

Health-related quality of life in a cohort of youths with type 1 diabetes

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SUMMARY

Health-related quality of life (HRQOL) in type 1 diabetes mellitus (T1DM) has been widely studied. The objectives of this study were to evaluate and identify the factors influencing the HRQOL of children and adolescents with T1DM.

MATERIAL AND METHODS: In total, 59 patients (9–16 years, T1DM for ≥ 1 year) responded to a version of the Diabetes Quality of Life Instrument for Youth (DQOLY) adapted to adapted to Brazilian patients, the Instrumento de Qualidade de Vida para Jovens com Diabetes (IQVJD). This instrument comprises 50 items (domains satisfaction, impact, and concerns, with the lowest scores corresponding to better HRQOL) and a questionnaire gathering social, demographic, and clinical parameters.

RESULTS: The mean age of the patients was 13.6 years, and 57.6% were girls. The median age at diagnosis was 7.16 years, 63% presented diabetic ketoacidosis (DKA) at diagnosis and 29% during follow-up. Mean glycated hemoglobin (HbA1c) in the previous year was 10%. All patients administered multiple insulin doses (mean 4.2 applications/day), 74.5% used rapid-acting and intermediate-acting insulin analogs, and 67.8% used pens for insulin application. The results of the DQOLY were within the cutoff limit for better HRQOL. An isolated analysis of each domain and the questionnaire results showed that the following factors were associated with better HRQOL: height Z-score, lower HbA1c, practice of physical activity, use of pen, fewer hospitalizations, and residence in a rural area. There was a high DKA rate at diagnosis, and the metabolic control was inappropriate in most patients. Despite coming from low-income households, most patients had access to the recommended treatment.

CONCLUSION: Among T1DM patients, 71% had IQVJD scores compatible with better HRQOL.

KEYWORDS: Quality of life. Child. Adolescent. Diabetes mellitus, type 1.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is the third most prevalent chronic disease in childhood and the most frequent type of diabetes in children ¹. The incidence of T1DM in this population has been increasing worldwide since 1960 at an approximate 3–5% yearly rate ². The causes of this epidemic are not well known, but

studies suggest the participation of multiple factors, including autoimmunity, genetic predisposition, diet, weight gain, viral infections, and early introduction of solid foods and cow's milk to infants ³⁻⁵. Approximately 80,000 children below the age of 15 years are estimated to develop T1DM annually across the world ⁶.

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Management of T1DM requires intensive treatment and adequate medical advice. Results from the Diabetes Control and Complications Trial (DCCT), the largest study conducted in T1DM patients, have shown that intensive treatment can prevent or delay the development of acute and chronic complications, and reduce the morbidity and mortality associated with the disease⁷.

For a long time, the mortality rate was a key determinant of the impact of a particular disease on public health. More recently, researchers have turned towards other determinants not confined to the medical dimension of a disease to include also subjective aspects related to health, such as health-related quality of life (HRQOL)⁸. Assessment of an individual's HRQOL offers a clear and objective analysis of the global impact that chronic diseases have on a patient's life since it encompasses several areas with potential health impact – physical, psychological, socioeconomic, and cultural satisfaction and well-being. Several studies have been relying on HRQOL as an indicator of treatment efficiency and as a basic parameter to understand an individual's perception of their condition and the impact of the disease on his health⁹.

Diabetes is often associated with substantial HRQOL impairment, imposing functional limitations, social and financial stress, emotional discomfort, and major depression. The reduction in HRQOL in patients with diabetes may result from complications associated with the disease and poor glycemic control, which is directly influenced by the patient's psychological profile and degree of acceptance of the disease⁷.

Considering the increasing incidence of diabetes in childhood and the lack of studies assessing HRQOL in this population, we conducted this study to evaluate and identify the factors that influence the HRQOL evaluated with the Instrumento de Qualidade de Vida para Jovens com Diabetes (IQVJD) in a group of children and adolescents with T1DM attending a reference center for diabetes in Curitiba (Brazil).

MATERIALS AND METHODS

This cross-sectional study was carried out between March and May 2013, at the outpatient diabetes clinic of *Unidade de Endocrinologia Pediátrica* (UEP) at *Hospital de Clínicas, Universidade Federal do Paraná* (UFPR). A total of 195 patients with diabetes (~95% of whom had T1DM) were seen at the clinic

during this period. We excluded patients younger than 9 years or older than 16 years of age, those diagnosed with diabetes for less than 1 year, with comorbidities that could interfere with their HRQOL (such as severe asthma or heart disease, blindness, and with genetic syndromes), with type 2 diabetes or with diabetes secondary to other diseases (cystic fibrosis or Fanconi anemia), illiterate, with cognitive disorders, or who refused to participate in the study. We selected by convenience 59 patients out of 79 who met the inclusion criteria.

We used the IQVJD to assess the HRQOL in our cohort. This adapted instrument maintained the three domains of the original Diabetes Quality of Life for Youth (DQOLY): satisfaction (17 items assessing patient's satisfaction with treatment and personal matters, such as family and friends), impact (22 items evaluating the impact of the diabetes on the patient's life), and worries (11 items assessing the patient's concerns with the diabetes and the future). The questions are presented on a Likert scale with five response options ranging from "very satisfied" to "very dissatisfied" in the satisfaction domain, and from "never" to "always" in the impact and concern domains. Scores are added to each domain, and the total scores are calculated by adding the scores in each domain, in which a lower score indicates a better HRQOL. It is worth noting that although this instrument has no cutoff values¹⁰, we adopted those values described in the study by Novato *et al.*¹⁰, which was performed in a similar geographical area as ours, characterizing as "worse" when the HRQOL was above the 75th percentile. The IQVJD is composed of 50 objective questions completed by the patient and an interview conducted by the researcher to gather sociodemographic data (gender, race, age, marital status, nationality, hometown location, who the patient lives with, and household income) and clinical data (age at diagnosis, disease duration, type of insulin administered, device used for insulin application, identification of the person in charge of the insulin administration, number of insulin applications per day, number of measurements of capillary glucose a day, associated diseases, occurrence of diabetic ketoacidosis [DKA] at diagnosis and during the course of the disease, number of hospital admissions during the treatment, physical activity, weight, height, body mass index [BMI, calculated with the formula weight/height²], pubertal stage according to the Tanner criteria, current glycosylated hemoglobin [HbA1c] level, and mean HbA1c level in the previous year). The same

researcher administered all questionnaires. Each patient completed the IQVJD individually in a room to prevent the caretaker from interfering with the answers. The researcher interviewed the caretakers and the patients to collect sociodemographic data.

For analysis purpose, we converted the weight, height, and BMI into z-scores using the software WHO AnthroPlus, version 10.4 ¹¹. Levels of HbA1c were measured by a turbidimetric method, and clinical data were collected from medical records.

For statistical analysis, we used the software Statistica (Statsoft®). To estimate the differences between continuous variables, we used the Student's *t* test, and for asymmetric variables, we used the Mann-Whitney test. The association between categorical variables was analyzed with Fisher's exact and Pearson's chi-square tests. A stepwise forward logistic regression model was applied to identify the key variables associated with HRQOL. We estimated the sample size considering a type I error fixed at 5%, type II error at 10%, and effect size of 30%, with a test power of 90%. We considered for all tests a significance level of 5% and a confidence interval of 95%.

TABLE 1 – PATIENTS' CHARACTERISTICS (N = 59).

Characteristics	n (%), mean, median
Gender	
Male	25 (42.4%)
Female	34 (57.6%)
Ethnicity	
White	43 (72.8%)
Mixed (Black/White)	16 (27.2%)
Origin	
Curitiba	24 (40.6%)
Metropolitan region of Curitiba	21 (35.6%)
Other regions in Paraná	14 (23.8%)
Level of education	
Elementary school	43 (72.8%)
Middle school	16 (27.2%)
Age	
Current	13.6 ± 1.5 years
At diagnosis	7.16 years (0.66 – 13.5)
Disease duration	6.5 years (1.3 – 14.5)
Clinical information	
Height z-scores	-0.35 (-2.12 – 2.04)
BMI z-scores	0.52 (-1.69 – 2.66)
Pubertal stage	
Pre-pubescent	08 (13.6%)
Pubescent	51 (86.4%)
Metabolic control	
HbA1c - latest assessment	10.2 ± 2.6%
HbA1c - average in the previous year	10.0 ± 1.6%

The Ethics and Research Committee at Hospital de Clínicas, UFPR, approved the study. All patients and their caretakers signed a free and informed consent form.

RESULTS

The study included 59 patients with an average age of 13.6 years, of which 34 (57.6%) were girls (Table 1). The median age at T1DM diagnosis was 7.16 years, and the median duration of the disease was 6.5 years. Most patients (66.1%) lived with both parents. The household *per capita* income was less than half of the minimum wage in 44.0% of the patients, between half and the minimum wage in 44.0%, and between one and two times the minimum wage in only 12.0% of the cohort. Overall, 37.0% of the parents had not completed the elementary education, and only 10.2% of the fathers and 8.5% of the mothers had a university degree. With regard to the degree of education of the patients, 43 were in elementary school, and 16 were in middle school. Twenty-four patients (40.7%) had experienced a school failure.

TABLE 2 - IQVJD RESULTS (N = 59).

Domain / Cutoff value for improved HRQOL	Mean ± SD
Satisfaction Improved HRQOL <41	34.9 ± 8.7
Impact Improved HRQOL <56	54.4 ± 10.6
Worries Improved HRQOL <28	25.3 ± 6.9
Overall sum of the domains Improved HRQOL <128	114.6 ± 22.0

IQVJD: Instrumento de Qualidade de Vida para Jovens com Diabetes; HRQOL: Health-related quality of life.

TABLE 3 - ASSOCIATION BETWEEN THE DOMAINS AND VARIABLES FOR IMPROVED QOL.

Domain	Variables associated with improved QOL	p
Satisfaction	Height z-score	0.02 (1)
	HbA1c	0.03 (2)
	Use of pen	0.04 (3)
	Practice of physical activity	0.01 (3)
Impact	Use of pen	0.04 (3)
	Practice of physical activity	0.04 (3)
	Lower number of hospital admissions	0.007 (3)
Worries	Height z-score	0.02 (1)
	HbA1c	0.03 (2)
	Hometown location (rural)	0.04 (3)

QOL: quality of life. (1) Mann-Whitney test; (2) Student's *t* test; (3) Fisher exact test.

In all, 54 patients performed some type of physical activity at an average of 3.2 times/week. DKA was present at the time of T1DM diagnosis in 63.0% of the patients and during the course of the disease in 29.0% of them. The mean number of hospital admissions in the course of the disease was 1.5 (range 0–6). The average HbA1c in the last assessment was 10.2% and the mean HbA1c in the previous year was 10.0%.

All patients were on a regimen of multiple insulin applications, ranging between 3 and 6 applications a day, with an average of 4.2. As for the type of insulin, 74.5% used a basal insulin analog (glargine) and a fast-acting insulin (lispro or aspart), 22.0% used an NPH and a regular insulin, and 3.5% used an NPH and a fast-acting insulin. To administer the insulin, 67.8% of the patients used insulin pens, 18.6% used syringes, and 13.6% used both pens and syringes. The persons in charge of administering the insulin were both the patient and caretaker in 45.7%, only the patient in 37.2%, only the caretaker in 11.8%, and another family member in 5.3% of the cases. The average number of capillary glucose measurements a day was 3.9 times, ranging from 2 to 10 measurements.

Chronic diabetes complications were absent in 93.0% of the participants, whereas 3.5% had nephropathy, and 3.5% had dyslipidemia. A total of 24.0% of the patients had Hashimoto's thyroiditis, 7.0% had celiac disease, and 5.0% had other diseases (rhinitis, congenital glaucoma, and psoriasis).

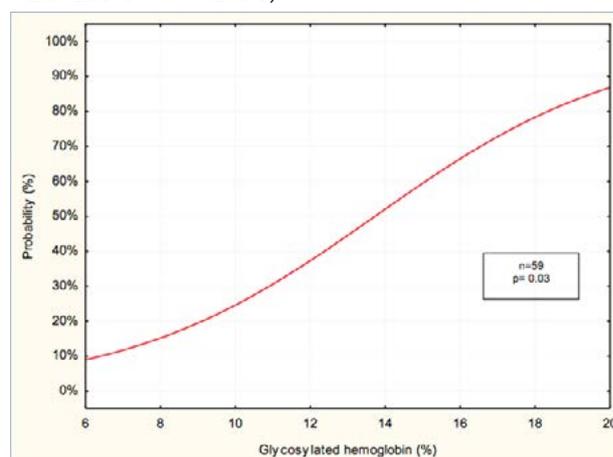
Table 2 presents the results of the IQVJD according to the different domains. The mean values in the overall cohort for the domains satisfaction, impact, worries, and overall sum of the scores were above the cutoff limit that characterizes the HRQOL as "better".

When we analyzed each domain separately considering the clinical and sociodemographic data, we observed that 43 patients scored above the cutoff limit in the satisfaction domain, whereas 16 patients scored below the limit in this domain. Compared with patients with lower scores, those with better scores showed higher height z-scores (-0.63 [range -1.56 to -0.06] versus -0.25 [range -2.12 to 2.04]; $p = 0.04$) and lower HbA1c levels (11.3% versus 9.7%, respectively; $p = 0.02$). On univariate logistic regression analysis, we observed that the higher the HbA1c, the higher was the likelihood of a worse score in the satisfaction domain ($p = 0.03$) (Figure 1). Patients who performed physical activity and used a pen to administer insulin were more likely to have a higher score in this domain ($p = 0.01$ and $p = 0.04$, respectively). The use

of a syringe and more than one hospital admission increased by 5 times and 4.4 times, respectively, the chance of a patient having worse scores in the satisfaction domain, whereas those without DKA on diagnosis had a 75.0% higher chance of having better scores in this domain.

In the satisfaction and impact domains, patients rated their own health answering the question "When compared with other adolescents of your age, would you say your health is". A total of 17% of the participants evaluated their lives as excellent, 49% as good, 24% as satisfactory, and 10% as poor. In 51% of the patients, the scores were below the cutoff limit in the impact domain. The use of insulin pen and practice of physical activity and a lower number of hospitalizations were indicative of a better score in the impact domain ($p = 0.04$, $p = 0.04$, and $p = 0.007$, respectively). The use of syringes increased by 7.5 times the chance of a worse score in the impact domain, while the presentation of DKA at diagnosis and after the diagnosis increased by 6 times and 15 times, respectively, the chance of a worse score in this domain. A total of 57.0% of the patients had a mean score above the cutoff level for better HRQOL in the worries domain. Compared with patients with worse HRQOL, those with better HRQOL presented higher height z-scores (-0.67 [range -0.92 to -0.41] versus -0.26 [range -0.4 to 0.24], respectively; $p = 0.02$) and lower HbA1c (10.6% versus 9.7%, respectively; $p = 0.03$), and lived in regions of Paraná other than Curitiba or its metropolitan region ($p = 0.04$) (Table 3). Other analyzed sociodemographic factors showed no association. In multivariate logistic regression in-

FIGURE 1 - RELATIONSHIP BETWEEN CURRENT HBA1C LEVEL AND WORSE SCORE IN THE SATISFACTION DOMAIN (UNIVARIATE LOGISTIC REGRESSION ANALYSIS).



cluding selected variables with significant p values, we found that no other variable was strongly associated with the quality of life domains, reflected by odds ratios close to 1 and unimpressive confidence intervals containing values of or close to 1.

DISCUSSION

Patients with T1DM included in this study showed an overall good HRQOL assessed with the IQVJD, a version of the DQOLY adapted to the Brazilian population. The mean scores in the satisfaction and worries domains were above the cutoff limit characterizing “better” HRQOL. In contrast, slightly more than half of the patients scored below the limit in the impact domain, reflecting a substantial impact of diabetes on these youths’ lives. Patients with a better HRQOL in this study were generally more likely to have higher height z-scores and lower HbA1c levels, a finding that corroborates the importance of the HRQOL as a determinant of health in diabetes.

Novato *et al.* applied the IQVJD to evaluate the HRQOL in a Brazilian cohort of 245 T1DM children and adolescents aged 10 to 19 years. The authors found average scores of 37.5 ± 9.8 in the satisfaction domain, 23.7 ± 7.9 in the concerns domain, and 110.3 ± 24.4 in the overall sum of the domains. These results are generally similar to those found in our study (Table 2), except in the impact domain in which the scores found by Novato *et al.*¹⁰ were lower (49.0 ± 11.3) than ours. This suggests that our cohort had a better HRQOL in the impact domain despite the fact that our study included patients of a lower social stratum. Since studies conducted in other countries use reduced versions of the DQOLY questionnaire, we were unable to compare our results with those of these studies.

Although most of the patients evaluated in our study belong to low-income households, all patients received the recommended treatment with multiple doses of insulin, conducted frequent self-monitoring, and had access to devices and insulin analogs when recommended. It would be valuable to compare our data with those of patients followed at a private setting in the same geographical area, but this was not possible. The frequency of patients with DKA at diagnosis was high, and the metabolic control was inadequate in most patients. The analysis of the HRQOL showed that 71% of the patients had scores compatible with better HRQOL, which was associated with a lower frequency of DKA at diagnosis and during the

course of the disease, better metabolic control, use of a pen to apply insulin, practice of physical activities, residence in rural areas of the state, and higher height z-scores.

The median age at T1DM diagnosis in our patients (7.16 years) was below that reported in the national^{12,13} and international¹⁴ literature (generally between the ages of 8 and 10 years). The prevalence of T1DM is currently higher in younger children, as evidenced in this study and in other Brazilian studies carried out in São Paulo (6.8 years) and Bahia (7.7 years)^{15,16}.

Overall, 80% of the patients reported a monthly household *per capita* income below the minimum wage. This information contrasts with the average family income in the state of Paraná, where only 44.7% of the families have incomes below the minimum wage. This may be explained by the fact that the study was carried out in a center that provides care exclusively for patients covered by the Brazilian Unified Health System (*Sistema Único de Saúde*, SUS)¹⁷. However, familial income was not associated with better or worse quality of life.

We found a high school failure rate when we compared our cohort with another with similar age range¹⁸, but the rate in our cohort was even higher than that reported by Alves *et al.*¹⁶ (25.8%) in patients with T1DM in northeast Brazil. There is growing evidence that children with T1DM have a higher risk of developing cognitive problems than children of similar age without diabetes. A history of an early T1DM diagnosis (below the age of 7 years), longer diabetes duration, recurrent hypoglycemia, and poor glycemic control are associated with cognitive impairment that adversely affects school performance and educational achievements^{19,20}. In addition, children with a history of severe hypoglycemia have reduced verbal and language functioning²¹. A recent study has shown that children with T1DM show slower growth of both white and gray matter when compared with controls without diabetes. This observation was associated with prolonged hyperglycemia and variability in blood glucose levels, but not with hypoglycemia²². Tolu-Kendir *et al.*²³ assessed the neurocognitive function of 60 T1DM patients between the ages of 6 and 12 years and 40 nondiabetic, age-matched controls. They applied specific questionnaires to assess several cognitive areas and observed that the group with T1DM had lower scores in tests evaluating information, arithmetic, and comprehension. The scores were even lower in children with earlier onset of the disease.

The frequency of patients with DKA at diagnosis was high in the present study (63%) but was similar to that reported in a study conducted in the southeast region of Brazil (66%)¹. Usher-Smith *et al.*²⁴ studied the frequency of DKA at diagnosis in 31 countries and observed a variation between 12.8% and 80.0%, with higher frequencies in the United Arab Emirates, Saudi Arabia, and Romania, and lower frequencies in Sweden, the Slovak Republic, and Canada. The frequency of DKA was inversely associated with the gross domestic product, latitude of the country, and incidence of T1DM. Other studies have also shown a great variability in the incidence of DKA in Europe and in the United States (15 to 70%) which is due in part to the different degrees of awareness of the disease and provision of health care^{24,25}. This reflects an urge in reducing the incidence of DKA. Vanelli *et al.*²⁶ showed that this is possible to achieve with an informative program. The authors implemented a program that presented signs and symptoms of childhood diabetes to children in public and private schools in Parma (Italy). The program successfully reduced the incidence of DKA at diagnosis from 78% (1987-1991, a period prior to the study) to 12.5% (1991-1997, the study period).

The average level of HbA1c in the patients evaluated in our study was above that recommended by both the ADA²⁷ and the ISPAD²⁸. Brazilian studies¹⁰ with patients of similar age groups showed similar HbA1c values (around 10%), while a multicenter study with children and adults with T1DM in several Brazilian areas showed a mean HbA1c of 9.4%, with only 12.2% of the patients achieving the goal of metabolic control²⁹. A Norwegian study showed that only 30% of the adolescents with T1DM had achieved the HbA1c goal, showing that the challenge in controlling blood glucose levels, particularly in adolescents, is common in different countries³⁰.

The frequency of each insulin regimen in our study differed from that in the study by Gomes *et al.*²⁹ in which 47% of the diabetics used NPH plus regular insulin and 22% used basal analog plus fast-acting in-

sulin. The frequency was also different from that in a study carried out in Salvador¹⁶, in which 91.5% of the patients used NPH insulin and 89.4% used regular insulin. This difference may be due to the fact that the state of Paraná is one of the few states in Brazil with a program in which the government (SUS) has been offering insulin analog to eligible patients since 2006³¹.

The method of insulin application in our study differed from that described in a study by Alves *et al.*¹⁶, in which 78.9% of the patients applied insulin using only syringe, 11.3% used only pen, and 9.9% used pen and syringe.

The average frequency of capillary glucose tests performed by our patients was within that recommended by the ADA of at least four measurements a day²⁷ and superior to that reported in the study conducted in Salvador, which was 2.1 times/day¹⁶.

The prevalence of diseases associated with T1DM in our study was similar to rates found in the literature. Kordonouri *et al.*³² reported a prevalence of Hashimoto thyroiditis between 3 and 8% and celiac disease between 1 and 10% in a population with T1DM, while Whitacker *et al.*³³ found in the southeastern region of Brazil a prevalence of celiac disease of 4% in children with T1DM. The prevalence of complications was low in our population. This is probably due to the short duration of diabetes in our patients (median 6.5 years) in contrast to the disease stage in which the complications of the disease usually develop (15 to 20 years)¹⁹.

CONCLUSION

The findings of our study corroborate the importance of assessing the HRQOL in children and adolescents with T1DM, supporting efforts to improve the care of the disease by approaching the patient and his health in more comprehensive ways, rather than from a medical perspective only. Similar studies should be conducted in patients with diabetes with higher socioeconomic levels in Brazil to assess the impact of HRQOL on disease control and care.

RESUMO

A qualidade de vida relacionada à saúde (HRQOL) no diabetes mellitus tipo 1 (T1DM) tem sido amplamente estudada. Os objetivos deste estudo foram avaliar e identificar os fatores que influenciam a HRQOL de crianças e adolescentes com T1DM.

MATERIAL E MÉTODOS: No total, 59 pacientes (9-16 anos, T1DM por ≥ 1 ano) responderam a uma versão do Instrumento de Qualidade de Vida para Jovens com Diabetes (DQOLY) adaptada aos pacientes brasileiros (IQVJD). Esse instrumento compreende satisfação, impacto e preocupações de domínios, com os menores índices correspondentes a uma melhor HRQOL, e um questionário que reúne parâmetros sociais, demográficos e clínicos.

RESULTADOS: A idade média foi de 13,6 anos e 57,6% eram meninas. A idade mediana no diagnóstico foi de 7,16 anos, 63% apresentaram cetoacidose diabética (DKA) no diagnóstico e 29% durante o seguimento. A hemoglobina glicada média (HbA1c) no ano ante-

rior foi de 10%. Todos os pacientes receberam doses múltiplas de insulina (média de 4,2 aplicações/ dia), 74,5% utilizavam análogos de insulina de ação rápida e de ação intermediária e 67,8% usavam canetas para aplicação de insulina. Os resultados do DQOLY estavam dentro do limite de corte para melhor HRQOL. Uma análise isolada de cada domínio e os resultados do questionário mostraram que os seguintes fatores estavam associados a uma maior HRQOL: score z de altura, HbA1c menor, prática de atividade física, uso de caneta, menos hospitalizações e residência em uma área rural. Houve uma alta taxa de cetoacidose diabética no diagnóstico, e o controle metabólico foi inadequado na maioria dos pacientes. Apesar de serem provenientes de famílias de baixa renda, a maioria dos pacientes teve acesso ao tratamento recomendado.

CONCLUSÃO: Entre pacientes com T1DM, 71% tinham escores IQVJD compatíveis com melhor HRQOL.

PALAVRAS-CHAVE: Qualidade de vida. Criança. Adolescente. Diabetes mellitus tipo 1.

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