

# Gender Differences in the Association Between Obstructive Sleep Apnea and Diabetes

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**Objective:** This study aimed to explore the association between obstructive sleep apnea (OSA) and diabetes in a Chinese population based on a cross-sectional analysis of patient data from a large tertiary care hospital in China and analyses whether there are any gender differences in this association.

**Methods:** A total of 794 (615 men and 179 women) inpatients were involved in this study. Polysomnography (PSG) was used to diagnose OSA, and overnight PSG testing was performed on each subject included in this study. All study subjects were also diagnosed with whether they had diabetes by an endocrinologist in the hospital.

**Results:** After adjusting for sex, age, smoking status, alcohol consumption and body mass index (BMI) groups, the results showed that the number of apnea–hypopnea index (AHI) events was a risk factor for diabetes, with a 9% (95% CI: 1–17%) increase in the risk of diabetes per unit increase, while subjects with higher (per unit increase) lowest oxygen saturation value monitored during the subject's sleep (LSaO<sub>2</sub>) with a 13% (95% CI: 4–22%) decrease in the risk of diabetes. Stratified analyses by gender, after adjustment, in men, OSA and its associated monitoring indicators were statistically significantly associated with diabetes [OR for severe OSA was 2.269 (95% CI: 1.164, 4.425), P=0.016, and OR for severe hypoxemia was 2.228 (95% CI: 1.145, 4.334), P=0.018], while not in women.

**Conclusion:** Our study found a significant association between OSA and diabetes in a Chinese clinical-based population as well as a dose–response relationship between the severity of AHI and severe hypoxemia (LSaO<sub>2</sub> < 80%) and blood glucose, the association has gender difference and was only present significant association in men, which demonstrated that diabetes prevention and blood glucose screening and management should be enhanced for Chinese men with OSA.

**Keywords:** obstructive sleep apnea, diabetes, gender differences, glucose, Chinese

## Introduction

Diabetes is a metabolic disease, an independent risk factor for cardiovascular and cerebrovascular diseases.<sup>1</sup> With the increase in the living standards of people in developing countries, diabetes incidence is increasing day by day and has become an epidemic chronic disease worldwide.<sup>2</sup> According to the latest report, in 2019, approximately 463 million adults aged 20–79 years worldwide had diabetes; it was expected to reach 700.2 million by 2045. IDF World Diabetes Map data of 2019 showed that China had the largest number of diabetic patients between the ages of 20–79 years, 116.4 (95% CI: 108.6–145.7) million people, and it was expected to reach 147.2 (95% CI: 134.7–176.2) million in 2045.<sup>3</sup> In 2019, about 4.2 million people (aged 20–79 years) died of diabetes or its complications, equivalent to

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1 person every 8 seconds, accounting for about 11.3% of all-cause deaths globally.<sup>4</sup> Type 2 diabetes mellitus (T2DM) is the most common type of diabetes.

Obstructive sleep apnea (OSA) is a highly prevalent respiratory disorder associated with sustained/intermittent reduction in blood oxygen saturation and tissue hypoxia, the prevalence in adults is between 35% and 58%.<sup>5</sup> The disorder causes intermittent hypoxemia and hypercapnia, increased oxidative stress, inflammatory response, and sleep fragmentation.<sup>6</sup> These signs and symptoms can further lead to cardiovascular disease, metabolic disease and even premature death.<sup>7–9</sup> Intermittent hypoxemia and recurrent awakenings associated with sleep apnea may affect glucose through activation of the sympathetic nervous system,<sup>10</sup> altered activity of the hypothalamic–pituitary–adrenal axis with increased circulating corticosteroid levels,<sup>11</sup> increased inflammatory markers and adipocyte-derived factors.<sup>12</sup> A number of recent studies have suggested that the increase in the prevalence of diabetes worldwide may be associated with the occurrence of OSA.<sup>13</sup> Although studies on the association between OSA and diabetes have shown inconsistent results,<sup>14,15</sup> a prospective analysis of 1453 non-diabetic participants showed that severe OSA was associated with greater risk of diabetes in the US population,<sup>14</sup> while the results from the Wisconsin Sleep Cohort showed that the association between OSA and diabetes was not significant.<sup>15</sup> Furthermore, some previous studies on the association have not adjusted for the influence of obesity, which is a common risk factor for OSA and diabetes.<sup>16</sup> And the studies on the association between OSA and diabetes in the Chinese population were limited. Therefore, this study aimed to explore the association between OSA and diabetes in a Chinese population based on a cross-sectional analysis of patient data from a large tertiary care hospital in China, and analyses whether there are any gender differences in this association.

## Design and Methods

### Study Sample

We used clinical data of all objectives from the Sleep Monitoring Unit, Chinese PLA General Hospital (a large tertiary hospital in China, Beijing) from August 2004 to December 2017.

We collected data regarding each participant's gender, age, alcohol and smoking consumption, diabetes and glucose status.

## Measurements

T2DM was defined according to the American Diabetes Association criteria<sup>17</sup> by endocrinologists in the hospital. That is T2DM is typically diagnosed when fasting plasma glucose (FPG)  $\geq 7$  mmol/L or 2-h post oral glucose load plasma glucose (2-h PG)  $\geq 11.1$  mmol/L or blood glucose  $\geq 11.1$  mmol/L at any time.<sup>17</sup> Blood glucose was analyzed using colorimetric method in a Modular P800 analyzer (Roche Diagnostics, Mannheim, Germany), and the unit of glucose was mmol/L. Polysomnography (PSG) is used to diagnose obstructive sleep apnea (OSA) and overnight PSG testing (from 10:00 p.m. to 7:00 a.m. and the sleep time is more than 7 hours) was performed on each subject included in this study. The PSG equipment model is EMBLA N7000. After automatic analysis of the original data, all corrections were manually verified. Two doctors who have worked in this field for more than 5 years provided a blinded interpretation of the objects' monitoring results. OSA was defined as the apnea–hypopnea index (AHI)  $\geq 5$  times/h with typical symptoms associated with OSA, such as inability to rejuvenate after sleep, daytime drowsiness, fatigue or insomnia, wheezing on awakening, playing snoring very loudly or having apnea, etc.), or although there are no obvious symptoms, but AHI  $\geq 15$  times/h.<sup>18</sup> Further, OSA patients were divided into a mild OSA group (AHI 5–15 times/h), a moderate OSA group (AHI 16–30 times/h), and a severe OSA group (AHI  $>30$  times/h) according to the AHI.<sup>19</sup> In overnight PSG testing, participants were defined as hypoxia when the lowest oxygen saturation (LSaO<sub>2</sub>)  $\leq 90\%$ .<sup>20</sup> According to the LSaO<sub>2</sub>, OSA patients were divided into a mild hypoxia group (LSaO<sub>2</sub> 86–90%), a moderate hypoxia group (LSaO<sub>2</sub> 80–85%), and a severe hypoxia group (LSaO<sub>2</sub>  $<80\%$ ).<sup>21</sup>

The included covariates include sex, age, smoking status, drinking status and body mass index (BMI). This information was collected by a trained primary nurse. An alcohol user was defined as a regular drinker who consumes alcohol almost every day and has been regularly consuming alcohol for more than six months. A former drinker was defined as having stopped regular alcohol consumption for more than six months.<sup>22</sup> A current smoker was defined as a person who, at the time of the survey, smoked a tobacco product. A former smoker was defined as a person who had smoked daily for at least 6 months during their lives but at the time of the survey did not use a tobacco product.<sup>23</sup> BMI (Kg/m<sup>2</sup>) is calculated as weight/

height<sup>2</sup>. According to WHO Asian standards, subjects were divided into four groups by BMI: low body mass group (BMI < 18.5 kg/m<sup>2</sup>), normal group (18.5 kg/m<sup>2</sup>–<BMI<24.0 kg/m<sup>2</sup>), overweight group (24 kg/m<sup>2</sup>–<BMI<28.0 kg/m<sup>2</sup>) and obese group (BMI ≥ 28.0 kg/m<sup>2</sup>).<sup>24</sup>

## Statistical Analysis

SPSS version 26.0 was used for the data analysis. The significance level for all tests was set at a two-tailed  $\alpha$  value of 0.05. The differences in means and proportions were evaluated using Student's *t*-test and the chi-square test, respectively. Multiple linear regression models and logistic regression models were used to identify the association between OSA (including the indexes of OSA) and T2DM (including glucose).

## Ethical Considerations

This study was conducted in accordance with the Declaration of Helsinki. And the committee for medical ethics of the Chinese PLA General Hospital examined and approved this study (No.S2017-327-03). Before completing the questionnaire, each involved participant signed an informed consent form.

## Results

A total of 794 (615 men and 179 women) inpatients were involved in this study. The average age was 57.4 ± 12.7 years (range: 19–90 years). There were 277 objectives with diabetes and 517 without. The prevalence of T2DM was 34.9% (277/794) in this sample, and the prevalence was 32.5% (200/615) in men, 43.0% (77/179) in women. And there were 688 objectives diagnosed by PSG with OSA and 106 without. The average ages of those who with and without T2DM were 59.7 ± 11.0 years (range: 28–87 years) and 56.2 ± 13.3 years (range: 19–90 years), respectively. The general characteristics (age, gender, smoking status, drinking status and BMI) of the participants are shown in Table 1. Compared with the T2DM group, the group without T2DM was younger, had a higher proportion of men, had a lower mean number of AHI events, had a higher mean LSAO<sub>2</sub>, and had a higher proportion who never drank alcohol (Table 1,  $p < 0.05$ ).

Using T2DM (dichotomous variable) as the dependent variable, OSA and its related monitoring indicators were included in the equation as independent variables, respectively. After adjusting for sex, age, smoking status, alcohol consumption and BMI groups, the results showed that the number of AHI events was a risk factor for T2DM, with

a 9% (95% CI: 1–17%) increase in the risk of T2DM per unit increase, while subjects with higher (per unit increase) lowest oxygen saturation value monitored during the subject's sleep (LSaO<sub>2</sub>) with a 13% (95% CI: 4–22%) decrease in the risk of T2DM (Table 2).

Stratified analyses by gender, after adjustment, in men, OSA and its associated monitoring indicators were statistically significantly associated with T2DM. Compared to men without OSA, the risk of T2DM in men with severe OSA (AHI > 30 events/h) was 2.269 (95% CI: 1.164, 4.425),  $P = 0.016$ , and the risk of T2DM in men with severe hypoxemia (LSaO<sub>2</sub> < 80%) was 2.228 (95% CI: 1.145, 4.334),  $P = 0.018$  (Table 2). In women, after adjustment, no statistically significant association was found between OSA/OSA associated monitoring indicators and T2DM (Table 2).

When glucose was involved in multiple linear regressions as a continuous outcome, OSA and its related monitoring indicators were included in the equation as independent variables, respectively. Models A to C showed that increased LSAO<sub>2</sub> was associated with decreased glucose of the objectives after adjustment ( $\beta = -0.011$ , 95% CI:  $-0.021$ ,  $-0.001$ ,  $P = 0.029$ , Table 3). In addition, after adjustment, in women, no significant association was found between OSA/OSA-related monitoring indicators and glucose, while in men, OSA severity was associated with glucose ( $\beta = 0.587$ , 95% CI: 0.038–1.136,  $p = 0.036$ ) and hypoxemia severity was also associated with glucose ( $\beta = 0.582$ , 95% CI: 0.036–1.128,  $p = 0.037$ ) (Table 3).

## Discussion

In this study, in a clinical-based Chinese population, we observed a significant association between OSA and T2DM as well as a dose–response relationship between the severity of AHI and hypoxemia and blood glucose, the association has gender difference and was only present in significant association in men.

Previous observational studies in both the US<sup>14</sup> and Japanese populations<sup>25</sup> have shown a significant association between OSA and the development of T2DM, and the results were consistent with this study. However, most studies did not perform PSG monitoring to diagnose OSA in all included subjects, instead using home multi-lead monitoring or pulse oximetry to monitor nocturnal hypoxia and determine OSA status, and the studies reporting gender differences are limited.

Celen et al<sup>26</sup> found that the contribution of OSA to diabetes development seems to be gender-dependent and

**Table 1** Sociodemographic Variables of the Participants

	Total	Without T2DM	T2DM	P
		(n=517)	(n=277)	
Age (years)	57.4 ± 12.7	56.2 ± 13.3	59.7 ± 11.0	<0.001
AHI (times/h)	25.2 ± 19.1	24.1 ± 18.4	27.2 ± 20.1	0.027
LSaO <sub>2</sub>	74.9 ± 16.0	76.2 ± 14.9	72.5 ± 17.5	0.002
Gender				0.010
Female	179 (22.5%)	102 (19.7%)	77 (27.8%)	
Male	615 (77.5%)	415 (80.3%)	200 (72.2%)	
Age group				<0.001
<45 ys	113 (14.2%)	94 (18.2%)	19 (6.9%)	
45–64 ys	484 (61.0%)	307 (59.4%)	177 (63.9%)	
≥65 ys	197 (24.8%)	116 (22.4%)	81 (29.2%)	
BMI group				0.015
<18.5 kg/m <sup>2</sup>	5 (0.6%)	5 (1.0%)	0 (0.0%)	
18.5–23.9 kg/m <sup>2</sup>	90 (11.3%)	62 (12.0%)	28 (10.1%)	
24.0–27.9 kg/m <sup>2</sup>	322 (40.6%)	224 (43.3%)	98 (35.4%)	
≥28.0 kg/m <sup>2</sup>	377 (47.5%)	226 (43.7%)	151 (54.5%)	
Smoking				0.057
Never	416 (52.4%)	263 (50.9%)	153 (55.2%)	
Former	151 (19.0%)	92 (17.8%)	59 (21.3%)	
Current	227 (28.6%)	162 (31.3%)	65 (23.5%)	
Drinking				0.024
Never	429 (54.0%)	263 (50.9%)	166 (59.9%)	
Former	257 (32.4%)	184 (35.6%)	73 (26.4%)	
Current	108 (13.6%)	70 (13.5%)	38 (13.7%)	
OSA				0.276
No	106 (13.4%)	74 (14.3%)	32 (11.6%)	
Yes	688 (86.6%)	443 (85.7%)	245 (88.4%)	
OSA with hypoxemia				0.180
No	134 (16.9%)	94 (18.2%)	40 (14.4%)	
Yes	660 (83.1%)	423 (81.8%)	237 (85.6%)	
AHI group				0.348
Without OSA	106 (13.4%)	74 (14.3%)	32 (11.6%)	
5–15 times/h	178 (22.4%)	121 (23.4%)	57 (20.6%)	
16–30 times/h	205 (25.8%)	134 (25.9%)	71 (25.6%)	
>30 times/h	305 (38.4%)	188 (36.4%)	117 (42.2%)	
Hypoxemia group				0.042
Without OSA	106 (13.4%)	74 (14.3%)	32 (11.6%)	
>85%	185 (23.3%)	122 (23.6%)	63 (22.7%)	
80–85%	163 (20.5%)	117 (22.6%)	46 (16.6%)	
<80%	340 (42.8%)	204 (39.5%)	136 (49.1%)	

only presents a significant association in women with an OR of 11.8. This inconsistency in the results may be due to the different study populations and the fact that although

the study was a cohort study design, the diagnosis of OSA cases at baseline was not all made using the PSG method, the diagnosis of T2DM was also self-reported by patients

**Table 2** The Odds Ratios (ORs) for T2DM

Exposure	Model A	P	Model B	P	Model C	P
AHI (times/h)	1.009 (1.001, 1.016)	0.027	1.011 (1.003, 1.019)	0.008	1.009 (1.001, 1.017)	0.031
LSaO <sub>2</sub>	0.986 (0.977, 0.995)	0.002	0.983 (0.974, 0.992)	0.000	0.987 (0.978, 0.996)	0.007
OSA	1.279 (0.821, 1.992)	0.276	1.316 (0.834, 2.079)	0.238	1.312 (0.834, 2.064)	0.240
OSA with hypoxemia	1.317 (0.880, 1.970)	0.181	1.365 (0.902, 2.064)	0.141	1.323 (0.874, 2.001)	0.185
AHI group						
Without OSA						
5–15 times/h	1.089 (0.647, 1.834)	0.747	1.122 (0.658, 1.912)	0.673	1.098 (0.646, 1.866)	0.730
16–30 times/h	1.225 (0.740, 2.030)	0.430	1.211 (0.722, 2.031)	0.468	1.264 (0.756, 2.113)	0.372
>30 times/h	1.439 (0.895, 2.313)	0.133	1.544 (0.944, 2.525)	0.084	1.502 (0.922, 2.447)	0.103
Hypoxemia group						
Without OSA						
>85%	1.194 (0.714, 1.997)	0.499	1.187 (0.699, 2.014)	0.525	1.298 (0.766, 2.198)	0.332
80–85%	0.909 (0.531, 1.555)	0.728	0.896 (0.517, 1.554)	0.696	0.893 (0.518, 1.542)	0.686
<80%	1.542 (0.965, 2.462)	0.070	1.673 (1.030, 2.715)	0.037	1.598 (0.986, 2.590)	0.057
Male						
AHI	1.010 (1.002, 1.019)	0.020	1.011 (1.002, 1.021)	0.013	1.009 (1.000, 1.019)	0.041
LSaO <sub>2</sub>	0.989 (0.979, 0.999)	0.029	0.987 (0.977, 0.997)	0.012	0.990 (0.980, 1.000)	0.050
OSA	2.061 (1.094, 3.880)	0.025	2.035 (1.075, 3.853)	0.029	2.017 (1.063, 3.826)	0.032
OSA with hypoxemia	1.981 (1.144, 3.433)	0.015	2.001 (1.150, 3.484)	0.014	1.962 (1.121, 3.431)	0.018
AHI group						
Without OSA						
5–15 times/h	1.872 (0.925, 3.791)	0.081	1.877 (0.921, 3.825)	0.083	1.823 (0.892, 3.726)	0.099
16–30 times/h	1.815 (0.906, 3.637)	0.093	1.738 (0.862, 3.504)	0.122	1.813 (0.898, 3.661)	0.097
>30 times/h	2.335 (1.208, 4.513)	0.012	2.340 (1.203, 4.553)	0.012	2.269 (1.164, 4.425)	0.016
Hypoxemia group						
Without OSA						
>85%	2.103 (1.049, 4.218)	0.036	1.976 (0.979, 3.987)	0.057	2.139 (1.056, 4.333)	0.035
80–85%	1.563 (0.757, 3.230)	0.228	1.516 (0.728, 3.158)	0.267	1.481 (0.710, 3.089)	0.295
<80%	2.279 (1.184, 4.386)	0.014	2.328 (1.202, 4.510)	0.012	2.228 (1.145, 4.334)	0.018
Female						
AHI (times/h)	1.010 (0.993, 1.026)	0.246	1.007 (0.990, 1.024)	0.420	1.010 (0.992, 1.028)	0.296
LSaO <sub>2</sub>	0.962 (0.937, 0.986)	0.003	0.961 (0.936, 0.986)	0.002	0.966 (0.942, 1.001)	0.051
OSA	0.839 (0.417, 1.692)	0.625	0.650 (0.306, 1.380)	0.262	0.773 (0.367, 1.629)	0.499
OSA with hypoxemia	0.855 (0.440, 1.664)	0.645	0.662 (0.324, 1.350)	0.256	0.761 (0.371, 1.559)	0.455
AHI group						
Without OSA						
5–15 times/h	0.558 (0.226, 1.375)	0.205	0.432 (0.168, 1.110)	0.081	0.514 (0.200, 1.319)	0.166
16–30 times/h	0.980 (0.425, 2.261)	0.962	0.761 (0.315, 1.839)	0.545	0.895 (0.371, 2.159)	0.806
>30 times/h	0.986 (0.431, 2.258)	0.974	0.766 (0.319, 1.840)	0.552	0.957 (0.391, 2.344)	0.924

(Continued)

**Table 2** (Continued).

Exposure	Model A	P	Model B	P	Model C	P
Hypoxemia group Without OSA						
>85%	0.556 (0.221, 1.398)	0.212	0.446 (0.169, 1.174)	0.102	0.572 (0.216, 1.512)	0.260
80–85%	0.463 (0.187, 1.149)	0.097	0.357 (0.138, 0.926)	0.034	0.432 (0.167, 1.114)	0.083
<80%	1.575 (0.706, 3.512)	0.267	1.182 (0.506, 2.762)	0.699	1.454 (0.615, 3.439)	0.394

Notes: Model A: crude model. Model B: adjusted for age and gender; Model C: adjusted for age, gender, smoking, drinking status and BMI.

**Table 3** The Association Between OSA/OSA Related Monitoring Indicators and Glucose

Exposure	Model A	P	Model B	P	Model C	P
AHI (times/h)	0.007 (−0.001, 0.016)	0.077	0.009 (0.000, 0.017)	0.042	0.006 (−0.003, 0.014)	0.187
LSaO <sub>2</sub>	−0.014 (−0.024, −0.004)	0.005	−0.015 (−0.025, −0.005)	0.002	−0.011 (−0.021, −0.001)	0.029
AHI GROUP Without OSA						
5–15 times/h	−0.055 (−0.597, 0.486)	0.841	−0.003 (−0.548, 0.542)	0.991	−0.078 (−0.615, 0.460)	0.778
16–30 times/h	0.133 (−0.395, 0.661)	0.621	0.175 (−0.357, 0.708)	0.518	0.120 (−0.404, 0.643)	0.654
>30 times/h	0.259 (−0.239, 0.757)	0.308	0.331 (−0.175, 0.837)	0.200	0.202 (−0.295, 0.700)	0.426
Hypoxemia group Without OSA						
>85%	−0.026 (−0.563, 0.512)	0.926	0.026 (−0.517, 0.570)	0.925	0.021 (−0.514, 0.556)	0.938
80–85%	−0.013 (−0.563, 0.538)	0.964	0.006 (−0.548, 0.561)	0.982	−0.065 (−0.611, 0.481)	0.816
<80%	0.304 (−0.187, 0.795)	0.225	0.379 (−0.118, 0.876)	0.135	0.240 (−0.253, 0.733)	0.340
OSA	0.140 (−0.320, 0.601)	0.551	0.194 (−0.273, 0.661)	0.416	0.102 (−0.356, 0.561)	0.661
OSA with hypoxemia	0.222 (−0.196, 0.640)	0.299	0.272 (−0.151, 0.695)	0.208	0.163 (−0.256, 0.581)	0.447
Male						
AHI (times/h)	0.011 (0.003, 0.020)	0.008	0.012 (0.003, 0.020)	0.007	0.009 (0.001, 0.018)	0.036
LSaO <sub>2</sub>	−0.012 (−0.021, −0.002)	0.017	−0.012 (−0.022, −0.003)	0.012	−0.009 (−0.019, 0.001)	0.070
AHI GROUP Without OSA						
5–15 times/h	0.402 (−0.194, 0.998)	0.186	0.396 (−0.199, 0.992)	0.193	0.351 (−0.242, 0.945)	0.246
16–30 times/h	0.532 (−0.052, 1.116)	0.075	0.509 (−0.075, 1.094)	0.088	0.498 (−0.082, 1.077)	0.093
>30 times/h	0.688 (0.137, 1.238)	0.015	0.676 (0.126, 1.227)	0.016	0.587 (0.038, 1.136)	0.036
Hypoxemia group Without OSA						
>85%	0.455 (−0.134, 1.045)	0.130	0.422 (−0.168, 1.012)	0.161	0.462 (−0.126, 1.049)	0.124
80–85%	0.454 (−0.155, 1.063)	0.144	0.432 (−0.178, 1.042)	0.166	0.374 (−0.232, 0.981)	0.227
<80%	0.683 (0.138, 1.228)	0.014	0.682 (0.137, 1.227)	0.014	0.582 (0.036, 1.128)	0.037
OSA	0.572 (0.052, 1.091)	0.031	0.558 (0.039, 1.077)	0.036	0.502 (0.015, 1.018)	0.047
OSA with hypoxemia	0.543 (0.083, 1.003)	0.021	0.539 (0.079, 0.999)	0.022	0.461 (0.000, 0.922)	0.050

(Continued)

**Table 3** (Continued).

Exposure	Model A	P	Model B	P	Model C	P
Female						
AHI (times/h)	-0.001 (-0.024, 0.022)	0.935	0.002 (-0.022, 0.025)	0.897	-0.004 (-0.028, 0.020)	0.737
LSaO <sub>2</sub>	-0.031 (-0.062, -0.001)	0.046	-0.031 (-0.062, -0.001)	0.045	-0.025 (-0.056, 0.005)	0.100
AHI GROUP						
Without OSA	0		0		0	
5–15 times/h	-0.737 (-1.997, 0.524)	0.254	-0.604 (-1.900, 0.691)	0.362	-0.635 (-1.851, 0.580)	0.307
16–30 times/h	-0.359 (-1.565, 0.848)	0.561	-0.235 (-1.483, 1.012)	0.712	-0.278 (-1.458, 0.903)	0.645
>30 times/h	-0.234 (-1.429, 0.962)	0.702	-0.117 (-1.357, 1.122)	0.853	-0.316 (-1.499, 0.867)	0.601
Hypoxemia group						
Without OSA	0		0		0	
>85%	-0.786 (-2.066, 0.494)	0.230	-0.706 (-2.013, 0.601)	0.291	-0.692 (-1.934, 0.550)	0.276
80–85%	-0.734 (-1.973, 0.505)	0.247	-0.609 (-1.886, 0.668)	0.351	-0.648 (-1.848, 0.552)	0.291
<80%	0.026 (-1.121, 1.174)	0.964	0.200 (-0.996, 1.396)	0.744	0.015 (-1.131, 1.160)	0.980
OSA	-0.423 (-1.428, 0.582)	0.411	-0.303 (-1.356, 0.750)	0.573	-0.404 (-1.386, 0.578)	0.421
OSA with hypoxemia	-0.233 (-1.188, 0.721)	0.632	-0.092 (-1.098, 0.915)	0.858	-0.162 (-1.109, 0.786)	0.738

**Notes:** Model A: crude model. Model B: adjusted for age and gender; Model C: adjusted for age, gender, smoking, drinking status and BMI.

with mailed questionnaires rather than diagnosed in hospital by a medical professional, and the fact that the study included only 31 women, of whom 7 developed T2DM in self-reported follow-up, all of which may have contributed to the inconsistent results.

In the present study, a dose–response association was observed not only between the severity of OSA and its monitoring indicators (AHI and LSaO<sub>2</sub>) for the risk of having T2DM but also between OSA and its monitoring indicators severity and blood glucose, independent of BMI and smoking and drinking habits. The association between OSA and blood glucose and the risk of having T2DM, independent of BMI, can be attributed to several possible mechanisms. For example, intermittent hypoxemia and recurrent awakenings associated with sleep apnea may affect glucose through activation of the sympathetic nervous system,<sup>27</sup> altered activity of the hypothalamic–pituitary–adrenal axis with increased circulating corticosteroid levels,<sup>11</sup> increased inflammatory markers (eg, hsCRP, interleukin-6, and tumor necrosis factor- $\alpha$ ) and adipocyte-derived factors (eg, leptin, adiponectin, and resistin).<sup>12</sup>

Previous study<sup>28</sup> has suggested that a higher proportion of men in the patients with OSA and women with OSA tend to be more obese and older than men with OSA, which partly explains the failure to observe an association between OSA and T2DM independent of BMI in women in this study.

There were differences in fat distribution, upper airway length and collapse, neurochemical control mechanisms, chemical response levels, arousal responses and sex hormone effects between the sexes.<sup>29</sup> Thus, men appear to be more susceptible to OSA than women because even with the same degree of obesity as women, men have a higher degree of peri-airway fat deposition,<sup>26,30</sup> suggesting a difference in pathogenic mechanisms between men and women, which could partially explain the association between OSA and T2DM observed only in men in this study.

This study had several limitations. First, due to the inherent limitations of cross-sectional studies, we are unable to infer a causal association between OSA and T2DM, and subsequent rigorously designed cohort studies are needed to verify whether OSA treatment can have a beneficial effect on blood glucose levels by improving AHI/LSaO<sub>2</sub>. Secondly, our sample may not be fully representative of OSA patients in China because our hospital is one of the best hospitals in China, and the proportion of patients here may differ from the proportion in other hospitals; however, the representativeness of our sample should not materially affect the internal validity of this study. Finally, we could not examine the hazard ratio of OSA with respect to T2DM because of the lack of detailed information regarding the onset time of OSA.

## Conclusion

In summary, our study found a significant association between OSA and T2DM in a Chinese clinical-based population, as well as a dose–response relationship between the severity of AHI and severe hypoxemia (LSaO<sub>2</sub> <80%) and blood glucose, the association has gender difference and was only present significant association in men. Both OSA and T2DM are diagnosed professionally by a doctor in the hospital. We found that OSA may be a risk factor for T2DM in men; however, further cohort studies should be conducted to verify the causal relationship. Our findings demonstrated that T2DM prevention and blood glucose screening and management should be enhanced for Chinese men with OSA.

## Disclosure

The authors report no conflicts of interest in this work.

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