Page 102 to 112

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Association between Sleep Quality and Glucose Control in Filipino Adults with Type 2 Diabetes Mellitus

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Abstract

Introduction: Studies show that patients with short or poor sleep quality affects glucoregulation and quality of life negatively. A review of local literature has not revealed any studies on the topic of the association between sleep quality and glucose control. The general objective of this study is to determine the association between sleep quality and glucose control among Filipino adults with T2DM.

Methods: Cross-sectional analytic study involving adult individuals with Type 2 diabetes mellitus seen consecutively at various out-patient clinics of the Lung Center of the Philippines and National Kidney and Transplant Institutes from September 2015 to May 2016.

Participants were 241 adults with type 2 diabetes (T2DM). Sleep quality was measured using the Pittsburg Sleep Quality Index Questionnaire. HbA1c within one month of the interview was used to assess glucose control with self-reported daytime sleepiness. Berlin Questionnaire and Epworth Sleepiness Scale were used to screen for obstructive sleep apnea and excessive daytime sleepiness respectively.

Result: Poor sleep quality was noted in 55% of Filipino diabetics in the study population. And among those with poor sleep, 70.45% have poor glycemic control. We found that sleep quality is directly although weakly correlated with glucose control.

Patients with poor glucose control were more likely to have poor sleep quality (OR 5.5012, 95% CI 3.0881 to 9.7997, p = 0.0000.

HbA1c, asthma/COPD, and lack of bedroom companion are predictors of poor sleep quality among adult diabetic Filipinos based on PSQI scoring.

Among the study population, 33% are high risk for sleep disordered breathing using the Berlin questionnaire and only 26% have excessive daytime sleepiness using ESS.

Conclusion: The prevalence of poor sleep among diabetic Filipinos is high at 55%. Poor sleep quality is directly correlated with poor glucose control. Factors that worsen sleep quality among T2DM are elevated hbA1c, obstructive airway disease and sleeping alone in a bedroom.

Keywords: *Glucose control; Type 2 Diabetes Mellitus; Sleep Quality*

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; ESS: Epworth Sleepiness Scale; HbA1C: Hemoglobin A1c; OSA: Obstructive Sleep Apnea; PEEP: Positive End Expiratory Pressure; PSQI:- Pittsburg Sleep Quality Index; SWS: Slow wave sleep; T2DM: type 2 Diabetes Mellitus

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Introduction

Type 2 diabetes is one of the most common non-communicable diseases. In 2014, there were 3.2 million cases of diabetes in the Philippines with 5.9% prevalence. [1] Diabetes related complications including cardiovascular disease, kidney disease, neuropathy, loss of vision and sexual dysfunction, significantly contribute to morbidity and mortality.

Aside from medications, lifestyle changes, weight loss management and increased physical activity are designed to prevent and manage diabetes. Despite these, incidence of diabetes is still on the rise and glycemic control is often difficult to achieve. [2-4] New strategies need to be developed to help with glucose control.

Studies have shown that short or disturbed sleep affects glucoregulation negatively (i.e. glucose intolerance and insulin resistance) [5] Diabetic patients also have poor sleep quality that affects their quality of life. [3,6] Sleep disorders were noted to have a negative impact on disease control on Chinese, Japanese, Korean and American population. [6-11] Filipinos have a higher rate of diabetes compared to other Asians. [12] A review of local literature has not revealed any studies on the topic of the association between sleep quality and glucose control.

The general objective of this study is to determine the association between sleep quality and glucose control among Filipino adults with T2DM. This study will also aim to determine the prevalence of having poor sleep quality among Filipino T2DM patients, their clinical profile; determine the correlation between sleep quality in terms of PSQI scoring and glucose control in terms of HbA1c and determine the factors that affect sleep quality among T2DM patients.

Methodology

Research design and setting

Cross-sectional analytic study involving adult individuals with Type 2 diabetes mellitus seen consecutively at various outpatient clinics of the Lung Center of the Philippines and National Kidney and Transplant Institutes from September 2015 to May 2016.

Inclusion criteria

1. Diagnosed type 2 diabetes patients by physicians at least six months prior using baseline clinical data. Diagnosis according to Philippine Practice Guidelines on the Diagnosis and Management of Diabetes Mellitus:

- Plasma glucose > 126 mg/dL (7.0 mmol/L) after an overnight fast (Fasting is defined as no caloric intake for at least 8 hours up to a maximum of 14 hours)

  or

- two-hour plasma glucose > 200 mg/dl (11.1 mmol/l) during an Oral Glucose Tolerance Test. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water after an overnight fast of between 8 and 14 hours

  or

- random plasma glucose > 200 mg/dl (11.1 mmol/l) in a patient with classic symptoms of hyperglycemia (weight loss, polyuria, polyphagia, polydipsia) or with signs and symptoms of hyperglycaemic crisis.

2. Hba1c within 1 month of the interview to ensure that control will coincide with the PSQI questionnaire which assesses 1 month subjective sleep quality and disturbances
3. of Filipino descent
4. aged 18-80, male or female

Exclusion criteria

1. Type 1 diabetes
2. diagnosed sleep disorders prior to diagnosis of diabetes
3. mental illness or use of any kind of psychotropic medication
4. other endocrine disorders, such as, thyroid disease or chronic use of glucocorticoids, or other drugs that can potentially affect glucose metabolism (antipsychotics, thyroid hormones, etc)
5. age < 18 years and above 80 years old
6. Pregnant
7. end stage renal disease patients on hemodialysis.

Sample Size

The sample size required for this study is 93 patients. This value was computed using the formula introduced by Schohenfield., *et al*. [18] designed for logistic regression using an odds ratio of 1.32 (where HBA1c > 7% patients has 1.32 times the odds of a poorer subjective sleep quality) based on the reference study [2]. We adjusted the sample size accordingly for a finite population of 150 patients.

$$N = \frac{(z_\alpha + z_{1-\alpha})^2}{P(1-P)E}$$

Where:

$$P = \frac{OR}{1+OR} = \frac{1.32}{1+1.32} = 0.5690$$

E = effect size = 0.367

Z_α = 1.960

Z_β = 0.842

Computation

$$N = \frac{(z_\alpha + z_{1-\beta})^2}{P(1-P)E^2}$$

$$N = \frac{(1.96+0.842)^2}{0.5690(1-0.5690)0.367^2}$$

$$N = 238$$

$$N_{adjusted} = \frac{ComputedSa\ mple}{1+\frac{ComputedSa\ mple - 1}{Population}}$$

$$N_{adjusted} = \frac{238}{1+\frac{238-1}{150}}$$

$$N_{adjusted} = 93$$

Study Outcomes

Independent variables

Sleep quality will be measured using Pittsburg Sleep Quality Index Questionnaire

Pittsburg Sleep Quality Index Questionnaire (PSQI) is a validated self-completed questionnaire that assesses subjective sleep quality and disturbances over the preceding 1 month. The scale included 19 individual items, which generate seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. The sum of scores for these seven components yields the PSQI global score. PSQI global scores < 5 are defined as ‘‘good sleep quality’’ and scores > 5 are defined as ‘‘poor sleep quality’’. A global PSQI score > 5 has a diagnostic sensitivity of 89.6% and specificity of 86.5% in differentiating poor from good sleepers. [13]

Presence of Obstructive Sleep Apnea (OSA) will be screened using 2 questionnaires

1. Presence of excessive daytime sleepiness (which may mean OSA) will be evaluated using the Epworth Sleepiness Scale (ESS) is a validated 8-item questionnaire. ESS scores range from 0 to 24 and higher scores represent greater daytime sleepiness. A score greater than 10 indicates excessive daytime sleepiness and scores were also dichotomized at ≤ 10 or > 10. [14]
2. Screening for the possibility of OSA will be done using The Berlin questionnaire consists of 10-items relating to snoring, non-restorative sleep, sleepiness while driving, apneas during sleep, hypertension, and body mass index. It categorizes patients to high-risk or low-risk for OSA. [15]

Other variables: Age, sex, status, educational attainment, occupation, number of persons in household and in the bedroom, years since diabetes diagnosis, comorbidities, and medications will also be noted

Dependent variable

The dependent variable in this study is the glycemic control as measured by the HbA1c for the last 3 months. An HbA1c of < 7.0% is considered to be of good control.

Ethical Considerations

Confidentiality and informed consent were the main ethical considerations. This paper underwent full board review approved by the Lung Center of the Philippines Institutional Ethics Review Board. A written informed consent was obtained from all participants.

Study Procedures

Recruitment was done by the PI at the clinic of consenting physicians during designated clinic days. Eligible patients were asked to fill out the PSQI questionnaire, the Epworth Sleepiness Score, and Berlin Questionnaire after giving their informed consent. The researcher was personally available during that time to clarify or answer any questions related to the research. Interview will be done in the clinic’s anteroom to ensure privacy. Medical records were reviewed for all patients to record information on age, sex, height and weight, duration of diabetes, medication usage, comorbidities, laboratory tests, including glycosylated hemoglobin A1c (HbA1c), fasting blood sugar (FBS) and creatinine, if available. HbA1c that will be included for control should be taken within 1 month of the interview to ensure that control will coincide with the PSQI questionnaire which assesses 1 month subjective sleep quality and disturbances

Statistical analysis

Plan of Analysis

Descriptive statistics was used to summarize the clinical characteristics of the patients. Frequency and proportion was used for nominal variables, median and IQR for ordinal variables, and mean and SD for interval/ratio variables. Spearman correlation was used to determine the level and direction of association between sleep quality in terms of PSQI scoring and glucose control in terms of HbA1c. Binary logistic regression was used to determine the risk factor of having poor quality sleep based on PSQI score. All valid data was included in the analysis. Missing variables was neither replaced nor estimated. Null hypothesis was rejected at 0.05α-level of significance. STATA 12.0 was used for data analysis.

Results

360 patients were screened but only 241 were eligible for the study. Forty-six patients have no HbA1c, 5 had type 1 diabetes mellitus, 3 were pregnant, 12 were on dialysis, 18 had endocrine disorders, 3 were over 80 years old and 32 did not give consent. They had an average age of 61.15 + 10.39 years. Majority of the recruited patients were female (60%) and married (72%). Almost half of the patients have been diagnosed with diabetes mellitus for more than 10 years (48%) and have been diagnosed with cardiovascular disease (77%). Table 1 provides their clinical and household characteristics.

	Frequency (%); Mean + SD; Median (Range)
Age (median, s.d.) (years)	61.15 + 10.39
Sex N (%)	
Male	98 (40.66)
Female	143 (59.34)
BMI (median, sd) (kg/m^2)	25.66 + 4.32
Civil Status N (%)	
Single	21 (8.71)
Married	174 (72.20)
Widowed	46 (19.09)
Educational Attainment	
Below college degree	60 (24.90)
College and Post graduate	181 (75.10)
Occupation N (%)	
Employed	63 (26.14)
Unemployed	134 (55.60)
Self-employed	44 (18.26)
Person in household N (%)	
6 or more	69 (28.63)
Below 6	172 (71.37)
Person in bedroom	2 (0 to 4)
Currently smoking	18 (7.47)
DM diagnosed more than 10 years	116 (48.13)
Comorbidities	
Cardiovascular disease	185 (76.76)
COPD/asthma	19 (7.88)
Arthritis	9 (3.73)
Stroke	9 (3.73)
DM neuropathy	4 (1.66)

Medicines	
Insulin	76 (31.54)
Statin	82 (34.02)
Beta blocker	21 (8.71)
Laboratory examination results	
FBS (mg/dl) (n = 209)	126.4 (58.5 to 369)
HbA1c	7.64 + 1.98

The quality of sleep of the patients were determined through administering the Pittsburgh Sleep Quality questionnaire. The overall median PSQI score was 6, indicative of poor sleep quality. The highest score obtained was 17, while the lowest was zero.

Table 1: *Demographic and clinical characteristics of diabetic adults assesed for sleep quality (N = 241).*

Domains	Median (Range)
Sleep duration	1 (0 to 3)
Sleep disturbance	1 (0 to 2)
Sleep latency	1 (0 to 3)
Daytime dysfunction	0 (0 to 3)
Habitual Sleep efficiency	1 (0 to 3)
Overall sleep quality	1 (0 to 3)
Use of sleeping medication	1 (0 to 3)
PSQI Total score	6 (0 to 17)

Table 2: *Pittsburgh Sleep Quality Index scores of the study population (n = 241).*

The prevalence of poor sleep quality using the three screening tools (Epworth Sleepiness scale and Berlin questionnaire) is summarized in Table 3. Using the PSQI, more than half of the patients were determined to have poor sleep quality (55%). However, only 26% of the patients had increased daytime sleepiness as assessed by the Epworth Sleepiness scale and only 33% of the patients were identified to have a high risk for sleep disordered breathing using the Berlin questionnaire.

	Frequency (%)
Poor sleep quality based on PSQI scoring	133 (55.19)
Excessive daytime sleepiness using Epworth Sleepiness Scale	63 (26.14)
High risk for Sleep disordered breathing using Berlin Questionnaire	79 (32.78)

Table 3: *Prevalence of poor sleep quality, excessive daytime sleepiness, and risk for sleep disordered breathing among diabetics (n = 241).*

Patients were categorized into either a good glucose control group or a poor glucose control based on their HbA1c (Table 4). Those with good control had median PSQI global score of 5 which was significantly lower than that of the patients with poor control (p 0.00). There were statistical differences between these two groups in terms of five PSQI factors, except for the habitual sleep efficiency and use of sleeping medications. In patients with HbA1c > 7, median sleep latency was significantly longer (30 mins vs. 20 mins p = 0.001) and sleep duration was significantly shorter duration (6 hrs vs. 6.5 hrs; p = 0.018).

	HbA1c > 7 (n = 129)	HbA1c < 7 (n = 111)	P-Value
	Median (Range)		
Sleep duration	1 (0 to 3)	1 (0 to 3)	0.008
Sleep disturbance	1 (0 to 2)	1 (0 to 2)	0.000
Sleep latency	2 (0 to 3)	1 (0 to 3)	0.001
Daytime dysfunction	1 (0 to 3)	1 (0 to 2)	0.000
Habitual Sleep efficiency	1 (0 to 3)	0 (0 to 3)	0.303
Overall sleep quality	1 (0 to 4)	1 (0 to 3)	0.000
Use of sleeping medication	1 (0 to 3)	0 (0 to 3)	0.069
PSQI Total score	7 (0 to 17)	5 (0 to 16)	0.000

Statistical test used: Mann-Whitney U test

Table 4: *Pittsburgh Sleep Quality Index scores of the study population.*

The correlation of the quality of sleep of patients to their HbA1c levels was determined. Based on the correlation coefficient, the two variables were determined to be directly, but weakly associated with each other. This relationship was deemed significant (p = 0.000).

Correlation Coefficient	Level of Association	P-Value
0.2804	Directly Weak Association	0.000

Table 5: *Correlation of Sleep quality based on PSQI and HbA1c (n = 241).*

We conducted binary logistic regression to determine the predictors of poor sleep quality (Tables 6 and 7). The initial regression model showed that HbA1c is the only predictor of poor sleep quality (p = 0.00). The variables enumerated below account for 15.83% of the variability in the sleep quality among the patients (p = 0.001).

	Poor sleep, PSQI > 6 (n = 133)	Good sleep, PSQI < 5 (n = 108)	Odds Ratio (95% CI)	P-Value
	Frequency (%); Mean + SD			
Age 60 and up	83 (62.41)	61 (56.48)	1.18 (0.54 to 2.58)	0.686
Female	82 (61.65)	61 (56.48)	1.31 (0.63 to 2.72)	0.472
BMI > 27.5	41 (30.83)	31 (28.70)	1.03 (0.47 to 2.25)	0.950
With companion in bedroom	92 (69.17)	84 (77.78)	0.5 (0.22 to 1.15)	0.102
DM diagnosed more than 10 years	72 (54.14)	44 (40.74)	1.01 (0.97 to 1.06)	0.536
Comorbidities				
COPD/Asthma	15 (11.28)	4 (3.70)	3.14 (0.71 to 13.87)	0.131
CVD	110 (82.71)	75 (69.44)	1.26 (0.48 to 3.26)	0.639
DM neuropathy	3 (2.26)	1 (0.93)	1.89 (0.12 to 30.04)	0.653
Arthritis	3 (2.26)	2 (1.85)	1.64 (0.21 to 12.52)	0.634
Stroke	6 (4.51)	3 (2.78)	1.41 (0.23 to 8.82)	0.712

Medicines				
Insulin	48 (36.09)	28 (25.93)	0.75 (0.34 to 1.65)	0.474
Statin	52 (39.10)	30 (27.78)	1.51 (0.69 to 3.29)	0.300
Beta blocker	13 (9.77)	8 (7.41)	0.79 (0.23 to 2.71)	0.712
Laboratory results				
FBS > 126	67 (58.77)	39 (41.05)	1.41 (0.67 to 2.99)	0.369
HbA1c > 7	93 (70.45)	36 (33.33)	5.39 (2.45 to 11.85)	0.000
Creatinine > 1.2	11 (10.48)	12 (13.19)	0.56 (0.19 to 1.65)	0.295

P-Value = 0.001; R^2 = 15.83%

Table 6: *Initial model to determine predictors of poor sleep quality among adult diabetic Filipinos based on PSQI scoring.*

In the final model, we selected bedroom companion, obstructive lung diseases, and HbA1c (Table 7). Patients who had a companion in the bedroom were less likely to have poor sleep quality (OR 0.4680, 95% CI 0.2431 to 0.9010, p = 0.023). Patients with COPD/Asthma were found to be thrice as likely to have poor sleep quality (OR 3.4508, 95% CI = 1.0144 to 11.7384, p =0.047). Patients with poor glucose control were more likely to have poor sleep quality (OR 5.5012, 95% CI 3.0881 to 9.7997, p = 0.0000. This model account for 13.24% of the variability in the sleep quality among these diabetic patients (p = 0.0000).

	Odds Ratio	95% Confidence Interval	P-Value
With companion in bedroom	0.4680	0.2431 to 0.9010	0.023
COPD/asthma	3.4508	1.0144 to 11.7384	0.047
HbA1c > 7	5.5012	3.0881 to 9.7997	0.000

P-Value = 0.0000; R^2 = 13.24%

Table 7: *Final model to determine predictors of poor sleep quality among adult diabetic Filipinos based on PSQI scoring.*

Discussion

Poor sleep quality was noted in 55% of Filipino diabetics in the study population. And among those with poor sleep, 70.45% have poor glycemic control. We found that sleep quality is directly although weakly correlated with glucose control. Among the study population, 33% are high risk for sleep disordered breathing using the Berlin questionnaire and only 26% have excessive daytime sleepiness using ESS. Bedroom companion, asthma/COPD, and HbA1c are predictors of poor sleep quality among adult diabetic Filipinos based on PSQI scoring. Patients who had a companion in the bedroom were less likely to have poor sleep quality (OR 0.4680, p = 0.023). Patients with asthma/COPD and poor glucose control were found to have poor sleep quality (OR 3.4508, 95% CI = 1.0144 to 11.7384, p =0.047) and (OR 5.5012, 95% CI 3.0881 to 9.7997, p = 0.0000) respectively.

These findings are similar with other studies noting significant associations between poor glucose control (HbA1c). Poor sleep quality is present in 33% (De Cunha, 2008 [17] n = 50), 60% (Tang, 2014 [18], n = 551), 71% (Tsai [19], n = 46) and 75% (Bing Qian, 2014 [7] n = 206) among the diabetic population with poor sleep quality using the PSQI questionnaire. Other studies also noted poorer sleep among diabetics in a community based setting using other parameters for sleep quality, with or without HbA1c. [3,5,6, 20-22]

There are many studies noting that insufficient sleep may predispose patients to increased risk for developing impaired fasting glucose and diabetes mellitus. [5, 23-25] Sleep deprivation stimulates increased insulin resistance, catecholamine and cortisol secretion, which could lead to increased plasma glucose. [9,10]

During sleep, initiation of slow-wave sleep (SWS) is temporally associated with transient decreased brain glucose utilization, stimulation of growth hormone release, inhibition of corticotropic activity, decreased sympathetic nervous activity, and increased vagal tone. [26] SWS suppression was investigated in 9 healthy individuals. This resulted in lower insulin sensitivity without compensatory increase in insulin release. An elevation in sympathovagal balance, which could be involved both in the decrease in insulin sensitivity and in the lack of appropriate compensatory increase in insulin in response to glucose. [26] Slow wave sleep was also noted to be significantly decreased amount of SWS in subjects with type 2 diabetes compared to nondiabetic control. [27] Yoda., *et al*. [23] however noted that among 63 T2DM patients, that among other sleep stages, REM latency alone had a significant and negative correlation with HbA1c (> 9).

A recent systematic review and meta-analysis by Lee., *et al*. [22] of 10 studies examining sleep quality and glucose control. They noted from the data pooled from 5 studies that there was no difference in the chance of attaining the goal of HbA1c less than 6.5% or 7% (risk ratio: 1.10; 95% CI: 0.85-1.42) in patients with a difficulty in initiating or maintaining sleep. When HbA1c levels were analyzed as a continuous variable, poorer sleep quality was associated with higher HbA1c levels, indicating poor glycemic control (WMD: 0.35%; 95% CI: 0.12-0.58).

In our study, those who have poor glucose control was 5x more likely to have poor sleep quality. This suggests that poor glucose control contributes to poor sleep quality. There was a statistically significant difference in the PSQI domains for sleep duration, sleep disturbance, sleep latency, day dysfunction and sleep quality between the 2 groups. A previous study also noted that a statistically significant difference in PSQI score with regard to glucose control. They also found a statistically significant difference in six of the seven PSQI domains between the 2 groups except the "use of sleeping medications". [7] We noted the same results where there is a statistically significant difference in sleep latency and sleep duration between the two groups. Poor glucose control are more likely to have poorer sleep quality, longer sleep latency (median 30 mins vs. 20 mins; p=0.001), and shorter duration (median 6 hrs vs. 6.5 hrs; p=0.018) between those with poor and good glucose control. A study noted that a perceived sleep debt of 3 hours per day was associated with an increase in HbA1c level by 1.1% above the median, while in patients with at least 1 complication, a 5-point increase in PSQI score was associated with an increase in HbA1c level by 1.9% above the median. [5]

COPD/asthma was found to be a predictor of poor sleep in our study. This is possibly due to nighttime arousals which could lead to fragmented sleep. COPD patients are found to have diminished amounts of deep sleep and REM sleep. An increased prevalence of insomnia, use of hypnotic medications and an increase in daytime sleepiness compared with the general population was also noted in patients with COPD. Possible mechanisms for frequent arousals in COPD are hypercapnia, increased inspiratory loads and intrinsic PEEP. Sleep deprivation is associated with a mild decrease in forced vital capacity (FVC) (-5%) and forced expiratory volume in 1s (FEV1) (-6%). [28-30] Poor sleep quality is common in patients with COPD, which could lead to worse outcomes.

Our results suggest that the presence of a bedroom companion is protective from poor sleep quality (OR 0.4680, 95% CI 0.2431 to 0.9010, p = 0.023). This finding is also noted in a previous study where they noted better sleep among those married and partnered. [6]

Chasens., *et al.* [6] noted that those with poor sleep quality and daytime sleepiness were associated with difficulty with multiple aspects of self-care and in reduced adherence to self- management behaviors, which may contribute to poor glucose control.

Sleep disordered breathing is more prevalent among diabetic patients ranging from 58-86% vs. 2-4% among non-diabetics. [6,11] In our study, only 33% are high risk for OSA using the Berlin Questionnaire. We also found that excessive daytime sleepiness occurred in 26% of the patients. This is higher compared to 8.5-20.5% of the patients in other diabetic populations. [8]

Since this is a cross-sectional study, we could not infer that poor sleep quality that "worsens" blood sugar, as well as poor sleep quality as a results of poor sugar control. Additional research is needed to establish whether improving sleep quality will improve glucose control. Other limitations of this study is that patients were not screened for insomnia and depression. Those noted to be high-risk for sleep apnea based on Berlin questionnaire and ESS did not undergo an overnight polysomnogram to confirm presence of sleep disordered breathing, the prevalence may be underestimated.

Conclusion

The prevalence of poor sleep among diabetic Filipinos is high at 55%. Poor sleep quality is directly correlated with poor glucose control. Factors that worsen sleep quality among T2DM are elevated hbA1c, obstructive airway disease and sleeping alone in a bedroom

Conflict of interest

There are no existing conflict of interest.

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