

Impact of subjective sleep quality on glycaemic control in type 2 diabetes mellitus

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Background. Glycaemic control is fundamental to the management of and risk reduction in microvascular complications of diabetes.

Objectives. The aim of this study was to investigate the association of sleep quality with glycaemic control and its impact on type 2 diabetic patients in an Asian population.

Methods. A total of 46 subjects with type 2 diabetes mellitus were enrolled. HbA1C was measured in each patient, and each patient completed the Chinese version of the Pittsburgh Sleep Quality Index (PSQI) questionnaire. Good sleep quality was defined as PSQI score ≤ 5 .

Results. After adjusting for age, gender and body mass index, the total PSQI score and sleep efficiency ($P < 0.05$) were significantly correlated with the level of HbA1C. Logistic regression analysis showed the adjusted odds ratio (OR) of sleep efficiency for HbA1C level was 6.83 [OR = 6.83, 95% confidence interval (CI) = 2.04–22.8, $P = 0.002$]. The adjusted ORs of worse glycaemic control for the poor sleep quality group was 6.94 with regard to the group of good sleep quality (OR = 6.94, 95% CI: 1.02–47.16, $P < 0.05$).

Conclusions. This study demonstrated that both poor sleep quality and less-efficient sleep are significantly correlated with worse glycaemic control in patients with type 2 diabetes. These findings are expected to contribute to the prevention and risk reduction of microvascular complications in type 2 diabetes.

Keywords. Diabetes mellitus, glycaemic control, HbA1C, PSQI, sleep quality.

Introduction

Insufficient sleep is one of the most common chief complaints in the practice of the general physician. Approximately 46–69% of patients presenting to a primary care physician report a complaint of at least occasional insomnia.^{1–3} Insomnia also has a negative impact on work efficiency and quality of life for many. At present, many experimental and epidemiological data have shown that poor sleep quantity and quality are related to an increased risk of chronic systemic diseases such as hypertension,⁴ obesity,^{5,6} cardiovascular disease,^{7,8} inflammatory conditions⁹ and insulin resistance.¹⁰ In addition, an association has been reported between difficulty in initiating sleep and risk of pre diabetes.¹¹ Another study has shown that both short and long duration of sleep are associated with greater prevalence of high fasting plasma glucose and high

A1c level;¹² however, there was insufficient documentation of how sleep quality influences the glycaemic control on type 2 diabetes in an Asian population.

It is well known that glycaemic control approaching the targeted glycaemic level helps to reduce the risk of microvascular complications in patients with type 2 diabetes.^{13,14} According to the 2010 clinical practice recommendations by the American Diabetes Association,¹⁵ lowering of A1c to $<7\%$ has been shown to reduce microvascular complications of type 1 and type 2 diabetes¹⁶ and also to reduce myocardial infarction if metformin is used in overweight diabetic patients.¹⁶ The Kumamoto study¹⁷ and the UK Prospective Diabetes Study (UKPDS)¹⁸ demonstrated that intensive glycaemic control was associated with long-term reduction in risk of microvascular complications. Since type 2 diabetes and its microvascular and macrovascular complications are increasingly prevalent worldwide

with major implications on the personal health, quality of life and public health, it is important to help the majority of these patients to reach the targeted glycaemic level, whether by lifestyle modification or with medication.

The aim of this study is to investigate the association of self-reported sleep quality with glycaemic control and to evaluate the impact of sleep quality on type 2 diabetes.

Methods

Participants

This is a cross-sectional study from February to August 2009. The protocol was approved by the Chang Gung Memorial Hospital institutional review board. A total of 108 patients were randomly selected from the 216 patients with type 2 diabetes mellitus who consecutively attended the family medicine department outpatient clinic in Chang Gung Memorial Hospital Linkou branch in Taiwan. We excluded patients who were newly diagnosed with type 2 diabetes within 1 year because they might not have achieved stable glycaemic levels. Patients who had macrovascular or microvascular complications such as impairment of renal function, diabetic retinopathy, neuropathy or prior cardiovascular events were also excluded because they might suffer from insomnia due to these co-morbidities. Patients with connective tissue disease (e.g. rheumatoid arthritis, systemic lupus erythematosus) were also excluded due to the possible influence of their specific symptoms (e.g. fever, bone or joint pain) or therapies (e.g. steroids, immunosuppressants) on sleep quality. Among 108 patients, 24 were treated with oral anti-diabetic agents (OADs) for <1 year, 15 had diabetic complications (2 with nephropathy, 4 with retinopathy, 3 with neuropathy, 1 with history of coronary artery disease, 1 with prior cerebral-vascular events and 4 with more than one complication) and 1 had rheumatoid arthritis (Fig. 1). In the rest of 68 patients, 22 denied the interview due to several reasons. After all, 46 patients who treated with mainly OADs for >1 year were included for the interview and blood tests. The participation rate was 46/68 (67.6%).

Study design

Each patient underwent measurement of body height, body weight, body mass index (BMI) and blood pressure, physical examination and laboratory testing of A1c at the time of the initial visit. Demographic data such as age and gender were collected. Each patient was also asked whether he or she had hypertension or dyslipidemia or had a history of cigarette smoking. Hypertension was defined as a repeatedly elevated blood pressure exceeding 140/90 mmHg or current use of antihypertensive medication in accordance with

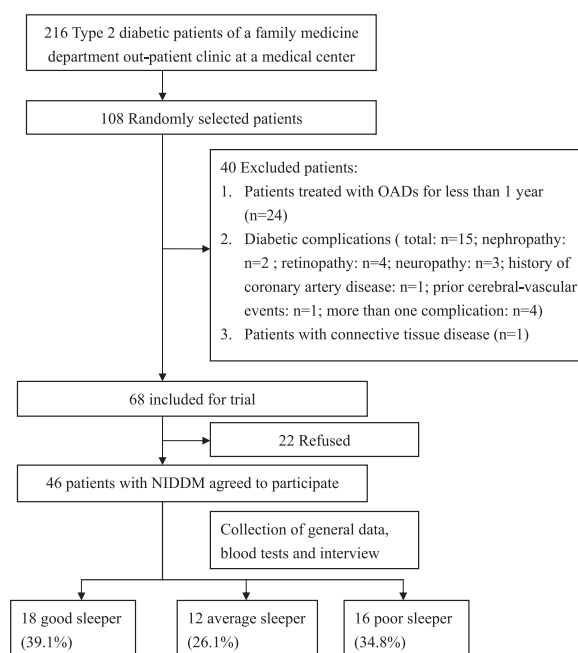


FIGURE 1 Study participant flow diagram

the guideline of JNC7. Dyslipidemia, including hypercholesterolemia and hypertriglyceridemia, was defined in accordance with ATP III guideline or current use of lipid lowering medication. ‘Current-smoker’ was defined as smoking cigarettes for the past month. At the end of the visit, each participant was interviewed using a questionnaire of Chinese version of the PSQI to assess their sleep quality.

The PSQI is a score derived by a self-rated questionnaire consisting of nine questions that assess a wide variety of factors related to sleep quality in the previous month. These included estimates of sleep duration and latency as well as frequency and severity of specific sleep-related problems. The nine questions were grouped into seven component scores, each weighted equally on a 0–3 scale. The seven components were then summed to yield a global PSQI score (range: 0–21); higher scores indicate worse sleep quality. The seven components of the PSQI are: (i) subjective sleep quality, (ii) sleep latency, (iii) sleep duration, (iv) sleep efficiency, (v) sleep disturbances, (vi) use of sleeping medications and (vii) daytime dysfunction. According to Buysse *et al.*,¹⁹ patients with a PSQI score >5 are defined as ‘good sleepers’. Accordingly, in this study design, a PSQI score ≤5 was also conventionally defined as ‘good sleep quality’, a PSQI score of 5–8 points was defined as ‘average sleep quality’, and a PSQI score > 8 was defined as ‘poor sleep quality’.

Because A1c is thought to reflect average blood sugar over several months²⁰ and has strong predictive value for diabetic complications,^{21,22} we used the level of A1c as the index for glycaemic control in type 2 diabetic patients in this study. The level of A1c < 7% was

defined as good glycaemic control based on the American Diabetes Association 2010 Guidelines while a level of A1c $\geq 7\%$ was considered poor glycaemic control. Subjects with a BMI $\geq 27 \text{ kg/m}^2$ are conventionally considered obese according to the criteria established by the Department of Health, Executive Yuan, ROC 200221.²³

Statistical analysis

We used chi-square tests to analyse the sampling distribution and Pearson correlation coefficients to analyse the correlation analysis among total PSQI score, the seven components of the PSQI and the level of A1c. Logistic regression analysis was performed to examine the associations of self-reported sleep quality and the seven components of the PSQI with plasma A1c levels. The A1c levels were input as dependent variables in Models I and II. The following parameters were input as independent variables in the Model I: age, BMI and the seven components of the PSQI which included subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medications and daytime dysfunction. In the Model II, gender, age, BMI and PSQI score were input as independent variables. The data were analysed using the Statistical Package for Social Sciences (SPSS) for Windows, Version 12.0 software (SPSS Inc., Chicago, IL).

Results

A total of 46 subjects ranging in age from 43 to 83 years with type 2 diabetes were recruited for this study. The mean age was 60.1 ± 9.7 years. Among them, 71% were < 65 years of age. The distribution of general characteristics of the participants is presented in Table 1.

In the study group of 46 patients, there were 28 men (61%) and 18 women (39%). Thirty-four patients (74%) were nonsmokers, and 31 (67%) were obese as defined by BMI $\geq 27 \text{ kg/m}^2$ using the criteria of the Department of Health, Executive Yuan, ROC 200221. Twenty-eight patients (61%) did not have the co-morbidity of dyslipidemia and among them, 13 (46%) had good glycaemic control and 15 (54%) had poor

glycaemic control. Twenty-nine patients (63%) had hypertension and among them, 12 (41%) had good glycaemic control and 17 (59%) had poor glycaemic control. In this study, overall, the proportion with poor sleep quality in the total study sample was 16/46 (34.8%). Eighteen patients (39.1%) had good glycaemic control and 28 patients (60.9%) had poor glycaemic control. Poor glycaemic control, defined by A1c $\geq 7\%$ using the ADA guideline 2010 was noted in 14 patients (87.5%) in the poor sleep quality group and in 8 patients (44.4%) in the good sleep quality group, while good glycaemic control was noted in 10 patients (55.6%) in the good sleep quality group. The complete demographic data of the participants are presented in Table 2.

The rate of poor glycaemic control was significantly greater in the poor sleep quality group than in the groups with good or average sleep quality. By using chi-square test, we demonstrated significant difference among the group of age ($\chi^2 = 4.29$, $P = 0.049 < 0.05$) and the group of sleep quality ($\chi^2 = 7.40$, $P = 0.02 < 0.05$).

By performing Pearson correlation statistical analysis, we found a significant positive correlation between the total PSQI score and the level of A1c ($P = 0.004 < 0.01$). Additionally, a robust positive correlation between sleep efficiency and the level of A1c ($r = 0.54$, $P < 0.05$) is also demonstrated. Thus, poor sleep quality and less-efficient sleep are both significantly associated with poor glycaemic control in type 2 diabetic patients.

Table 3 shows the logistic regression analysis of the seven components of the PSQI questionnaire and the level of A1c. We found that each one point increase in sleep efficiency score leads to a 6.83-fold increase in risk of poor glycaemic control [odds ratio (OR) = 6.83, 95% CI = 2.04–22.8, $P = 0.002 < 0.05$]. Apart from sleep efficiency, no other significant associations were found with any of the other PSQI components.

In Table 4, we assumed a dummy variable and set good sleep quality group (PSQI ≤ 5) as the reference group in logistic regression analysis to analyse the impact of sleep quality by using PSQI score on glycaemic control. The results showed that the adjusted OR for poor sleep quality group was 6.94 [OR = 6.94, 95% confidence interval (CI) = 1.02–47.16, $P = 0.05$] compared with the group with good sleep quality. This also demonstrates that the PSQI score is a predictor on glycaemic control in type 2 diabetic patients.

TABLE 1 General characteristics of the participants

	Minimum	Maximum	Mean
Age (years)	43	83	60.11 ± 9.69
Height (cm)	148	180	162.59 ± 9.52
Body weight (kg)	40	115	69.39 ± 14.78
BMI (kg/m^2)	18.26	37.33	26.04 ± 3.80
PSQI score	0	15	6.33 ± 3.50
A1c (%)	5.1	14.9	8.32 ± 2.20

Discussion

In this study, we found a robust and significant positive association between sleep quality and A1c level even after adjusting for a large number of possible confounders. The adjusted OR of sleep efficiency and

TABLE 2 Demographic data of participants (n = 46)

	Numbers (%)	A1c		$c\chi^2$	P value
		<7% (n = 18) n (%)	≥7% (n = 28) n (%)		
All	46	18 (39.1)	28 (60.9)		
Gender					
Male	28 (60.9)	13 (46.4)	15 (53.6)	1.60	0.23
Female	18 (39.1)	5 (27.8)	13 (72.2)		
Age (years)					
<65	33 (71.7)	16 (48.5)	17 (51.5)	4.29	0.049
≥65	13 (28.3)	2 (15.4)	11 (84.6)		
Smoking					
No	34 (73.9)	11 (32.4)	23 (67.6)	2.51	0.17
Yes	12 (26.1)	7 (58.3)	5 (41.7)		
BMI (kg/m ²)					
<27	15 (32.6)	5 (33.3)	10 (66.7)	0.31	0.75
≥27	31 (67.4)	13 (41.9)	18 (58.1)		
Dyslipidemia					
No	28 (60.9)	13 (46.4)	15 (53.6)	1.60	0.23
Yes	18 (39.1)	5 (27.8)	13 (72.2)		
Hypertension					
No	17 (37.0)	6 (35.3)	11 (64.7)	0.17	0.76
Yes	29 (63.0)	12 (41.4)	17 (58.6)		
Sleep quality					
Good (PSQI ≤ 5)	18 (39.1)	10 (55.6)	8 (44.4)	7.40	0.02
Average (6 ≤ PSQI ≤ 7)	12 (26.1)	6 (50.0)	6 (50.0)		
Poor (PSQI ≥ 8)	16 (34.8)	2 (12.5)	14 (87.5)		

TABLE 3 Logistic regression analysis of PSQI components and A1c

	β -value	SD	Odds Ratio	95% CI	P value
Age	0.05	0.05	1.05	0.95–1.16	0.35
BMI	0.01	0.12	1.01	0.81–1.27	0.93
Subjective sleep quality	–0.24	0.58	0.79	0.25–2.47	0.68
Sleep latency	0.59	0.47	1.81	0.73–4.51	0.20
Sleep duration	–0.32	0.59	0.72	0.23–2.29	0.58
Sleep efficiency	1.92	0.62	6.83	2.04–22.8	0.002
Sleep disturbances	0.26	0.90	1.29	0.22–7.60	0.78
Use of sleep medications	–0.67	0.59	0.51	0.16–1.62	0.25
Daytime dysfunction	0.42	0.52	1.52	0.55–4.22	0.43

sleep quality for A1c level were 6.83 (OR = 6.83, $P = 0.002 < 0.05$, 95% CI = 2.04–22.8) and 6.94 (OR = 6.94, $P = 0.05$, 95% CI = 1.02–47.16). These findings suggest that both poor sleep quality and less-efficient sleep are strongly related to worse glycaemic control in type 2 diabetic patients.

The average PSQI score was significantly higher among the female participants than among the male participants. Furthermore, the score of sleep latency in the subcomponents of PSQI was significantly different between men and women ($t = 3.43$, $P = 0.001$).

One study conducted in Italy on the association of sleep abnormalities of diabetes and plasma glucose levels reached the following conclusions.²⁴ Firstly, univariate analysis showed lower sleep maintenance ($P = 0.002$) and sleep efficiency ($P = 0.005$) in patients with

type 2 diabetes. A1c level correlated inversely with sleep efficiency ($r = -0.29$; $P = 0.047$). The above findings suggest that better sleep efficiency was associated with lower A1c level and which is similar to the results of this study ($r = 0.54$, $P < 0.001$).

We highlight two possible mechanisms to explain this association. Firstly, sleep deprivation stimulates the cerebral cortex, cerebral limbic system and hypothalamus, which induces the secretion of catecholamines from the sympathetic ganglion and adrenal medulla and of cortisol from the pituitary–adrenal system.²⁵ These hormones may function to increase the plasma glucose level. Secondly, several physiologic experiments have demonstrated that the blood cortisol concentration and insulin resistance are increased as a consequence of sleep deprivation.^{26–28}

Because microvascular complications of diabetes remain the leading causes of blindness and renal failure in developed countries and are much more closely associated with hyperglycemia than with macrovascular complications, sleep quality and efficiency are important to address.²⁸ For prevention of microvascular disease in type 2 diabetes, the A1c goal for non-pregnant patients with type 2 diabetes (in general) is <7%. According to our study results, better sleep quality and sleep efficiency might probably lead to closer approximation of the target A1c goal.

Our study limitations are as follows. Firstly, although A1c level is the most frequently used index to reflect average plasma glucose levels in the past 3

TABLE 4 Logistic regression analysis of sleep quality and A1c level

	β -value	SD	Odds Ratio	95% CI	P value
PSQI					
Good sleep quality (PSQI \leq 5)			1		
Average sleep quality (6 \leq PSQI \leq 7)	0.07	0.78	1.07	0.23–4.98	0.93
Poor sleep quality (PSQI \geq 8)	1.94	0.98	6.94	1.02–47.16	0.05
Gender					
Female			1		
Male	–0.65	0.71	0.52	0.13–2.12	0.37
Age	0.02	0.04	1.02	0.95–1.11	0.56
BMI	0.01	0.01	1.01	0.84–1.22	0.91

months, it is difficult to illustrate the real-time blood glucose level precisely. The details of fluctuation in blood glucose are not demonstrated by A1c. Secondly, patients with either microvascular or macrovascular diabetic complications were excluded from this study. The exclusion of such patients would hide the impact of sleep quality on glycaemic control in diabetic patients who already are affected with the co-morbidities of diabetic complications. A study conducted by the University of Chicago Hospitals showed that glycaemic control was associated with perceived sleep debt rather than PSQI score in patients without diabetic complications. In patients with at least one complication, A1c level was associated with PSQI score but not perceived sleep debt. The predicted increase in A1c level for a 5-point increase in PSQI was 1.9% above the median. Sleep duration and quality constitute a key marker to predict the level of A1c.²⁹ Thirdly, patients who were affected with obstructive sleep apnoea were not excluded from this study. This might be a potential confounding factor because it is difficult to discern the actual effect of sleep quality on the A1c level. Fourthly, because sleep quality and quantity have been shown to change with age, the wide age range of the study participants would be a possible confounding factor.

In the future, a longitudinal cohort study will be needed to evaluate of the efficacy of therapeutic interventions on sleep quality, with the goal of testing the hypothesis of causality between sleep quality and glycaemic control and of evaluating the extent of reduction in A1c level in patients with type 2 diabetes mellitus.

Conclusion

This study demonstrates that poor sleep quality and less-efficient sleep was closely associated with poor control of A1c level in type 2 diabetes. In the future, it is an important work to treat sleep disturbances in type 2 diabetic patients, which in turn may lead to much better glycaemic control of these patients as well as improvement in quality of life. Better glycaemic

control as evidenced by glycosylated haemoglobin values in the target range helps to decrease the progression of microvascular complications of diabetes.

Declaration

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Ethical approval: Chang Gung Memorial Hospital Institutional Review Board (Ethical Review Committee)

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Conflict of interest: none.

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