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The effect of glycemic control on sleep quality in type 2 diabetes mellitus

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ABSTRACT

Objectives: There are publications showing sleep quality is impacted in type 2 diabetes mellitus (T2DM) cases. In our study, we planned to assess the prevalence of sleep disorder in these patients compared to society, and investigate whether poor glycemic regulation and increased body mass index (BMI) caused disruption of sleep quality or not.

Methods: Sleep quality was compared between patients followed in our clinic with T2DM (n = 534) for minimum 5 years and a control group (n = 269). Assessment was performed for whether increased glycated haemoglobin (HbA1c) and increased BMI caused an increase in Pittsburgh Sleep Quality Index (PSQI) score or not. Cases with any comorbid disease or drug use affecting sleep quality were excluded from the study.

Results: T2DM patients had higher PSQI points compared to the control group. A statistically significant, very low-level positive correlation was identified between BMI measurements and PSQI scores (as BMI increased, PSQI increased). A statistically significant, very low-level positive correlation was identified between HbA1c measurements and PSQI scores (as HbA1c increased, PSQI increased). HbA1c measurements of those in the good sleep quality group were significantly lower compared to those in the moderate sleep quality and poor sleep quality groups. The BMI measurements in the poor sleep quality group were significantly higher than those in the good sleep quality group.

Conclusions: The sleep quality of T2DM cases was worse compared to the control group, while the increase in HbA1c level further disrupted sleep quality. The increase in BMI is another factor disrupting sleep quality in diabetic patients.

Keywords: Glycemic control, type 2 diabetes mellitus, sleep quality, glycated haemoglobin

Type 2 Diabetes Mellitus (T2DM) is a disease requiring continuous medical care, progressing with increased insulin resistance in the liver and muscles mainly [1]. If appropriate medical treatment is not received or necessary precautions not taken, a variety of microvascular and macrovascular complications develop associated with the disease in the long term. Apart from these well-known and defined complications, there are a range of diseases and situations lowering quality of life in T2DM. Negative changes in sleep quality is one of these.

The daily mean sleep duration recommended for adults is 7-9 hours [2]. Quality sleep assists in preserving mental health, physical health and quality of life. For the initiation and continuation of sleep, functions must occur in many cortical and subcortical brain re-

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gions. To initiate sleep, firstly, there must be cyclical stimuli from the pre-hypothalamus and the ventrolateral preoptic nucleus in the hypothalamus is accepted as playing a role in line with endogenous chemical stimuli. Sleep comprises two periods of rapid eye movement (REM) and non-rapid eye movement (NREM) [3]. Just as disruption in any of these systems may cause sleep disorder, it is necessary for these systems to operate flawlessly for quality sleep.

The circadian rhythm and sleep control important daily physiological situations for metabolic health. All sleep disorders like inadequate sleep, narcolepsy, short sleep, continuous insomnia, sleep apnea, circadian rhythm disruption, and shift work may contribute to metabolic disruption. Sleep disorders and circadian rhythm disorders associated with metabolic irregularity cause visceral fattening by changing the amount and time of food intake and changing and disrupting energy metabolism leading to inflammation, insulin resistance and glucose intolerance contributing to weight gain, obesity and T2DM. The importance of disruptions to the circadian rhythm and sleep disorders is understood by considering the rapidly increasing prevalence of metabolic diseases [4]. We aimed to compare the sleep quality of patients with T2DM diagnosis with the normal population and to research whether there was a correlation between glycemic regulation and sleep disorder frequency.

METHODS

The study was a prospective and controlled study performed between July 2021-October 2021. A total of 803 people, including 534 T2DM cases and 269 non-diabetic controls, who applied to the internal medicine polyclinic were included in the study. The diagnosis of diabetes was based on a previous diagnosis of T2DM or a random plasma glucose level of 200 mg/dL or higher, together with classic features of DM, such as polyuria, polydipsia, polyphagia and weight loss,or a fasting blood glucose level of > 126 mg/dL or glycated haemoglobin (HbA1c) levels of 6.5% or higher. The cases were included in the study with a diagnosis of T2DM for a minimum of 5 years. The control group included non-diabetic patients with similar sex and age distribution to the diabetic group. The demographic data, comorbid diseases patients were questioned and recorded. The Pittsburgh Sleep Quality Index (PSQI) was completed by the researcher, an internal medicine specialist, when consent was obtained from patients.

Exclusion criteria for the study groups were the existence of any comorbid diseases of congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, obstructive sleep apnea,; insomnia, neurodegenerative disease like alzheimer, dementia, parkinson; terminal period chronic disease or malignancy; receiving any treatment crossing the blood-brain barrier and disrupting sleep patterns (antihistaminic, antiepileptic, antidepressant use etc.), working shift work, Type 1 Diabetes Mellitus and pregnancy. Ethical committee approval was obtained for our study (Decision no: 2021/514/204/17).

Pittsburgh Sleep Quality Index

The PSQI was developed by Buysse *et al*. [5] and subjectively assesses sleep disorders. The PSQI is a scale about sleep difficulties examined in seven groups of subjective sleep quality, sleep duration, sleep latency, habitual sleep activity, sleep disorders, use of sleeping drugs and daytime function disorder. The re-

Table 1. Distribution of descriptive characteristics

	Data
Sex	
Female	465 (57.90)
Male	338 (42.10)
Age (years)	
Mean ± SD	55.82 ± 10.06
Median (Min-Max)	56 (22-89)
BMI (kg/m^2)	
Mean ± SD	29.09 ± 5.12
Median (Min-Max)	28 (19.10-43)
Glucose (mg/dL)	
Mean ± SD	131.72 ± 69.15
Median (Min-Max)	103 (76-490)
HbA1c (%)	
Mean ± SD	6.84 ± 2.07
Median (Min-Max)	6.40 (4.10-18.60)

SD = standard deviation

sponse to each component is given points from 0-3, and the general PSQI points from 0 to 21 are the total of the seven components. According to the points, patients are divided into 3 groups as those with points ≤ 5 in the good sleep quality group; PSQI 6-8 in the moderate sleep quality group and PSQI ≥ 9 in the poor sleep quality group. The PSQI is a subjective sleep quality assessment tool.

Statistical Analysis

For statistical analyses the Number Cruncher Statistical System (NCSS) 2007 program was used (Kaysville, Utah, USA). When assessing study data, descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used. The fit of quantitative data to normal distribution was tested with the Shapiro-Wilk test, graphical investigations and Mann-Whitney U test used for comparisons between two groups. For comparison of quantitative variables without normal distribution in more than two groups, Bonferroni correction, the Kruskal Wallis test and Dunn-Bonferroni test were used. Assessment of correlations between quantitative variables used the Spearman correlation analysis. Statistical significance was accepted as $p < 0.05$.

RESULTS

The research was performed with a total of 803 cases (534 T2DM, 269 controls) including 57.90% females (n = 465) and 42.10% males (n = 338) attending the internal diseases clinic from July 2021 to October 2021. The ages of the cases varied from 22 to 89 years, with mean age identified as 55.82 ± 10.06 years (Table 1).

The sleep duration questioned within the scope of the PSQI was mean 7.05 ± 4.32 hours in the T2DM group, while it was mean 4.76 ± 3.34 hours in the control group. According to groups, there were statistically significant differences in the Pittsburgh scores of cases ($p = 0.001$ and $p < 0.01$).

Points received by cases with T2DM on the PSQI were higher than points received by those in the control group, with the T2DM group having worse sleep quality. According to group, there were statistically significant differences identified between the sleep quality of cases ($p = 0.001$ and $p < 0.01$) (Table 2).

Those in the control group had higher good sleep quality rates, while those in the patient group had higher moderate and poor sleep quality rates. There was a positive (as BMI increased, PSQI score increased), statistically significant, very low level of correlation identified between the BMI measurements of participants with PSQI scores (r = 0.178; $p = 0.001$ and $p < 0.01$).There was a positive (HbA1c increased, PSQI score increased), statistically significant, very low level of correlation identified between HbA1c measurements of participants with PSQI scores (r = 0.217; $p = 0.001$ and $p < 0.01$) (Table 3).

There were statistically significant differences in sleep quality of cases according to BMI measurements ($p = 0.001$ and $p < 0.01$). With the aim of determining the source of the difference, two-way comparisons found the BMI measurements in the group with poor

Table 2. Assessment of PSQI according to groups

	DM patients	Control	*p value*
PSQI score			**[a]0.001****
Mean ± SD	7.05 ± 4.32	4.76 ± 3.34	
Median (Min-Max)	6 (0-21)	4 (1-19)	
Sleep quality, n (%)			**[b]0.001****
Good	237 (44.40)	203 (75.50)	
Moderate	119 (22.30)	42 (15.60)	
Poor	178 (33.30)	24 (8.90)	

PSQI = Pittsburgh Sleep Quality Index, SD = standard deviation
[a]Mann Whitney U Test, [b]Fisher Freeman Halton Test, **$p < 0.01$

Table 3. Correlation of PSQI points with BMI and HbA1c

		PSQI
BMI (kg/m^2)	r	0.178
	p value	**0.001****
HbA1c (%)	r	0.217
	p value	**0.001****

PSQI = Pittsburgh Sleep Quality Index, BMI = Body Mass Index, HbA1c = Glycated haemoglobin glycated haemoglobin r = Spearman Correlation Coefficient

sleep quality were significantly higher compared to those in the group with good sleep quality ($p = 0.001$ and $p < 0.01$). According to HbA1c measurements, there were statistically significant differences identified for the sleep quality of cases ($p = 0.001$ and $p < 0.01$). Two-way comparisons performed with the aim of determining the source of the difference found the HbA1c measurements in the group with good sleep quality were significantly lower compared to those with moderate sleep quality and with poor sleep quality ($p = 0.001$, $p = 0.001$ and $p < 0.01$) (Table 4).

DISCUSSION

Our study researching the effect of T2DM on sleep quality and whether there is a connection between HbA1c and PSQI score indicates that patients with T2DM diagnosis had higher PSQI scores than the control group. Rajendran *et al*. [6] identified mean PSQI score as 7.08 in a study including 120 T2DM cases, and while this situation was associated with poor sleep quality in T2DM, the same study did not observe a correlation between HbA1c and PSQI scores. Cho *et al*. [7] found 49% had poor sleep quality among 614 individuals with T2DM, while HbA1c levels were not associated with poor sleep quality. Telford *et al*. [8] could not form a correlation between HbA1c levels with sleep quality in a study of 279 T2DM cases. However, Tang *et al*. [9] showed weak glycemic control among those with inadequate sleep in a study investigating 551 cases with T2DM diagnosis. A study by Zhu *et al*. [10], similarly, found an inverse correlation between high HbA1c level with sleep quality, with individuals with HbA1c of 7% and above having significantly higher PSQI scores. Bener *et al*. [11] showed that individuals with HbA1c level 7% and below had better sleep quality compared to individuals with levels above 7% in a study investigating 871 T2DM cases. Tsai *et al*. [12] identified a significant correlation between HbA1c level with PSQI score among 46 T2DM cases. They showed a very strong statistically significant correlation between increased HbA1c level and poor sleep quality in T2DM cases. Cappuccio *et al*. [13] showed sleep quality was consistent in predicting T2DM development risk in a meta-analysis including 10 studies and 3586 T2DM cases. As mentioned in the article, while studies by Rajandran *et al*. [6], Cho *et al*. [7] and Telford *et al*. [8] did not show a correlation between poor sleep quality and HbA1c, Tang *et al*. [9], Zhu *et al*. [10], Bener *et al*. [11] and Tsai *et al*. [12] showed a correlation between poor sleep quality and poor glycemic index, as

Table 4. Assessment of sleep quality according to BMI and HbA1c measures

	Sleep Quality			*p value*
	Good	**Moderate**	**Poor**	
BMI (kg/m^2)				**[c]0.001****
Mean ± SD	28.40 ± 5.00	29.32 ± 5.10	30.41 ± 5.15	
Median (Min-Max)	27.20 (19-53)	28.50 (20-47)	30.50 (19-46)	
HbA1c (%)				**[c]0.001****
Mean ± SD	6.55 ± 2.12	7.06 ± 1.96	7.30 ± 1.99	
Median (Min-Max)	5.80 (3.90-16.30)	6.60 (3.90-13.60)	6.80 (4.70-18.60)	

BMI = Body Mass Index, HbA1c = Glycated haemoglobin glycated haemoglobin
[c]Kruskal Wallis Test, **$p < 0.01$

illustrated in our study. Experimental studies support our study results. A variety of studies showed that ≤ 6 hours sleep was associated with glucose intolerance and insulin resistance [14], increased diabetes incidence [15, 16] and high diabetes risk [17]. A meta-analysis investigating 12 studies reported that the pooled probability rate was 1.09 between exposure to shift work and diabetes risk [18]. Buxton *et al*. [19] showed a relative reduction in insulin sensitivity following circadian misalignment and sleep loss in cases with 5.6 hours sleep limitation in 24 hours during experimental studies with 45 cases. T2DM is a disease causing disruption of sleep quality. At the same time, low level of correlation was observed between HbA1c level with PSQI score. The HbA1c values in the group with good sleep quality were identified to be significantly lower compared to the group with poor sleep quality. It appears that sleep quality is disrupted by a significant level after T2DM has developed. These are the most powerful results obtained from our study. Just as there are studies supporting our results, there are publications that are not in line with our results.

Additionally, another result obtained in our study was between poor glycemic control and BMI. There were statistically significant differences observed between sleep quality of cases according to BMI measurements and two-way comparisons to determine the source of this difference identified that BMI measurements in the group with poor sleep quality were significantly high compared to those in the group with good sleep quality. Similarly, a study investigating 1031 cases showed a correlation between poor sleep index and high BMI, with high BMI causing a reduction in sleep duration [20]. A study by Vargas *et al*. [21] including 515 participants identified that 51% of individuals with BMI > 25 kg/m2 had PSQI score above 5moderate or poor sleep quality. In reducing the sleep quality of BMI; increased sympathetic activity, changes in cortisol, leptin and ghrelin levels and insulin resistance have beel suggested as factors explaining this relationship [22].

In our study, the median BMI value was 28 kg/m^2, and T2DM and obesity frequently accompany each other. Just as glycemic outcomes in T2DM may cause disrupted sleep quality, we think increased BMI may contribute to disruption of sleep quality. The results of our study support this idea.

The results of our study are consistent with the general literature results in terms of both T2DM-sleep quality and BMI-sleep quality. Strong aspects of our study are the adequate case numbers, balanced distribution of age and sex in the case and control groups, assessment of patient BMI, exclusion criteria (especially apnea, OSAS, CAD), confirmation of results with two-way statistical comparisons, assessment by a single internal diseases specialist when completing case assessment and PSQI index in the clinical section of the study and standardization specific to the study by using the subjective PSQI index. Apart from experimental studies, no study investigating T2DM-sleep quality included a non-diabetic control group and generally compared the T2DM group with nondiabetic population when investigating the relationships with HbA1c and PSQI score. All these reasons make our study unique and valuable.

Limitations

In spite of being able to assess glycemic fluctuations and especially nighttime hypoglycemia with continuous glucose monitoring (CGM), CGM is not sufficiently common or easily accessible in our country. For this reason, the presence of nocturnal hypoglycemia cannot be excluded. Though it may be considered that some of our patients were controlled according to HbA1c level, a significant portion of these cases experienced proven severe hypoglycemia. We think glycemic fluctuations reduce sleep quality. OSAS is generally an obesity problem, and our study excluded those with diagnosis of cases describing apnea. Though not a practical approach, exclusion of OSAS among our cases without a polysomnographic study by a chest diseases expert is a limitation.

CONCLUSION

In conclusion, we identified a positive low level significant correlation between HbA1c level with PSQI score. Our T2DM cases had significantly high PSQI scores, and poor sleep quality. Diabetic patients should be questioned about sleep quality and those with advanced sleep disorder should be assessed in detail. It should be considered that low sleep quality is both a cause and an outcome in uncontrolled DM patients.

After better glycemic control in diabetic patients with regulated treatment, repeated sleep scales may further explain this topic.

Authors' Contribution

Study Conception: ZK, BB, SA, ÖK, NA; Study Design: ZK, BB, SA, ÖK, NA; Supervision: ZK, BB, SA, ÖK, NA; Funding: ZK; Materials: ZK; Data Collection and/or Processing: ZK; Statistical Analysis and/or Data Interpretation: ZK; Literature Review: ZK; Manuscript Preparation: ZK and Critical Review: ZK.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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