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Glycemic Control Rate in Patients With Type 1 Diabetes Treated at a Public Tertiary Referral Hospital in Rio de Janeiro, Brazil

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Abstract

Background: The incidence of type 1 diabetes (T1D) has been increasing worldwide, leading to a serious public health problem resulting in reduced life expectancy and increased morbidity. The aim of this study was to determine the glycemic control rate and its demographic and clinical factors, in T1D followed up at a tertiary referral hospital in Brazil.

Methods: An observational and retrospective study was conducted between October 2014 and October 2015. Data were obtained from 140 medical records.

Results: Satisfactory glycemic control rate was found in 22.14% of patients. There was no difference between the pediatric group and adult group regarding control rate. However, a worse HbA1C level was found in the pediatric group (P = 0.001). The use of long-acting insulin analogue (P = 0.03) was associated with satisfactory glycemic control, and a tendency was observed for both the combination of long-acting and ultra-rapid acting analogues (P = 0.08), and the absence of ketoacidosis during the course of diabetes (P = 0.08). In the group with satisfactory glycemic control, the median number of consultations (1 (1 - 4)) was significantly lower than in the uncontrolled group (2 (1 - 4)) (P = 0.003). Regarding the two major microvascular complications, 23.53% had retinopathy and 12.09% had nephropathy.

Conclusions: The majority of patients did not obtain a satisfactory HbA1C level. Good glycemic control factors were directly associated with the use of long-acting insulin analogues, and the combination of long-acting and ultra-rapid analogues as well as the absence of ketoacidosis during T1D's evolution tended also to be associated with better metabolic control.

Keywords: Type 1 diabetes mellitus; Glycosylated hemoglobin A; Brazil

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Introduction

Type 1 diabetes (T1D) is a heterogeneous disorder characterized by the destruction of pancreatic beta cells, gradually leading to absolute insulin deficiency [1, 2].

The International Diabetes Federation (IDF) estimates that 415 million individuals between 20 and 79 years old have diabetes, with a worldwide prevalence of 8.8% [3]. Among children and adolescents with T1D aged up to 14 years, an overall incidence and prevalence of 86,000 per year and 542,000 are estimated, respectively [3]. In Brazil, the estimated incidence and prevalence correspond to 5.0/1,000/year and 31.1/1,000, respectively [4]. The epidemiology of T1D in adults is less well characterized than in children aged 0 - 14 years old. Studies show that T1D incidence has been increasing approximately 3% each year [5-8].

T1D is a chronic disease, usually diagnosed in children and young adults, requiring indefinite multidisciplinary treatment, making it an extremely onerous disease. In Brazil, for example, an average annual cost of US$1,319.15 per patient is estimated for nominal T1D treatment [9]. Moreover, T1D has an important negative impact on life quality and expectancy, mainly due to the disease-specific vascular complications [10].

After the Diabetes Control and Complications Trial (DDCT) and later, the Epidemiology of Diabetes Interventions and Complications (EDIC) results were published, it became clear that diabetic complications were directly related to poor glycemic control, recognizing the need of achieving the best glycemic and metabolic control as soon as T1D diagnosis is established [11-13]. Despite this knowledge, it is extremely difficult to achieve strict glycemic control in clinical practice.

This study aims to assess glycemic control rate and its demographic and clinical factors, and analyze the prevalence of microvascular complications in patients with T1D in a public

Brazilian tertiary referral hospital.

Materials and Methods

Study design and population

An observational, retrospective study, between October 2014 and October 2015, at the Endocrinology Section of Hospital Federal da Lagoa (HFL) was performed. All patients were seen by an endocrinologist. Inclusion criteria were predefined as follows: patients (adults and children) diagnosed with T1D, with a regular follow-up and at least one visit and a glycated hemoglobin (HbA1C) assessment during the studied period. Exclusion criteria included: 1) other types of diabetes (such as type 2 diabetes, latent autoimmune diabetes in adults (LADA), maturity-onset of diabetes of the young, and gestational diabetes); 2) an irregular follow-up with no medical appointment in the studied period; 3) patients treated with another option besides insulin injections (including insulin pump); and 4) those with unavailable HbA1C measurement.

Data collection

The following data were collected from data available in medical records: age at the last consultation, age at diagnosis (in years), gender, diabetes duration (in months), type of insulin, self-monitoring of blood glucose (SMBG), presence and frequency of hypoglycemia with the latest treatment, history of diabetic ketoacidosis, presence of nephropathy or retinopathy, body mass index (BMI), waist circumference and HbA1C.

According to age range, the participants were divided into two groups: individuals aged 18 years or less were included in the pediatric group and above 18 years in the adult group. Three groups were created to classify the type of insulin injection: intermediate insulin (NPH) + rapid insulin (regular), intermediate insulin + ultra-rapid insulin analogue (glulisine, lispro or aspart), or long-acting insulin analogue (detemir, glargine or degludec) + ultra-rapid insulin analogue. SMBG was analyzed through glycemic profile and divided into: < 1 time/day; 1 - 3 times/day and > 4 times/day. BMI was determined dividing the weight in kg by the square of the height in meter, and considered normal below the 85th percentile adjusted for age and sex for participants younger than 20 years of age and below 25 kg/m^2 for adults ≥ 20 years old. Overweight and obesity were classified as a BMI between p85 and p94 adjusted for age and sex for individuals < 20 years of age or BMI between 25 and 30 for adults ≥ 20 years of age, and ≥ 95th percentile for participants < 20 years of age and BMI ≥ 30 kg/m^2 for adults ≥ 20 years of age, respectively [14]. Waist circumference was measured at midpoint between the lowest rib and the iliac crest [14].

HbA1C was determined by high performance liquid chromatography, a certified method by the Glycohemoglobin Standartization Program, in the equipment Premier Hb9210^{TM}, with the software Affinity^{TM}, with an acceptable error range of 0.067. Satisfactory control target was defined as an HbA1C lower than 7.5% for children and adolescents aged up to 18 years old and below 7.0% for patients older than 18 years old, according to the American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) [2, 15].

Patients who had more than 5 years of diabetes were analyzed regarding the two major microvascular complications: 1) nephropathy was assessed by identifying the presence of urine albumin-to-creatinine ratio > 30 mg/g in a random spot urine collection or albuminuria > 30 mg/24 h urine [16]; and 2) retinopathy was screened with fundoscopic examination performed at the Ophthalmology Section, and considered positive when microvascular alterations leading to retinal ischemia or neovascularization were present [17]. In other words, if mild, moderate or severe non-proliferative retinopathy or proliferative retinopathy was present.

Diabetic neuropathy was not analyzed due to the lack of standardization of different test methods.

Statistical analysis

The statistical analyses were performed using SPSS version 20.0 for MacOS (SPSS Inc., Chicago, IL). Most of the variables, except BMI and waist circumference, were found not to follow a normal distribution using the Kolmogorov-Smirnov test. For the descriptive analysis, categorical variables were expressed as the percentage and frequency, and numerical variables were expressed as mean ± SD or median (minimum - maximum) according to their distribution pattern. Student's *t*-test or the Mann-Whitney U test was performed to compare the numerical variables between the two groups according to their distributions. A Kruskal-Wallis test was performed to compare the numerical variables between the three groups (insulin injection and SMBG). Fisher's exact test and a Chi-square test were used to compare categorical variables. A P-value < 0.05 was considered statistically significant, except for comparison between two of the three groups (insulin injection and SMBG), when P-value < 0.017 was considered significant (Bonferroni *post hoc* analysis). P-values ≥ 0.05 and ≤ 0.09 were considered to indicate a tendency towards statistical significance.

Results

Out of 173 patients selected with T1D diagnosis, 33 were not eligible (18 patients were excluded due to unavailable HbA1c, 11 did not have any consultation during the studied period and four had LADA). Clinical and epidemiological data of the 140 patients included in this study are shown in Table 1.

Regarding age at diagnosis, 78.58% of patients were diagnosed with T1D between 5 and 19.9 years. The majority of patients had one or two consultations per year (70%) and most of them had ≥ 4 blood glucose tests per day (46.21%), while 43.94% performed 1 - 3 tests daily and 9.85% less than once a day. Regarding the type of insulin, the majority (67.15%) used intermediate-acting insulin instead of long-acting insulin analogue (32.85%). Likewise, the majority (55.71%) used ultra-

Table 1. Clinical and Epidemiological Data

Variables	Total, n (%)
Male/female	70 (50%)/70 (50%)
Age[a] (years)	19.0 (6 - 64)
0 - 18	69 (49.30%)
> 18	71 (50.70%)
Age at diagnosis (years)	10.0/1 - 33
0 - 5	14 (10%)
5 - 9.9	50 (35.72%)
10 - 14.9	39 (27.86%)
15 - 19.9	21 (15%)
20 - 29.9	15 (10.71%)
≥ 30	1 (0.71%)
Diabetes duration (months)	84 (2 - 660)
Treatment	
Basal intermediate action insulin	94 (67.15%)
Basal long duration analogues	46 (32.85%)
Bolus rapid action insulin	62 (44.29%)
Bolus ultra-rapid action insulin	78 (55.71%)
Self-monitoring of blood glucose (n = 132)	
< 1 time/day	13 (9.85%)
1 - 3 times/day	58 (43.94%)
≥ 4 times/day	61 (46.21%)
Consultations/year	2 (1 - 4)
1	50 (35.71%)
2	48 (34.29%)
3	28 (20%)
4	14 (10%)
Ketoacidosis at diagnosis (n = 91)	47 (51.65%)
Ketoacidosis during the evolution of the disease (n = 78)	21 (26.92%)
Retinopathy (n = 102)	24 (23.53%)
Nephropathy (n = 91)	11 (12.09%)
Waist circumference (cm)	78.94 ± 12.42
BMI (kg/m^2)	21.97 ± 4.88
Overweight or obesity (n = 104)	39 (27.85%)

[a]Age, patient's age obtained at the last consultation. BMI: body mass index.

rapid-acting insulin analogue instead of rapid-acting insulin (44.29%). Moreover, 27.85% of patients were overweight or obese. Retinopathy was found in 23.53% and nephropathy in 12.09% of cases. All of the retinopathy cases and 90.90% of patients with nephropathy were diagnosed in adulthood (Table 1).

The global glycemic control rate was 22.14%. Comparing the patients' profile according to age range, the median HbA1C level found in the pediatric group was significantly higher (9.2% (5.2-16.5%)) than in the adult group (7.9% (5.6-16.2%)) (P = 0.001). However, there was no significant difference regarding glycemic control rate between these groups (21.74% and 22.53%, respectively; P = 0.910), nor regarding the median number of consultations per year (2 (1 - 4); P = 0.6).

Concerning the type of insulin, the group treated with long-acting analogue + ultra-rapid analogue tended to have a better control rate (32.6%; P = 0.08) and obtained a lower HbA1C (7.90%; P = 0.01) when compared to other groups (Table 2).

SMBG was more frequent in younger patients (≥ 4 times/day: 14 years old (6 - 56); 1 - 3 times/day: 21 years old (7 - 64);

Table 2. Profile of Patients According to the Type of Insulin

Variables	NPH + R (n = 62)	NPH + UR (n = 32)	L + UR (n = 46)	P value
Sex	F: 35 (56.45%) M: 27 (43.55%)	F: 13 (40.62%) M: 19 (59.38%)	F: 22 (47.83%) M: 24 (52.17%)	NS
Age[a] (years)	20 (6 - 64)	18.5 (8 - 60)	16.50 (7 - 56)	NS
Age at diagnosis (years)	11.5 (1 - 27)*	11.5 (1 - 22)	9.0 (1 - 33)*	0.02
Diabetes duration (months)	80 (2 - 660)	78 (6 - 492)	108 (9 - 492)	NS
BMI (kg/m^2)	22.38 ± 4.92	21.39 ± 4.39	21.87 ± 5.22	NS
Waist circumference (cm)	81.87 ± 12.27	71.13 ± 8.87	78.47 ± 12.97	NS
Hypoglycemia	44/53 (83%)	18/24 (75%)	27/41 (65.85%)	NS
Retinopathy	15/48 (31.25%)	1/22 (4.54%)	8/32 (25%)	0.05
Nephropathy	6/44 (13.63%)	1/18 (5.55%)	4/29 (13.79%)	NS
HbA1C (%)	8.3 (5.2 - 16.5)	9.4 (5.6 - 14.3)**	7.9 (6 - 11.3)**	0.01
Control rate[b]	12/62 (19.35%)	4/32 (12.50%)	15/46 (32.60%)	0.08

[a]Age, patient's age obtained at the last consultation. [b]For this analysis, we considered ADA's goals for T1D patients as: HbA1C < 7.5% for children and adolescents up to 18 years old and < 7.0% for patients ≥ 18 years old. *Significant difference between the groups: NPH + R and L + UR (P = 0.006) - Kruskal-Wallis test and Bonferroni *post hoc* analysis. **Significant difference between the groups NPH + UR and L + UR (P = 0.002) - Kruskal-Wallis test and Bonferroni *post hoc* analysis. BMI: body mass index; F: female; M: male; NS: not significant; NPH: (basal) intermediate insulin; R: (bolus) rapid insulin; L: (basal) long-acting insulin analogue; UR: (bolus) ultra-rapid insulin analogue.

< 1 time/day: 20 years old (10 - 38), P = 0.03), and in those using long-acting (≥ 4 times/day: 69.05%; 1 - 3 times/day: 28.57%; < 1 time/day: 2.38%, P = 0.001) or ultra-rapid insulin analogues (≥ 4 times/day: 56.94%; 1 - 3 times/day: 38.89%; < 1 time/day: 4.17%, P = 0.007). No statistical difference was found between SMBG and the presence of retinopathy or nephropathy.

The use of long-acting insulin analogue (P = 0.03) was a factor of satisfactory glycemic control and a tendency was observed for combination of long-acting and ultra-rapid acting analogues (P = 0.08), as well as for the absence of ketoacidosis during the course of diabetes (P = 0.08). Regarding the group that had satisfactory glycemic control, the median number of consultations (1 (1 - 4)) was significantly lower than in the uncontrolled group (2 (1 - 4)) (P = 0.003) (Table 3).
SMBG was not a factor of glycemic control.

Discussion

In this study, we analyzed T1D patients' characteristics according to glycemic control rate, considering the cutoff points for age determined by ADA's and ISPAD's latest recommendations [2, 15]. Only few studies in Brazil are available analyzing glycemic control, and trying to establish satisfactory glycemic control factors among T1D patients. In this series, satisfactory glycemic control rate was about 22%, and the main positive factor of good control was the use of long-acting insulin analogue and the negative factor was the number of consultations per year. It is important to know which factors are associated with diabetes control not only for the patient's care but also to ensure effective health policies.

Studies conducted by the Brazilian Type 1 Diabetes Study Group (BrazDiab1 SG) demonstrated a control rate of 23.2% and 11.6% among T1D younger than 18 years old and adults, respectively [5, 10]. Previous Brazilian data showed an even worse control rate among T1D patients over 18 years old (10%) [18]. Moreover, in a study that analyzed the control rate in Latin America, Chan et al [19] observed an overall control rate of 21.1%. Regarding US data, where approximately 60% of the studied population were using insulin pump, considered to be the gold standard therapy for T1D, the control rate was 17-23% in patients younger than 18 years old, 14% in subjects aged 18 - 25 years old, and about 30% among adults over 25 years old, with a mean HbA1c of 8.2-9.0%, 8.7% and 7.6-7.7%, respectively [20].

In our study, only 22.14% of the patients (21.74% individuals ≤ 18 years old and 22.53% adults > 18 years old) reached the recommended goal, which is in agreement with that reported in the literature [5, 10, 20, 21]. A greater number of consultations per year also did not imply in a better glycemic control. However, the difficulty of achieving satisfactory glycemic control in T1D is not exclusive to our service, as it appears to be global and should be seen as an important treatment challenge in T1D [5, 10, 19, 20, 22, 23]. Strict metabolic control plays an important role in preventing the onset and progression of chronic complications, as evidenced by the DCCT in which the progression of microvascular complications was so profoundly reduced in patients with intensive glucose control that the trial ended early after a mean time of 6.5 years, and all patients were placed into intensive therapy. This strict control should be sought even among children and adolescents from the beginning, as the early glycemic environment is remembered in target organs as a form of metabolic memory, mostly due to the existence of residual beta cell function. Hyperglycemia has long-lasting deleterious effects in diabetes and glycemic control, if not started at a very early stage of

Table 3. Distribution of Patients According to Glycemic Control Rate

Variables	HbA1C < target[a] (n = 31; 22.14%)	HbA1C > target[a] (n = 109; 77.86%)	P-value
Male/female	41.94%/58.06%	52.30%/47.70%	NS
Age[b] (years)	20 (6 - 64)	19 (6 - 64)	NS
Age at diagnosis (years)	12 (5 - 22)	10 (1 - 33)	NS
Diabetes duration (months)	60 (2 - 660)	88 (2 - 660)	NS
Consultations/year	1 (1 - 4)	2 (1 - 4)	0.003
Types of insulin			0.08
NPH + R	12/62 (19.35%)	50/62 (80.65%)	
NPH + UR	4/32 (12.50%)	28/32 (87.50%)	
L + UR	15/46 (32.60%)	31/46 (67.40%)	
SMBG (n = 132)			NS
< 1 time/day	0/29 (0%)	13/103 (12.62%)	
1 - 3 times/day	13/29 (44.83%)	45/103(43.69%)	
≥ 4 times/day	16/29 (55.17%)	45/103 (43.69%)	
Hypoglycemia (n = 124) present	20/28 (71.43%)	54/96 (56.25%)	NS
Hypoglycemia's frequency (n = 118)			NS
≥ 2 - 3 times/week	9/27 (33.33%)	20/91 (21.98%)	
≤ 1 time/week	18/27 (66.67%)	71/91 (78.02%)	
Ketoacidosis at diagnosis (n = 91)	12/20 (60%)	35/71 (49.30%)	NS
Ketoacidosis during the disease evolution (n = 78)	2/18 (11.10%)	19/60 (31.66%)	0.08
BMI (kg/m^2)	22.13 ± 5.44	21.94 ± 4.76	NS
Waist circumference (cm)	73.63 ± 10,69	79.98 ± 12.59	NS
HbA1C	6.8 (5.2 - 7.5)	9.0 (7.10 - 16.5)	< 0.001

[a]For this analysis, we considered ADA's goals for T1D patients as: HbA1C < 7.5% for children and adolescents up to 18 years old and < 7.0% for patients ≥ 18 years old. [b]Age, patient's age obtained at the last consultation. BMI: body mass index; HbA1C: glycated hemoglobin; L: long-acting insulin analogue; NPH: intermediate insulin; NS: not significant; R: rapid insulin; UR: ultra-rapid insulin analogue; SMBG: self-monitoring of blood glucose.

the disease. Strict metabolic control is associated with better glycemic control, lower hypoglycemia risk and long-lasting vascular benefits. Additionally, treatment optimization from the early stages of the disease significantly reduces the risks of complications [12].

There was no statistically significant difference between the pediatric group and adult group with respect to control rate; however, a worse HbA1C level was found in the pediatric group, also consistent with literature data [11, 20]. In the DCCT, for example, the intensively treated adolescent cohort achieved a mean HbA1c of 8.06%, whereas subjects in the corresponding adult cohort achieved a mean HbA1c of 7.1% [11]. In our study, this difference could be explained by the fact that our study gathered mostly adolescents (65% of them during puberty), which, of all age groups, are currently the farthest from achieving target HbA1c lower than 7.5% [21, 22]. Lack of concern regarding their disease, as well as psychological and hormonal changes can partially explain poor diabetes management during puberty. Moreover, both children and parents and even the medical team fear hypoglycemia, which may lead to overtreatment of initial symptoms, being more permissive in its treatment and instituting looser insulin regimens, even though the rates of hypoglycemia found in our study were similar in both the pediatric and adult groups [24-27].

In our study, although the use of ultra-rapid-acting insulin analogue was prescribed more often than regular insulin because it is routinely supplied in our hospital only for children and adolescents, its use did not correlate with better glycemic control when compared to rapid-acting insulin (24.36% vs. 19.35%), findings that are still controversial in the literature [28, 29]. On the other hand, a better glycemic control rate was directly associated with the use of long-acting insulin analogues and a trend with the combination of long-acting and ultra-rapid analogues. Similarly, studies showed that the use of long-acting analogues was superior to intermediate-acting insulin leading to small but significant reduction in HbA1c, as well as decrease in the frequency of severe and nocturnal hypoglycemia and mostly lower glycemic variability (nowadays considered as an additional marker of glucose control) [30, 31]. In addition, a Brazilian study conducted in T1D patients showed superior control rate (16.7% vs. 11.6%) with similar average HbA1c in patients using long-acting insulin analogues, compared to findings from a multicenter study where different types of insulin regimens were used [5, 32]. Furthermore, considering HbA1C as the outcome, no important clinical benefit was reported in systematic reviews per-

formed in T1D patients comparing human insulins with insulin analogues [33]. Although ultra-rapid insulin analogues are superior to rapid-acting insulin regarding the reduction of postprandial hyperglycemia and severe hypoglycemia, its greater efficacy in reducing HbA1c is still debatable [28, 33-35]. Despite the evident association between insulin analogues and a lower frequency of hypoglycemia, this finding was not observed in our study [28, 30, 31, 34, 35].

In our study, glycemic control tended to correlate to the type of insulin and presence of ketoacidosis during disease evolution. In addition, social and economic factors may also have contributed to glycemic control, since our hospital is a public institution whose attended population has lower economic and social status.

According to the literature, there is no consensus regarding which factors are directly associated with better glycemic control rates. Chan et al [19] noted that a short disease duration, SMBG and training by diabetes educators were associated with better glycemic control among patients with T1D in Latin America.

Furthermore, among our patients, 27.85% were overweight or obese. According to Gomes et al [10] in the BrazDiab1 study with T1D aged up to 18 years, 20.2% were overweight and 9.2% were obese. In another study by the same group, overweight was present in 25.6% and obesity in 6.9% of adults between 30 and 69 years [5]. Miller et al [20] observed a global rate of 25.65% and 16.4% in overweight and obesity, respectively.

Regarding SMBG, the optimal frequency in patients with T1D is unclear but ADA and ISPAD recommend that SMBG should be performed usually 4 - 6 times a day [15, 21]. In our study, most of the patients (46.21%) had ≥ 4 tests per day, while a minority (9.85%) less than once a day, even though patients have access to inputs required to perform at least three tests daily. Several studies have demonstrated a strong correlation between SMBG frequency and glycemic control [15, 19, 21, 36-39], which was not observed in our study. A database study of almost 27,000 children and adolescents with T1D showed that increased daily frequency of SMBG was significantly associated with lower HbA1C (-0.2% for one additional test per day) and with fewer acute complications [36].

Even though each patient was seen by an endocrinologist in a tertiary referral hospital, 27.15% did not undergo screening for retinopathy, which delays its early diagnosis and consequently the chance to treat and prevent further sequelae, also resulting in compromised quality of life of a significant proportion of our patients. This fact could be explained by the difficulties found when scheduling consultations and therefore having access to the Ophthalmology Service, which reinforces the importance of a specialized multidisciplinary team and the need to build partnerships. Likewise, despite the fact that microalbuminuria and/or albuminuria assessment is available in our hospital, 35% of our patients were not screened for diabetic nephropathy. Our findings were consistent with those found in other studies [5, 10, 19].

Our study has some limitations. Since this is a retrospective study, the socio-economic analysis of the patients was impaired. Recently diagnosed (< 1 year) T1D patients were not excluded to decrease the potential impact of residual insulin production, nor were analyzed factors that could interfere with HbA1C, such as hemoglobinopathy.

In conclusion, achieving adequate control in T1D is difficult, which is seen globally. In our study, the majority did not have a satisfactory glycemic control rate. Good glycemic control factors were directly associated with the use of long-acting insulin analogues, and the combination of long-acting and ultra-rapid analogues, as well as the absence of ketoacidosis during T1D's evolution tended also to be associated with better metabolic control.

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Conflicts of Interest

The authors have nothing to declare.

Author Contributions

Study design: Leonardo Vieira Neto. Study conduct: Leonardo Vieira Neto and Raissa Barros Mota. Literature review: Leonardo Vieira Neto, Raissa Barros Mota, Elisa Baranski Lamback, Michelle Botelho Caarls and Mariana Arruda. Data collection: Raissa Barros Mota and Natasha Reis Lozovey. Data analysis: Leonardo Vieira Neto and Raissa Barros Mota. Data interpretation: Leonardo Vieira Neto, Raissa Barros Mota, Elisa Baranski Lamback, Michelle Botelho Caarls and Mariana Arruda. Drafting manuscript: Raissa Barros Mota and Elisa Baranski Lamback. Revising manuscript content: Leonardo Vieira Neto, Michelle Botelho Caarls and Mariana Arruda. Approving final version of manuscript: Leonardo Vieira Neto, Raissa Barros Mota, Elisa Baranski Lamback, Natasha Reis Lozovey, Michelle Botelho Caarls and Mariana Arruda. Leonardo Vieira Neto takes responsibility for the integrity of the data analysis.

Abbreviations

ADA: American Diabetes Association; BMI: body mass index; BrazDiab1 SG: Brazilian Type 1 Diabetes Study Group; DDCT: Diabetes Control and Complications Trial; EDIC: Epidemiology of Diabetes Interventions and Complications; F: female; HbA1C: glycated hemoglobin; HFL: Hospital Federal da Lagoa; IDF: International Diabetes Federation; ISPAD: International Society for Pediatric and Adolescent Diabetes; L: long-acting insulin analogue; M: male; NPH: intermediate in-

sulin; NS: not significant; R: rapid insulin; SMBG: self-monitoring of blood glucose; T1D: type 1 diabetes; UR: ultra-rapid insulin analogue

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