Assessment of Sleep Quality in Patients with Type 2

Diabetes Mellitus: A Case-control Study

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ABSTRACT

Sleep disorders increase risk for impaired glucose tolerance, insulin resistance, and type 2 diabetes mellitus through changes in hormone release involved in energy homeostasis; on the other hand, complications occurring in patients with type 2 diabetes mellitus also lead sleep disorders. In the present study, it was aimed to assess sleep quality in patients with type 2 diabetes mellitus.

The study included 40 patients (aged 18-65 years) diagnosed as type 2 diabetes mellitus (21 women; 19 men) and 42 healthy controls (26 women; 16 men). The data were collected using demographic data sheet, Pittsburgh Sleep Quality Index (PSQI) in this case-control study.

In patients with type 2 diabetes mellitus, total PSQI score and component scores for sleep duration, sleep disturbance, use of sleep medication and daytime dysfunction were significantly higher when compared to controls. In addition, the proportion of patients with poor sleep quality was significantly higher in the patients with type 2 diabetes mellitus compared to controls (82.5% vs. 59.5%; χ^2 = 5.224, p=0.022). The age and body mass index were higher in patients with type 2 diabetes mellitus compared to controls.

It was found that sleep quality was poorer in patients with type 2 diabetes mellitus. It is important to identify problems that may result from sleep disorders and adverse effects of type 2 diabetes mellitus on sleep quality. To achieve glucose control in patients with type 2 diabetes mellitus, it is essential to improve sleep quality in addition to current approaches used in clinical practice.

Keywords: Sleep quality, Pittsburgh Sleep Quality Index, type 2 diabetes mellitus

Introduction

Although sleep is one of the primary physiological needs for maintaining well-being, sleep disorders have become a common problem due to living conditions, physiological and psychological problems (1, 2). It has been reported that sleep disorders are common in type 2 diabetes mellitus (T2DM) (3-6). It is also known that, in case of insufficient sleep duration, the risk for obesity, hyperglycemia and insulin resistance is increased due to alterations in release of hormones involved in energy metabolism (7-10). The impaired sleep quality and excessive sleep have negative effects on glucose metabolism. In previous studies, it was shown that, despite adequate sleep duration, changes in sleep quality also increase risk for impaired glucose tolerance and are also associated with insulin resistance and glucose metabolism (11, 12); in addition, both prolonged and shortened sleep duration is associated with T2DM

and sleep duration <6 hours or \geq 9 hours increases risk for T2DM (13,14). In many studies, it was found that sleep duration leads impaired glucose metabolism and that irregular sleep pattern (manifest as delayed sleep and awake time) plays role in the onset of abnormal eating behaviors by affecting glucose metabolism adversely and playing an important role in the pathophysiology T2DM (15-18).The impaired glucose of metabolism resulting from sleep disorders is associated with neurohormonal changes. In case of sleep disorder, there is an increase in sympathetic activity and cortisol level with decreased growth hormone. Neuropathic pain, diabetic foot ulcers and sleep apnea also lead impaired sleep efficiency and quality, resulting in a vicious cycle by further disrupting glycemic control via inadequate sleep (2). Thus, it is important to identify problems caused by sleep disorders and changes in the sleep quality in patients with diabetes mellitus.

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In the present study, it was aimed to assess sleep quality in patients diagnosed as T2DM and to compare with healthy controls.

Materials and Methods

Study Design and Ethic Statement: This casecontrol study was conducted between July, 2019 and February, 2020. The study was approved by Local Ethics Committee (approval#2017-KAEK-189-2019.08.21-01). All patients gave written informed consent before participation. The study was conducted in accordance to Helsinki Declaration.

Study Population: This study included patients with type 2 diabetes mellitus presented to internal medicine outpatient clinic. The inclusion criteria were age, diagnosis of type 2 diabetes mellitus, absence of known physical or psychiatric disease, absence of diseases that may cause sleep disorders and no drug use other than anti-diabetic agents. Exclusion criteria were known sleep disorder, alcohol or substance abuse, pregnancy and lactation. The control group was selected among patients presented to internal medicine outpatient clinic. Overall, 40 patients with diabetes mellitus and 44 healthy cases (controls) were included to the study.

Data Collection Tools: Data were collected using a socio-demographic data sheet and Pittsburgh Sleep Quality Index (PSQI). Data regarding weight, height, HbA1c and fasting blood glucose (FBG) were retrospectively gathered from internal medicine outpatient clinic records. Body mass index (BMI) was calculated as weight (kg) divided by height square (m²) and classified as follows: lean, <18.5 kg/m²; normal weight, 18.5-24.9 kg/m²; overweight, 25.0-29.9 kg/m²; and obese, >30.0 kg/m².

Socio-demographic Data Sheet: It was developed by researchers and included 10 items about age, gender, educational status, marital status, height, weight, and medication.

Pittsburgh Sleep Quality Index: The Pittsburgh Sleep Quality Index (PSQI) was developed by Buysse et al. (20). The Turkish validity and reliability study was proven by Agargün et al. [21]. PSQI is a 19-item, self-rated scale, which assess sleep quality and disorder within prior month. PSQI includes 24 questions, 19 of which are rated by subject and 5 of which are rated by sleep partner. The scale includes 7 components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, and sleep disorders, use of sleep medication and daytime dysfunction. Each component is rated by a 4-points scale (0-3). Sum of component scores gives total PSQI score (0-21). Higher scores indicate poorer sleep quality. Total PSQI score>5 indicates clinically relevant, poor sleep quality.

Data Analysis: Data were analyzed using SPSS version 22.0. Normal distribution of data was Shapiro-Wilk The assessed using test. relationships between categorical variables were examined with Chi-square test. For correlation analyses, Pearson's correlation coefficient was used for normally distributed variables while Spearman's correlation for non-normal distributed data. Mean values were compared using Independent samples t test between groups with normal distribution and using Mann Whitney U test between groups with skewed distribution. Logistic regression analysis was used to determine effects of age, BMI, HbA1c and FBG on sleep quality while multiple regression analysis was used to determine effects of age, BMI, HbA1c and FBG on PSQI scores. A p value <0.05 was considered as statistically significant.

Results

The study included 40 patients with type 2 diabetes mellitus and 42 controls. There were 21 women (52.5%) and 19 men (47.5%) in the T2DM group whereas 26 women (61.9%) and 16 men (38.1%) in the control group. Mean age was 50.4 ± 1.8 years in the study population while it was T2DM 61.05±9.61 years in group and 40.33 ± 16.46 years in the control group. Mean age, FBG and HbA1c level, BMI and total PSQI scores were significantly higher in the patient group when compared to control (Table 1). In the post hoc power analysis, it was found that study had power of 0.93 with effect size of 0.750 at alpha level of 0.05.

As seen in Table 2, PSQI component 3 (sleep duration), 5 (sleep disturbance), 6 (use of sleep medication) and 7 (daytime dysfunction) scores were significantly higher in the patient group as compared to controls.

There was a positive correlation between PSQI scores and age, BMI and HbA1c levels, indicating an increase in PSQI scores by increasing age, BMI and HbA1c (Table 3).

As seen in Table 4, an increase of one unit in HbA1c level resulted in 2.37-folds worsening in sleep quality.

	Patient	Control	Compa	rison
	(n: 40)	(n: 42)	t+	р
			(df: 80)	
Age	61.05±9.61a	40.33±16.46	6.997	0,001
FBG	147.59±57.70 a	96.67±23.95	5.172	0,001
HbA1c	8.37±2.69a	5.54 ± 0.70	6.454	0,001
BMI	32.34±6.38	26.92 ± 5.35	4.169	0,001
PSQI	9.50±4.20 a	6.79 ± 2.96	3365	0,001
Gender			χ^{2++}	р
Female	21 (52.5%)	26 (61.9%)	0.406	0.503
Male	19 (47.5%)	16 (38.1%)		
Sleep quality			χ^{2++}	р
Good	7 (17.5%)	17 (40.5%)	5.224	0.022
Poor	33 (82.5%) a	25 (59.5%)		

Table 1. Comparison of age, FBG, HbA1c, BMI and PSQI scores between patients with type 2 diabetes mellitus and controls

*Independent samples t test, ** Chi-square test, FBG: Fasting blood glucose, HbA1C: Hemoglobin A1C, BMI: Body mass index, PSQI: Pittsburgh Sleep Quality Index

^a Significantly higher as compared to controls

Table 2. Comparison PSQI components between patients with type 2 diabetes mellitus and com	ntrols
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	Patient	Control	Compa	Comparison+	
	(n:40)	(n:42)	Z	р	
	Median (Mean Rank)	Median (Mean Rank)			
Component 1	1 (44.61)	1 (38.54)	-1.244	0.213	
Component 2	2 (45.00)	2 (38.17)	-1.379	0.168	
Component 3	0 (47.13)a	0 (36.14)	-2.775	0.006**	
Component 4	0 (43.68)	0 (39.43)	-1.421	0.155	
Component 5	2 (49.45)a	1.5 (33.93)	-3.530	0.001**	
Component 6	0 (46.45)a	0 (36.79)	-2.405	0.016*	
Component 7	2.5(50.05)a	2 (33.36)	-3.364	0.001**	

+Mann-Whitney-U Test

Component 1: Subjective sleep quality Component 2: Sleep latency Component 3: Sleep duration Component 4: Sleep efficiency Component 5: Sleep disturbance Component 6: Use of sleep medication Component 7: Daytime dysfunction, ^a Significantly higher compared to controls

As seen in Table 5, multiple regression analysis showed that advancing age contributed to increase in PSQI score by 18.6%.

Discussion

In our study, total PSQI score was higher in the patient group when compared to controls. The proportion of patients with poor sleep quality was higher in the patient group than controls. The advancing age explained 18.6% of increase in PSQI score. The sleep quality was worsened by 2.37 folds per unit increase in HbA1c level.

In our study, mean age was significantly higher in the patient group than controls (Table 1). In a

study on diabetic patients, it was reported that mean PSQI scores were comparable among age groups (22). In a study by Öztürk et al., sleep quality was reported as poor by 62.2% of individuals' aged 60-74 years and by 53.1% of individuals' aged ≥ 75 years (16). In a longitudinal follow-up study by Björkleund et al., sleep complaints were periodically followed over 32 years and authors found that sleep complaints were increased in all age groups over time (4). Although it has been suggested that advanced age is associated with poor sleep quality (23), it is well-known that the risk for chronic diseases such as diabetes mellitus is also increased by advancing age.

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	Age		BMI		PSQI	
	r	р	r	р	r	р
Age	-	-	-	-	0.345	0.001**
BMI	0.414	0.001**	-	-	0.221	0.046*
FBG	0.410	0.001**	0.253	0.022*	-0.020	0,452
HbA1C	0.556	0.001**	0.414	0.001**	0.388	0.001**

Table 3. Correlation between slee	o quality and age	BMI, FBG and HbA1c ^a
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^aSpearman's correlation analysis, BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c, PSQI: Pittsburgh Sleep Quality Index

Table 4. Effects of as	ge, BMI, HbA1c	and FBG on im	pairment in sleer	o quality: L	ogistic regres	ssion analysis
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	В	Wald	OR	95 % CI for OR		р
				Lower	Upper	
Age	-0.18	0.960	0.982	0.947	1.018	0.327
HbA1c	0.866	4.545	2.376	1.072	5.266	0.033
FBG	-0.016	1.596	0.985	0.961	1.009	0.206
BMI	0.054	1.021	1.055	0.951	1.1172	0.312

OR: Odds ratio, BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c

In our study, mean FBG level was found as 147.59 ± 57.70 mg/dL and mean HbA1c level as $8.37\pm2.69\%$. The mean FGB and HbA1c levels were significantly higher in the patient group when compared to controls.

In a study on patients with T2DM, Livia et al. reported higher mean HbA1c and blood glucose levels in diabetic patients compared to controls in agreement with our study (5, 25).

In our study, mean BMI value was 32.34 ± 6.38 in the patient group and significantly higher than controls.

In the literature, it has been suggested that the relation between obesity and diabetes mellitus is associated with insulin resistance and that hyperinsulinemia and that insulin resistance are primary mechanisms underlying type 2 diabetes mellitus. Lipotoxicity is another mechanism proposed to explain mechanistic interaction between obesity and diabetes mellitus development. It was proposed that excessive triglyceride accumulation at muscles, liver and pancreas islet cells causes dysfunction of the cells (25). In our study, significantly higher mean BMI value in the patient group can be attributed to above-mentioned changes occurring in type diabetes mellitus.

In our study, it was found that the proportion of patients with higher total PSQI score and poor

sleep quality was significantly higher in the patient group than controls.

In a study on patient with T2DM, Fiorentini et al. found that poor sleep quality was more common that good sleep quality among patients (26). In another study on patients with T1DM or T2DM, it was found that total sleep quality score was higher while sleep quality was poorer in patients with T2DM compared to those with T1DM (27) Our results are in agreement with literature suggesting that sleep disorders are prevalent among diabetic patients (27).

In our study, we evaluated 7 components of PSQI in all subjects. The sleep duration (component 3) was significantly higher in the patient group than controls.

In previous studies, it has been suggested that changes in sleep duration and irregular sleep patterns had negative effect on glucose metabolisms (15, 17). Moreover, it has been also suggested that impaired sleep quality and oversleep negatively affect glucose metabolisms and that alterations in sleep quality is associated with impaired glucose tolerance, insulin resistance and glucose metabolism despite sufficient total sleep duration (11, 12). Tare et al. reported that shorter or longer duration of sleep is associated with T2DM (13) while Pyykkönen et al. reported that sleep duration <6 hours of >9 hours led

Table 5. Effects of age, BMI, HbA1c and FBG on PSQI scores: Multiple regression analysis

	Ba	Std. Error	β^{b}	t	р
Age	0.075	0.028	0.331	2.632	0.010
HbA1c	0.210	0.229	0.131	0.915	0.363
FBG	0.002	0.011	0.020	0.146	0.884
BMI	0.024	0.073	0.041	0.335	0.738

B^a: non-standardized regression coefficient, β^b: standardized regression coefficient,

BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c, PSQI: Pittsburgh Sleep Quality Index

increased risk for T2DM (14). Based on our results together with studies reported in the literature, it can be concluded that changes in the glucose metabolism have negative effect on both sleep duration and quality in type 2 diabetes mellitus.

In our study, sleep disturbance level (component 5) was found to be significantly higher in the patient group as compared to controls.

The sleep disturbance was found in 33.7% of patients with diabetes mellitus in the study by Sridhar and Madhu (28) and in 34% of patients with diabetes mellitus in the study by Gunes et al. (22). Thus, it is expected that sleep disturbance can also occur as a result of poor sleep quality in patients diabetes mellitus.

In a study involving patients with T1DM or T2DM, it was reported that patients with T2DM used more sleep medication and there was a positive correlation with use of sleep medication and PSQI scores. In our study, use of sleep medication (component 6) level was significantly higher in the patient group than controls in agreement with literature.

Similarly, in our study, there was a significant difference in daytime dysfunction (component 7) level between groups, which was originated from patient group.

In a study on diabetic patients, it was found that 41.2% of patient experienced daytime dysfunction during prior month and that 42.3% experienced daytime dysfunction in less than one occasion per week (22). In a study by Öztürk et al., it was found that only 29.3% of patients felt sleepy after wake up (16). On contrary to our study, these findings indicate that the patients less frequently experienced daytime dysfunction due to sleep disorder.

In our study, there was a positive correlation between PSQI level and age, BMI and HbA1c level (Table 3), indicating an increase in PSQI level by increasing age, BMI and HbA1c level.

In the literature, it has been suggested that, by advancing age, several changes occur in sleep pattern; that sleep disorders including problems in sleep latency and maintaining sleep, awakening early at morning, excessive daytime sleepiness become more common; and that sleep quality is negatively affected (30, 31). The increase in PSQI score by advancing age in our study may be explained above-mentioned findings.

In a study on patients with heart failure by Gökçe et al., it was shown that sleep quality score was higher in patient with BMI>30 kg/m² when compared to remaining groups, suggesting that sleep quality is positively correlated with BMI (32). In a study by Altın et al., it was found that sleep quality was poor in 66.7% of lean patients whereas in 38.3% of those with normal weight, 52.9% of obese patients and 75.0% of morbid obese patients, indicating a significant difference (33). Likewise, in another study, it was reported that 81.3% of obese individuals had poor sleep quality (34). In our study, PSQI score was increased by increasing BMI in agreement with literature.

In logistic regression analysis, the effect size of age, BMI, HbA1C and FBG on worsening of sleep quality, it was found that the effect size was 0.9 for age, 0.98 for FBG and 1.05 for BMI. It was also found that sleep quality was significantly worsened by 2.37-folds per unit increase in HbA1c.

In a study on adolescents with T1DM, there was no significant correlation between HbA1c and sleep quality score, however patients with poor sleep quality had higher mean HbA1c value (35). In a German study on adolescents with T1DM, it was shown that HbA1c was decreased by 1.1 mmol/mol per one point increase in sleep quality (36).

In a study on patients with T2DM, it was reported that mean HbA1c level was higher in patients with poor sleep quality; that there was a significant positive correlation between HbA1c and total PSQI score; and that sleep quality was impaired by increasing HbA1c level (37). In a study on patients with T2DM, Rajendran et al. found mean HbA1c level as $8.52\pm2.07\%$ with no significant correlation between HbA1c level and PSQI score (38). In a study by Yüksel et al., mean HbA1c level was found as $7.5\pm1.7\%$ with no significant difference between poor and good sleep quality groups (25).

Based on literature, the impaired sleep quality has negative effect on glucose metabolism and elevated HbA1c level indicates poor glucose control. In uncontrolled diabetes mellitus, it is more likely to experience incident acute and chronic complications (39). Thus, it should be suggested that sleep quality is adversely affected by increasing HBA1c.

In conclusion, many studies have shown that sleep and sleep disorders are important factors in control of blood glucose; in addition, it is also known that diabetes mellitus can lead sleep disorders.

In our study, it was found that sleep quality was poorer in diabetic patients and that there was a significant association between diabetic symptoms and sleep quality. To identify adverse effects caused by sleep disorders and impairment in sleep quality in diabetic patients, to determine adverse effects of diabetes mellitus on sleep quality can contribute evaluation of sleep status in all patients with meeting need for sleep and prevention of sleep disorders in diabetes mellitus.

In addition, it is recommended to include factors having negative influence on sleep quality in type 2 diabetes mellitus sleep-related issues into diabetes mellitus guidelines.

Study Limitations: This study has some limitations. Firstly, it was conducted in a single center. Secondly, our sample was relatively smaller; thus, our results cannot be generalized. In addition, we used a self-rated scale without polysomnography studies to evaluate sleep quality. However, comparison with healthy individuals can provide better understanding about results obtained in patients with type 2 diabetes mellitus. Further multi-center studies with larger sample size are needed.

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