

Prevalence of obstructive sleep apnea syndrome in hospitalized patients with type 2 diabetes in Beijing, China

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Keywords

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ABSTRACT

Aims/Introduction: To estimate the prevalence, and patient clinical and demographic profile, as well as risk factors associated with obstructive sleep apnea syndrome (OSAS) in hospitalized patients with type 2 diabetes mellitus in Beijing, China.

Materials and Methods: Hospitalized adult patients with type 2 diabetes mellitus were consecutively screened and invited for an overnight polysomnography from four hospitals in Beijing, China, from May 2016 to February 2017. We used the American Academy of Sleep Medicine 2012 polysomnography recording techniques and scoring criteria to identify the type of apnea and the severity of OSAS. The χ^2 -test was used to evaluate differences between groups regarding the prevalence, and demographic and other clinical parameters.

Results: A total of 735 patients were found eligible for the study, of whom 309 patients completed the overnight polysomnography. The mean age of the patients was 58.2 ± 10.9 years, and most (67.3%) were men. The prevalence of overall (apnea hypopnea index $\geq 5/h$), moderate-to-severe (apnea hypopnea index $\geq 15/h$) and severe (apnea hypopnea index $\geq 30/h$) OSAS was 66.3% (95% confidence interval 60.8–71.6%), 35.6% (95% confidence interval 30.3–41.2%) and 16.5% (95% confidence interval 12.5–21.1%), respectively. Central and mixed apnea contributed 12% to all sleep-disordered breathing. With the aggravation of OSAS, the combined prevalence for central, mixed and obstructive apnea increased from 57% to 70%. We found OSAS to be associated with older age, obesity, self-reported snoring and apnea, and diabetes complications.

Conclusions: Guidelines on screening and treatment of OSAS among hospitalized patients with diabetes are needed to direct the routine practice for diabetes endocrinologists for optimal clinical care of such patients.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) refers to repeated partial (hypopnea) and complete (apnea) obstruction of the upper airway during sleep. However, due to normal respiratory drive in the central nervous system, the chest and abdominal

respiratory efforts still exist¹. Consequences of OSAS include sleep disorders, accidents related to daytime drowsiness, and increased risk of coronary heart disease², hypertension and cerebrovascular disease³. Observational studies in different regions and races have shown the severity of OSAS to be associated with insulin resistance, abnormal glucose metabolism and metabolic syndrome, and is independent of obesity^{4–9}. A few cohort studies in Western countries¹⁰ suggested that OSAS

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might increase the risk of developing diabetes or worsening the condition if it is already existent. In addition, a multitude of conditions, including diabetic kidney disease², diabetic retinopathy¹¹, diabetic nephropathy¹² and diabetic peripheral neuropathy¹³, are associated with OSAS. The International Diabetes Federation calls on specialists to be fully aware of the correlation between OSAS and diabetes, to test for glucose tolerance in all patients with sleep apnea, and to carry out sleep apnea-related tests, and early detection and treatment of all patients with diabetes¹⁴.

In the past decade, just three studies were carried out to estimate the prevalence of OSAS among the Chinese population with diabetes. Whereas Lam *et al.*¹⁵ reported a rate of OSAS of 53.9% among 165 patients with diabetes in one Hong Kong hospital using a polysomnogram, Zhang *et al.*¹⁶ and Zhang *et al.*¹⁷, who used the portable monitor, reported 66.7% among 210 patients in four Beijing hospitals and 60.0% among 880 participants from 12 cities around China, respectively. Of these, only one study, comprising a small sample size, used the gold standard of polysomnogram to diagnose obstructive sleep apnea. Therefore, more robust studies with larger sample sizes at different settings are required to verify the prevalence, patient characteristics and risk factors of OSAS among patients with diabetes.

The aim of the present study was to assess the prevalence of OSAS among hospitalized patients with type 2 diabetes. We further intended to estimate the proportion of patients with mild, moderate and severe OSAS, and identify the patient-related profiles in those with central, mixed, and obstructive apnea and hypopneas. Finally, we sought to explore the association between OSAS with potential predictors and related complications. We expect that this work will provide a basis for the development of clinical guidelines regarding the screening, diagnosis and treatment of OSAS among hospitalized patients with diabetes.

MATERIALS AND METHODS

Study design and participants

A multicenter, observational cross-sectional study of hospitalized patients with type 2 diabetes was carried out in four tertiary hospitals in Beijing, China, from May 2016 to February 2017. These hospitals were: The Department of Endocrinology and Metabolism at Peking University People's Hospital, Xuanwu Hospital, Beijing Hospital and the Third Medical Center of Chinese Hospital of People's Liberation Army. Overnight polysomnography was used as a standard method for OSAS diagnosis. Patient information was collected from medical records and a pre-designed questionnaire. The study was approved by the ethics committees of the four hospitals, respectively. Written informed consent was obtained from all the participants.

Eligible participants were hospitalized patients with type 2 diabetes, aged ≥ 18 years, and willing to join the study and sign the informed consent. Patients were excluded if they were suffering from chronic obstructive pulmonary disease, bronchial asthma, acute upper respiratory tract infection, acute coronary syndrome or congestive heart failure. We also excluded patients

with new onset stroke within the past 6 months or a previous stroke with significant neurological impairment, and uncontrolled severe neuropsychiatric disorders. Patients who were pregnant or lactating women and were participating in other clinical trials were also excluded.

Participants were recruited consecutively during the study period and screened for eligibility during their hospitalization to ensure as representative a sample as possible. The minimum sample size was 271 based on a two-sided 95% confidence interval with a width of relative 10% and applying an estimated prevalence of OSAS of 60% according to a previous study in a comparable setting.

Data collection and measurement

A pre-designed questionnaire was used to collect study information including demographic data, disease and medication history, patient clinical characteristics, the Epworth Sleepiness Scale, and the Berlin questionnaire. All eligible patients completed the Epworth Sleepiness Scale and Berlin questionnaire about the frequency and extent of snoring, and the extent of daytime fatigue. Reported snoring was categorized as snoring or not; snoring loudly was defined as snoring louder than speaking; the frequency of snoring with apnea during sleep was defined by times per month; observed snoring sleep apnea referred to snoring observed by other people. We reviewed patients' medical records to collect information on age; sex; year of diabetes diagnosis; and clinical characteristics, including height (cm), weight (kg), neck circumference (cm) and waist circumference (cm). Body mass index (BMI; kg/m^2) was calculated as weight divided by height squared. We recorded medication used for diabetes, hypertension and dyslipidemia within 1 week before hospitalization.

We defined hypertension as either systolic blood pressure of ≥ 140 mmHg, diastolic blood pressure of ≥ 90 mmHg or use of antihypertensive drugs in the past week before hospitalization or diagnosis of hypertension in the past. We considered a patient to have dyslipidemia if they used drugs for the treatment of dyslipidemia in the past week before hospitalization or if they had a diagnosis of dyslipidemia in the past or had low-density lipoprotein cholesterol of ≥ 2.6 mmol/L.

We collected laboratory test records on glycated hemoglobin, fasting plasma glucose and low-density lipoprotein cholesterol levels. The complications of diabetes, such as coronary heart disease, cerebral infarction, diabetic retinopathy, diabetic nephropathy and diabetic peripheral neuropathy, were recorded according to the physician's diagnosis in the hospital records (Appendix 1).

Polysomnography study

An overnight polysomnography study (Respironics Alice6; Philips, Murrysville, PA, USA) was carried out in a sleeping room for all participants starting from 22.00 hours to 06.00 hours the next morning. To be regarded as successful, the monitoring had to be recorded for at least 6 h. The polysomnography

study included electrooculogram left outer canthus and right outer canthus positive signal electrode; electroencephalogram C3, C4, O1 and O2 signal electrode; electroencephalogram A1 and A2 signal electrode; electrocardiogram II Limb Guide; electromyography on both sides of the lower chin electrode; leg sensor on double sides; airflow by using oronasal thermistors and nasal pressure transducer; chest and abdominal breathing belt; microphone snoring and body position sensor; as well as a peripheral blood oxygen saturation detector.

The following polysomnographic variables were obtained: apnea hypopnea index (AHI), oxygen desaturation index (ODI), time of oxygen saturation <90%, minimum pulse oxygen saturation, total sleep time, non-rapid eye movement sleep phases 1–4 and rapid eye movement sleep.

All records were analyzed by trained polysomnography technicians and sleep physicians using the current recording techniques and scoring criteria according to the revised 2012 American Academy of Sleep Medicine (AASM) manual 2012¹⁸. Apnea was scored when there was a complete cessation of airflow or $\geq 90\%$ drop in the peak thermal sensor excursion for at least 10s. Apnea was classified as either obstructive sleep apnea, central sleep apnea or mixed sleep apnea. The AHI was defined as the sum of the numbers of apnea and hypopnea that occur during sleep divided by the total sleep time. The diagnosis of sleep disordered breathing required an apnea hypopnea index (AHI) score of five or more events/h. Furthermore, AHI ≥ 15 events/h was considered moderate-to-severe, while AHI ≥ 30 events/h was interpreted as severe OSAS. ODI was defined as the number of events of oxyhemoglobin desaturation $>4\%$ per hour of sleep. Hypopneas were defined as a drop in nasal pressure signal excursion by $\geq 30\%$ with a drop in oxygen saturation by $\geq 3\%$ or an associated arousal.

Statistical analysis

Mean (\pm standard deviation) values are used to describe continuous variables that were normally distributed. For variables that were not normally distributed, data are presented as the median together with the corresponding interquartile range. Categorical data are presented as frequency and percentages. Comparisons between mean values were made using *t*-tests, whereas differences in frequencies were evaluated using χ^2 -tests. The prevalence of OSAS and the 95% confidence intervals (CI) were evaluated for different categories including age, sex, BMI, neck circumference, waist circumference, hypertension, reported snoring, snoring loudly, sleep apnea and diabetes complications. We transformed continuous variables, such as age and BMI levels, into categorical variables, and the χ^2 -test was carried out to assess differences between groups. A two-sided *P*-value <0.05 was considered statistically significant. The SAS EG 7.1 software package (SAS Institute, Cary, NC, USA) was used for all analyses.

RESULTS

A total of 1,735 eligible patients were registered sequentially, of whom 309 successfully completed both the questionnaire and

overnight polysomnography (Figure 1). No significant difference in age was observed between patients who completed the polysomnography test ($n = 309$, 58.2 ± 10.9 years) and those who declined ($n = 426$, 58.7 ± 12.6 years). However, those who declined to participate in the study were mainly men (60.0% vs 67.3%, $P = 0.040$) and had a slightly lower BMI (25.97 ± 3.48 vs 26.57 ± 4.40 kg/m², $P = 0.020$) when compared with those who participated in the study.

The demographic and potential OSAS-relevant characteristics of the 309 patients included in the study are summarized in Table 1. The patients had a mean diabetes duration of 10.79 years, with most of them (255, 82.5%) reporting having some form of diabetes complications.

The prevalence of OSAS and the accompanying results after univariate comparisons among specific subgroups of severity are shown in Table 2. Significant differences were noted in the prevalence rates of OSAS, with at least one severity level between categories of age, obesity, neck circumference, waist circumference, snoring, snoring loudly, observed sleep apnea and diabetes complications ($P < 0.05$). There were, however, no differences in OSAS severity based on sex, hypertension or dyslipidemia status.

Among all OSAS patients (AHI $>5/h$), central (7%) and mixed (5%) apnea contributed 12% to the total sleep-disordered breathing, respectively. When OSAS worsened from mild to severe, the proportion of all kind apnea increased from 57% to 70%; this was accompanied by a decrease in the proportion of hypopnea episodes from 42% to 29% (Table 3).

Three parameters of nocturnal hypoxemia measured by ODI, time of oxygen saturation $<90\%$ and minimum pulse oxygen

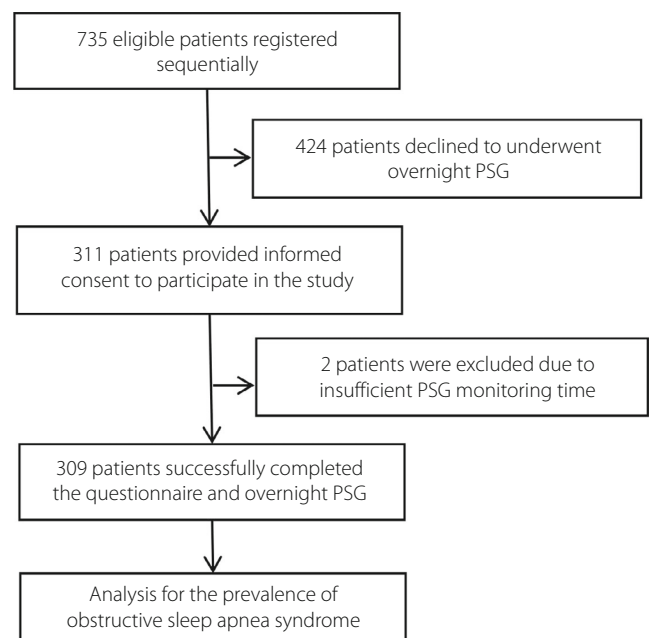


Figure 1 | Flowchart of selection of study participants. PSG, polysomnography.

Table 1 | Baseline characteristics

| Characteristics | Without OSAS (AHI <5) (n = 104) | With OSAS (AHI ≥5) (n = 205) | Total (n = 309) | P-value* |
|---|------------------------------------|---------------------------------|--------------------|----------|
| Mean age, years (SD) | 54.4 (10.8) | 60.2 (10.5) | 58.2 (10.9) | <0.001 |
| Male, n (%) | 66 (63.5%) | 142 (69.3%) | 208 (67.3%) | 0.304 |
| Mean BMI, kg/m ² (SD) | 26.24 (5.09) | 26.74 (4.01) | 26.57 (4.40) | 0.343 |
| Mean waist circumference, cm (SD) | 94.45 (8.82) | 97.30 (9.68) | 96.34 (9.48) | 0.013 |
| Mean neck circumference, cm (SD) | 38.25 (3.36) | 38.91 (3.35) | 38.69 (3.36) | 0.114 |
| Hypertension, n (%) | 62 (59.6%) | 140 (68.3%) | 202 (65.4%) | 0.130 |
| Self-reported snoring, n (%) | 67 (65.7%) | 163 (79.5%) | 230 (74.9%) | 0.008 |
| Self-reported snoring loudly, n (%) | 21 (20.6%) | 80 (39.2%) | 101 (33.0%) | 0.001 |
| Observed sleep apnea, n (%) | 18 (18.6%) | 59 (29.5%) | 77 (25.9%) | 0.044 |
| Mean diabetes duration, years (SD) | 9.17 (7.04) | 11.61 (8.07) | 10.79 (7.81) | 0.009 |
| Median ESS score (Q1, Q3) | 4.0 (2.0, 8.0) | 5.0 (2.0, 9.0) | 5.0 (2.0, 9.0) | 0.096 |
| Mean HbA1c, (SD) | 8.40 (1.83) | 8.56 (2.05) | 8.51 (1.98) | 0.512 |
| Mean FPG (SD) | 8.85 (3.21) | 8.73 (4.21) | 8.77 (3.89) | 0.808 |
| Mean LDL (SD) | 2.52 (0.90) | 2.59 (0.78) | 2.57 (0.82) | 0.489 |
| Mean TSH (SD) | 1.90 (1.13) | 2.11 (1.55) | 2.04 (1.42) | 0.218 |
| Any diabetes complications [†] , n (%) | 76 (73.1%) | 179 (87.3%) | 255 (82.5%) | 0.002 |

*P-values for continuous variables are from the *t*-test, and P-values for categories are from the χ^2 -test. [†]Any diabetes complications: patients have at least one of the following diabetes complications: diabetic kidney disease, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, cardiovascular disease or cerebral infarction events.

AHI, apnea hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein; OSAS, obstructive sleep apnea syndrome; TSH, thyroid-stimulating hormone

saturation suggested that nocturnal hypoxemia was more severe in the patients with OSAS. However, the profiles of rapid eye movement sleep, and stage 1 and stage 2 sleep were indistinguishable between patients with OSAS and those who did not have the condition (Table 4).

DISCUSSION

To the best of our knowledge, we are the first in China to estimate the prevalence of OSAS in hospitalized patients with type 2 diabetes, and to quantify differences in the prevalence rates based on demographic and clinical categories (such as age, obesity and disease-related complications) based on the gold standard, polysomnography examination. This multicenter study confirmed the high prevalence of OSAS among patients with diabetes. We also found that central and mixed apnea contributed approximately 12% to the total sleep-disordered breathing. In addition, although the proportion of occurrence of apnea increased with the aggravation of OSAS, the opposite trend was observed with hypopnea. When nocturnal hypoxemia was reported, it was frequently associated with more severe OSAS.

The prevalence of OSAS in participants with type 2 diabetes reported in the present study was 66.3%, which was higher than another polysomnography-based study among Chinese people¹⁵. A recent study¹⁹ in Xiamen, China, observed similar OSAS prevalence to the present study. The variations in the prevalence across the studies might be due to differences in the sleep monitoring devices, as well as the version of AASM

criteria that were applied in the respective studies²⁰. Geographical differences and other potential biases can also contribute to varying outcomes in these studies. For example, in the Xiamen study, 330 patients, from one hospital, with type 2 diabetes and aged 52.7 ± 14.2 years were diagnosed using the latest AASM 2012 scoring criteria¹⁸. Although they also reported a prevalence of 66%, as is the case with the present study, the accuracy of their results can be a subject of debate due to the demanding nature of the technique and unpleasant experience of overnight sleep monitoring. Combined, these factors can provoke potential bias from technicians and a low response rate among study participants. In contrast, the present study featured four hospitals, and applied a rigorous assessment of OSAS to provide the prevalence. We believe that our approach offers more robust observations.

Compared with white European people (75.2%)²¹ and those in the USA (86%)²², the prevalence of OSAS among patients with type 2 diabetes in the present study (66.3%) was much lower. The difference in prevalence rates between Chinese and Western patients could be mainly accounted for by differences in the age distribution and BMI. In the studies mentioned previously, patients were slightly older (mean age 59.3–64.1 years) and frequently obese (mean BMI 36.5–37.4 kg/m²). This contrasts the age (mean 58.2) and BMI (26.5) profile of patients in the present study. Notably, when patients across the studies are matched for age and BMI (obesity status), the influence of ethnicity in the prevalence of OSAS appears to diminish. For instance, considering patients aged ≥ 60 years

Table 2 | Prevalence of obstructive sleep apnea syndrome, moderate-to-severe obstructive sleep apnea syndrome and severe obstructive sleep apnea syndrome among different subgroups[†]

| Population subgroups | Overall OSAS (AHI ≥5) | | Moderate-to-severe OSAS (AHI ≥15) | | Severe OSAS (AHI ≥30) | |
|------------------------------------|-----------------------|---------|-----------------------------------|---------|-----------------------|---------|
| | % (95% CI) | P-value | % (95% CI) | P-value | % (95% CI) | P-value |
| Total | 66.3 (60.8, 71.6) | | 35.6 (30.3, 41.2) | | 16.5 (12.5, 21.1) | |
| Age (years) | | | | | | |
| <60 | 56.3 (48.2, 64.2) | <0.001 | 30.4 (23.3, 38.2) | 0.059 | 17.7 (12.1, 24.6) | 0.573 |
| ≥60 | 76.7 (69.1, 83.2) | | 40.7 (32.7, 49.0) | | 15.3 (10.0, 22.1) | |
| Sex | | | | | | |
| Male | 68.3 (61.5, 74.5) | 0.304 | 38.0 (31.4, 45.0) | 0.209 | 19.2 (14.1, 25.3) | 0.064 |
| Female | 62.4 (52.2, 71.8) | | 30.7 (21.9, 40.7) | | 10.9 (5.6, 18.7) | |
| BMI (kg/m ²) | | | | | | |
| <28 | 62.2 (55.3, 68.8) | 0.019 | 30.1 (24.0, 36.9) | 0.003 | 11.5 (7.5, 16.6) | <0.001 |
| ≥28 | 75.8 (66.1, 83.8) | | 47.5 (37.3, 57.8) | | 27.3 (18.8, 37.1) | |
| Neck circumference | | | | | | |
| <36 | 59.6 (44.3, 73.6) | 0.175 | 23.4 (12.3, 38.0) | 0.007 | 6.4 (1.3, 17.5) | <0.001 |
| 36–42 | 65.6 (58.5, 72.3) | | 34.9 (28.2, 42.0) | | 12.8 (8.5, 18.3) | |
| ≥42 | 76.4 (63.0, 86.8) | | 52.7 (38.8, 66.3) | | 38.2 (25.4, 52.3) | |
| Waist circumference (female, male) | | | | | | |
| <80, 85 | 70.4 (49.8, 86.2) | 0.081 | 37.0 (19.4, 57.6) | 0.328 | 7.4 (0.9, 24.3) | 0.033 |
| 80–90, 85–95 | 56.8 (45.8, 67.3) | | 29.5 (20.3, 40.2) | | 10.2 (4.8, 18.5) | |
| ≥90, 95 | 70.2 (63.1, 76.5) | | 38.7 (31.8, 46.0) | | 20.9 (15.4, 27.4) | |
| Hypertension | | | | | | |
| No | 60.7 (50.8, 70.0) | 0.130 | 29.9 (21.4, 39.5) | 0.128 | 11.2 (5.9, 18.8) | 0.068 |
| Yes | 69.3 (62.4, 75.6) | | 38.6 (31.9, 45.7) | | 19.3 (14.1, 25.4) | |
| Dyslipidemia | | | | | | |
| No | 62.7 (53.3, 71.4) | 0.260 | 33.9 (25.4, 43.2) | 0.600 | 16.1 (10.0, 24.0) | 0.865 |
| Yes | 68.9 (61.8, 75.4) | | 36.8 (30.0, 44.1) | | 16.8 (11.8, 22.9) | |
| Snoring | | | | | | |
| Without snoring | 54.5 (42.8, 65.9) | 0.008 | 19.5 (11.3, 30.1) | <0.001 | 7.8 (2.9, 16.2) | 0.016 |
| With snoring | 70.9 (64.5, 76.7) | | 41.3 (34.9, 48.0) | | 19.6 (14.6, 25.3) | |
| Snoring loudly | | | | | | |
| No | 60.5 (53.4, 67.2) | 0.001 | 30.7 (24.5, 37.5) | 0.007 | 11.2 (7.2, 16.4) | <0.001 |
| Yes | 79.2 (70.0, 86.6) | | 46.5 (36.5, 56.7) | | 27.7 (19.3, 37.5) | |
| Observed sleep apnea | | | | | | |
| No | 64.1 (57.4, 70.4) | 0.044 | 30.9 (24.9, 37.5) | 0.004 | 11.8 (7.9, 16.8) | <0.001 |
| Yes | 76.6 (65.6, 85.5) | | 49.4 (37.8, 61.0) | | 31.2 (21.1, 42.7) | |
| Any diabetes complications | | | | | | |
| No | 48.1 (34.3, 62.2) | 0.002 | 18.5 (9.3, 31.4) | 0.004 | 11.1 (4.2, 22.6) | 0.240 |
| Yes | 70.2 (64.2, 75.7) | | 39.2 (33.2, 45.5) | | 17.6 (13.2, 22.9) | |

[†]Prevalence (%) was defined as the proportion of participants diagnosed as obstructive sleep apnea syndrome (OSAS), moderate-to-severe OSAS and severe OSAS among those who were recruited and effectively completed the polysomnography sleep test (denominator *n* = 309). AHI, apnea hypopnea index.

and with comorbid obesity (BMI ≥28 kg/m²) in the current study shows a prevalence of OSAS of 85.4% with the moderate-to-severe type of OSAS of 46.3%, as reported for the patients in the other two studies in Europe and the USA. Usually, OSAS is common in the elderly, increasing significantly in those aged ≥65 years, and with obesity²⁰. However, some investigators have reported that ethnicity was an independent risk factor for OSAS, even after controlling for BMI^{20,23}. In the study by Ong and Clerk²³ among Asian patients, OSAS was more severe compared with the experience

by white patients matched for age, sex and BMI. Caution is thus needed in making direct comparisons as far as the prevalence of OSAS between Chinese and Western studies are concerned, as this could be influenced by the type of recording techniques and scoring criteria applied. Furthermore, the pathogenesis of OSAS is complex, and other factors beyond age and BMI, which have not been not considered in the study, such as the upper airway anatomy and neuromuscular control of breathing, could also contribute to the differences in prevalence of OSAS across races^{20,24}.

Table 3 | Level and composition of sleep-disordered breathing among patients with different severity of obstructive sleep apnea syndrome

| Patient group | <i>n</i> | Total AHI | Central apnea | Mixed apnea | Obstructive apnea | Hypopnea |
|---|----------|-----------|---------------|-------------|-------------------|-------------|
| All patients | 309 | 16.03 | 1.13 (7%) | 0.80 (5%) | 6.95 (43%) | 6.98 (44%) |
| Patients with sleep-disordered breathing (AHI ≥ 5) | 205 | 23.02 | 1.82 (8%) | 1.31 (6%) | 9.80 (43%) | 9.69 (42%) |
| Patients with moderate and Severe sleep-disordered breathing (AHI ≥ 15) | 110 | 34.32 | 3.23 (9%) | 2.40 (7%) | 15.43 (45%) | 13.00 (38%) |
| Patients with severe sleep-disordered breathing (AHI ≥ 30) | 51 | 50.35 | 5.36 (11%) | 4.32 (9%) | 24.96 (50%) | 14.48 (29%) |

Data presented as the mean (%). AHI, apnea hypopnea index.

Table 4 | Comparison of polysomnography results between patients with and without obstructive sleep apnea syndrome

| Polysomnography Parameters | Without OSAS (AHI <5) (<i>N</i> = 104) | With OSAS (AHI ≥ 5) (<i>N</i> = 205) | <i>P</i> value* |
|-----------------------------------|--|--|-----------------|
| Total sleep time, min | 355.09 (58.73) | 345.26 (70.57) | 0.223 |
| AHI, events/h | 2.25 (1.50) | 23.02 (17.85) | <0.001 |
| ODI, events/h | 4.42 (10.60) | 24.34 (23.40) | <0.001 |
| Time, SpO ₂ <90% (min) | 9.36 (42.05) | 24.40 (48.68) | 0.023 |
| Minimum SpO ₂ , % | 88.26 (5.46) | 81.92 (8.30) | <0.001 |
| REM sleep, % | 11.15 (10.03) | 10.13 (8.44) | 0.392 |
| Stage 1 sleep, % | 10.98 (8.33) | 12.92 (9.31) | 0.151 |
| Stage 2 sleep, % | 56.15 (11.79) | 58.21 (12.29) | 0.259 |
| Stage 3 sleep, % | | | |

Data presented as the mean (%). **P* values are from the *t*-test. AHI, apnea hypopnea index; ODI, oxygen desaturation index; OSAS, obstructive sleep apnea syndrome; REM, rapid eye movement.

As observed by others, we noted a higher prevalence of OSAS among patients who were older, had obesity, reported snoring and those who had any diabetes complication^{15–17,22,25}. Epidemiological studies have reported that OSAS prevalence is higher in men than women, and more prevalent in patients with hypertension and dyslipidemia^{15,25}. This was the case in the present study, although the differences between respective groups were not significant, probably due to the small sample size.

Nocturnal hypoxemia parameters could show the severity of OSAS. We found progressive worsening of nocturnal hypoxemia, from mild to severe OSAS, with a correlation between OSAS severity and the minimum pulse oxygen saturation, ODI and time of oxygen saturation <90%. Consistent results have been reported in a study by Chen *et al.*²⁴ in the general Chinese population. However, it is unknown whether OSAS patients had disruption of sleep structure and excessive daytime sleepiness. In the same study, the researchers found non-rapid eye movement sleep phase 1/2 to be increased, and slow wave sleep (non-rapid eye movement sleep phase 3/4) was decreased significantly from mild to severe OSAS, in the general population. In contrast, we found these parameters to be similar between those with and without OSAS.

Increasing evidence shows that most patients with type 2 diabetes suffer from OSAS, which also increases the risk of micro- and macrovascular complications. There are, however, no strategies, guidelines or tools specially developed to aid in

the screening, diagnosis and treatment of OSAS. We believe that the present results provide a useful resource toward initiating OSAS screening and treatment of hospitalized patients with type 2 diabetes.

A key strength of the present study is that, to the best of our knowledge, we are the first to estimate the prevalence of OSAS in patients with type 2 diabetes in China using the latest polysomnography recording techniques and revised scoring criteria (AASM 2012). We, therefore, have confidence in the results in the context of current recommendations¹⁸. In addition, the present study features multiple centers in which consecutive recruitment of study participants was carried out, enabling the extrapolation of the findings to a larger diabetes population. Finally, we excluded, by design, those with sleep-disordered breathing conditions, such as chronic obstructive pulmonary disease, congestive heart failure, severe anxiety and depression, thus minimizing the likelihood of misclassification bias.

Despite the notable strengths of the present study, our results should be considered in the context of some limitations. As study participants were drawn from type 2 diabetes inpatients in the four selected tertiary hospitals only, the study findings cannot be generalized to patients in primary and secondary hospitals or to outpatients with fewer diabetes complications. In addition, 57% of participants declined to undergo polysomnography, which might contribute to selection bias and, potentially,

an over estimation of prevalence. Nevertheless, we anticipate minimal consequences of the probable bias mentioned earlier, as the age distribution, sex and BMI profile in the present study was similar to those reported previously among patients with type 2 diabetes in China^{15–17,19}.

In conclusion, the present study showed that two out of every three patients with type 2 diabetes suffer from OSAS, and that 50% of the OSAS are moderate to severe. The aggravation of OSAS is positively related to increased apnea and severe nocturnal hypoxemia. We strongly suggest the development of strategies and guidelines for endocrinologists to carry out OSAS screening, diagnosis and treatment during their routine practice for this category of patients.

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DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: The study was approved by the ethics committee of the four hospitals, respectively.

Informed consent: Written informed consent was obtained from all the participants.

Registry and the registration no. of the study/trial: N/A.

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2. Diabetic nephropathy was considered if any result of the following seven laboratory tests was beyond the normal ranges: (i) serum creatinine 44–133 $\mu\text{mol/L}$; (ii) urinary albumin to creatinine ratio 30 mg/g; (iii) urinary albumin excretion rate $<20 \mu\text{g/min}$; (iv) microalbuminuria $<20 \text{mg/L}$; (v) urinary albumin in 24 h urine collection $<30 \text{mg/day}$; (vi) urine protein “negative”; or (vii) 24-h proteinuria $<0.3 \text{g/day}$ (Improving Global Outcomes [KDIGO] CKD Work Group. *KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease*).

APPENDIX 1

DIAGNOSIS CRITERIA FOR DIABETIC RETINOPATHY, DIABETIC NEPHROPATHY, DIABETIC PERIPHERAL NEUROPATHY AND CARDIOVASCULAR EVENTS

1. Diabetic retinopathy was diagnosed by fundal photographs, ophthalmoscope or fluorescein angiography according to staging criterion adopted at the Chinese Medical Association Third National Conference of Ophthalmology (Xiaoxin Li. Diabetic ocular fundus diseases prevention and treatment guideline. *Chinese Journal of Practical Ophthalmology* 2014; 50).
3. The diagnosis of diabetic peripheral neuropathy was made by physicians using comprehensive analysis of clinical manifestations, neurological examination and auxiliary examination according to the “diabetic peripheral neuropathy diagnostic and treatment recommendations” established by the Chinese Endocrinologist Association metabolic practitioner branch in 2019 (Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care* 2017;40:136–154. DOI:10.2337/dc16-2042).
4. Cardiovascular events in this study included acute myocardial infarction, abnormal coronary angiography, coronary artery bypass graft, percutaneous coronary intervention, cerebral ischemic stroke and hemorrhagic stroke. Patients who had any of these cardiovascular events before the study were considered to have a history of cardiovascular events.