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ORIGINAL RESEARCH

Association Between Sleep Duration and Albuminuria in Patients with Type 2 Diabetes: A Cross-Sectional Study in Ningbo, China

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Purpose: Type 2 diabetes mellitus (T2DM) can lead to microvascular complications including diabetic kidney disease. Albuminuria is an important marker to diagnose kidney injury in T2DM patients and healthy sleep duration is important for maintaining good health in patients with T2DM. However, the association between sleep duration and albuminuria in T2DM patients is unclear. Thus, this study aimed to investigate the association between sleep duration and albuminuria in patients with T2DM in Ningbo, China.

Methods: A cross-sectional study was conducted at National Metabolic Management Centre (MMC) - Ningbo First Hospital from March 2018 to February 2021. Adult patients with T2DM were included in the study. The sleep duration (daytime and nocturnal) was self-reported. Albuminuria was defined as the presence of urinary albumin-creatinine ratio ≥30 mg/g. Logistic regression analyses were performed to identify the association.

Results: There were 2688 T2DM patients in the study. In the unadjusted model (1), the odds of albuminuria increased with the daytime sleep duration (31–60 minutes: OR 1.36, 95% CI 1.09–1.71; ≥61 minutes: 1.73, 1.33–2.24). Similarly, after adjusting for age and sex (model 2), the odds of albuminuria increased with the daytime sleep duration (31–60 minutes: 1.34, 1.07–1.68; ≥61 minutes: 1.69, 1.30–2.20). After adjusting for age, sex, physical activity, smoking, alcohol drinking, overweight/obesity, hypertension, hyperuricaemia, duration of T2DM, glycated haemoglobin, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker usage and nocturnal sleep duration (model 3), the odds of albuminuria increased with the daytime sleep duration (31–60 minutes: 1.33, 1.04–1.71; ≥61 minutes: 1.71, 1.29–2.26). However, no relationship was found between nocturnal sleep duration and albuminuria.

Conclusion: Longer daytime sleep is found to be associated with albuminuria in patients with T2DM in Ningbo, China but no association is found between nocturnal sleep duration and albuminuria. The findings are exploratory, and there is a need for longitudinal studies on this topic.

Keywords: type 2 diabetes mellitus, sleep, albuminuria, China

Introduction

Type 2 diabetes mellitus (T2DM) is a serious chronic condition. In China, around 140 million people have diabetes, the largest T2DM population in the world.[1] T2DM can lead to microvascular complications like diabetic kidney disease.[2] In fact, T2DM is the primary cause of chronic kidney disease and can finally lead to end-stage kidney disease.[3] Diabetic kidney disease is common in China, especially among middle-aged and older adults.[4] A meta-analysis reported the prevalence of diabetic kidney disease in China is 22%.[5] Albuminuria, defined as the urinary albumin-creatinine ratio (UACR) ≥30 mg/g, is not only one of the diagnostic indicators of diabetic kidney disease but also plays a key role in the

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progression of diabetic kidney disease.[6] T2DM patients with an increased UACR level have a higher risk of end stage kidney diseases (ie, estimated glomerular filtration rate (eGFR)< 15mL/min/1.73m^2 or renal replacement therapy).[7]

The duration of sleep is associated with a range of health conditions including T2DM.[8–10] Adults are recommended to sleep seven to eight hours per night.[11] Sleep deprivation is common in China, and a meta-analysis of 47 studies reported that 36% of older adults had sleep disturbances,[12] and 23% of T2DM patients sleep for less than six hours per day compared to only 12% of healthy people in China.[13]

Previous studies have found an association between sleep duration and albuminuria in the general population.[14,15] Similar studies conducted in patients with T2DM have predominantly considered nocturnal sleep duration or total sleep duration but not daytime napping[16–18] considering daytime napping is a common practice in China,[19,20] and the findings have been inconsistent.[16–18,21] To the best of the authors' knowledge, no such study on daytime napping has been conducted in patients with T2DM in China. Thus, the study aimed to investigate the association between daytime as well as nocturnal sleep duration and albuminuria in patients with T2DM in Ningbo, China. The findings could support the need for appropriate actions to address this issue.

Methods

Study Design, Site, Population, Data Source and Period

A cross-sectional study was conducted and data were collected through the National Metabolic Management Centre (MMC) - Ningbo First Hospital from 1st March 2018 to 28th February 2021. Please see STROBE checklist (Supplementary Material). MMC is a multi-hospital-based programme running across mainland China to provide standardised management for metabolic diseases and led by Ruijin Hospital, Shanghai.[22] A total of 3170 patients with metabolic diseases were registered and managed at this MMC in the study. The study inclusion criteria were patients aged 18 to 75 years, visiting this MMC for the first time and diagnosed with T2DM based on the World Health Organization (WHO) criteria (1999).[23] In the present study, patients <18 years of age (n=19) and >75 years of age (n=15) and with type 1 diabetes (n=65), gestational diabetes (n=5), other types of diabetes (n=76) and missing data on the exact disease condition (n=87), sleep duration (n=48) and UACR (n=167) were excluded. The rest of the 2688 patients were eligible and included in the present study.

Data Collection and Study Variables

A standardised questionnaire developed and piloted by MMC was used for this purpose, and the physiological, anthropometric and biochemical parameters were measured/analysed by the trained nurse/laboratory staff using the MMC standardised protocol.[22] In this study, the following variables were used: (a) self-reported sociodemographic factors, namely, age (18 to 39 years, 40 to 59 years or ≥60 years) and sex (male or female); (b) self-reported lifestyle factors, namely, physical activity (low, medium or high; assessed using the Chinese version of the International Physical Activity Questionnaire-short (IPAQ),[24] smoking and alcohol drinking (current status); (c) health conditions, namely, overweight/obesity (yes or no; defined as body mass index (BMI) ≥24kg/m^2;[25] body weight and height were measured with light clothes and without shoes in standing position using a calibrated automatic digital weight and height scale (HNH-318, Omron, Japan); weight was measured to the nearest 0.1 kg, height was measured to the nearest 0.5 cm and BMI was calculated as weight in kg divided by height in m^2), hypertension (yes or no; defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg on the day of visit;[26] measured using an automated blood pressure monitor (HBP-1100U, Omron, Japan) in a seated position), hyperuricaemia (yes or no; defined as serum uric acid >7 mg/dL;[27] measured using an enzymatic method (AU5800, Beckman Coulter, USA)), duration of T2DM (<5 years, ≥5 to <10 years or ≥10 years)[28] and glycated hemoglobin (HbA1c; <7% (< 53 mmol/mol) or ≥7% (≥ 53 mmol/mol);[29] measured using the high-performance liquid chromatographic (HPLC) method (D-10 Hemoglobin Analyzer, Bio-Rad, USA)); (d) usage of medicines associated with kidney functions and urinary albumin, namely, angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blocker (ARB) (yes or no); (e) self-reported sleep duration, namely, daytime sleep (none, ≤30 minutes, 31 to 60 minutes or ≥61 minutes)[21,30] and nocturnal sleep (<7 hours, ≥7 to <8 hours, ≥8 to <9 hours or ≥9 hours);[31] and (f) albuminuria (yes or no; defined as the presence of UACR ≥30 mg/g;[32]

UACR was calculated by dividing the urinary albumin value by the urinary creatinine value; urinary albumin and creatinine were measured in the spot urine sample using the immunonephelometry and enzymatic methods, respectively (AU5800, Beckman Coulter, USA)).

Ethics

Ethics approval was obtained from the Research Ethics Committees of Ruijin Hospital (2017-42) and Ningbo First Hospital (2019-R057). Written informed consent was obtained from all the patients.

Statistics Analyses

Numbers and percentages are reported for categorical data, means and standard deviations (SD) for normally distributed continuous data and median and interquartile range (IQR) for skewed continuous data. To identify any association between sleep duration and increased albuminuria, the following models were created: in model 1, simple logistic regression analyses were performed. The dependent variable was albuminuria (yes or no; defined as the presence of UACR ≥30 mg/g), and the independent variable was sleep duration (daytime sleep or nocturnal sleep); in model 2, multiple logistic regression analyses were performed and adjusted for age and sex; and in model 3, multiple logistic regression analyses were performed and adjusted for age, sex, physical activity, smoking, alcohol drinking, overweight/obesity, hypertension, hyperuricaemia, duration of T2DM, HbA1c, ACEI/ARB usage and sleep duration (in the daytime sleep analysis, the nocturnal sleep was adjusted for and vice versa). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Data missing (unknown) on the adjusted variables were included in the adjusted models. A p-value ≤0.05 was considered statistically significant. IBM SPSS statistics version 28.0 for Windows was used for data analyses.

Results

There were 2688 T2DM patients in the study. Table 1 reports the characteristics of the study participants. The mean age was 51 years (SD ±12), and 65% were men. The median daytime sleep duration was 10 minutes (IQR 60 minutes). The mean nocturnal sleep duration was 8 hours (SD ±1). 25.8% of them had albuminuria.

Table 1 Characteristics of T2DM Patients in the Study

	Total (n=2688, 100%)
Age (years)	
18–39	499 (18.6%)
40–59	1486 (55.3%)
≥60	703 (26.2%)
Sex	
Male	1748 (65.0%)
Female	940 (35.0%)
Physical activity	
Low	1182 (44.0%)
Medium	1301 (48.4%)
High	178 (6.6%)

(*Continued*)

Table 1 (Continued).

	Total (n=2688, 100%)
Unknown	27 (1.0%)
Current smoker	
Yes	874 (32.5%)
No	1814 (67.5%)
Current alcohol drinker	
Yes	1189 (44.2%)
No	1498 (55.7%)
Unknown	1 (0.0%)
Overweight/obesity	
Yes	1691 (62.9%)
No	997 (37.1%)
Hypertension	
Yes	986 (36.7%)
No	1700 (63.2%)
Unknown	2 (0.1%)
Hyperuricaemia	
Yes	427 (15.9%)
No	2213 (82.3%)
Unknown	48 (1.8%)
Duration of T2DM (years)	
<5	1019 (37.9%)
≥5-<10	565 (21.0%)
≥10	772 (28.7%)
Unknown	332 (12.4%)
HbA1c (%)	
<7	878 (32.7%)
≥7	1761 (65.5%)
Unknown	49 (1.8%)
ACEI/ARB usage	
Yes	987 (36.7%)
No	1701 (63.3%)

(*Continued*)

Table 1 (Continued).

	Total (n=2688, 100%)
Daytime sleep (minutes)	
None	1322 (49.2%)
≤30	474 (17.6%)
31–60	553 (20.6%)
≥61	339 (12.6%)
Nocturnal sleep (hours)	
<7	430 (16.0%)
≥7-<8	766 (28.5%)
≥8-<9	879 (32.7%)
≥9	613 (22.8%)
Albuminuria	
No	1994 (74.2%)
Yes	694 (25.8%)

Table 2 reports the association between sleep duration and albuminuria in T2DM patients. In model 1, the odds of albuminuria increased with the increasing daytime sleep duration (31 to 60 minutes: OR 1.36, 95% CI 1.09 to 1.71; ≥61 minutes: OR 1.73, 95% CI 1.33 to 2.24). Similarly, in model 2, the odds of albuminuria increased with the daytime sleep duration (31 to 60 minutes: OR 1.34, 95% CI 1.07 to 1.68; ≥61 minutes: OR 1.69, 95% CI 1.30 to 2.20). In model 3, the

Table 2 Association Between Sleep Duration and Albuminuria in Patients with T2DM

	OR (95% CI)	**p-value**
Daytime sleep (minutes)		
Model 1		
None	1	
≤30	1.18 (0.93, 1.51)	0.180
31–60	*1.36 (1.09, 1.71)*	*0.007*
≥61	*1.73 (1.33, 2.24)*	*<0.001*
Model 2		
None	1	
≤30	1.18 (0.92, 1.50)	0.193
31–60	*1.34 (1.07, 1.68)*	*0.012*
≥61	*1.69 (1.30, 2.20)*	*<0.001*

(*Continued*)

Table 2 (Continued).

	OR (95% CI)	p-value
Model 3		
None	1	
≤30	1.23 (0.94, 1.60)	0.128
31–60	*1.33 (1.04, 1.71)*	*0.023*
≥61	*1.71 (1.29, 2.26)*	*<0.001*
Nocturnal sleep (hours)		
Model 1		
<7	1.02 (0.78, 1.34)	0.892
≥7-<8	1	
≥8-<9	0.95 (0.76, 1.19)	0.680
≥9	1.14 (0.90, 1.45)	0.277
Model 2		
<7	1.01 (0.77, 1.32)	0.972
≥7-<8	1	
≥8-<9	0.95 (0.76, 1.19)	0.638
≥9	1.12 (0.88, 1.42)	0.368
Model 3		
<7	0.96 (0.72, 1.29)	0.799
≥7-<8	1	
≥8-<9	0.97 (0.76, 1.23)	0.773
≥9	1.16 (0.89, 1.51)	0.263

Notes: Model 1 - Unadjusted. Model 2 - Adjusted for age and sex. Model 3 - Adjusted for age, sex, physical activity, smoking, alcohol drinking, overweight/obesity, hypertension, hyperuricaemia, duration of T2DM, HbA1c, ACEI/ARB usage and sleep duration (in the daytime sleep analysis, the nocturnal sleep was adjusted for and vice versa). Italic = statistically significant.

odds of albuminuria increased with the daytime sleep duration (31 to 60 minutes: OR 1.33, 95% CI 1.04 to 1.71; ≥61 minutes: OR1.71, 95% CI 1.29 to 2.26). However, no relationship was found between nocturnal sleep duration and albuminuria.

Discussion

In the present study, longer daytime sleep was associated with albuminuria among T2DM patients in Ningbo, China. Considering the adverse effects of longer daytime sleep, a maximum of 30 minutes of daytime sleep can be allowed and anything more than this is not recommended.[33] The study finding is consistent with a study conducted among T2DM patients in Japan (beta coefficient 0.01, 95% CI 0.01 to 0.02).[21] Another study conducted in the general Chinese population found that those who slept during the daytime were at higher risk of albuminuria compared to those who did not sleep during the daytime (0–1 h/day: OR 1.55, 95% CI 1.44 to 1.67; 1–1.5 h/day: OR 1.30, 95% CI 1.14 to 1.49; >1.5 h/day: OR 1.57, 95% CI 1.35 to 1.81).[14] Among newly diagnosed T2DM patients in Turkey, daytime sleep was

found to be associated with 24-h urinary albumin excretion (beta coefficient 0.04, p-value 0.043).[17] Studies conducted in Japan and Singapore have reported a U-shaped association between total sleep duration and albuminuria in T2DM patients.[16,18] This dissimilarity could be due to the fact that they focused on the total sleep duration, and the present study focused separately on daytime and nocturnal sleep durations.

The underlying mechanism behind the association between daytime sleep duration and albuminuria in patients with T2DM remains unclear. It could be due to the following reasons: first, longer sleep duration is likely to indicate less physical activity and energy consumption, which are known to be associated with hyperglycaemia[34] and overweight and obesity.[35] These health conditions can lead to endothelial dysfunction[36] and finally kidney injury.[37] Second, most renal physiological activities follow a circadian rhythm, including renal blood flow, GFR, sodium and water excretion.[38] Longer sleep may disrupt the sleep-wake cycle, affect the circadian rhythm and lead to kidney dysfunction.[39] Circadian disorganisation can cause albuminuria, glomerulosclerosis and renal fibrosis.[40] Third, blood pressure varies throughout the day and is maintained at different times by different control systems. A prolonged daytime sleep could lead to sympathetic reactivation, resulting in a rapid increase in blood pressure[41] and finally leading to kidney injury.[42] Fourth, longer daytime sleep may indicate insufficient nocturnal sleep or poor quality of sleep.[43] The poor quality of sleep increases the inflammatory markers, which contributes to albuminuria.[44] In the present study, nocturnal sleep duration was adjusted for, however, the quality of sleep was not recorded and adjusted for.

In our previous study, shorter nocturnal sleep duration was found to be associated with higher body weight, BMI and visceral fat area.[45] Considering the close relationship between visceral fat accumulation and urinary albumin,[46] the present study explored the relationship between nocturnal sleep duration and albuminuria in T2DM patients. However, no association was found between nocturnal sleep duration and albuminuria. This is also consistent with the study conducted among T2DM patients in Japan.[21] Nocturnal sleep was negatively associated with 24-h urinary albumin excretion in the study conducted on newly diagnosed T2DM patients in Turkey.[17] A study conducted among T2DM patients in China found an association between <6 hours of nocturnal sleep and diabetic kidney disease (defined as the presence of eGFR <60 mL/min/1.73 m^2/UACR >30 mg/g).[47] In these previous studies, different definitions of nocturnal sleep were used and daytime sleep was not adjusted for, and these could be the reasons for different study findings.

The present study has several strengths and weaknesses. To the best of the authors' knowledge, this was the first study to examine the association between daytime sleep duration and albuminuria among T2DM patients in China. The study included a relatively large number of T2DM patients, and the routinely collected data quality was high. Missing data on adjusted variables were low in the study, and multiple logistic regression analyses included the sample with missing data. The sleep duration was self-reported by T2DM patients which may not provide an objective measure of sleep duration. A previous study reported a good correlation between self-reported sleep duration and polysomnography results.[48] Nevertheless, objective measures of sleep should be used in future studies. The UACR level in the body, used to define albuminuria, is affected by multiple factors.[49] Using the average of multiple assessments over a few months could have provided a more accurate assessment of albuminuria. However, the data in the study were coming from a single one-time cross-sectional assessment. Since it was a cross-sectional study, the causal relationship between sleep duration and albuminuria could not be determined, and there is a need for longitudinal studies. The present study did not consider the influence of sleep quality and obstructive sleep apnoea/hypopnoea syndrome, and these need to be explored in future studies.

Conclusions

In the present cross-sectional study, longer daytime sleep is found to be associated with albuminuria in patients with T2DM in Ningbo, China but no association is found between nocturnal sleep duration and albuminuria. The findings are exploratory, and there is a need for longitudinal studies on this topic.

Data Sharing Statement

The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

Ethics Approval

The Research Ethics Committee of Ruijin Hospital, China (2017-42) and the Research Ethics Committee of Ningbo First Hospital, China (2019-R057) approved the study.

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Disclosure

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