Effects of Sleep Disorders on Hemoglobin A1c Levels in Type 2 Diabetic Patients

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Abstract

Background: Studies have reported the presence of sleep disorders in approximately 50–70% of diabetic patients, and these may contribute to poor glycemic control, diabetic neuropathy, and overnight hypoglycemia. The aim of this study was to determine the frequency of sleep disorders in diabetic patients, and to investigate possible relationships between scores of these sleep disorders and obstructive sleep apnea syndrome (OSAS) and diabetic parameters (fasting blood glucose, glycated hemoglobin A1c [HbA1c], and lipid levels).
Methods: We used the Berlin questionnaire (BQ) for OSAS, the Epworth Sleepiness Scale (ESS), and the Pittsburgh Sleep Quality Index (PSQI) to determine the frequency of sleep disorders and their possible relationships with fasting blood glucose, HbA1c, and lipid levels.
Results: The study included 585 type 2 diabetic patients admitted to family medicine clinics between October and December 2014. Sleep, sleep quality, and sleep scores were used as the dependent variables in the analysis. The ESS scores showed that 54.40% of patients experienced excessive daytime sleepiness, and according to the PSQI, 64.30% experienced poor-quality sleep. The BQ results indicated that 50.20% of patients were at high-risk of OSAS. HbA1c levels correlated significantly with the ESS and PSQI results ($r = 0.23$, $P < 0.001$ and $r = 0.14$, $P = 0.001$, respectively), and were significantly higher in those with high-risk of OSAS as defined by the BQ ($P < 0.001$). These results showed that HbA1c levels were related to sleep disorders.
Conclusions: Sleep disorders are common in diabetic patients and negatively affect the control of diabetes. Conversely, poor diabetes control is an important factor disturbing sleep quality. Addressing sleep disturbances in patients who have difficulty controlling their blood glucose has dual benefits: Preventing diabetic complications caused by sleep disturbance and improving diabetes control.

Key words: Hemoglobin A1c; Obstructive Sleep Apnea Syndrome; Sleep Disorders; Type 2 Diabetes Mellitus

Introduction

Diabetes mellitus is a chronic metabolic disorder caused by deficiency and/or ineffectiveness of insulin. With its increasing frequency of acute and chronic complications and its increasing morbidity and mortality, diabetes has caused a considerable loss of labor and exerted a heavy economic burden on society. Sleep disorders are described as disturbances in falling asleep or staying asleep and the having nonrestful sleep. Epidemiological studies have suggested that sleep disorders are common in society.[1,2] Sleep disorders can lead to important negative consequences: Adversely affecting lives by impairing school or business performance, marriage, etc., Studies have reported the presence of sleep disorders in approximately 50–70% of diabetic patients.[3]

Sleep disorders in diabetic patients may contribute to poor glycemic control, diabetic neuropathy, and

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overnight hypoglycemia. Studies have revealed that there is a bidirectional relationship between sleep disorders and diabetes: Diabetes may cause sleep disorders, while sleep disorders may also complicate the control of diabetes. Shorter or longer duration of sleep can increase the complication rate.[4-6]

The presence of sleep disturbances is a factor in increasing the rate of complications in chronic diseases.[5,7] The prevalence of obstructive sleep apnea syndrome (OSAS) is directly proportional to age and weight and occurs frequently in diabetic patients. Approximately 36–60% of diabetics are reported to experience OSAS. Increased severity of OSAS has been reported to increase glycated hemoglobin A1c (HbA1c) levels.[3,8-10] This study aimed to determine the frequency of sleep disorders in diabetic patients by using the Berlin questionnaire (BQ) for OSAS, the Epworth Sleepiness Scale (ESS), and the Pittsburgh Sleep Quality Index (PSQI) and to investigate possible relationships between scores of these sleep disorders and OSAS and the diabetic parameters (fasting blood glucose, HbA1c, and lipid levels).

Methods

Patients

This study included 585 type 2 diabetic patients admitted to family medicine clinics between October and December 2014. Inclusion criteria were: (1) the diagnosis of type 2 diabetes mellitus and (2) aged over 18 years. Type 1 diabetic patients were excluded. Five hundred and ninety-six patients were originally included, but 11 patients with known sleep disturbances (OSAS) under treatment were excluded. Ethical approval was obtained from Ethics Committee of Turgut Özal Medical Center Clinical Research, Inonu University. All patients provided informed consent prior to their participation in the study.

Demographic characteristics (age, gender, weight, height, smoking, and drugs used) were recorded. The patients' complete blood counts, liver function tests, and thyroid-stimulating hormone values were within normal limits.

Blood samples

Routine blood analysis included parameters of diabetes control (HbA1c, fasting blood glucose, and lipid profiles). Blood samples were collected 12 h after fasting from all patients. Blood glucose, total cholesterol, triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein were measured using the immunometric chemiluminescence method. HbA1c values were measured by high-performance liquid chromatography.

Epworth Sleepiness Scale

The ESS is a self-rating questionnaire used to assess average daytime sleepiness, consisting of eight questions scored 0–3. The questions examine the possibility of falling asleep in certain situations in an ordinary nontiring day, using the following scale: 0 = "would never doze or sleep"; 1 = "slight chance of dozing or sleeping"; 2 = "moderate chance of dozing or sleeping"; and 3 = "high chance of dozing or sleeping". A total score of 10 or more from the 8 questions reflects above-normal daytime sleepiness (inadequate sleep and the need to improve sleep hygiene) and indicates a need for further evaluation.[11] The patient were divided into normal sleep group and very sleepy group according to ESS results.

Pittsburgh Sleep Quality Index

The PSQI evaluates the quality of sleep across seven component domains: Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. After processing, each of the components has a score from 0 to 3, with 3 indicating the greatest sleep problems. The scores for the seven components are added, and a total score of 5 or greater is indicative of poor sleep quality.[12] The patients were divided into poor and good quality groups according to PSQI scores.

Berlin questionnaire for obstructive sleep apnea syndrome

The BQ is a questionnaire designed for community screening for OSAS. There are a total of 10 questions across three categories. Each category is evaluated in itself, and if two or more categories have positive results, the subject is considered to have a high-risk for OSAS.[13]

Statistical analysis

The data are shown as a mean ± standard deviation (SD), percentages, or median (interquartile range [IQR]). The Shapiro–Wilk test was used to assess the normality of the data. For groups with nonnormally distributed data, the Mann–Whitney U-test was used to compare two groups and the Kruskal–Wallis H-test to compare three or more groups. Spearman correlation coefficients were used to determine the correlation between nonnormally distributed variables. Pearson's Chi-squared test was used in the analysis of cross tables. The odds ratio (*OR*) with 95% confidence intervals (*CI*s) was used to determine the risk factors. SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Sleep, sleep quality, and sleep scores were taken as dependent variables. A P value of <0.05 was considered as statistically significant.

Results

A total of 585 patients with type 2 diabetes mellitus were enrolled in the study (193 males, 392 females, median age 57 years [50–64 years]). Since 10 patients did not complete PSQI, only 575 patients were included in the statistical analysis for PSQI; 579 patients were included for ESS since 6 patients did not complete ESS, and 580 patients were for BQ since 5 patients did not complete BQ. Of these, 18.50% were smokers and 52.20% were obese (the median body mass index [BMI] was 29.98 kg/m^2 [26.83–33.70 kg/m^2]). The median disease duration was 7 years (3–12 years); 174 patients (29.74%)

were receiving insulin therapy. The median HbA1c level was 6.90% (6.20–8.20%), with 37.80% of the patients in the range considered normal (≤6.5%). The median LDL level was 1.27 g/L (1.04–1.49 g/L), and median TG level was 1.50 g/L (1.11–1.96 g/L). An evaluation of drug histories showed that none of the patients was using medication affecting sleep quality, such as sedative-hypnotic drugs.

Comparing patients with normal HbA1c (≤6.5%) and high HbA1c, there were no significant difference in smoking rate (17.2% vs. 19.4%, $P > 0.05$) and BMI (median: 29.73 kg/m^2 [27.42–33.29 kg/m^2] vs. 30.06 kg/m^2 [26.44–34.13 kg/m^2], $P = 0.966$); however, there was a significant difference in the gender ratio (normal HbA1c: Male 26.20%, female 78.20%; high HbA1c: Male 37.40%, female 62.60%; $\chi^2 = 7.652$, $P = 0.006$). The mean PSQI score was 6.18 ± 3.42, with 64.30% of patients having poor sleep quality, and the mean ESS score was 8.96 ± 5.70, with 54.40% of patients having excessive daytime sleepiness. According to the BQ results, 50.20% of patients were at high-risk of OSAS. Statistical analysis indicated that BMI was positively correlated with ESS and PSQI ($r = 0.11$, $P = 0.009$ and $r = 0.17$, $P < 0.001$, respectively). There was a significant association between obesity and a high-risk of OSAS ($P < 0.001$). HbA1c levels correlated significantly with the ESS and PSQI scores ($r = 0.23$, $P < 0.001$ and $r = 0.14$, $P = 0.001$, respectively) and were significantly higher in those with high-risk of OSAS ($P < 0.001$). Compared with patients with normal HbA1c levels, those with high HbA1c (>6.5%) had a greater risk of excessive daytime sleepiness according to the ESS results (*OR*: 2.08, 95% *CI*: 1.47–2.96, $P < 0.001$), poor sleep quality according to the PSQI results (*OR*: 1.54, 95% *CI*: 1.08–2.18, $P = 0.017$), and having a high-risk of OSAS (*OR*: 1.84, 95% *CI*: 1.30–2.59, $P < 0.001$). Duration of diabetes was positively correlated with the ESS and PSQI scores ($r = 0.101$, $P = 0.016$ and $r = 0.142$, $P = 0.001$, respectively). Comparisons of good and poor sleep quality grouped by PSQI results are shown in Tables 1 and 2.

There was no significant difference between genders in the ESS and BQ scores, but PSQI score levels were significantly higher in female patients than in male patients (6.63 ± 3.57 vs. 5.27 ± 2.91, $P < 0.001$). ESS scores were significantly higher in smokers than in nonsmokers (9.84 ± 5.05 vs. 8.76 ± 5.82, $P = 0.043$), but there were no significant differences in the BQ and PSQI results. Comparisons of normal sleep and very sleepy patients grouped by ESS results are given in Tables 3 and 4. Comparisons of low risk and high risk patients for OSAS grouped by BQ results are given in Tables 5 and 6.

Fasting blood glucose levels showed significantly different between normal and high BQ results (151.03 ± 76.81 vs. 159.05 ± 72.06; $P = 0.017$) and were positively correlated with ESS and PSQI scores ($r = 0.213$, $P < 0.001$ and $r = 0.157$, $P < 0.001$, respectively).

The variables thought to influence the BQ, ESS, and PSQI scores were age, gender, BMI, smoking status, and HbA1c levels. Binary logistic regression analysis was used to examine the impact of these variables on the study group results. Age, BMI, and HbA1c levels were found to have effects on BQ scores (*OR* = 1.02, $P = 0.004$; *OR* = 1.09, $P < 0.001$; and *OR* = 1.13, $P = 0.020$, respectively). Age, BMI, smoking status, and HbA1c levels were found to have effects on ESS scores (*OR* = 1.02, $P = 0.037$; *OR* = 1.03, $P = 0.032$; *OR* = 1.698, $P = 0.021$; and *OR* = 1.19, $P = 0.001$, respectively). Gender and HbA1c levels were found to have effects on PSQI scores (*OR* = 1.89, $P = 0.001$ and *OR* = 1.15, $P = 0.011$, respectively).

When the patients' LDL levels were compared with the results of the sleep disturbance scales, they did not significantly correlate with the results of the ESS, BQ, or PSQI. When the patients' TG levels were compared with the results of the sleep disturbance scales, they did not significantly correlate with the results of the ESS and BQ. However, the TG levels were significantly higher in a poor sleep quality group than in the good quality sleep group (152.00 [118.75–201.00] vs. 14.00 [97.75–182.25], $P = 0.016$).

Discussion

Diabetes mellitus is a chronic disorder. With its increasing frequency of acute and chronic complications, and its increasing morbidity and mortality, diabetes has caused a considerable loss of labor and exerted a heavy economic burden on society. It is also associated with an increase in psychological disorders and sleep disorders, both of which complicate the metabolic control of diabetes.

Sleep disorders are quite common in the community and are considered as cardiovascular risk factors. They also

Table 1: Comparison of patients with good and poor sleep quality according to PSQI results by using Mann–Whitney *U*-test

Parameters	Good sleep quality group ($n = 205$)	Poor sleep quality group ($n = 370$)	Total ($N = 575$)	Standardized statistics	*P*
Age (years)	57 (51–64)	59 (51–64)	58 (51–64)	1.198	0.231
BMI (kg/m^2)	29.22 (26.31–31.99)	30.59 (27.53–34.28)	30.06 (26.95–33.91)	2.477	0.013
Waist/hip ratio	0.92 (0.86–0.97)	0.90 (0.86–0.96)	0.91 (0.86–0.96)	−1.190	0.234
HbA1c (%)	6.70 (5.91–7.53)	7.20 (6.21–8.40)	6.90 (6.18–8.20)	2.817	0.005
Duration of DM (years)	5.50 (2.62–10.00)	8.00 (4.00–14.75)	7.00 (3.00–13.00)	3.458	0.001
Fasting blood glucose (g/L)	1.30 (1.08–1.54)	1.43 (1.10–1.89)	1.37 (1.10–1.80)	2.841	0.004

Data are shown as median (interquartile range). PSQI: Pittsburgh Sleep Quality Index; BMI: Mean body mass index; HbA1c: Hemoglobin A1c; DM: Diabetes mellitus.

Table 2: Comparison of good and poor sleep quality according to PSQI results by using chi-square test, *n* (%)

Parameters	Good sleep quality group (*n* = 205)	Poor sleep quality group (*n* = 370)	Total (*N* = 575)	χ^2	*P*
Gender				10.208	0.001
Male	85 (44.73)	105 (55.27)	190 (100)		
Female	120 (31.16)	265 (68.84)	385 (100)		
Cigarette				0.310	0.578
Smoker	41 (37.96)	67 (62.04)	108 (100)		
Nonsmoker	164 (35.11)	303 (64.89)	467 (100)		
HbA1c*				5.746	0.017
≤6.5%	91 (41.93)	126 (58.07)	217 (100)		
>6.5%	111 (31.98)	236 (68.02)	347 (100)		
Treatments†				3.479	0.176
No drugs	10 (47.61)	11 (52.39)	21 (100)		
Oral antidiabetics	140 (36.93)	239 (63.07)	379 (100)		
Insulin	53 (30.63)	120 (69.37)	173 (100)		

*HbA1c values could only be obtained from 564 patients; †Treatment history could only be obtained from 573 patients. HbA1c: Hemoglobin A1c; PSQI: Pittsburgh Sleep Quality Index.

Table 3: Comparison of normal sleep and very sleepy groups according to ESS results by using Mann–Whitney *U*-test

Parameters	Normal sleep group (*n* = 315)	Very sleepy group (*n* = 264)	Total (*N* = 579)	Standardized statistics	*P*
Age (years)	56 (51–63)	59 (52–65)	58 (51–64)	2.402	0.016
BMI (kg/m^2)	29.21 (26.55–33.72)	30.66 (27.59–34.13)	30.06 (26.95–33.91)	2.462	0.014
Waist/hip ratio	0.91 (0.85–0.96)	0.92 (0.86–0.96)	0.91 (0.86–0.96)	1.239	0.215
HbA1c (%)	6.60 (5.90–7.50)	7.40 (6.40–8.60)	6.90 (6.18–8.20)	4.878	<0.001
Duration of DM (years)	6.00 (3.00–11.00)	8.00 (3.00–14.00)	7.00 (3.00–13.00)	1.484	0.138
Fasting blood glucose (g/L)	1.25 (1.05–1.57)	1.52 (1.18–2.01)	1.37 (1.10–1.80)	4.340	<0.001

Data are shown as median (interquartile range). ESS: Epworth Sleepiness Scale; BMI: Mean body mass index; HbA1c: Hemoglobin A1c; DM: Diabetes mellitus.

Table 4: Comparison of normal sleep and very sleepy groups according to ESS results by using chi-square test, *n* (%)

Parameters	Normal sleep group (*n* = 315)	Very sleepy group (*n* = 264)	Total (*N* = 579)	χ^2	*P*
Gender				0.037	0.847
Male	105 (54.97)	86 (45.03)	191 (100)		
Female	210 (54.12)	178 (45.88)	388 (100)		
Cigarette				4.352	0.037
Smoker	48 (45.28)	58 (54.72)	106 (100)		
Nonsmoker	267 (56.44)	206 (43.56)	473 (100)		
HbA1c*				17.315	<0.001
≤6.5%	143 (65.29)	76 (34.70)	219 (100)		
>6.5%	164 (47.39)	182 (52.61)	346 (100)		
Treatments†				4.392	0.085
No drugs	16 (72.72)	6 (27.28)	22 (100)		
Oral antidiabetics	213 (56.61)	170 (44.39)	383 (100)		
Insulin	85 (49.41)	87 (50.59)	172 (100)		

*HbA1c values could only be obtained from 565 patients. †Treatment history could only be obtained from 577 patients. ESS: Epworth Sleepiness Scale; HbA1c: Hemoglobin A1c.

complicate the control of chronic diseases such as diabetes, obesity, and hypertension.[14] Sleep disorders increase the risk of the emergence of cardiovascular, neurologic, and metabolic diseases. Conversely, the prevalence of sleep disorders increases with diabetes and such co-existence results in poor glycemic control and more chronic complications (i.e., diabetic neuropathy).[4,15]

In this study, we observed the following results: According to the ESS results, 54.40% of the patients had excessive daytime sleepiness; according to the PSQI results, 64.30% of the patients had poor sleep quality; and according to the BQ results, 50.20% of the patients were considered to have high-risk for OSAS. Therefore, in our study, the sleep disorders were found in 50–64% of patients.

Table 5: Comparison of patients with high-risk and low risk according to BQ for OSAS by using Mann–Whitney *U*-test

Parameters	Low risk group (n = 289)	High-risk group (n = 291)	Total (N = 580)	Standardized statistics	P
Age (years)	56 (48–64)	59 (52–64)	58 (50–64)	2.721	0.006
BMI (kg/m^2)	29.27 (26.19–32.73)	31.06 (27.68–35.37)	30.11 (27.01–33.98)	4.728	<0.001
Waist/hip ratio	0.91 (0.85–0.96)	0.92 (0.87–0.96)	0.91 (0.86–0.96)	0.907	0.365
HbA1c (%)	6.60 (5.90–7.54)	7.35 (6.30–8.43)	6.90 (6.11–8.27)	3.679	<0.001
Duration of DM (years)	7.00 (2.25–12.00)	7.50 (3.00–13.00)	7.00 (3.00–13.00)	1.071	0.284
Fasting blood glucose (g/L)	1.30 (1.06–1.63)	1.47 (1.14–1.90)	1.38 (1.11–1.81)	2.393	0.017

Data are shown as median (interquartile range). BQ: Berlin questionnaire; OSAS: Obstructive sleep apnea syndrome; BMI: Mean body mass index; HbA1c: Hemoglobin A1c; DM: Diabetes mellitus.

Table 6: Comparison of patients high-risk and low risk for OSAS according to BQ by using chi-square test, *n* (%)

Parameters	Low risk group (n = 289)	High-risk group (n = 291)	Total (N = 580)	χ^2	P
Gender				2.712	0.100
Male	105 (54.69)	87 (45.31)	192 (100)		
Female	184 (47.43)	204 (52.57)	388 (100)		
Cigarette				0.079	0.778
Smoker	52 (48.60)	55 (51.40)	107 (100)		
Nonsmoker	237 (50.10)	236 (49.90)	473 (100)		
HbA1c*				12.246	<0.001
≤6.5%	129 (58.90)	90 (41.90)	219 (100)		
>6.5%	152 (43.80)	195 (56.20)	347 (100)		
Treatments†				9.216	0.010
No drugs	17 (77.27)	5 (27.73)	22 (100)		
Oral antidiabetics	195 (50.90)	188 (49.10)	383 (100)		
Insulin	76 (39.37)	97 (60.63)	173 (100)		

*HbA1c values could only be obtained from 566 patients; †Treatment history could only be obtained from 578 patients. BQ: Berlin questionnaire; OSAS: Obstructive sleep apnea syndrome; HbA1c: Hemoglobin A1c.

We also found that there was a bidirectional relationship between sleep quality and diabetes. Sleep disorders increased the risk of the elevated HbA1c level, and a high level of HbA1c was a risk factor for sleep disorders. This finding was consistent with other studies. Studies have indicated that both the development and control of diabetes are affected by quality and duration of sleep. Sleep disorders were found to be associated with impaired glucose tolerance, increased type 2 diabetes, and elevated fasting blood glucose and HbA1c levels.[16]

Sleep apnea is defined as at least 10 s of cessation of breathing during sleep; 90–95% of apneas are obstructive. The prevalence of OSAS is correlated with age and weight, and it is a common sleep disorder in diabetic patients. In our study, we found from the BQ results that 50.20% of patients were considered to have a high-risk for OSAS. Several studies have shown that the prevalence of OSAS in diabetic subjects is 36–60%.[3,10] Studies have also shown an increased incidence of diabetes in patients with OSAS.[17] Studies including both diabetic and nondiabetic individuals revealed a positive correlation between HbA1c levels and the severity of OSAS.[15]

In this study, the risk of not achieving the target HbA1c was 1.84-fold higher in patients at high-risk of OSAS (according to the results of BQ) than those at low risk of OSAS. This finding suggested that a higher risk of OSAS might be a factor that complicates control in diabetic patients. Ignoring OSAS in diabetic patients could complicate the control of diabetes, and treatment for OSAS can result in improvements in diabetes parameters.[18,19] When treating diabetic patients, physicians should be aware of this disease, which is highly prevalent in diabetic patients. We believed that the BQ, with its ease of use, might be effective in screening for this disease.

The quality of sleep can predict the risk of developing diabetes, and the metabolic control of diabetes might be affected by quality and duration of sleep.[20,21] Daytime sleepiness causes a general decline in motivation, and, as a result, may have a negative effect on the psychological status of patients with diabetes.[22] It is well known that chronic diseases such as diabetes cause an emotional stress load to patients. The prognosis of diabetes can be affected by sleep quality and psychological distress and symptoms.[23,24] Sleep can have a modulator effect on the glycemic control of diabetes through hormones. Sleep disturbance is a stress factor that can alter blood glucose levels, and psychological defense mechanisms and high levels of HbA1c are associated with insomnia.[25,26]

However, this study has some limitation. This study only included type 2 diabetes mellitus and did not set the control groups (i.e., people without diabetes), which will be studied in the future.

In summary, sleep disorders are common in diabetes and have a negative impact on its control. Conversely, poor control of diabetes is an important factor for disturbing sleep quality. In diabetic patients with poor regulation of blood glucose, it is important to address sleep problems, both for eliminating the complications caused by the sleep disorders and for improving the control of diabetes.

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Conflicts of interest

There are no conflicts of interest.

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