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Generic and disease-specific quality of life in adolescents with type 1 diabetes: comparison to age-matched healthy peers

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Abstract

Background: This study aimed to evaluate the health-related quality of life (HRQoL) of adolescents with type 1 diabetes (T1DM) on the basis of the pediatric quality of life inventory™ (PedsQL™) generic and diabetes-specific modules, and to compare it to that of healthy peers.
Methods: This retrospective case-control study involved 650 participants between ages of 13 and 19 years including 296 adolescents with T1DM from four diabetes centers and 354 healthy peers matched for age and gender from three different cities of the country. Participants completed the validated PedsQL™ for assessing the HRQoL. The analysis included an independent t-test to compare the means of the total and subscales of the PedsQL™ between boys and girls as well as between a healthy group and a group with T1DM. Gender differences in exercise, insulin therapy modalities were evaluated with the Pearson χ^2-test.
Results: Adolescents with T1DM have similar HRQoL in all domains when compared to their healthy counterparts. Females report worse HRQoL regardless of the presence of the disease. Insulin pump therapy facilitates better glycemic control and HRQoL. Regular exercise positively correlates with the generic HRQoL in both groups; however, it has no relationship with glycemic control.
Conclusions: Optimal metabolic control and improved HRQoL are the eventual goals of diabetes management. Despite the difficulties, adolescents with diabetes can manage their disease well and live normal lives, similar to their healthy peers. Although diabetes-related problems exist, it seems that regular exercise and staying physically active, as well as promoting insulin pump therapy where it is applicable are related to favorable HRQoL.

Keywords: adolescents; health-related quality of life; regular exercise; type 1 diabetes.

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Introduction

Type 1 diabetes mellitus (T1DM) is a leading chronic disease in the pediatric population and its incidence is continuously rising worldwide [1, 2]. As there is no recovery from the disease, overall health-related quality of life (HRQoL) is a concern amongst health care experts. The perceived self-assessed health status is considered to be a predictor of mortality and morbidity [3, 4]. Adolescent patients with T1DM are challenged to cope with diverse short- and long-term complications of the disease. They seem to display worse metabolic control compared to other diabetic age groups [5, 6] as well as problems in psychosocial wellbeing [7]. Metabolic control reflects the physiological results of diabetes management whereas the HRQoL outcomes represent the psychological perspective of the treatment and care. Nowadays, the ultimate goals of the diabetes management do not focus only on achieving and maintaining optimal metabolic control which contributes to prevent long-term consequences such as retinopathy, nephropathy and neuropathy but they also put an emphasis on promoting improved HRQoL among patients with T1DM [8, 9]. There are a few studies examining the HRQoL of adolescents with T1DM [10, 11], however, different results were demonstrated in surveys in relation to the healthy population. Some studies showed similar HRQoL to that of the normative samples [12, 13], others observed worse HRQoL in youths with diabetes [14, 15]. Therefore, this study primarily focuses on general HRQoL of patients with T1DM that allows comparison to the healthy population. However, disease-specific tools are more sensitive to symptoms experienced by patients as well as to the implications of

different treatments. For understanding what influence the disease has on the patients' HRQoL, the diabetes-specific questionnaire should be applied [16]. It seems that regardless of the type of questionnaire (generic or disease-specific) females tend to report more impaired HRQoL than males [10, 17, 18]. Therefore, we evaluated the HRQoL of our participants separately by gender.

The results of the diabetes control and complications trial (DCCT) showed the benefits of intensive insulin therapy for achieving tight blood glucose control and reducing the risk of micro- and macro-vascular complications, but found no differences on patients' HRQoL between intensive and conventional diabetes treatment [19]. Due to technical improvements of insulin pumps in the last decades, there is some evidence that the insulin pump therapy [continuous subcutaneous insulin infusion (CSII)] has positive effect on patients' HRQoL and may be better than multiple daily injections (MDI) for glycemic control [20, 21].

It is well known that regular exercise has physiological and psychological benefits for all age groups, but for youths with T1DM, it is an integrated part of the diabetes management [22]. Patients with T1DM are at increased risk for development of cardiovascular diseases and regular exercise plays an important role in prevention [23]. Moreover, its benefits include decreasing insulin requirements, improving glucose control, lowering hypertension, improving fitness and overall wellbeing [24].

The primary objective of this study was to evaluate the general HRQoL of adolescents with T1DM, and we compared responses to the healthy peers of the similar age separately by gender. We also aimed to examine whether the glycemic control, regular exercise and insulin therapy modalities were in relation to the diabetes-specific HRQoL in our participants.

Materials and methods

Adolescent participants and procedure

This retrospective case-control study involved 650 participants between the ages of 13 and 19 years including 296 adolescents with T1DM and 354 healthy peers matched for age and gender. Both groups completed a generic HRQoL questionnaire that had an average time of 10 min. In addition, patients with T1DM completed a disease-specific questionnaire which took about 10 more minutes to complete. Parents were informed in written form about the purpose, method and voluntary nature of the study and written consent from parents and assent from adolescents were obtained before the study procedure. The management of the schools were contacted by telephone to confirm their willingness and obtain their permission to participate in this research study. Healthy participants filled in the questionnaire in a classroom setting where they studied with the help of the headmaster whereas the patients with T1DM filled it in the waiting room at the regularly scheduled appointment with the help of the health assistant. The teachers and assistants received instructions on the appropriate application of the instrument.

The study was approved by the Regional Scientific and Research Ethics Committee and in conjunction with the Helsinki Declaration on human research.

Patients with type 1 diabetes

Patients with T1DM were recruited from four pediatric diabetes centers located in different parts of the country. Patients were included if they were diagnosed with T1DM for at least 1 year, were 13–19 years old, and visited the outpatient cares during the study measurement (between October 2014 and February 2015). We had a total of 296 patients including 163 males and 133 females with an average year of 15.54 (±1.84). The average duration of diabetes was 7.12 (±3.94), the average glycemic control [expressed by hemoglobin A_{1c} (HbA_{1c})] was 8.26% (±1.37)/66.8 mmol/mol (±11.08). All participants were receiving intensive insulin treatment of three to four injections per day or insulin pump therapy and had no evidence of diabetic complications by regular assessments for retinopathy (fundal photography), nephropathy (microalbuminuria), and neuropathy (nerve conduction velocity and cardiovascular reflex tests). All the approached families agreed to take part in the study, however, we achieved 83% of the available adolescent population, because some of the adolescents failed to appear for routine care during the study period.

Demographic and clinical characteristics of the participants are displayed in Table 1.

Table 1: Demographic and clinical characteristics of adolescents with type 1 diabetes by gender (n=296).

Mean (SD)	Males	Females	Range
Sample size	163	133	
Age, year	15.59 (1.88)	15.48 (1.79)	13–19
Disease duration, year	6.98 (4.02)	7.31 (3.85)	1–16
HbA_{1c}, %	8.18 (1.49)	8.37 (1.22)	5.30–14.00
HbA_{1c}, mmol/mol	65.9 (12.00)	68.0 (9.91)	34.4–129.5
Insulin pump therapy, %	48.8	51.2	
Engaged with regular exercise, %	56.1	50.8	
Socioeconomic status, %			
Low:middle:high	9:79:12	10:81:9	

There were no significant differences in the parameters between males and females. There was no significant difference between patients treated with insulin pump therapy to those on multiple daily injections in regular exercise. Socioeconomic status is classified as living in a low, middle or high income family.

Healthy controls

Adolescents in the control group were randomly selected from three different cities and schools of the country. We assessed all the students who attended the chosen classes, were aged 13–19; had no other chronic or acute disease; and were present in the class at the time when the assessment was carried out. Students completed the questionnaire if the informed consent was returned. There were 23 unsigned forms returned, 28 had other chronic or acute disease, and 32 students were absent at the study protocol. Characteristics of the control group are presented in Table 2.

Health-related quality of life measurements

Generic health-related quality of life: The pediatric quality of life inventory (PedsQL™) is a modular instrument for evaluating HRQoL in the pediatric population from age range of 2 to 18 [25, 26]. The generic core scales (GCS) distinguish between healthy children and children affected by acute or chronic diseases. This questionnaire includes 23 items which is distributed into four subscales: physical functioning (eight items), emotional functioning (five items), social functioning (five items) and school functioning (five items). The participants rated their HRQoL on a 5-point Likert-type response scale (0=never a problem, 1=almost never a problem, 2=sometimes a problem, 3=often a problem, 4=almost always a problem). Items were reverse scored and linearly transformed to a scale ranged from 0 to 100. The normal range of total and subscale scores is not available in the literature. Generally, higher scores indicate better HRQoL. In this study, the item – total internal consistency reliability (Cronbach's α) was good both in the healthy group (α=0.851) and the group with diabetes (α=0.895) [27]. The GCS has been previously validated by Berkes et al. in the Hungarian population [28].

Health-related quality of life of adolescents with T1DM: Disease-specific HRQoL was measured by using the multidimensional PedsQL™ 3.0 Diabetes Module [29]. This module encompasses five subscales: diabetes symptoms (Ds) (11 items), treatment barriers (Tb) (four items), treatment adherence (Ta) (seven items), Worry (W) (three items) and Communication (C) (three items). The scoring method is the same as applied in the GCS. Based on the research of Nansel et al. [30] we used the total score of the diabetes module for evaluating the disease-specific global HRQoL. The PedsQL 3.0 Diabetes Module has previously been validated for Hungarian usage [31].

Table 2: Characteristics of healthy controls by gender (n=354).

Mean (SD)	Males	Females	Range
Sample size	169	185	
Age, year	15.50 (1.62)	15.51 (1.61)	13–19
Engaged with regular exercise, %	71.0[a]	45.9	
Socioeconomic status, %			
Low:middle:high	12:75:13	13:77:10	

[a]significant gender difference is found in exercise (χ^2=22.692; p<0.001). Socioeconomic status is classified as living in low, middle or high income families.

In this study, we found a Chronbach α=0.883 item – total internal consistency reliability.

Exercise

Adolescents were classified into regular exercising and non-regular exercising groups. Youths doing moderate exercise at least 3 times a week for 1 h beyond the normal Physical Education classes, were considered regular exercising individuals, all the others belonged to the non-exercising group. Regular exercise was identified with an additional question. "Have you been exercising regularly at least for 60 min long 3 times a week beyond the normal Physical Education classes during the last month?" The possible answers were: yes/no, or not regular.

Glycemic control

Glycemic control was assessed by glycated hemoglobin (HbA_{1c}) values that were measured from the venous blood the day of the study protocol except in some cases, when the latest values were extracted from the medical records. Both the DCCT and International Federation of Clinical Chemistry (IFCC) units were marked. The HbA_{1c} test is the most accepted measure of glycemic control and diagnostic test for diabetes [32].

Socioeconomic status

Socioeconomic status (SES) was identified by the parents according to the latest data of the Hungarian Central Statistical Office. There were three categories to choose from: low, middle and high income. This information was obtained together with the written consent.

Statistical analysis

Data analysis was performed with SPSS 22.0 statistical software (IBM Corp, Armonk, NY, USA). Descriptive statistics were presented as mean, standard deviation (±), minimum and maximum for continuous variables, and percentage for discrete variables. The analysis included the Mann-Whitney U-test to compare the means of the total and subscales of the PedsQL between boys and girls as well as between healthy group and the group with T1DM. Gender differences in exercise, insulin therapy modalities were evaluated with the Pearson χ^2-test. Correlation between indicator variables (gender and method of intensive therapy) with the HRQoL was analyzed with the F-test. Cronbach α was used to estimate the reliability of the GCS and Diabetes Module in this study. Multiple regression analysis with backward elimination was used to find predictors of HRQoL. Significance level was set at p-values $\leq$0.05.

Results

Our investigated groups were matched in age, gender and SES. Adolescent boys and girls with T1DM reported similar

Table 3: Health-related quality of life between groups and genders using the PedsQL™ Generic Core Scales (n=650).

Mean (SD)	Males (n=332)		Females (n=318)	
Scores	D (n=163)	C (n=169)	D (n=133)	C (n=185)
PedsQL GCS	79.74 (11.16)[b]	79.51 (10.41)[d]	75.71 (12.96)	74.07 (10.37)
Physical	83.65 (11.43)[c]	83.90 (12.55)[d]	77.33 (14.16)	76.69 (12.07)
Emotional	72.04 (15.88)[b]	70.35 (16.21)[d]	65.76 (17.16)[a]	60.72 (16.59)
Social	88.02 (14.43)	89.01 (12.72)	88.91 (14.22)	88.37 (12.41)
School	72.92 (15.63)	72.19 (14.91)[b]	69.93 (18.16)	68.91 (15.57)

D, adolescents with diabetes; C, healthy controls; GCS, generic core scales. [a]p<0.05 (between healthy girls and girls with T1DM). [b]p<0.05; [c]p<0.01; [d]p<0.001 (between healthy boys and girls as well as of diabetes).

HRQoL to the healthy controls. The only significant difference was observed in emotional functioning, girls with T1DM had higher scores than healthy girls. When analyzing generic HRQoL by gender and groups, significant differences were observed in global score and in most of the subscales with boys presenting better HRQoL (Table 3).

Regarding the diabetes-specific HRQoL, we also found gender differences in the PedsQL Diabetes Module global scores and most of the subscales scores (Table 4).

The treatment modalities correlated with the diabetes-specific HRQoL (F=12,873; p<0.001) and the glycemic control (F=8019; p<0.01). Patients treated with insulin pump therapy had better HbA_{1c} values (8.04±1.10) and more favorable HRQoL (74.80±11.15) than those who were on MDI (8.50±1.59; p=0.005) (69.93±12.03; p<0.001). Regular exercise positively correlated with the Ds (F=5312; p<0.05), however, it had no relationship with the glycemic control. When we examined the generic HRQoL regarding regular exercise, a strong association was found with the global HRQoL scores [Control group (C): F=11,978; p=0.001; Group with T1DM (D): F=5065; p<0.05], specifically the strongest association was observed with the physical functioning subscale score in both investigated groups (C: F=12,688; p<0.001; D: F=14,564; p<0.001). A significant difference was found in regular exercise between the healthy boys and boys with T1DM ($\chi^2_{(1)}$=7756; p=0.006), but it was not observed in the case of girls. Boys with T1DM were less engaged in regular exercise than their healthy peers.

In the multiple regression model, the only significant predictor of the generic HRQoL was exercise (t=–2.223; p=0.028). When diabetes-specific HRQoL was added as a dependent variable, gender (t=–2.229; p=0.027) and intensive insulin treatment modality (t=–3.268; p=0.001) were significant predictors. The Ds subscale was predicted by exercise (t=2.010; p=0.045) and intensive insulin therapy modality (t=2.492; p=0.013).

Discussion

The primary aim of this study was to compare the generic HRQoL of adolescents with T1DM with a healthy age- and gender-matched control group from the same homogenous pediatric population. We consider important to use the same cohort and mutatis mutandis, apply the same self-report questionnaire for the comparison of HRQoL. In our study, there was no difference in HRQoL between the

Table 4: Diabetes-specific health-related quality of life between boys and girls with type 1 diabetes using PedsQL™ Diabetes Module (n=269).

Mean (SD)	Adolescents with T1DM (n=296)	Males (n=163)	Females (n=133)
Scores			
PedsQL total score	72.40 (11.81)	74.11 (10.47)[a]	70.26 (13.04)
PedsQL subscales			
Diabetes symptoms	63.49 (13.48)	64.43 (12.30)	62.32 (14.76)
Treatment barriers	71.65 (21.70)	74.88 (19.51)[a]	67.64 (23.62)
Treatment adherence	82.73 (15.27)	84.10 (13.49)	81.03 (17.14)
Worry	69.88 (21.63)	73.87 (20.27)[b]	64.92 (22.32)
Communication	81.38 (21.42)	85.28 (17.58)[b]	70.26 (13.04)

[a]p<0.05; [b]p<0.01.

healthy group and the group with T1DM. This result confirms the findings by Hesketh et al. and Upton et al. [33, 34]. Our results suggest that diabetes management, which includes regular blood glucose monitoring, diet, keeping track of carbohydrates, giving multiple daily insulin shots or managing the procedures of the insulin pump does not disturb the youths' vigor and vitality. Even the girls with T1DM reported more stable emotional functioning when compared to the healthy counterparts. Wagner et al. also experienced better psychological wellbeing in adolescents compared to the healthy peers [35]. Perhaps these youths, who have undergone several procedures from the diagnosis of the disease, are more sensitive to issues of positive thinking and treating with other people with respect [36]. Females are especially characterized by this empathy. Consistent with previous studies [18, 37] girls had a lower HRQoL perception than boys not only in the population with diabetes but also in the healthy group [38, 39]. It is recommended to take this gender difference into consideration in HRQoL measurements.

In the last two decades, insulin pump therapy has become popular among children and adolescents. It is well known that they should be treated with intensive insulin therapy to achieve optimal glycemic control, either with CSII or MDI [40]. In our sample, half the patients were treated with CSII and the other half were on MDI. We found that CSII patients had significantly better HRQoL and glycemic control, as assessed by HbA_{1c}. This fact also needs consideration in the future surveys. Such a correlation has been revealed with other diabetes-specific HRQoL measures [21, 41] but this association is not seen with generic measures. There is an issue about the association between HRQoL and glycemic control. Similar to other studies [42–44], we found no significant relationship between generic or disease-specific HRQoL and glycemic control. Due to hormonal and other pubertal changes, metabolic control may fluctuate even in the case of previously well-established therapy. Although regular exercise presents challenges in diabetes management, its health, mental and social benefits are indisputable. As it is stated in the Position Statement of the American Diabetes Association, being engaged in regular exercise, being physically active improves the individual's well-being [23]. In our study, both the adolescents with diabetes and healthy controls demonstrated better generic HRQoL compared to those who were physically less active. Interestingly, the boys with diabetes were remarkably inactive in comparison to the healthy peers. Fear of hypoglycemia may discourage youths from engaging in appropriate regular exercise [45]. The reason why we did not experience the same difference in the case of girls is that the adherence to doing regular exercise decreased in the group of healthy girls in adolescence as well [46]. We found that regular exercise is an evincible factor that explains the favorable generic HRQoL in group with diabetes. It seems that regular exercise is associated with less problematic Ds such as shaking, being sweaty, irritable, feeling tired or fatigued, having stomach- or headaches, as well as experiencing low blood glucose levels, which impairs the HRQoL of youths with diabetes.

Conclusions

Optimal metabolic control and improved HRQoL are the eventual goals of diabetes treatment and care. It seems remarkable that despite the difficulties caused by the disease, adolescent patients with T1DM can manage their diabetes well and live normal lives, similar to their healthy peers. Although diabetes-related problems exist, it seems that regular exercise and staying physically active, as well as promoting insulin pump therapy where it is applicable are related to favorable HRQoL.

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