

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established that in patients with T1D, early near-normalization of blood glucose with glycated hemoglobin (HbA_{1c}) <7.0% prevents or delays progression of long-term microvascular complications [3]. However, optimizing glycemic control in children and adolescents with T1D is particularly challenging, given the physiological and behavioral challenges that confront individuals in this age group [4]. Despite the progress of new technology widely available in developed countries such as improved glucose monitoring devices, insulin pumps, and insulin analogs, a substantial proportion of youth with T1D still fail to achieve target HbA_{1c} levels <7.5% [5–7]. Family relationships, psychosocial factors, and race–ethnicity continue to be associated with glycemic outcomes in youth with T1D [4, 8]. To date, there is a paucity of studies of adolescents with T1D in less-resourced countries examining the relationships of factors affecting glycemic control in this population. The objectives of the present study were to determine which HbA_{1c} levels can be achieved in unselected children and adolescents <18 years of age with T1D and to examine the possible relationships to various parameters such as insulin regimen, insulin dose, sex, age, diabetes duration, body mass index (BMI), frequency of self-monitoring of blood glucose (SMBG), adherence, and psychosocial factors (socioeconomic status, family functioning, and quality of life (QoL)) in pediatric patients with good glycemic control compared with those with poor glycemic control.

Materials and methods

Participants

The study protocol was reviewed and approved by the institutional review board of Faculty of Medicine, Chulalongkorn University (certificate of approval no. 787/2014). Written informed consent was obtained from the parents or guardians of each patient, and the assent was obtained from each child. We enrolled 58 patients (28 boys and 30 girls; aged 13.6 ± 4.0 years) with T1D who had been diagnosed for >12 months and had been regularly followed up (at least every 3–4 months) at our pediatric diabetes clinic at King Chulalongkorn Memorial Hospital (KCMH), a tertiary-care university teaching hospital in Bangkok, Thailand, during 2014–2015. We excluded children who had intellectual deficits that may interfere with their psychosocial functioning and children who were not regularly followed up (seen in the clinic <3 visits over the past 12 months).

Patients were divided into 2 subgroups according to their average HbA_{1c} levels in the last 3 visits. In accordance with the International Society for Pediatric and Adolescent Diabetes guidelines, an HbA_{1c} cutoff of 7.5% was chosen to define excellent glycemic control for T1D. Thus, in the present study, "good glycemic control" (excellent to fairly good) was defined as average HbA_{1c} <8.0%, and "poor control" was defined as average HbA_{1c} ≥8.0%.

Study protocol

Data were obtained from each patient's medical record at the time of their most recent visit, which included age, sex, onset characteristics, BMI, pubertal status, duration of diabetes, and current HbA_{1c} levels. Pubertal status was assessed by the method of Marshall and Tanner [9, 10]. Prepuberty was defined by using criteria of Tanner stage I for breasts in girls and testicular volume 3 mL or less for boys by Prader orchidometry at the study visit. Boys with testicular volume >3 mL, girls with Tanner breast stage of at least 2, and patients with a Tanner pubic hair stage of at least 2 were classified as having entered puberty. Details of diabetes management including insulin dosage, insulin regimen, and frequency of SMBG were collected. The patient and the parent or guardian who accompanied the child to the clinic were asked to complete a set of questionnaires during the most recent visit when the medical records of that visit were obtained.

Questionnaires

Parents completed a set of questionnaires regarding their marital status, educational levels, and financial and employment statuses and a "Family relationship and functioning questionnaire" [11], which is a 7-item questionnaire that assesses the family's ability to be flexible, supportive, communicative, and have enough income and time to support their child.

Youth with T1D were asked to complete a set of questionnaires including (1) "family APGAR scales" [12, 13] to assess the participant's perception of family functioning by examining his or her satisfaction with 5 parameters of family relationships (namely, adaptability, partnership, growth, affection, and resolve); (2) "problem and conflict solving questionnaire" [14, 15], which is a 5-item questionnaire to assess the participant's ability to manage conflict or solve problems; (3) psychological well-being and the diabetes-specified QoL scales were assessed by use of a modified

World Health Organization-5 Well-being Index and; and QoL was measured by use of a modified Diabetes Attitudes, Wishes, and Needs (DAWN) survey [16, 17]. Patient participants were asked to rate how they felt during the last 2 weeks and to what extent they agreed with each statement.

All the questionnaires used in the present study had been translated and validated. Higher scores of these psychosocial indicators suggest stronger family support, good family relationship, better adaptive and problem-solving skills, and better QoL.

Adherence

Data regarding adherence to the diabetes management were obtained from the record of data downloaded from a glucometer and the medical chart from 12 months before the child's study visit. Four adherence measures were obtained: (1) the frequency of missing blood glucose checks in the week before the study visit (at least 4 checks per day were recommended for all children), (2) the number of missing insulin injections in the week before the study visit, (3) the number of the clinic visits that each child did not bring the blood glucose meter during the last 3 visits, and (4) the number of the clinic visits that each child did not bring the diabetes logbook during the last 3 visits. To obtain a single measure of adherence, we created a single composite score of the 4 adherence variables described earlier. We defined the adherence composite scores ranging from 0 to 8. We defined "good adherence" if the scores were ≥6 and "poor adherence" if the scores were <6. In addition, patient participants completed the "8-item Morisky Medication Adherence Scale (MMAS) questionnaire" [18], which is a self-rated inventory used as a quick screening measure to quantify medication adherence (on a scale of 0–8). Higher values of the adherence composite score and MMAS scores indicate better adherence.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0. Normally distributed data were expressed as mean ± standard deviation (SD), whereas non-normally distributed data were expressed as median and interquartile range (IQR; Q1, Q3). Comparisons between 2 groups were analyzed using a Fisher's exact or chi-square test for categorical data and an unpaired *t* test or Mann–Whitney *U* test for continuous data. Receiver operating characteristic curves were used to analyze the reasonable cutoff values of selected psychosocial indices for predicting poor glycemic control. Univariate logistic regression analysis was used to assess differences between the good control and poor control groups in various characteristics. $P < 0.05$ was considered significant in tests of statistical inference.

Results

Demographic and clinical characteristics

We enrolled 58 patients (28 boys and 30 girls) in the present study. Their demographic and clinical characteristics are shown in **Table 1**. Thirty-nine (67%) patients were on a basal-bolus insulin regimen with 4 or more daily injections, 12 (21%) patients were on twice-daily injections with premixed insulin, 2 patients (3%) were on twice-daily injections, and 5 patients (9%) were on thrice-daily injections with split mixed human insulin (RI/NPH) (modified conventional regimen) (**Table 2**). There were no patients using an insulin pump in the present study. Mean HbA_{1c} levels were

Table 1. Demographic and clinical characteristics of patient participants in the groups with good and poor glycated hemoglobin control

Characteristic	Total	HbA_{1c} (%)		*P*
		Good control (<8.0%), n = 13	Poor control (≥8.0%), n = 45	
Sex				
Male	28 (48%)	8 (62%)	20 (44%)	0.27
Female	30 (52%)	5 (39%)	25 (56%)	
Age (years)	13.6 ± 4.0	14.4 ± 5.6	13.4 ± 3.5	0.45
BMI-SDS	0.5 (–0.13, 1.04)	–0.10 (–1.06, 0.7)	0.56 (0.14, 1.15)	0.07
Pubertal status				
Prepuberty	13 (22%)	4 (31%)	9 (20%)	0.46
Puberty	45 (78%)	9 (69%)	36 (80%)	
Duration of T1D (years)				
Median (range)	4.1 (1–18)	4.3 (1–18)	3.5 (1–13)	
≤2 years	21 (36%)	6 (46%)	15 (33%)	0.61
>2 years	37 (64%)	7 (54%)	30 (67%)	0.40

Values are presented as frequency (%), mean ± SD, median (IQR; Q1, Q3), or median (range). *P*-value corresponds to chi-square, *t*, and Mann–Whitney *U* tests

BMI-SDS, body mass index-standard deviation score; HbA_{1c}, glycated hemoglobin; IQR, interquartile range; SD, standard deviation; T1D, type 1 diabetes mellitus

Table 2. Insulin regimen, dose, frequency of self-monitoring of blood glucose, and glycemic control

Factor	HbA_{1c}	*P*
	Good control (<8.0%), n = 13	Poor control (≥8.0%), n = 45	
Insulin regimen			
Basal-bolus insulin regimen (≥4 injections/day)	10 (77%)	29 (64%)	0.52
Other regimens:	3 (23%)	16 (36%)	
2 injections/day with premixed or split mixed human insulin	3	11	
3 injections/day with split mixed human insulin	0	5	
Units of insulin per body weight (U/kg/day)	0.79 ± 0.28	0.99 ± 0.30	0.04*
Frequency of SMBG			
0–1	1 (8%)	9 (20%)	0.53
2	4 (31%)	12 (27%)	
3	2 (15%)	11 (24%)	
≥4	6 (46%)	13 (29%)	

P corresponds to Fisher's exact and unpaired *t* tests. *$P < 0.05$.
HbA_{1c}, glycated hemoglobin; SMBG, self-monitoring of blood glucose.

Table 3. Adherence and glycemic control

Variable	HbA_{1c}		*P*
	Good control (<8.0%), n = 13	Poor control (≥8.0%), n = 45	
Frequency of missing SMBG in 1 wk			
Never forget	10 (77%)	22 (49%)	0.11
Forget at least 1 time/wk	3 (23%)	23 (51%)	
Frequency of missing insulin injection in 1 wk			
Never forget	11 (85%)	37 (82%)	>0.99
Forget at least 1 time/wk	2 (15%)	8 (18%)	
Frequency of missing log book in the last 3 visits			
Never forget	8 (62%)	25 (56%)	0.76
Forget at least 1 time	5 (38%)	20 (44%)	
Frequency of missing glucose meter in the last 3 visits			
Never forget	9 (69%)	30 (67%)	>0.99
Forget at least 1 time	4 (31%)	15 (33%)	
Composite adherence score	6.2 ± 2.1	5.8 ± 2.1	0.51
MMAS score	6.4 ± 1.4	6.03 ± 1.3	0.35

P-value corresponds to Fisher's exact and unpaired *t* tests.
HbA_{1c}, glycated hemoglobin; SMBG, self-monitoring of blood glucose; MMAS, Morisky Medication Adherence Scale

9.2 ± 1.9%. By the definition in the present study, there were 13 (22%) patient participants considered to have good control (average HbA_{1c} 7.0 ± 0.7%) and 45 (78%) patient participants in the group considered to have poor control (average HbA_{1c} 9.9 ± 1.6%). Age, sex, duration of diabetes, and the pubertal status were not different between the group with good control and the group with poor control. Weight did not differ significantly between groups, but those in the group with poor control tended to have a higher median BMI-standard deviation score (BMI-SDS) than those in the group with good control (**Table 1**).

Insulin regimen, dose, and the frequency of SMBG

The insulin regimen and the frequency of SMBG did not differ between patient participants in the group with good control and those in the group with poor control. Patient participants in the group with poor control required a significantly higher insulin dose than those in the group with good control (**Table 2**).

Adherence

There was no significant difference between the groups with poor or good control in terms of the frequency of missing SMBG or insulin injections in 1 week or the number of routine clinic visits in the last 3 visits to which patients had not brought glucometers or log books. Neither the composite adherence score nor the MMAS score was different between groups (**Table 3**).

Socioeconomic status

Family income was significantly different between the groups with poor or good glycemic control. Eleven of 13 (85%) patients in the group with good control and 15 of 45 (33%) patients in the group with poor control had family income ≥30,000 Thai baht (THB)/month ($P = 0.01$). The average monthly household income in Thailand in 2015 (National Statistical Office of Thailand) was 26,915 THB or 786 U.S. dollars (USD; 1 USD equivalent to 34.241 THB, U.S. Federal Reserve Bank G5.A annual average rate 2015). There were no significant differences in financial self-sufficiency, parental age, parents' education, or marital status between the groups (data not shown).

Family support and QoL

The median scores (IQR) of family relationship and functioning as reported by primary caregivers did not differ

significantly between the groups with good and poor control (**Table 4**). Most of the psychosocial variables assessed by the child were significantly different between the groups. The family APGAR scores were higher in the good control group than those in the poor control group, and the scores for QoL were also higher in the good control group. Participants in the good control group appeared to have higher scores for problem and conflict solving than those in the group with poor glycemic control, but the difference was not significant, possibly because of the small sample size.

Factors associated with poor glycemic control

After performing the univariate analysis, significant factors ($P < 0.05$) were entered into a univariate logistic regression model to identify those most importantly associated with poor glycemic control. The only remaining significantly associated factor of poor glycemic control was a QoL score <25 (**Table 5**).

Table 4. Family support and quality of life and glycemic control

Psychosocial indicators	HbA_{1c}		*P*
	Good control (<8.0%), n = 13	Poor control (≥8.0%), n = 45	
Family relationship and functioning (7–35)	31 (29, 32.5)	27 (24.5, 32)	0.17
Family APGAR scores (0–20)	20 (17, 20)	15 (12, 19)	0.005*
Problem- and conflict-solving skill (0–15)	9 (7, 11.5)	7 (5, 9)	0.054
QoL (0–39)	27 (22.5, 28.5)	21 (17, 24)	0.019*

Minimum and maximum scores of each questionnaire are given in the brackets. Higher scores of these indicators generally suggest stronger family support and better relationships. Values are presented as median (IQR; Q1, Q3). *P*-value corresponds to a Mann–Whitney *U* test. *$P < 0.05$
HbA_{1c}, glycated hemoglobin; IQR, interquartile range; QoL, quality of life

Table 5. Factors associated with poor glycemic control by univariate logistic regression analysis

Factor	Adjusted odds ratio	95% confidence interval		*P*
		Lower	Upper	
Family income <30,000 THB/month	5.68	0.89	36.31	0.07
Quality of life score <25	6.19	1.01	37.87	0.049*
Family APGAR score <16	3.81	0.34	43.19	0.28
Problem- and conflict-solving score <11	1.99	0.18	21.67	0.57

Discussion

In the present study, we found that the mean HbA_{1c} level in Thai youth with T1D was 9.2% and that the majority of children and adolescents could not achieve satisfactory glycemic control. The challenge in achieving targeted glycemic control in youth with T1D has been observed in several studies from Thailand and various countries worldwide [19–23]. Notably, data from the DCCT study showed that the mean HbA_{1c} level was 8.1% in adolescents who were under intensive insulin therapy and closed monitoring compared with 7.1% in adults treated with the same protocol [24].

The results of the present study suggested that that daily insulin dosage, family income, family problem and conflict-solving ability, family structure and support, and QoL differed between patients in the groups with good and poor control. Various factors affecting glycemic control have been found in studies of pediatric patients. A large study of >2,579 children and adolescents in France with T1D found strong associations between HbA_{1c} levels and age, daily insulin dosage per kilogram, mother's age, and frequency of SMBG [20]. Dorchy et al. [21] studied 144 children and adolescents with T1D and showed that HbA_{1c} levels were not related to sex, number of insulin injections, or age, and after age of 2 years, HbA_{1c} was negatively correlated with the frequency of SMBG. Data from the T1D Exchange database from 58 diabetes clinics in the USA showed that children and adolescents with excellent glycemic control tended to exhibit better diabetes self-management techniques than those with poor control, i.e., using insulin pumps, performing SMBG ≥5×/d, missing fewer boluses, using meal-specific insulin to carbohydrate ratios, and using a lower mean total daily insulin dose than those with poor control [25]. A meta-analysis in 2009 also supported the adherence–glycemic control link in pediatric T1D [26]. By contrast, we could not demonstrate any association between glycemic control and treatment adherence, which could possibly be explained by the small sample size. However, we observed that patients in the group with good glycemic control tended to have less missing SMBG. In addition, we found that patients in the group with poor control tended to have higher BMI-SDS than those with good control, suggesting that BMI may play a role in glycemic control. However, we did not assess other factors, i.e., eating habits or physical activity that could contribute to BMI or daily insulin dosage requirement.

Similarly, several other studies demonstrated that behavioral and psychosocial issues in children and adolescents with T1D importantly impact their glycemic control and QoL outcomes. Wu et al. [27] found that higher levels of caregiver support during adolescence were a protective factor from the expected decline in diabetes self-management adherence. Rechenberg et al. [28] showed that socioeconomic status was associated with diabetes outcomes in adolescents with T1D. Those in higher income groups reported significantly lower HbA_{1c}, better diabetes problem-solving, lower levels of stress, and better QoL. Family structure and functioning also impact outcomes in youth with T1D. Cohen et al. [29] found that better glycemic control was predicted by high family cohesion and the presence of internalizing behavior problems. Iskander et al. [30] found that baseline positive communication during preadolescent years predicted adherence 3 years later, suggesting the importance of improving family communication before entering puberty.

A strength of the present study is that it attempts to characterize the comprehensive medical and psychosocial factors affecting glycemic control in children and adolescents with T1D in a less-resourced country. However, there are some limitations to our present study. First, the study was retrospective with a small sample size. Not all the patients we attempted to recruit were willing to participate or their parents or guardians did not provide consent to participate, leading to a recruitment rate of around just 65%. Thus, the study may lack sufficient power for some associated factors, and there were not sufficient data for multivariable logistic regression analysis. However, by univariate logistic regression analysis, we found that the only significant factor associated with poor glycemic control was the QoL. Similarly, Hood et al. [31] found that psychosocial burden, especially poor diabetes-related QoL, was a strong contributor to poor glycemic outcomes. Second, although all patients in this study had diabetes duration ≥1 year, there is concern that short diabetes duration may affect the outcome of glycemic control. However, a previous study suggested that most children with T1D were out of the honeymoon (partial remission) period within 12 months of diagnosis [32]. Finally, a significant proportion of patients in our clinic were still on a suboptimal insulin regimen, which may affect their glycemic outcome. T1D has a low prevalence in Thailand; hence, it is relatively ignored by the government and policy makers. Unlike in some developed countries, most patients have to buy glucometer strips from their own resources as these are not covered by universal health care coverage in Thailand, which might impact the frequency of SMBG. Unfortunately, more advanced diabetes technologies including an insulin pump and continuous glucose monitoring are not covered by any schemes of health care coverage. The cost of an insulin pump is not affordable for a majority of the patients in Thailand [33]. Moreover, T1D is a social stigma in Thailand and other Southeast Asian countries [34]. Thus, many children with T1D avoid insulin injection during lunch time at school. In addition, most school personnel will not help young children with T1D with the injection. In Thailand, we have not yet had any antidiscrimination or civil rights statute that ensures that the needs of students with T1D are met adequately. Consequently, many children with T1D have to use a modified conventional insulin regimen, using NPH in the morning to cover their lunch time.

Conclusions

In this study, we found that adolescents with good glycemic control significantly had a higher family income and higher scores for family support and QoL than those in the group with poor control. According to univariate logistic regression analysis, lower QoL is the strongest risk factor for poor glycemic control. Lower socioeconomic status, poor family problem and conflict-solving skills, poor family support, and lower QoL are risk factors for poor glycemic control in youth with T1D. Therefore, diabetes care providers should seek and take action targeted to these psychosocial risk factors. Further studies should emphasize the effect of psychosocial intervention, especially targeting the parent–child relationship, family functioning, and problem-solving skills. Management of T1D in Thailand remains suboptimal because of country-specific challenges; therefore, it is essential to promote understanding of the disease to the public and healthcare professionals, as well as strengthen the government healthcare infrastructure, to improve healthcare equality and coverage, which could improve the QoL and disease outcomes for these patients with T1D.

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Conflict of interest statement. The authors have each completed and submitted the ICMJE Uniform Disclosure Form for Potential Conflicts of Interest. None of the authors disclose any conflict of interest.

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