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Sleep quality and glycemic control in children and adolescents with type 1 diabetes mellitus

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Abstract. – OBJECTIVE: This study aimed to investigate the frequency of sleep disorders, and the relationship between glycemic control and sleep characteristics in diabetic children and adolescents.

PATIENTS AND METHODS: Sixty-one patients followed for at least one year for type 1 diabetes mellitus (T1DM) aged 6-16 years old, and eighty-three group-matched healthy controls were included in the study. Time in range (TIR) and hypoglycemia episode numbers were recorded using the freestyle libre sensor data. The sleep characteristics were evaluated using the Sleep Disturbance Scale for Children (SDSC) validated survey. The diabetic patients were trichotomized according to SDSC scores, as low, medium, and high score groups.

RESULTS: Sleep duration, SDSC total score, and subgroup scores except for sleep hyperhidrosis (3.11±1.53 *vs.* 2.16±0.85, $p<0.001$, respectively) were similar ($p>0.05$) between the diabetic and control group. According to the survey, 1.6% of diabetic cases and 6.1% of the control group had clinically significant sleep disturbances ($p>0.05$). Duration of diabetes (DD) was lower ($p=0.01$), and the level of HbA1C was higher ($p=0.02$) in the high-score group than the others. Regression analysis revealed that TIR was the only independent determinant for the SDSC score (β=-1.27, $t=-1.90$; $p=0.012$).

CONCLUSIONS: Sleep habits and problems should be routinely evaluated in diabetic children and adolescents.

Key Words:
Sleep disorder, Diabetes mellitus, Pediatrics, Hypoglycemia, Glycemic control.

Introduction

Type 1 diabetes mellitus (T1DM) is one of the most encountered chronic diseases in children and adolescents. Good metabolic control is essential in preventing acute and chronic complications in patients with T1DM. Healthy sleep has a crucial role in children's growth and development as a physiological activity. Researchers in diabetic patients were interested in sleep duration and sleep problems[1-7]. In the literature, sleep measurement methods varied, including questionnaires, polysomnographic (PSG) data, and actigraphic data[8]. It has been shown that sleep-related problems such as reduced neurocognitive functioning, daytime behavioral problems, difficulty initiating and maintaining sleep, longer sleep apnea syndrome, and night-time restlessness are more common in children with T1DM, and are associated with poor metabolic control[2,9-12]. Glycemic control and sleep quality may be bidirectional in diabetic patients. Sleep quality may deteriorate in diabetic children due to night-time hypoglycemia episode or parents' attempts to control blood sugar excessively[1]. On the other hand, poor diabetic control may also affect sleep[13]. This study aimed to compare sleep disturbances in children with and without T1DM and investigate the relationship between glycemic control and sleep characteristics.

Patients and Methods

This cross-sectional study was conducted in a tertiary-level hospital. Sixty-one patients followed for at least one year for T1DM aged 6-16 years old, and eighty-three group-matched healthy controls were included in the study. Those with chronic disease, obesity, chronic tonsillitis or a history of tonsillectomy, or a known sleep disorder were excluded from the study. Hypoglycemia and time in range (TIR) were defined as blood glucose level lower than 70 mg/dL[14] and between 70-180 mg/dL[15]. Percent time in range (TIR%) and hypoglycemia episode numbers from the last 14 days were recorded for all diabetic patients using the freestyle libre sensor data. Sleep disturbances were evaluated with the Sleep Disturbance Scale for Children (SDSC) questionnaire that was validated for Turkish children[16,17]. This questionnaire (SDSC), developed by Bruni et al[17] in 1996, is a Likert-type scale that in-

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vestigates sleep disturbances in the last 6 months, in children aged 6-16 years. It consists of 26 questions, and a 5-point Likert scale is used for each question (1=least severe and 5=most severe). There are six different domains of sleep; disorders of arousal (DA); disorders of excessive somnolence (DES); disorders of initiating and maintaining sleep (DIMS); sleep breathing disorders (SBD); sleep hyperhidrosis (SH); sleep-wake transition disorders (SWTD). As in the original scale, a T-score of >70 was considered clinically significant. Questionnaires were performed by a single interviewer. To investigate the effect of diabetes-related variables on the total score of the SDSC Questionnaire, the diabetic patients were trichotomized according to 33rd and 67th percentiles total score as fallow; low score group (1st-33rd percentile), medium score group (34th-66th percentile), and high score group (67th-100th percentile). The study protocol was approved by the Sivas Cumhuriyet University ethics committee (Date: 27.07.2022, Number: 2022-07/04). Following a thorough explanation of the research protocol, all children and their parents/guardians completed informed assent and consent forms, respectively.

Statistical Analysis

SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical calculations. Kolmogorov-Smirnov test used for investigating normality. Student *t*-test, Mann-Witney-U test, Kruskal-Wallis test, and the Chi-square test were used to evaluate associations between continuous or categorical variables, whichever is appropriate. Correlations between diabetes and sleep were estimated using the Pearson correlation coefficient analysis. Backward multiple regression was conducted to identify the effect of number of hypoglycemic attacks in the last 14 days, diabetes duration, daily insulin per kg, Hemoglobin A1 (HbA1C), and TIR % in predicting the total score of the questionnaire. Assumptions of linearity, normally distributed errors, and uncorrelated errors were checked and fulfilled. Values except gender were expressed as the mean±standard deviation (SD) or median (interquartile range); $p<0.05$ was considered statistically significant.

Results

Age, sex, body weight, body weight-SDS (standard-deviation-scores), height, height-SDS, body mass index (BMI), and BMI-SDS were similar ($p>0.05$) in the case and control groups (Table I). Sleep duration, SDSC total score, and subgroup scores except sleep hyperhidrosis were also comparable ($p>0.05$) (Table I). Sleep hyperhidrosis score was higher in the diabetic group than the control group (3.11±1.53 *vs.* 2.16±0.85, $p<0.001$, respectively). Diabetes duration, HbA1C, total daily insulin level, TIR, and number of hypoglycemia episodes in diabetic patients were given in Table I.

When the T score was accepted as >70, 4.2% of all study group had a clinically significant sleep disturbance score. This rate was 1.6% in diabetic cases and 6.1% in the control group ($p>0.05$). There was also no significant difference in SDSC scale subgroups ($p>0.05$). However, when the T score was >50, the frequency of SH (31.1% *vs.* 4.8%; $p<0.001$) and SBD (42.6% *vs.* 24.1%; $p=0.015$) was higher in the diabetic group (Table II).

There was a significant correlation between SDSC total score with HbA1c ($r=0.28$, $p=0.03$), and number of hypoglycemia episodes ($r=-0.33$, $p=0.01$) in the diabetic group. We also found a statistically significant correlation between TIR with Hba1c ($r=-0.46$, $p=0.01$), and the number of hypoglycemia episodes ($r=0.33$, $p=0.01$), as expecteded.

When the study group was divided into three groups according to a total score of SDSC questionnaire, age, sex, BMI-SDS, daily insulin per kg, TIR, and number of hypoglycemia episodes were similar between groups ($p>0.05$). However, the duration of diabetes was significantly lower ($p=0.01$), and the level of HbA1C was significantly higher ($p=0.02$) in the high-score group than the others (Table III).

Backward multiple regression was conducted to identify the effect of diabetes duration, number of hypoglycemic attacks in the last 14 days, daily insulin per kg, HbA1C, and TIR % in predicting total score of the questionnaire. TIR was the only variable that statistically significantly contributed to the final model ($\beta=-1.27$, $t=-1.90$; $p=0.012$).

Discussion

The main finding of the study was that poor glycemic control is related to poor sleep quality; the HbA1c level was higher in the group with higher SDSC total score and, the score was significantly associated with TIR evaluated by multiple regression analysis. Additionally, we showed that distribution of pathological T score (>70) according to SDSC survey was similar in children and adolescents with T1DM and non-diabetic controls. To the best of our knowledge, this is the first study showing that the TIR ratio is associated with sleep disturbance in children

Table I. Demographic data.

	Case group (n=61)	Control group (n=83)	p
Age, *year*	11.76±2.58	11.42±2.38	0.42
Sex (female %)	54.1	63.9	0.30
Body weight, *kg*	41.79±11.61	41.12±14.14	0.77
Body-weight-SDS	-0.26±1.17	-0.20±1.01	0.76
Height, *cm*	148.32±15.16	145.71±14.41	0.32
Height-SDS	-0.22±1.19	-0.25±1.03	0.87
BMI, kg/m^2	3±17	18±66	0.05
BMI-SDS	-0.18±1.07	-.04±0.93	0.13
SDSC Scores			
DIMS	11.70±3.65	12.32±5.17	0.40
SBD	4.04±1.96	3.61±1.59	0.15
DA	3.60±1.68	3.40±0.92	0.41
SWTD	9.24±3.59	9.64±3.86	0.52
DES	7.24±2.86	7.21±3.22	0.95
SH	3.11±1.53	2.16±0.85	<0.001
Total	38.96±12.77	38.23±10.28	0.70
Sleep duration (Hour)	8.37±1.23	8.46±1.16	0.73
Diabetes Duration, year	4.32±2.89	-	
HbA1c, %	8.82±1.92	-	
Daily insulin/kg, Unit	0.91±0.36	-	
TIR (%)		-	
<70 mg/dL	5.26±6.49	-	
70-180 mg/dL	35.80±18.96	-	
>180 mg/dL	58.93±20.52	-	
Number of Hypoglycemia *			
Day	1 (3)		
Night	1 (5)		
Total (Day and Nigh)	3 (7)		

DA, Disorders of Arousal; DES, Disorders of excessive somnolence; DIMS, Disorders of initiating and maintaining sleep; SBD, Sleep breathing disorders; SDSC, Sleep Disturbance Scale for Children; SH, Sleep hyperhidrosis; SWTD, Sleep-Wake Transition Disorders; TIR, Time in Range. * Median (Minimum of hypoglycemia of two weeks).

with T1DM. In addition, this is the first study to evaluate the SDSC questionnaire in Turkish children with T1DM. In this study, the original validity and reliability study for Turkish children, the total frequency of sleep disturbances and their components were comparable[16]. There are limited studies[2,7,18] in the literature evaluating sleep disorders in children with T1DM using the SDSC survey. Among these studies, Adler et al[18] showed that total SDSC scores for the T1DM and control groups were similar. However, the authors found a higher frequency of sleep disorders in T1DM cases than in our study. We think that the difference may be due to the accepted T score value (50 *vs.* 0). As a matter of fact, in our study, we found similar rates when score was accepted as >50 for sleep disorder risk. Additionally, they also suggested that SDSC score was significantly higher in those using continuous glucose monitoring (CGM) *vs.* glucose meters. In another study, Caruso et al[2] found that SDSC scores for total, DIMS, SWTD, and DES were higher in the diabetic group. However, in our study, only SH score was higher at T1DM. The higher SH score may be related to sympathetic hyperactivity due to glycemic variability.

The minimum sleep recommendations of The American Academy of Sleep Medicine (AASM)[8] are 9 hours per 24 hours for 6-12 years-old children and 8 hours per 24 hours for 13-18 years old teenager. In this study we found that self-reported sleep duration and percent of sufficient sleep duration were similar in diabetic and healthy controls. Similarly, Macaulay et al[19] showed that children and adolescents with T1DM and their

Table II. Distribution of pathological scores on the Sleep Disturbances Scale for Children Questionnaires scores between children with diabetes mellitus and healthy controls.

	Total	Case	Control	p
T score>70				
DIMS	6 (4.2%)	5 (1.6%)	5 (6.0%)	0.62
SBD	5 (3.5%)	2 (3.3%)	3 (3.6%)	0.91
DA	6 (4.2%)	3 (4.9%)	3 (3.6%)	0.77
SWTD	11 (7.7)	4 (6.6%)	7 (8.5%)	0.65
DES	5 (3.5%)	1 (1.6%)	4 (4.8%)	0.28
SH	3 (1.1%)	2 (3.3%)	1 (1.2%)	0.39
Total	6 (4.2%)	1 (1.6%)	5 (6.1%)	0.24
T score>50				
DIMS	55 (38.2%)	19 (31.1%)	36 (43.4%)	0.09
SBD	46 (31.9%)	26 (42.6%)	20 (24.1%)	0.015
DA	35 (24.3%)	16 (26.2%)	19 (21.9%)	0.39
SWTD	56 (39.2)	24(39.3%)	32 (39%)	0.55
DES	48 (33.3%)	24 (39.3%)	24 (28.9%)	0.12
SH	23 (16%)	19 (31.1%)	4 (4.8%)	<0.001
Total	46 (32.1%)	16 (26.2%)	30 (36.6%)	0.12

DA, Disorders of Arousal; DES, Disorders of excessive somnolence; DIMS, Disorders of initiating and maintaining sleep; SBD, Sleep breathing disorders; SH, Sleep hyperhidrosis; SWTD, Sleep-Wake Transition Disorders.

relatives without T1DM had similar sleep duration measured by PSG. However, in some other studies[9,10] sleep duration with polysomnography in diabetic adolescents was lower than controls. In a recent systematic review and meta-analysis, Reutrakul et al[3] showed that self-reported sleep duration was comparable in adults with T1DM and controls. One of the reasons for different results may be related to measuring methods and the different age groups. Self-reported and objectively measured sleep duration in the same cohort may be different[5].

There are conflicting results investigating sleep quality and glycemic control in diabetic patients. Most of the studies[3,20] suggested that there is no difference in Hba1c levels between good or poor sleep quality in adults. However, some studies[3,20,21] suggested that self-reported good sleep quality of pa-

Table III. Diabetic parameters according to trichotomized total score of the Sleep Disturbance Scale For Children questionnaire.

	Low Score Group	Medium Score Group	High Score Group	p
Age, year	12 (4.5)	12.5 (4.5)	13.50 (4.50)	0.28
Sex (female %)	68.2	50	42.1	0.21
BMI-SDS	-0.46 (2.38)	0.37 (0.64)	-0.19 (1.32)	0.36
Diabetes Duration, year	3 (3.5)	5.50 (2.8)	2.50 (2.8)	0.01 *
HbA1c, %	8.6 (1.9)	7.80 (1.40)	10.05 (2.83)	0.02 *
Daily insulin/kg, Unit	0.90 (0.42)	0.75 (0.47)	1.03 (0.43)	0.30
TIR (%)				
<70 mg/dL	4 (9)	3 (10)	2 (4)	0.13
70-180 mg/dL	38 (29)	40.50 (26)	29 (25)	0.18
>180 mg/dL	58 (59)	58.50 (22)	70 (22)	0.09
Number of hypoglycemia				
Day	2 (3)	1 (2)	0.50 (2)	0.09
Night	1 (5)	2 (9)	0 (2)	0.05
Total (Day and Night)	6 (6)	3.50 (13)	2 (3)	0.09

*Post hoc analysis (Tamhane) indicated that the differences arose from High score group.

tients with T1DM had lower Hba1c levels than those with poor sleep quality. Sleep stages were also evaluated in adults, it has been shown that those with well-controlled type 1 diabetes mellitus (Hba1c <7) have lower non-REM stage 2 duration and higher stage 3 duration, but the difference was not significant[1]. We found that HbA1c level was higher in the group with higher SDSC total score and, the score was significantly associated with TIR, evaluated by multiple regression analysis. Similarly, studies[22,23] in T1DM adolescents have shown that poor sleep quality is associated with increased HbA1c. In their study, Jaser et al[24] showed that sleep efficiency increased in adolescents included in the sleep-promoting intervention program, but they observed no change in Hba1c level. We did not find any association between sleep quality and nocturnal hypoglycemia episodes. It may be related to relatively small sample size. Similarly, Matyka et al[25] showed that profound hypoglycemia episode was not related to sleep quality. However, Griggs et al[13] showed that increased glucose variability and hypoglycemia episodes were associated with earlier waking, indicating worse sleep quality. Additionally, studies[6,9,25-27] have found that nocturnal hypoglycemia episodes in T1DM are associated with longer time in deep sleep (stage 3), as well as lower sleep efficiency.

Limitations

The study has some limitations: sleep duration and sleep disturbances were evaluated by standardized questionnaire[16] instead of objective measurements including polysomnography, actigraphy or wireless sleep monitor. Additionally, the relatively small sample size is another limitation.

Conclusions

Sleep habits and problems should be routinely evaluated in diabetic children and adolescents.

Ethics Approval

Ethics Committee Approval was obtained from Sivas Cumhuriyet University School of Medicine, Clinical Research Ethics Committee (Date: 27.07.2022, Number: 2022-07/04) and the principles of the Helsinki Declaration were followed.

Informed Consent

Written informed consent was obtained from the patients' first-degree relatives, after informing them about the study rationale and their right to withdraw from the study at any time without any consequences.

Availability of Data and Materials

The complete de-identified dataset is available from the corresponding author on a reasonable request.

Conflict of Interest

All authors declare that they do not have any competing.

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Authors' Contributions

EB: Planning, designing, data collection, literature survey. NC: Planning, designing, statistical analysis, interpretation of the results, writing, submission. All authors have agreed to conditions noted on the Authorship Agreement Form. The authors read and approved the final manuscript.

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