Sleep Medicine 109 (2023) 132–142

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Associations between sleep characteristics and glycemic variability in youth with type 1 diabetes

Necla İpar [a, b, **], Perran Boran [a, c, *], Hatice Ezgi Barış [a, c], Mahmut Caner Us [a], Burcu Aygün [a], Belma Haliloğlu [d], Tuğba Gökçe [e], Ecem Can [e], Elif Eviz [e], Neslihan Gökmen İnan [f], Gül Yeşiltepe Mutlu [e], Abdullah Bereket [d], Şükrü Hatun [e]

[a] Institute of Health Sciences, Social Pediatrics PhD Program, Marmara University, Istanbul, Turkey
[b] Department of Pediatrics, Koc University School of Medicine, Istanbul, Turkey
[c] Department of Pediatrics, Division of Social Pediatrics, Marmara University School of Medicine, Istanbul, Turkey
[d] Department of Pediatrics, Division of Pediatric Endocrinology, Marmara University School of Medicine, Istanbul, Turkey
[e] Department of Pediatrics, Division of Pediatric Endocrinology, Koç University School of Medicine, Istanbul, Turkey
[f] College of Engineering, Department of Computer Engineering, Koc University, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 19 April 2023
Received in revised form
15 June 2023
Accepted 18 June 2023
Available online 27 June 2023

Keywords:
Type 1 diabetes
Sleep
Actigraphy
Chronotype
Continuous glucose monitoring
Youth

ABSTRACT

Objective: This study aimed to determine sleep characteristics and their associations with glycemic variability in youth with type 1 diabetes (T1D).
Material and methods: This cross-sectional study conducted at two pediatric diabetes centers in Istanbul, Turkey, included 84 children with T1D (mean age 10.5 years). Sleep characteristics and glycemic variability were determined by actigraphy, DSM-5 Level 2-Sleep Disturbance Scale Short Form and continuous glucose monitoring. Circadian preference was evaluated by the Children's Chronotype Questionnaire. Sleep disturbances were assessed by the. The sleep quality was determined by actigraphy-derived sleep measures.
Results: Eighty-eight percent of participants had insufficient age-appropriate total sleep time (TST) (<9 h for 6–13-year-olds and <8 h for 14–17-year-olds). Chronotype was classified as intermediate in 50%, evening in 45.2%, and morning in 4.8%. A higher chronotype score indicating a stronger eveningness preference was associated with more time spent in hypoglycemia ($\beta = 0.433$, $p = 0.002$). On nights when participants had lower sleep efficiency and longer sleep onset latency, they had significantly higher overnight glycemic variability ($\beta = -0.343$, $p = 0.016$, $\beta = 0.129$, $p = 0.017$, respectively). Prolonged nocturnal wake duration was significantly associated with more time spent in daytime hypoglycemia ($\beta = 0.037$, $p = 0.046$) and higher overnight glycemic variability (J index, $\beta = 0.300$, $p = 0.015$). The associations between TST and glycemic variability indices were not significant.
Conclusions: Sleep quality rather than TST was significantly associated with glycemic variability in children with T1D. Eveningness preference might contribute to an increased risk of hypoglycemia. Addressing sleep patterns and chronotypes can be crucial in management plans for youth with T1D.

Abbreviations: ADA, American Diabetes Association; BMI, Body Mass Index; CGM, Continuous Glucose Monitoring; CV, Coefficient of variation; HbA1c, Glycated Hemoglobin A1c; HBGI, High Blood Glucose Index; LBGI, Low Blood Glucose Index; TST, Total Sleep Time; T1D, Type 1 Diabetes; T2D, Type 2 Diabetes; SOL, Sleep Onset Latency; WASO, Wake After Sleep Onset.

* Corresponding author. Marmara University, School of Medicine, Başıbüyük Mah, Maltepe. Başıbüyük Yolu sok No: 9/1. Istanbul, Turkey,
** Corresponding author. Koç Üniversitesi Hastanesi, Çocuk Sağlığı ve Hastalıkları Kliniği, Davutpaşa Cd. No:4, 34010 Zeytinburnu, Istanbul, Turkey.
E-mail addresses: nipar@kuh.ku.edu.tr (N. İpar), perran.boran@marmara.edu.tr (P. Boran), ezgi_aksu@yahoo.com (H.E. Barış), mcanerus@gmail.com (M.C. Us), burcudir@hotmail.com (B. Aygün), bh566@medschl.cam.ac.uk (B. Haliloğlu), tgokce@kuh.ku.edu.tr (T. Gökçe), eccan@kuh.ku.edu.tr (E. Can), EVIZ@ku.edu.tr (E. Eviz), NINAN@ku.edu.tr (N.G. İnan), gmutlu@kuh.ku.edu.tr (G.Y. Mutlu), abdullahbereket@gmail.com (A. Bereket), sukruhatun@gmail.com (Ş. Hatun).

https://doi.org/10.1016/j.sleep.2023.06.018
1389-9457/

1. Introduction

Type 1 Diabetes Mellitus (T1D) is one of the most common chronic diseases in childhood [1]. Its prevalence was reported as 7.5% in Turkey [2]. Recent studies have addressed a close relationship between type 1 diabetes and sleep problems [3–6]. Studies found that 87.5% of children with T1D had short total sleep time (TST) [7], as much as 26 min as compared with controls [4]. Short TST has been shown to contribute to insulin resistance and impaired glucose metabolism, both of which are closely associated with suboptimal blood glucose levels [4,8]. Adequate TST, on the other hand, is associated with better self-management of diabetes [9].

Sleep health is a multi-dimensional construct including different domains other than adequate duration, such as subjective satisfaction, appropriate timing, high efficiency and alertness during waking hours [10]. While adequate sleep and good sleep quality are essential for youth without chronic conditions, they are much more important in youth with diabetes because poor sleep health may negatively affect diabetes self-care behaviors and glycemic outcomes [6,11]. Nocturnal glycemic variability, use of devices such as pumps, continuous glucose monitoring alarms in diabetes treatment, and associated conditions such as anxiety, stress, and depressive symptoms are likely to play a role in the poor sleep health of people with diabetes [3,12,13]. In 2017, the American Diabetes Association (ADA) emphasized that sleep assessment should be incorporated into the routine medical evaluation of patients with diabetes [14].

Chronotypes indicate the behavioral manifestations of the circadian system that governs preferred timing of sleep and wake, and are classified as morning, intermediate, and evening types [15]. There has been an increasing trend in the pediatric literature to draw attention to chronotypes in the context of sleep health, particularly disorders of initiating and maintaining sleep, non-restorative sleep, and excessive somnolence, associated with eveningness [15]. Although the literature is abundant on T2DM and adult patients with T1DM, limited studies explored chronotypes and glycemic control in children and adolescents with T1DM [16,17]. Social changes such as reduced parental control on bedtimes, irregular sleep-wake schedules, increased social networks, increased use of electronics, and caffeine, increased academic demands, biologically delayed circadian timing of dim light melatonin onset resulting in later sleep onset times, and slower build-up of homeostatic sleep pressure triggered with the onset of puberty often interact in adolescents posing challenges to several sleep health dimensions resulting in short TST, late timing, and reduced regularity of sleep [18,19].

Studies on sleep health in youth with T1DM are limited, with insufficient sample size and inconsistent findings [1,3,5,6,16,20–22]. Furthermore, studies have relied primarily on inter-person differences, failing to capture within-person fluctuations. It is essential to understand how changes in sleep quality covary with daily fluctuations in glycemic measures. Thus, the current study was conducted to determine sleep characteristics, chronotypes, and glycemic variability of youth with T1DM between individuals and examine the within-person fluctuations in glycemic variables and prior night's sleep quality.

2. Materials and methods

This prospective study was conducted at two outpatient clinic settings from university hospitals in Istanbul between December 2020 and 2021. The study was conducted following the principles in the Declaration of Helsinki on experimentation involving human subjects; the study protocol was approved by the Marmara University ethics review board (protocol ID; 09.2020.299) and registered at Clinical Trails.gov (NCT04978662-Registration Date: July 27, 2021).

2.1. Participants

Children and families were informed about the study during routine outpatient visits, and those who accepted to participate were included in the study. Informed written consent was obtained from the parents of all participants.

The eligibility criteria for the study included children between 6 and 18 years of age with a diagnosis of type 1 diabetes for at least six months, current use of continuous glucose monitoring (CGM), and current use of multiple insulin injections daily.

Exclusion criteria included intensive care unit admission within the past month, any previous diagnoses of neurological, genetic, or psychiatric diseases, obstructive sleep apnea syndrome, and the use of an insulin infusion pump.

The study enrolled 123 eligible children, 6–18 years of age, with a diagnosis of type 1 diabetes. Thirty-eight declined to participate, and one child was excluded from the study because he denied wearing an Actigraphy at home. Analyses were made based on the data from 84 children. The study flow chart is shown in Fig. 1.

2.2. Procedures

All participants were invited to the pediatric outpatient clinic and had clinical examinations to determine their developmental stages according to the Tanner classification and anthropometric measurements. Clinical and laboratory findings of the participants, including the duration of diabetes and the most recent HbA1c levels, were retrieved from the electronic hospital records.

All parents or youth were asked to complete three questionnaires, including a sociodemographic form developed by the authors, the DSM-5 Level 2-Sleep Disturbance Scale short form, and the Childhood Chronotype Questionnaire. The child form of the DSM-5 Level 2 Sleep Disturbance Scale short form and the Childhood Chronotype Questionnaire were completed by the parent and the adolescent form was completed by the adolescent.

Children were asked to wear an actigraphy device for at least 3 days and to fill out sleep diaries. Before device delivery to the participants, both devices (actigraphy and CGM) were synchronized by the investigators (Nİ, EB, BD).

All the participants completed the questionnaires. In two children, CGM data were not available due to recording failures.

2.3. Sleep questionnaire

The short form of DSM-5 Level 2-Sleep Disturbance Scale was used to evaluate sleep disturbances. It is an 8-item scale that assesses self-reported perceptions of restlessness and any perceived difficulties related to falling and staying asleep in children and adolescents within the past 7 days. Each item is rated on a 5-point scale (1 = never; 2 = rarely; 3 = sometimes; 4 = often, and 5 = always). The total score ranges from 8 to 40 points, with higher scores indicating more severe sleep disturbances.

Its validity and reliability in Turkish children were shown by Erkuran et al. [23]. The child form of the DSM-5 Level 2 Sleep Disturbance Scale short form was completed by the parent, and the adolescent form was completed by the adolescent.

2.4. The Childhood Chronotype Questionnaire

The Childhood Chronotype Questionnaire was used to evaluate the chronotype in children. This 27-item questionnaire was

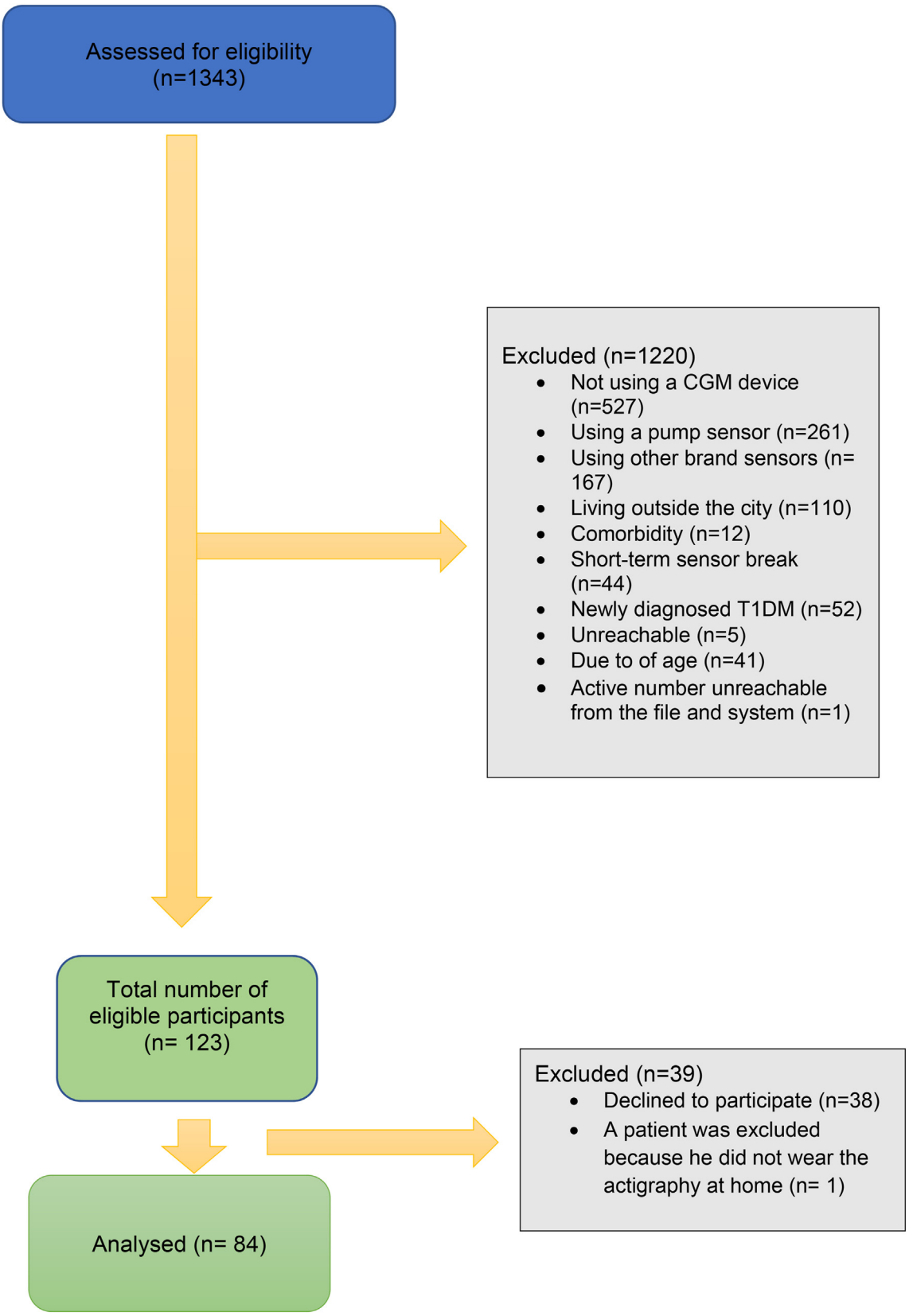

Fig. 1. Flowchart.

developed for Turkish children in the light of the Munich Chronotype Questionnaire [24] and the Mornings-Evenings Questionnaire [25]. Its validity and reliability studies for Turkish children were conducted by Dursun et al. [26]. The chronotypes were classified as morning, intermediate and evening types, with corresponding scores of ≤23, 24–32 and ≥ 33 [26,27]. The child form of the Childhood Chronotype Questionnaire was completed by the parent and the adolescent form was completed by the adolescent.

2.5. Objective sleep measurements with actigraphy

Actigraphy is an objective and non-invasive method that evaluates sleep-wake patterns at 30-s epochs with activity-based recordings [28,29]. Sleep variables were recorded and processed using 6.1.0 Actigraphy (Actiwatch-2, Philips Resipronics®, USA) software. The actigraphy and the CGM device were simultaneously worn to examine usual sleep and daily routines for at least 3 days. The actigraphy was worn on the non-dominant wrists and was removed only during bathing. Due to the disruption of school and normal life routines adopted during lockdowns, weekend parameters were not obtained to analyze weekday and weekend differences in the current study. At the end of recordings, each actigraphy was returned to the pediatric outpatient clinic, and data were downloaded to a computer by the investigators (Nİ, EB, BD). The mean duration of actigraphy monitoring was 3.2 ± 0.87 days (range 3–5 days).

According to the manufacturer's instructions, the thresholds for low, medium, and high activities were 20, 40 and 80, respectively. In the current study, the medium activity threshold was used based on the literature [30].

Sleep onset was defined as five consecutive minutes of null activity, scored as sleep, whereas a period of at least 5 min of activity above the medium threshold was defined as wakefulness. Actigraphy measures bedtime, wake time, TST, sleep efficiency, sleep latency (SOL), and the number of awakenings. Sleep efficiency was calculated using the formula: (TST/TST + total waking time)* 100. Wake up after sleep onset (WASO) was defined as the total of awakening minutes throughout the sleep period [31]. Actigraphy data were evaluated by taking sleep diaries into consideration.

The sleep quality definition used in the current study included actigraphy-derived items related to sleep continuity as recommended by National Sleep Foundation's (NSF) consensus recommendations for sleep quality assessment [32]. Sleep quality was categorized as 'poor' when at least one of the following criteria was met: (1) sleep efficiency <85%; (2) WASO ≥41 min; (3) the number of awakenings ≥4 per night; 4) SOL >30 min based on the NSF criteria. The optimum TST was defined according to the NSF criteria [33]. Children who slept below the optimum duration for their age (<9 and < 8 h for ages 6–13 and 14–17, respectively) were evaluated as having a short TST.

2.6. Parameters for glycemic variability

The devices used for daytime and overnight glucose monitoring included Dexcom G6 (Dexcom, San Diego, USA) or FreeStyle Libre (Abbott Diabetes Care, Alameda, USA). The data were exported for calculations using GlyCulator 3.0 software [34].

The Dexcom G6 device provides real-time, dynamic glycemic variability every 5 min [35], while Freestyle Libre is an instant glucose measurement system at 15-min intervals [36]. While the former has an alarm during hypoglycemia and hyperglycemia, the latter does not.

Daytime was defined as the period from 06:00 a.m. to 00:00 a.m., overnight as the period from 00:00 a.m. to 06:00 a.m. and total as the 24-h period [37].

For 24-h continuous glucose monitoring, the targeted percentages of time were >70% at 70–180 mg/dL for glycemic control, <4% at <70 mg/dL for hypoglycemia, <1% at <54 mg/dL for severe hypoglycemia, <25% at >180 mg/dL for hyperglycemia and <5% at >250 mg/dL for severe hyperglycemia [38]. Achieving a percentage of >70% for time in the target glucose range (70–180 mg/dL) was defined as 'good metabolic control'.

The hemoglobin A1c level and the amount of insulin used per kilogram of body weight per day were determined at enrollment, with an HbA1c value ≥ 7.5% indicating suboptimal blood glucose levels [39].

There is a lack of clarity as to which glycemic variability metrics are most appropriate for clinical use in T1D patients on insulin therapy. Glycemic variability was calculated from the CGM data [35] using the J index to determine the quality of glycemic control (calculated as 0:001 × (mean +SD) [34], the low blood glucose index (LBGI) to determine the risk of hypoglycemia and the high blood glucose index (HBGI) to determine the risk of hyperglycemia [35].

The coefficient of variation (CV) specifies percentage fluctuations in blood glucose, with a CV ≤ 36% indicating a stable glucose profile and a CV>36% indicating an unstable glucose profile [38].

2.7. Statistical analysis

Data were processed using SPSS 28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp). Descriptive statistics were used to define demographic data. The Kolmogorov-Smirnov test was used to determine the normal or non-normal distribution of the variables. Categorical variables were compared with Pearson Chi-Square Test.

In order to investigate the effect of independent variables such as glycemic variability on the dependent variable such as sleep characteristics Multiple Linear Regression was used. Backward variable selection was utilized to determine which choice of predictive variables is carried out by an automatic procedure. The variance Inflation Factor (VIF) value was evaluated to check the multicollinearity assumption and Durbin-Waston statistics was used to test for the presence of serial correlation among the residuals.

All participants were involved in the restricted maximum likelihood (RML) estimation. Analyses were performed by importing lme 4, rml packages in R. Within- and inter-person (day and person levels, respectively) effects of glycemic variability on sleep characteristics were examined using a linear mixed-effect model, which utilizes a restricted maximum likelihood to handle missing data. Each sleep parameter corresponded to day and person average glycemic variability parameters. The models are subject to the fewest constraints in this method, which also permits free estimation of variances and covariances from the data. The person level (inter-person) and day level (within-person) were used to determine how the average glycemic variability indices and daily glucose levels, respectively, were associated with sleep characteristics. The analysis of variance (ANOVA) test was used in model selection. Data criteria such as AIC and BIC were evaluated to determine the appropriate model.

3. Results

3.1. Descriptive analyses

The median age of the participants was 10.5 (8.0–12.9) years, and 47 were male (56%). The median age at the diagnosis of diabetes was 6.5 (4.1–9.6) years and the median diabetes duration was 3.1 (1.4–5.0) years. At enrollment, the median HbA1c was 7.1%

(6.4–7.6%). The sociodemographic and clinical characteristics of the study population are presented in Table 1.

Most participants wore the FreeStyle Libre device (n = 71, 84.5%). A comparison of daytime and overnight glycemic parameters is presented in Table 2. The overall median percentage of time in severe hypoglycemic ranges (<54 mg/dL) was 0.60% (0–5.05), and the average percentage of time in hypoglycemia ranges (<70-54 mg/dL) was 6.01% (2.20–13.28).

The majority of the participants (n = 74, 88.1%) slept less than the recommended duration for their age, 90.6% (n = 58) for the age range of 6–12 years and 80.0% (n = 16) for the age range of 13–18 years. There were no gender differences in TST (p = 0.098).

Data on sleep characteristics are presented in Table 3.

Sleep quality was classified as poor in 56% of the participants. Sleep quality was not different according to gender, diabetes duration, insulin use, HbA1c levels, and pubertal stage (appendix). Overnight glycemic variability was not different according to sleep quality. Participants who spent less time in the target glucose range were at increased risk for worse sleep quality than those who spent optimal time in the target range (p: 0.023, RR: 2.92%95 CI: 1.14–7.42).

The chronotype median score was 32 (28–36). The participants were classified into the following chronotypes: morning (n = 4, 4.8%), intermediate (n = 42, 50%), and evening (n = 38, 45.2%) types. Although total DSM-5 scores were higher in the evening group than in the intermediate group, the difference was not significant. Glycemic variability was not different according to chronotype. Multiple linear regression analysis showed a higher chronotype score indicating a stronger eveningness preference was associated with more time spent in hypoglycemia (<54 mg/dL, β = 0.433, p = 0.002) and higher LBGI (β = 0.147, p = 0.008). Other CGM parameters showed no associations with chronotype scores.

No differences were observed between the good and poor metabolic control groups regarding sleep parameters, chronotype, and DSM-5 scores during daytime and overnight.

Longer SOL and later bedtime were associated with higher HbA1c levels (Table 4). Wake time, TST, sleep efficiency, WASO, and awakenings showed no associations with HbA1c. The effects of actigraphy-derived sleep parameters on HbA1c are presented in Table 4.

3.2.1. Bivariate associations between sleep characteristics and daytime glycemic variability indices-inter-person level

Associations between sleep characteristics and daytime glycemic variability indices throughout actigraphy monitoring in the inter-person level are presented in Table 5. In bivariate modeling, sleep efficiency was significantly associated with daytime LBGI. The number of awakenings was significantly associated with CV and more time spent in daytime hypoglycemia. There were no significant associations between bedtime, waketime, TST, WASO and daytime glycemic variability.

Table 1
Sociodemographic and clinical characteristics of the participants.

Characteristics	N: 84
Age, years, median (IQR)	10.5 (8.0–12.9)
Gender, Male, n (%)	47 (56)
BMI Z-score, median (IQR)	0.57 (0.04–1.1)
Pubertal status, n (%)	
Prepubertal	42 (50)
Pubertal	42 (50)
Maternal education, years, mean ± SD	12.12 ± 4.00
Screen exposure 1 h before going to sleep, n (%)	63 (75)
Diabetes duration, years, median (IQR)	3.1 (1.4–5.0)
Age at the diagnosis of diabetes, median (IQR)	6.5 (4.1–9.6)
Insulin requirement, IU/kg, median (IQR)	0.8 (0.7–0.96)
HbA1c, %, median (IQR)	7.1 (6.4–7.6)
Suboptimal (≥7.5) n (%)	22 (27.5)
Optimal (<7.5) n (%)	58 (72.5)

*IQR= Interquartile range; BMI: body mass index; HbA1c: glycated hemoglobin A1c.

3.2.2. Bivariate associations between sleep characteristics and overnight glycemic variability indices-inter-person level

Associations between sleep characteristics and overnight glycemic variability indices throughout actigraphy monitoring inter-person level are presented in Table 6. In bivariate modeling, later bedtime was significantly associated with higher overnight glycemic variability. Sleep efficiency was significantly associated with lower overnight mean glucose level, lower overnight glycemic variability (J index), overnight higher time in the target range, less time spent in overnight hyperglycemia, and lower overnight HBGI. WASO was significantly associated with higher overnight mean glucose levels, overnight higher glycemic variability (J index), and more time spent in overnight hyperglycemia. Awakenings were significantly associated with lower overnight time in the target range. There were no significant associations between waketime, TST, SOL, and overnight glycemic variability.

3.3.1. Multilevel models of sleep indices and daytime glycemic variability

Both within-person and inter-person daytime glycemic variability was determined in relation to actigraphy derived sleep parameters. Glycemic variability was significantly associated with most sleep parameters (bedtime, wake time, sleep efficiency, WASO), mostly within-person (Table 7).

On nights when participants had a later bedtime and wake time, they spent less time in daytime hypoglycemia (Table 7). The association between late bedtime and daytime hyperglycemia was not significant.

On nights when participants had higher sleep efficiency, they had significantly lower daytime glycemic variability (J index), lower high blood glucose index and spent less time in hyperglycemia (Table 7). On the contrary, higher inter-person sleep efficiency was significantly associated with higher daytime hypoglycemia.

On nights when participants had higher SOL, there was also higher daytime glycemic variability (J index) and higher daytime HBGI.

On nights when participants had prolonged WASO, there was also more time spent in daytime hypoglycemia, whereas the inter-person prolonged WASO was significantly associated with less time spent in daytime hypoglycemia.

Within-person and inter-person TST and awakenings showed no associations with daytime glycemic variability indices in multilevel models.

3.3.2. Multilevel models of sleep indices and overnight glycemic variability

On nights when participants had higher SOL and lower sleep efficiency, they had significantly higher overnight glycemic variability (CV). On nights when participants had higher WASO, they had significantly higher overnight glycemic variability (J index) and more time spent in overnight hyperglycemia. Within-person and inter-person bedtime, wake time, TST, and awakenings showed no associations with overnight glycemic variability indices in multilevel models (Table 8).

4. Discussion

The current study examined the associations between sleep characteristics and glycemic variability in the T1D youth sample. Our findings identified significant associations between lower sleep

Table 2
Comparison of daytime and overnight glycemic parameters.

	Daytime, Median (Min-Max) N = 82	Overnight, Median (Min-Max) N = 82	p
Mean glucose, mg/dL	142.51 (41.63–312.39)	139.35 (87.42–229.36)	0.942
CV, %	34.4 (19.13–58.88)	18.26 (5.46–52.03)	< **0.001**
J index	36.16 (4.65–188.04)	30.23 (11.59–71.85)	**0.039**
Hypoglycemia (Time <54 mg/dL) %	0.46 (0–29.17)	0 (0–34.72)	0.126
Hypoglycemia (Time <70 mg/dL), %	4.63 (0–48.08)	2.78 (0–44.44)	0.358
Time in range of 70–180 mg/dL, %	60.34 (0–95.65)	0.83 (19.44–100)	0.429
Hyperglycemia (Time >180 mg/dL), %	22.47 (0–88.47)	21.76 (0–80.56)	0.753
Hyperglycemia (Time >250 mg/dL), %	5.09 (0–60.8)	0 (0–41.67)	0.576
Low blood glucose index	1.29 (0–11.47)	1.24 (0–13.53)	0.194
High blood glucose index	4.65 (0–37.82)	4.07 (0.07–18.4)	0.679

CV: Coefficient of variation.

Table 3
Actigraphy-derived sleep characteristics (N = 84).

Bedtime hour, median (IQR)	22:59 (22:09–23:45)
Wake up hour, median (IQR)	08:26 (07:41–09:12)
Total sleep time, hour, median (IQR)	7.6 (6.8–8.3)
SOL, minute, median (IQR)	11.79 (4.58–24.47)
Sleep efficiency, %, median (IQR)	86.1 (81.6–89.7)
WASO, minute, median (IQR)	37.85 (29.47–50.69)
Awakenings, median (IQR)	0.33 (0–1.0)
DSM-5, median (IQR)	14 (10.25–18)

*IQR= Interquartile range; SOL: sleep onset latency; WASO: wake after sleep onset.

efficiency, longer SOL, longer WASO, and higher overnight glycemic variability in children with T1D, highlighting the importance of adequate sleep for children with T1D. Although our findings indicate that participants who spent less time in the target glucose range were at 2.9 times increased risk for worse sleep quality compared to those who spent optimal time in the target range, overnight glycemic variability was not different in youth with poor sleep quality compared to those with good sleep quality. Children with eveningness preference had higher sleep disturbances scores than the intermediate group and higher chronotype scores, indicating a stronger eveningness preference was associated with an increased risk of hypoglycemia. Eighty-eight percent of the participants slept less than the age-appropriate recommended TST, but TST showed no associations with daytime and overnight glycemic variability indices in multilevel models.

The current ADA guidelines recommend screening for sleep health in people with diabetes, including symptoms of sleep disorders, disruptions to sleep due to diabetes symptoms or management needs, and sleep-related concerns [40]. However, despite its high prevalence, insufficient TST and poor sleep quality are still

Table 4
The effect of actigraphy-derived sleep parameters on HbA1c.

	Unstandardized coefficients		Standardized coefficients	T	Sig.	VIF
	Beta	Standard error	Beta			
Constant	−2372	3048		−0,7778	0,440	
SOL	0,044	0013	0,410	3275	**0,002**	1032
Bedtime	0,005	0002	0,402	2990	**0,004**	1191

VIF: Variance Inflation Factor; SOL: sleep onset latency.

Table 5
Bivariate associations between sleep characteristics and daytime glycemic variability indices-inter-person level (N = 82).

	Bedtime β ± SE (P)	Wake time β ± SE (P)	Total sleep time β ± SE (P)	SOL β ± SE (P)	Sleep efficiency β ± SE (P)	WASO β ± SE (P)	Awakenings β ± SE (P)
Mean	0.022 ± 0.023 (0.341)	0.021 ± 0.034 (0.538)	2.150 ± 2.477 (0.387)	0.147 ± 0.174 (0.401)	−0.642 ± 0.492 (0.194)	0.079 ± 0.107 (0.464)	0.278 ± 0.235 (0.238)
CV	−0.008 ± 0.006 (0.147)	−0.001 ± 0.008 (0.823)	1.045 ± 0.647 (0.108)	−0.011 ± 0.046 (0.806)	0.033 ± 0.130 (0.796)	−0.004 ± 0.027 (0.860)	**0.124±0.061 (0.044)**
J index	0.008 ± 0.001 (0.420)	0.005 ± 0.001 (0.740)	−0.201 ± 1.243 (0.871)	−0.017 ± 0.085 (0.836)	−0.179 ± 0.240 (0.456)	0.033 ± 0.055 (0.545)	0.136 ± 0.119 (0.256)
Hypoglycemia <54 mg/dL, %	−0.001 ± 0.003 (0.595)	−0.003 ± 0.005 (0.48)	0.612 ± 0.382 (0.111)	−0.047 ± 0.026 (0.076)	0.144 ± 0.073 (0.051)	0.002 ± 0.001 (0.906)	**0.078±0.035 (0.029)**
Hypoglycemia <70 mg/dL, %	−0.002 ± 0.005 (0.582)	−0.003 ± 0.008 (0.663)	0.601 ± 0.606 (0.323)	**−0.099±0.041 (0.018)**	0.134 ± 0.117 (0.253)	0.012 ± 0.028 (0.676)	0.083 ± 0.057 (0.144)
Time in range of 70 −180 mg/dL, %	−0.013 ± 0.011 (0.237)	0.020 ± 0.017 (0.253)	1.960 ± 1.251 (0.119)	0.022 ± 0.087 (0.798)	0.157 ± 0.246 (0.523)	−0.006 ± 0.054 (0.901)	−0.123 ± 0.118 (0.298)
Hyperglycemia >180 mg/dL, %	0.009 ± 0.001 (0.346)	−0.002 ± 0.016 (0.893)	0.082 ± 1.186 (0.944)	0.102 ± 0.080 (0.208)	−0.404 ± 0.228 (0.078)	0.034 ± 0.053 (0.519)	0.141 ± 0.110 (0.202)
Hyperglycemia >250 mg/dL, %	0.007 ± 0.005 (0.179)	0.005 ± 0.009 (0.566)	−0.417 ± 0.669 (0.533)	0.035 ± 0.047 (0.450)	−0.161 ± 0.127 (0.207)	0.013 ± 0.029 (0.644)	0.055 ± 0.063 (0.387)
Low blood glucose index	−0.008 ± 0.001 (0.477)	−0.008 ± 0.001 (0.643)	0.246 ± 0.139 (0.078)	**−0.023±0.009 (0.014)**	**0.055±0.026 (0.039)**	0.001 ± 0.006 (0.843)	0.024 ± 0.013 (0.060)
High blood glucose index	0.003 ± 0.002 (0.215)	0.003 ± 0.004 (0.447)	0.076 ± 0.289 (0.791)	0.008 ± 0.002 (0.966)	−0.052 ± 0.055 (0.349)	0.010 ± 0.013 (0.408)	0.041 ± 0.027 (0.136)

SOL: sleep onset latency; WASO: wake after sleep onset; CV: Coefficient of variation.

Table 6
Bivariate associations between sleep characteristics and daytime glycemic variability indices-inter-person level (N = 82).

	Bedtime β ± SE (P)	Wake time β ± SE (P)	Total sleep time β ± SE (P)	SOL β ± SE (P)	Sleep efficiency β ± SE (P)	WASO β ± SE (P)	Awakenings β ± SE (P)
Mean	0.009 ± 0.003 (0.772)	0.016 ± 0.047 (0.734)	−2.055 ± 3.944 (0.603)	0.528 ± 0.288 (0.068)	−2.210 ± 0.765 (**0.004**)	**0.372±0.161 (0.023)**	0.611 ± 0.347 (0.081)
CV	**0.015±0.006 (0.018)**	0.002 ± 0.010 (0.795)	−1.220 ± 0.771 (0.116)	0.007 ± 0.005 (0.902)	0.077 ± 0.154 (0.619)	−0.035 ± 0.029 (0.233)	−0.095 ± 0.071 (0.184)
J index	0.010 ± 0.014 (0.492)	0.002 ± 0.021 (0.927)	−2.014 ± 1.798 (0.264)	0.238 ± 0.131 (0.071)	**−1.115±0.346 (0.001)**	**0.161±0.073 (0.030)**	0.272 ± 0.158 (0.088)
Hypoglycemia <54 mg/dL, %	−0.001 ± 0.008 (0.845)	0.005 ± 0.013 (0.677)	1.450 ± 1.070 (0.178)	−0.081 ± 0.078 (0.302)	0.324 ± 0.210 (0.126)	−0.034 ± 0.043 (0.425)	0.095 ± 0.095 (0.319)
Hypoglycemia <70 mg/dL, %	0.003 ± 0.011 (0.75)	0.008 ± 0.019 (0.670)	1.145 ± 1.507 (0.449)	−0.108 ± 0.108 (0.322)	0.373 ± 0.291 (0.203)	−0.063 ± 0.060 (0.298)	−0.002 ± 0.135 (0.986)
Time in range of 70 −180 mg/dL, %	−0.008 ± 0.020 (0.684)	−0.013 ± 0.032 (0.681)	0.950 ± 2.568 (0.712)	−0.254 ± 0.186 (0.175)	**1.320±0.493 (0.008)**	−0.114 ± 0.104 (0.276)	**−0.609±0.223 (0.007**)
Hyperglycemia >180 mg/dL, %	−0.010 ± 0.017 (0.566)	0.020 ± 0.029 (0.485)	−3.320 ± 2.367 (0.163)	0.321 ± 0.168 (0.058)	**−1.474±0.440 (0.001)**	0.154 ± 0.100 (0.128)	0.231 ± 0.211 (0.275)
Hyperglycemia >250 mg/dL, %	0.003 ± 0.009 (0.726)	−0.015 ± 0.015 (0.296)	−0.669 ± 1.221 (0.585)	0.077 ± 0.089 (0.388)	**−0.679±0.234 (0.004)**	**0.111±0.049 (0.025)**	0.151 ± 0.108 (0.163)
Low blood glucose index	−0.000 ± 0.002 (0.904)	0.006 ± 0.004 (0.897)	0.461 ± 0.374 (0.220)	−0.020 ± 0.027 (0.458)	0.099 ± 0.072 (0.172)	−0.015 ± 0.015 (0.297)	0.016 ± 0.033 (0.630)
High blood glucose index	−0.008 ± 0.005 (0.872)	−0.000 ± 0.006 (0.881)	−0.356 ± 0.586 (0.544)	0.058 ± 0.043 (0.183)	**−0.355±0.116 (0.002**)	0.034 ± 0.022 (0.133)	0.069 ± 0.050 (0.175)

SOL: sleep onset latency; WASO: wake after sleep onset; CV: Coefficient of variation.

Table 7
Within- and inter-person-level effects of sleep characteristics on daytime glycemic variability-multilevel models (N = 82).

Predictors		Bedtime β ± SE (*P*-value)	Wake time β ± SE (*P*-value)	Total sleep time β ± SE (*P*-value)	SOL β ± SE (*P*-value)	Sleep efficiency β ± SE (*P*-value)	WASO β ± SE (*P*-value)	Awakenings β ± SE (*P*-value)
Mean glucose	Within-person	0.015 ± 0.026 (0.569)	0.037 ± 0.030 (0.231)	3.363 ± 2.283 (0.143)	0.267 ± 0.177 (0.135)	−0.845 ± 0.453 (0.066)	0.099 ± 0.121 (0.414)	0.059 ± 0.191 (0.757)
	Inter-person	−0.001 ± 0.009 (0.123)	−0.009 ± 0.001 (0.403)	−0.078 ± 0.791 (0.541)	−0.007 ± 0.007 (0.283)	0.010 ± 0.020 (0.608)	0.002 ± 0.005 (0.650)	−0.004 ± 0.008 (0.582)
CV	Within-person	−0.005 ± 0.005 (0.379)	−0.011 ± 0.006 (0.090)	−0.193 ± 0.560 (0.730)	0.008 ± 0.041 (0.835)	−0.075 ± 0.101 (0.463)	0.022 ± 0.028 (0.426)	−0.056 ± 0.044 (0.206)
	Inter-person	0.002 ± 0.002 (0.286)	0.002 ± 0.002 (0.423)	0.023 ± 0.025 (0.359)	−0.002 ± 0.001 (0.162)	0.007 ± 0.005 (0.160)	0.006 ± 0.001 (0.996)	0.001 ± 0.002 (0.506)
J index	Within-person	0.011 ± 0.010 (0.338)	0.002 ± 0.015 (0.896)	0.489 ± 1.112 (0.661)	**0.186±0.084 (0.029)**	**−0.446±0.213 (0.040)**	0.017 ± 0.056 (0.764)	−0.069 ± 0.094 (0.464)
	Inter-person	−0.000 ± 0.000 (0.134)	−0.007 ± 0.006 (0.237)	0.003 ± 0.049 (0.943)	−0.003 ± 0.003 (0.246)	0.009 ± 0.009 (0.319)	0.006 ± 0.002 (0.833)	−0.002 ± 0.004 (0.616)
Hypoglycemia <54 mg/dL %	Within-person	**−0.008±0.004 (0.032)**	**−0.011±0.005 (0.040)**	−0.028 ± 0.39 (0.943)	−0.055 ± 0.029 (0.060)	0.011 ± 0.075 (0.884)	**0.037±0.018 (0.046)**	0.034 ± 0.033 (0.298)
	Inter-person	0.001 ± 0.001 (0.404)	0.002 ± 0.001 (0.912)	0.010 ± 0.015 (0.528)	−0.008 ± 0.001 (0.399)	**0.006±0.002 (0.043)**	**−0.001±0.008 (0.047)**	0.008 ± 0.001 (0.951)
Hypoglycemia <70 mg/dL %	Within-person	**−0.016±0.006 (0.013)**	−0.016 ± 0.008 (0.055)	0.236 ± 0.605 (0.697)	−0.071 ± 0.045 (0.116)	0.106 ± 0.117 (0.365)	0.028 ± 0.029 (0.329)	−0.033 ± 0.051 (0.519)
	Inter-Person	0.002 ± 0.002 (0.249)	−0.005 ± 0.002 (0.842)	0.002 ± 0.002 (0.993)	−0.004 ± 0.001 (0.799)	0.005 ± 0.004 (0.262)	−0.001 ± 0.001 (0.156)	0.008 ± 0.002 (0.701)
Time in range of 70 −180 mg/dL %	Within-person	−0.000 ± 0.014 (0.951)	0.002 ± 0.001 (0.984)	0.496 ± 1.153 (0.667)	−0.071 ± 0.090 (0.429)	0.230 ± 0.234 (0.327)	−0.049 ± 0.061 (0.423)	0.075 ± 0.096 (0.436)
	Inter-person	−0.009 ± 0.005 (0.870)	−0.000 ± 0.000 (0.822)	−0.058 ± 0.050 (0.246)	0.002 ± 0.003 (0.434)	−0.008 ± 0.010 (0.440)	−0.003 ± 0.003 (0.303)	−0.005 ± 0.004 (0.213)
Hyperglycemia >180 mg/dL %	Within-person	0.010 ± 0.014 (0.471)	0.024 ± 0.015 (0.119)	1.329 ± 1.152 (0.250)	0.152 ± 0.087 (0.084)	**−0.492±0.228 (0.032)**	0.099 ± 0.058 (0.090)	0.034 ± 0.095 (0.718)
	Inter-person	−0.006 ± 0.005 (0.899)	−0.002 ± 0.005 (0.660)	−0.014 ± 0.048 (0.775)	−0.003 ± 0.003 (0.318)	0.008 ± 0.009 (0.385)	0.003 ± 0.002 (0.263)	−0.002 ± 0.004 (0.962)
Hyperglycemia >250 mg/dL %	Within-person	0.008 ± 0.005 (0.152)	0.007 ± 0.007 (0.327)	0.073 ± 0.556 (0.895)	0.062 ± 0.041 (0.138)	−0.164 ± 0.097 (0.091)	−0.005 ± 0.002 (0.998)	−0.043 ± 0.047 (0.356)
	Inter-Person	−0.003 ± 0.002 (0.184)	−0.002 ± 0.003 (0.493)	−0.004 ± 0.002 (0.986)	−0.001 ± 0.001 (0.561)	0.004 ± 0.005 (0.394)	0.004 ± 0.001 (0.976)	−0.003 ± 0.002 (0.892)
Low blood glucose index	Within-person	**−0.004±0.001 (0.009)**	**−0.004±0.002 (0.037)**	0.009 ± 0.143 (0.947)	−0.015 ± 0.010 (0.147)	0.015 ± 0.027 (0.581)	0.010 ± 0.006 (0.126)	0.001 ± 0.012 (0.901)
	Inter-person	0.005 ± 0.005 (0.309)	−0.004 ± 0.006 (0.949)	0.002 ± 0.005 (0.679)	−0.001 ± 0.003 (0.630)	0.001 ± 0.001 (0.151)	−0.005 ± 0.003 (0.063)	0.001 ± 0.005 (0.773)
High blood glucose index	Within-person	0.004 ± 0.002 (0.093)	0.001 ± 0.003 (0.625)	0.066 ± 0.26 (0.800)	**0.048±0.019 (0.014)**	**−0.114±0.049 (0.023)**	0.004 ± 0.013 (0.733)	−0.016 ± 0.022 (0.445)
	Inter-person	−0.000 ± 0.000 (0.079)	−0.002 ± 0.001 (0.160)	−0.005 ± 0.011 (0.661)	−0.005 ± 0.007 (0.500)	0.001 ± 0.002 (0.600)	0.002 ± 0.006 (0.675)	−0.006 ± 0.001 (0.551)

SOL: sleep onset latency; WASO: wake after sleep onset; CV: Coefficient of variation.

Table 8
Within- and inter-person-level effects of sleep characteristics on overnight glycemic variability-multilevel models (N = 82).

Predictors		Bedtime β ± SE (*P*-value)	Wake time β ± SE (*P*-value)	Total sleep time β ± SE (*P*-value)	SOL β ± SE (*P*-value)	Sleep efficiency β ± SE (*P*-value)	WASO β ± SE (*P*-value)	Awakenings β ± SE (*P*-value)
Mean	Within-Person	−0.003 ± 0.051 (0.944)	0.097 ± 0.070 (0.169)	8.070 ± 5.295 (0.130)	0.244 ± 0.446 (0.586)	0.506 ± 1.105 (0.647)	0.382 ± 0.255 (0.138)	0.579 ± 0.486 (0.235)
	Inter-Person	−0.001 ± 0.001 (0.151)	−0.006 ± 0.001 (0.670)	0.056 ± 0.172 (0.744)	0.001 ± 0.011 (0.929)	0.020 ± 0.031 (0.526)	0.003 ± 0.010 (0.763)	−0.007 ± 0.012 (0.586)
CV	Within-Person	−0.011 ± 0.009 (0.217)	0.001 ± 0.012 (0.899)	−1.026 ± 0.854 (0.234)	**0.129±0.053 (0.017)**	**−0.343±0.139 (0.016)**	0.012 ± 0.050 (0.808)	−0.007 ± 0.075 (0.312)
	Inter-Person	0.003 ± 0.002 (0.204)	0.000 ± 0.000 (0.313)	0.024 ± 0.031 (0.429)	0.002 ± 0.002 (0.295)	−0.008 ± 0.006 (0.215)	0.001 ± 0.002 (0.461)	0.002 ± 0.002 (0.338)
J index	Within-Person	−0.019 ± 0.023 (0.393)	0.041 ± 0.031 (0.189)	0.055 ± 0.077 (0.472)	0.078 ± 0.201 (0.698)	0.040 ± 0.511 (0.936)	**0.300±0.120 (0.015)**	0.292 ± 0.219 (0.184)
	Inter-Person	−0.000 ± 0.000 (0.313)	0.004 ± 0.007 (0.995)	3.903 ± 2.366 (0.101)	0.002 ± 0.005 (0.625)	−0.002 ± 0.014 (0.838)	0.004 ± 0.004 (0.331)	−0.005 ± 0.005 (0.930)
Hypoglycemia <54 mg/dL %	Within-Person	0.006 ± 0.001 (0.960)	−0.012 ± 0.018 (0.500)	−0.539 ± 1.393 (0.700)	0.035 ± 0.116 (0.760)	0.152 ± 0.294 (0.604)	−0.089 ± 0.070 (0.208)	−0.192 ± 0.125 (0.128)
	Inter-Person	0.000 ± 0.000 (0.479)	0.000 ± 0.000 (0.343)	0.006 ± 0.046 (0.884)	−0.002 ± 0.003 (0.541)	0.001 ± 0.008 (0.894)	0.002 ± 0.002 (0.410)	0.005 ± 0.003 (0.109)
Hypoglycemia <70 mg/dL %	Within-Person	−0.005 ± 0.018 (0.761)	−0.020 ± 0.025 (0.428)	−1.154 ± 2.001 (0.567)	−0.044 ± 0.163 (0.788)	0.153 ± 0.420 (0.717)	−0.089 ± 0.096 (0.357)	−0.192 ± 0.125 (0.128)
	Inter-Person	0.000 ± 0.000 (0.408)	0.000 ± 0.000 (0.373)	0.034 ± 0.063 (0.588)	−0.002 ± 0.004 (0.630)	0.005 ± 0.001 (0.996)	0.009 ± 0.003 (0.816)	−0.192 ± 0.125 (0.128)
Time in range of 70 −180 mg/dL %	Within-Person	0.004 ± 0.031 (0.877)	−0.021 ± 0.042 (0.614)	−3.440 ± 3.299 (0.300)	−0.096 ± 0.276 (0.728)	−0.434 ± 0.686 (0.528)	−0.305 ± 0.171 (0.080)	−0.015 ± 0.296 (0.958)
	Inter-Person	0.001 ± 0.008 (0.216)	0.000 ± 0.001 (0.909)	−0.069 ± 0.110 (0.527)	0.001 ± 0.007 (0.862)	−0.004 ± 0.020 (0.839)	−0.008 ± 0.006 (0.223)	−0.004 ± 0.008 (0.576)
Hyperglycemia >180 mg/dL %	Within-Person	−0.020 ± 0.028 (0.478)	0.041 ± 0.038 (0.293)	2.275 ± 2.888 (0.432)	−0.103 ± 0.250 (0.681)	0.603 ± 0.604 (0.321)	0.126 ± 0.137 (0.361)	−0.332 ± 0.270 (0.221)
	Inter-Person	0.002 ± 0.007 (0.970)	0.000 ± 0.000 (0.910)	0.089 ± 0.102 (0.385)	0.002 ± 0.006 (0.672)	−0.008 ± 0.018 (0.622)	**0.011±0.005 (0.047)**	0.008 ± 0.008 (0.295)
Hyperglycemia >250 mg/dL %	Within-Person	−0.004 ± 0.015 (0.759)	0.034 ± 0.020 (0.095)	2.275 ± 2.888 (0.432)	0.053 ± 0.133 (0.689)	−0.096 ± 0.326 (0.768)	**0.214±0.074 (0.005)**	0.112 ± 0.145 (0.443)
	Inter-Person	−0.005 ± 0.004 (0.892)	0.000 ± 0.000 (0.708)	0.013 ± 0.052 (0.796)	0.002 ± 0.003 (0.994)	0.009 ± 0.009 (0.319)	−0.001 ± 0.003 (0.524)	−0.001 ± 0.004 (0.743)
Low blood glucose index	Within-Person	0.000 ± 0.004 (0.924)	−0.004 ± 0.006 (0.469)	−0.278 ± 0.501 (0.582)	−0.005 ± 0.041 (0.899)	0.046 ± 0.105 (0.662)	−0.023 ± 0.024 (0.340)	−0.067 ± 0.042 (0.117)
	Inter-Person	0.000 ± 0.000 (0.346)	0.000 ± 0.000 (0.413)	−0.002 ± 0.015 (0.861)	−0.003 ± 0.001 (0.787)	−0.009 ± 0.003 (0.764)	0.006 ± 0.009 (0.520)	0.001 ± 0.001 (0.153)
High blood glucose index	Within-Person	−0.004 ± 0.009 (0.639)	0.009 ± 0.013 (0.489)	−0.752 ± 1.114 (0.501)	−0.091 ± 0.079 (0.249)	−0.087 ± 0.210 (0.679)	0.091 ± 0.052 (0.086)	−0.122 ± 0.092 (0.187)
	Inter-Person	0.008 ± 0.002 (0.745)	0.009 ± 0.002 (0.680)	−0.001 ± 0.025 (0.948)	0.000 ± 0.001 (0.662)	−0.001 ± 0.005 (0.752)	0.000 ± 0.001 (0.620)	−0.000 ± 0.001 (0.817)

SOL: sleep onset latency; WASO: wake after sleep onset; CV: Coefficient of variation.

unrecognized in youth with T1D, and it has not been possible to standardize sleep assessment as part of the management for wider clinical use [41].

Although previous research has suggested a link between sleep and glycemic variability, few studies have concurrently investigated sleep characteristics and chronotypes in relation to glycemic variability in youth with T1D. Besides the glycemic and sleep measures, the present study reports chronotypes in youth with T1D. Consistent with a recent study [15], we observed that half of the sample presented an intermediate type (50%), followed by the evening type (45.2%) and morning type (4.8%). This finding suggests that a significant proportion of youth with T1D may have difficulty adjusting to the demands of a typical school schedule. Despite the finding that the glycemic variability did not differ among children between chronotypes, regression analysis showed a higher chronotype score indicating a stronger eveningness preference was associated with more time spent in hypoglycemia and low blood glucose index. Our findings might partly be explained by the high levels of stress hormones and unhealthy eating habits observed in evening chronotypes [42,43] contributing to suboptimal blood glucose levels and increased risk of hypoglycemia. Further, a study in young adolescents showed that later chronotype preferences are associated with higher BMI [43]. In our study, neither BMI nor HbA1c differed significantly between participants with the intermediate and eveningness chronotypes. A study in adolescents with T1D found no association between chronotype scores and HbA1c [16]. Reutrakul et al. found that evening chronotypes were associated with poorer glycemic control in adults with type 2 diabetes independently of sleep disturbances [44]. In contrast, Silva et al. found that adolescents with higher HbA1c had more daytime sleepiness and a morning chronotype [45]. The relationship between chronotype and diabetes is complex, and our findings suggest that eveningness preference might contribute to an increased risk of hypoglycemia. Further research is needed to understand the mechanisms underlying these associations fully. Additionally, pediatricians need to take into consideration the patient's chronotype when developing management plans for diabetes.

4.1. Total sleep time

Although the recommended minimum TST among children between 6 and 13 years has been determined to be 9 h, 90.6% of the participants slept less. Eighty percent of the children over 13 years slept less than 8 h showing no gender differences. Furthermore, the percentage of patients with diabetes over 13 years with insufficient TST was higher compared to adolescents who do not have diabetes with insufficient TST (40.1%) reported in a recent study from Turkey [46]. Previous studies have reported similar results [5,8,47]. In a

meta-analysis, nearly half of the children and up to 77% of adolescents with T1D were found to have insufficient sleep [5]. Patel et al. found that only 23% of adolescents with T1D had adequate sleep [48]. In another meta-analysis, children and adolescents with T1D slept approximately 26 min less than those without diabetes [22], but found no significant association between TST and glycemic outcomes. Although short TST was reported to be associated with suboptimal blood glucose levels in some previous studies [4,8,39,49], other studies found no significant associations between TST and glycemic variability [3,7,48]. The findings of the present study suggest that the TST may not be the only factor influencing glycemic outcomes in youth with T1D and that addressing only sleep duration may not be sufficient to achieve glycemic targets in these children.

4.2. Sleep quality

Findings on the association of sleep quality with glycemic variability were contrary to our anticipation. Sleep quality was classified as poor in 56% of the sample using a composite of objective actigraphy-derived sleep parameters (sleep latency, number of awakenings, wake after sleep onset, and sleep efficiency) as the predictors based on the NSF's consensus criteria [32]. Sleep quality was not different according to gender, diabetes duration, total daily insulin dose, HbA1c levels, and pubertal stage. Nonetheless, our findings showed that participants who spent less time in the target glucose range were at 2.9 times increased risk for worse sleep quality than those who spent optimal time in the target range. A recent study in adults with T1D found significant associations between sleep quality and overnight glycemic variability but no association with time spent in the target glucose range [50]. Notably, the criteria to define sleep quality was different between that and the current study. The findings of our study suggest that there is an association between poor sleep quality and an increased risk for poor glycemic outcomes in youth with T1D. However, overnight glycemic variability was not different in youth with poor sleep quality compared to those with good sleep quality. This suggests that poor sleep quality may be associated with poor glycemic outcomes through other mechanisms. As such, a study of older adolescents with T1D showed that perceptions of poor sleep quality were related to a greater risk of hyperglycemia [51]. More research is needed to understand the mechanisms underlying these conditions fully.

Previous studies were primarily concerned with inter-person analysis [5,17,39]. To date, within-person analysis of sleep parameters and glycemic variability has been rarely conducted [3,52]. The current study examined sleep characteristics and glycemic variability in inter-person and within-person analyses for multiple days in children with T1D. There is a lack of evidence supporting the use of a specific parameter as an index for glycemic variability. The current study used CV and J index as indicators for glycemic variability.

Increased nocturnal hypoglycemic episodes were associated with frequent awakenings in adolescents and young children with T1D [53,54]. Considering CV as the measure of glycemic variability with the best ability to predict the risk of hypoglycemia [55], our findings support the previous study findings. Bivariate analyses showed that higher overall daytime glycemic variability was associated with greater inter-person sleep disruptions, such as lower sleep efficiency and more awakenings. This suggests that poor glycemic targets during the day may be associated with poor sleep quality at night.

Bivariate analyses showed that later bedtime and longer WASO were significantly associated with higher overnight glycemic variability. Moreover, awakenings were significantly associated with lower overnight time in the target range. The findings of this study suggest that there may be a relationship between sleep patterns and overnight glycemic variability in youth with T1D. Consistent with our findings, in a young adult study, a longer WASO was associated with greater inter-person glycemic variability (quality of glycemic control, J index), and delayed bedtime was associated with hyperglycemia [52]. In contrast, some studies found no significant associations between sleep parameters and blood glucose levels [7,39,49].

Whereas better sleep efficiency is associated with less overnight glycemic variability, more time in target range, and less overnight risk for hyperglycemia. Our findings align with the findings of a recent study conducted among young adults with T1D [52], which showed that nights with higher sleep efficiency were associated with a lower J index, which reflects overall glycemic variability, and a lower HBGI, which reflects the proportion of time spent in hyperglycemic ranges. Additionally, participants with higher sleep efficiency had significantly lower overnight glycemic variability as measured by the CV index, which reflects the degree of variation in glucose levels. On the other hand, a similar study in children with T1D found no association between sleep efficiency and glycemic variability [3]. In studies conducted with different methods, children with T1D and without diabetes were found to have similar sleep efficiency [39,56]. Our findings suggest that sleep efficiency plays an important role in achieving treatment targets for children with T1D. Specifically, better sleep efficiency is associated with better daytime glycemic stability and lower overnight glycemic variability.

Prolonged WASO was associated with more time spent in daytime hypoglycemia and higher overnight glycemic variability as measured by the J index, which reflects both the amplitude and frequency of glucose excursions. Additionally, prolonged WASO was associated with more time spent in overnight hyperglycemia. Consistent with our findings, in an adolescent study with T1D, a longer WASO was associated with greater within-person overall glycemic variability [3]. In a young adult study, a longer WASO was associated with greater inter-person glycemic variability [52]. These findings highlight the importance of addressing sleep patterns and promoting healthy sleep habits in youth with T1D. Prolonged WASO may interfere with glucose regulation and increase the risk for both hypoglycemia during the day and hyperglycemia during the night.

On nights when participants had higher SOL, they had higher overnight glycemic variability as measured by the CV index. Additionally, participants with higher SOL, and delayed bedtime had significantly higher HbA1c, which reflects long-term poor glycemic outcomes. Our findings align with the previous works. Frye et al. found that, later bedtimes predicted a worse glycemic outcome [17]. Macaulay et al. found that suboptimal glycemic stability was associated with longer sleep onset latency in children with T1D [39]. Salah et al. found that children with T1D had longer SOL than controls [57].

5. Limitations and strength

This current study has some limitations. The cross-sectional design and lack of a control group limit the generalization of temporal associations, and it is difficult to determine whether poor sleep led to poor glycemic variability or vice versa.

Another limitation is that despite the enrollment of a sample at risk of sleep disorders, the study's sample of youth with T1D had relatively good glycemic stability, which may limit the generalizability of the findings to children with poorer glycemic outcomes.

Another limitation of the study is that the presence of an alarm system on Dexcom G6 might have confounded the evaluation of

sleep parameters. Moreover, the study did not assess other potential confounding variables that might influence the relationship between sleep and glycemic variability, such as stress, diet, and physical activity. Longitudinal studies and studies that assess multiple confounding variables would provide more insight into the complex relationship between sleep and glycemic stability.

Finally, the current study does not measure every dimension of sleep health as recently proposed by Buysse [10]. This conceptual model of sleep health focuses on positive dimensions of sleep and wakefulness that may exist to some degree in every person rather than detecting sleep disorders. In adolescents prone to eveningness, better sleep health indicated by higher sleep health composite scores was associated with reduced risks in emotional, cognitive, and emotional health domains [19]. Even though its psychometric properties are limited due to the lack of studies in clinical samples or adolescents without chronic diseases, investigating the sleep of youth with T1D within the framework of sleep health may help find existing positive dimensions to support their overall health and well-being.

However, the strengths of this study may outweigh the limitations. Objective sleep assessment by actigraphy and continuous blood glucose monitoring metrics were simultaneously obtained for at least three consecutive days in combination with subjective sleep diaries and sleep questionnaires and determination of chronotypes not only in adolescents but also in a younger age group.

6. Conclusion

Our findings showed that sleep efficiency, SOL, WASO, and bedtime play important roles in glycemic outcomes for children with T1D. These findings suggest that sleep quality rather than TST is significantly associated with glycemic variability in children with T1D. Additionally, our findings suggest that eveningness preference might contribute to an increased risk of hypoglycemia. These highlight the importance of addressing sleep patterns and the patient's chronotype when developing management plans for youth with T1D, as promoting healthy sleep habits can improve their glycemic outcomes and long-term complications. It is also important to note that there are multiple factors that can affect regulation of blood glucose levels. Therefore, further research is needed to fully understand the mechanisms underlying these associations.

Funding

This research was supported by The Scientific and Technological Research Council of Türkiye (TUBİTAK) with grant numbers 120S789, which are gratefully acknowledged.

CRediT authorship contribution statement

Necla İpar: Conceptualization, Funding acquisition, Formal analysis, Data curation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Perran Boran:** Conceptualization, Funding acquisition, Formal analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Hatice Ezgi Barış:** Formal analysis, Data curation, Writing – review & editing. **Mahmut Caner Us:** Data curation. **Burcu Aygün:** Data curation. **Belma Haliloğlu:** Formal analysis, Methodology, Resources. **Tuğba Gökçe:** Data curation. **Ecem Can:** Data curation. **Elif Eviz:** Data curation. **Neslihan Gökmen İnan:** Formal analysis. **Gül Yeşiltepe Mutlu:** Resources, Writing – review & editing. **Abdullah Bereket:** Funding acquisition, Resources, Supervision, Writing – review & editing. **Şükrü Hatun:** Funding acquisition, Resources, Supervision, Writing – review & editing.

Trial registration

Clinical Trails.gov identifier, NCT04978662 (Registration Date: July 27, 2021).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix. Assessment according to sleep quality

	Sleep quality		p
	Poor n = 37	Good n = 47	
Gender (n,%)			
Female	17 (36.2)	20 (54.1)	0.10[a]
Male	30 (62.8)	17 (45.9)	
HbA1c (n,%)			
Suboptimal (≥7.5)	11 (24.4)	11 (31.4)	0.48[a]
Optimal (<7.5)	34 (75.6)	24 (68.6)	
Pubertal status, (n,%)			
Prepubertal	23 (48.9)	19 (51.4)	0.82[a]
Pubertal	24 (51.1)	18 (48.6)	
Total daily insulin dose (Unit/kg)	0.80 (0.70–0.97)	0.82 (0.71–0.97)	0.93[b]
Diabetes duration, year	2.86 (1.55–4.73)	3.26 (1.36–5.67)	0.70[b]

[a] Chi-squared test.
[b] Mann-Whitney *U* Test.

References

[1] Caruso NC, Radovanovic B, Kennedy JD, Couper J, Kohler M, Kavanagh PS, et al. Sleep, executive functioning and behaviour in children and adolescents with type 1 diabetes. Sleep Med 2014;15:1490–9.
[2] Yeşilkaya E, Cinaz P, Andıran N, Bideci A, Hatun Ş, Sarı E, et al. First report on the nationwide incidence and prevalence of Type 1 diabetes among children in Turkey. Diabet Med 2017;34:405–10.
[3] Griggs S, Redeker NS, Jeon S, Grey M. Daily variations in sleep and glucose in adolescents with type 1 diabetes. Pediatr Diabetes 2020;21:1493–501.
[4] Reutrakul S, Thakkinstian A, Anothaisintawee T, Chontong S, Borel AL, Perfect MM, et al. Sleep characteristics in type 1 diabetes and associations with glycemic control: systematic review and meta-analysis. Sleep Med 2016;23:26–45.
[5] Ji X, Wang Y, Saylor J. Sleep and type 1 diabetes mellitus management among children, adolescents, and emerging young adults: a systematic review. J Pediatr Nurs 2021;61:245–53.
[6] Macaulay GC, Galland BC, Boucher SE, Wiltshire EJ, Haszard JJ, Campbell AJ, et al. Impact of type 1 diabetes mellitus, glucose levels, and glycemic control on sleep in children and adolescents: a case-control study. Sleep 2020;43.
[7] Rechenberg K, Griggs S, Jeon S, Redeker N, Yaggi HK, Grey M. Sleep and glycemia in youth with type 1 diabetes. J Pediatr Health Care 2020;34:315–24.
[8] Jaser SS, Foster NC, Nelson BA, Kittelsrud JM, DiMeglio LA, Quinn M, et al. Sleep in children with type 1 diabetes and their parents in the T1D Exchange. Sleep Med 2017;39:108–15.
[9] McDonough RJ, Clements MA, DeLurgio SA, Patton SR. Sleep duration and its impact on adherence in adolescents with type 1 diabetes mellitus. Pediatr Diabetes 2017;18:262–70.
[10] Buysse DJ. Sleep health: can we define it? Does it matter? Sleep 2014;37:9–17.
[11] Perez KM, Hamburger ER, Lyttle M, Williams R, Bergner E, Kahanda S, et al. Sleep in type 1 diabetes: implications for glycemic control and diabetes management. Curr Diabetes Rep 2018;18:1–8.
[12] Hazen RA, Fehr KK, Fidler A, Cousino MK, MacLeish SA, Gubitosi-Klug R. Sleep disruption in adolescents with Type 1 diabetes mellitus: relationships with adherence and diabetes control. Diabetes Manag 2015;5:257.
[13] Farabi SS. Type 1 diabetes and sleep. Diabetes Spectr 2016;29:10–3.
[14] Standards of medical care in diabetes-2017: summary of revisions. Diabetes Care 2017;40:S4–5.
[15] Eid B, Bou Saleh M, Melki I, Torbey PH, Najem J, Saber M, et al. Evaluation of

chronotype among children and associations with BMI, sleep, anxiety, and depression. Front Neurol 2020;11:416.
[16] von Schnurbein J, Boettcher C, Brandt S, Karges B, Dunstheimer D, Galler A, et al. Sleep and glycemic control in adolescents with type 1 diabetes. Pediatr Diabetes 2018;19:143–9.
[17] Frye SS, Perfect MM, Silva GE. Diabetes management mediates the association between sleep duration and glycemic control in youth with type 1 diabetes mellitus. Sleep Med 2019;60:132–8.
[18] Crowley SJ, Wolfson AR, Tarokh L, Carskadon MA. An update on adolescent sleep: new evidence informing the perfect storm model. J Adolesc 2018;67:55–65.
[19] Dong L, Martinez AJ, Buysse DJ, Harvey AG. A composite measure of sleep health predicts concurrent mental and physical health outcomes in adolescents prone to eveningness. Sleep Health 2019;5:166–74.
[20] Yeshayahu Y, Mahmud FH. Altered sleep patterns in adolescents with type 1 diabetes: implications for insulin regimen. Diabetes Care 2010;33:e142.
[21] Jaser SS, Lord JH, Simmons JH, Malow BA. Brief report: sleep disturbances in young children with type 1 diabetes. Diabetes Res Clin Pract 2016;120:232–4.
[22] Reutrakul S, Thakkinstian A, Anothaisintawee T, Chontong S, Borel A-L, Perfect MM, et al. Sleep characteristics in type 1 diabetes and associations with glycemic control: systematic review and meta-analysis. Sleep Med 2016;23:26–45.
[23] Erkuran HÖ, Yalin Sapmaz Ş, Herdem A, Ozturk M, Ö Bilaç, Önen Ö, et al. DSM-5 Düzey 2 Uyku Bozukluğu Ölçeği Türkçe Formunun Güvenirliği ve Geçerliği (11-17 yaş çocuk formu ve 6-17 yaş ebeveyn formu). Arch. Neuropsychiatry 2018;55:256–60.
[24] Zavada A, Gordijn MC, Beersma DG, Daan S, Roenneberg T. Comparison of the Munich chronotype questionnaire with the horne-östberg's morningness-eveningness score. Chronobiol Int 2005;22:267–78.
[25] Carskadon M, Vieira C, Acebo C. Association between puberty and a circadian phase delay. Sleep 1993;16:258–62.
[26] Dursun OB, Ogutlu H, Esin IS. Turkish validation and adaptation of children's chronotype questionnaire (CCTQ). Eurasian J. Med. 2015;47:56–61.
[27] Durmuş FB, Arman AR, Ayaz AB. Chronotype and its relationship with sleep disorders in children with attention deficit hyperactivity disorder. Chronobiol Int 2017;34:886–94.
[28] Meltzer LJ, Montgomery-Downs HE, Insana SP, Walsh CM. Use of actigraphy for assessment in pediatric sleep research. Sleep Med Rev 2012;16:463–75.
[29] Kushida CA, Chang A, Gadkary C, Guilleminault C, Carrillo O, Dement WC. Comparison of actigraphic, polysomnographic, and subjective assessment of sleep parameters in sleep-disordered patients. Sleep Med 2001;2:389–96.
[30] Fekedulegn D, Andrew ME, Shi M, Violanti JM, Knox S, Innes KE. Actigraphy-based assessment of sleep parameters. Annu. Work Expo. Health 2020;64:350–67.
[31] Farabi SS, Quinn L, Carley DW. Validity of actigraphy in measurement of sleep in young adults with type 1 diabetes. J Clin Sleep Med 2017;13:669–74.
[32] Ohayon M, Wickwire EM, Hirshkowitz M, Albert SM, Avidan A, Daly FJ, et al. National Sleep Foundation's sleep quality recommendations: first report. Sleep Health 2017;3:6–19.
[33] Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health 2015;1:233–43.
[34] Czerwoniuk D, Fendler W, Walenciak L, Mlynarski W. GlyCulator: a glycemic variability calculation tool for continuous glucose monitoring data. J Diabetes Sci Technol 2011;5:447–51.
[35] Wagner J, Tennen H, Wolpert H. Continuous glucose monitoring: a review for behavioral researchers. Psychosom Med 2012;74:356–65.
[36] Piona C, Dovc K, Mutlu GY, Grad K, Gregorc P, Battelino T, et al. Non-adjunctive flash glucose monitoring system use during summer-camp in children with type 1 diabetes: the free-summer study. Pediatr Diabetes 2018;19:1285–93.
[37] Danne T, Nimri R, Battelino T, Bergenstal RM, Close KL, DeVries JH, et al. International consensus on use of continuous glucose monitoring. Diabetes Care 2017;40:1631–40.
[38] Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care 2019;42:1593–603.
[39] Macaulay GC, Galland BC, Boucher SE, Wiltshire EJ, Haszard JJ, Campbell AJ, et al. Impact of type 1 diabetes mellitus, glucose levels, and glycemic control on sleep in children and adolescents: a case–control study. Sleep; 2019.
[40] ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 5. Facilitating positive health behaviors and well-being to improve health outcomes: standards of care in diabetes-2023. Diabetes Care 2023;46:S68–96.
[41] Adapp Committee. 14. Children and adolescents: standards of medical care in diabetes—2022. Diabetes Care 2021;45:S208–31.
[42] Lucassen EA, Zhao X, Rother KI, Mattingly MS, Courville AB, de Jonge L, et al. Evening chronotype is associated with changes in eating behavior, more sleep apnea, and increased stress hormones in short sleeping obese individuals. PLoS One 2013;8:e56519.
[43] Arora T, Taheri S. Associations among late chronotype, body mass index and dietary behaviors in young adolescents. Int J Obes 2015;39:39–44.
[44] Reutrakul S, Hood MM, Crowley SJ, Morgan MK, Teodori M, Knutson KL, et al. Chronotype is independently associated with glycemic control in type 2 diabetes. Diabetes Care 2013;36:2523–9.
[45] Silva RAE, Ganen AP, Fernandes VFT, Evangelista NMA, Figueiredo CC, Pacheco LA, et al. Evaluation of sleep characteristics of children and adolescents with type 1 diabetes mellitus. Rev. Paul Pediatr. 2021;40:e2020407.
[46] Orhon F, Ergin A, Topçu S, Çolak B, Almiş H, Durmaz N, et al. The role of social support on the relationships between internet use and sleep problems in adolescents during COVID-19 pandemic: a multicentre study. Child Adolesc Ment Health 2023;28:117–23.
[47] Rechenberg K, Griggs S, Jeon S, Redeker N, Yaggi HK, Grey M. Sleep and glycemia in youth with type 1 diabetes. J Pediatr Health Care 2020;34:315–24.
[48] Patel NJ, Savin KL, Kahanda SN, Malow BA, Williams LA, Lochbihler G, et al. Sleep habits in adolescents with type 1 diabetes: variability in sleep duration linked with glycemic control. Pediatr Diabetes 2018;19:1100–6.
[49] Perfect MM, Patel PG, Scott RE, Wheeler MD, Patel C, Griffin K, et al. Sleep, glucose, and daytime functioning in youth with type 1 diabetes. Sleep 2012;35:81–8.
[50] Brandt R, Park M, Wroblewski K, Quinn L, Tasali E, Cinar A. Sleep quality and glycaemic variability in a real-life setting in adults with type 1 diabetes. Diabetologia 2021;64:2159–69.
[51] Turner SL, Queen TL, Butner J, Wiebe D, Berg CA. Variations in daily sleep quality and type 1 diabetes management in late adolescents. J Pediatr Psychol 2016;41:661–9.
[52] Griggs S, Grey M, Strohl KP, Crawford SL, Margevicius S, Kashyap SR, et al. Variations in sleep characteristics and glucose regulation in young adults with type 1 diabetes. J Clin Endocrinol Metab 2022;107:e1085–95.
[53] Radan I, Rajer E, Ursic Bratina N, Neubauer D, Krzisnik C, Battelino T. Motor activity during asymptomatic nocturnal hypoglycemia in adolescents with type 1 diabetes mellitus. Acta Diabetol 2004;41:33–7.
[54] Pillar G, Schuscheim G, Weiss R, Malhotra A, McCowen KC, Shlitner A, et al. Interactions between hypoglycemia and sleep architecture in children with type 1 diabetes mellitus. J Pediatr 2003;142:163–8.
[55] Gómez AM, Muñoz OM, Marin A, Fonseca MC, Rondon M, Robledo Gómez MA, et al. Different indexes of glycemic variability as identifiers of patients with risk of hypoglycemia in type 2 diabetes mellitus. J Diabetes Sci Technol 2018;12:1007–15.
[56] Kostkova M, Durdik P, Ciljakova M, Vojtkova J, Sujanska A, Pozorciakova K, et al. Short-term metabolic control and sleep in children and adolescents with type 1 diabetes mellitus. J. Diabet. Complicat. 2018;32:580–5.
[57] Salah NY, Abido AY, Rashed HR. Relationship of glycaemic derangement using continuous glucose monitoring system with sleep pattern among children with type 1 diabetes. Diabetes. Metab. Res. Rev. 2021;37:e3407.