

SCIENTIFIC INVESTIGATIONS

## Prevalence of Type 2 Diabetes in Patients with Obstructive Sleep Apnea in a Multi-Ethnic Sample

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**Study Objectives:** Relationship of obstructive sleep apnea (OSA) with insulin resistance and type 2 diabetes in Caucasians has been studied, but this association has not been investigated in Hispanic and African-Americans. The objective of this study is to determine the prevalence of type 2 diabetes in patients evaluated for OSA in a predominantly African American and Hispanic sample. The secondary objective is to evaluate the relationship of REM related OSA and type 2 diabetes.

**Methods:** 1008 consecutive patients who had a comprehensive polysomnography were evaluated. OSA was defined as an obstructive apnea-hypopnea index (AHI) of  $\geq 5$  per hour. REM AHI of  $\geq 10$  was considered to indicate REM related OSA.

**Results:** The prevalence of type 2 diabetes was 30.1% in the group with OSA compared to 18.6% in those without OSA. The subjects with OSA had significantly increased odds of type 2 diabetes compared with those without OSA (odds ratio = 1.8, 95% confidence interval: 1.3–2.6) but this association became non-significant when controlled

for confounding variables and covariates (odds ratio = 1.3, 95% confidence interval: 0.9–2.0). Middle-aged participants with OSA had 2.8 times higher odds for type 2 diabetes, when compared to younger or middle aged without OSA, controlling for covariates. Finally, the odds of type 2 diabetes were 2.0 times higher in patients with REM AHI of  $\geq 10/h$  independent of confounding variables.

**Conclusions:** OSA is not independently associated with type 2 diabetes in a predominantly African American and Hispanic sample. However, the relationship of REM related OSA with type 2 diabetes may be statistically significant.

**Keywords:** Type 2 diabetes mellitus, Obstructive sleep apnea, REM sleep

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More than 24 million Americans have diabetes mellitus (DM), and nearly one million new cases of diabetes are diagnosed every year.<sup>1</sup> Type 2 diabetes accounts for 90% to 95% of all cases of diabetes. Diabetes mellitus was the sixth leading cause of death in 2002, with the risk of death almost twice that of non-diabetic patients of similar age.<sup>2</sup> According to the Centers for Disease Control and Prevention, African Americans have a 1.8-fold increase and Hispanic Americans have a 1.7-fold increase in the prevalence of diabetes mellitus compared to Caucasian Americans.<sup>2</sup>

In addition to ethnicity, sleep disordered breathing (SDB) is independently associated with glucose intolerance and insulin resistance,<sup>3,4</sup> and may also contribute to the pathogenesis of type 2 DM. These findings were reported by the Sleep Heart

Health Study, which comprised 93.4% Caucasian Americans.<sup>4</sup> The Wisconsin Sleep Cohort study reported a high prevalence of type 2 DM with SDB in a population that comprised 96% Caucasian Americans,<sup>5</sup> but the incidence was not increased after 4 and 8 years of follow-up. The relationship between SDB and type 2 DM has not been defined in Hispanic or African Americans. The objective of our study is to determine whether obstructive sleep apnea (OSA) is associated with type 2 DM in a sample consisting of predominantly Hispanic and African Americans.

Studies have suggested that REM related SDB is more common in mild to moderate cases of OSA,<sup>6</sup> and thus, may be a marker of early obstructive sleep apnea. We hypothesized that the relationship of REM related OSA and type 2 DM could be independent in this racially diverse sample.

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### RESEARCH DESIGN AND METHODS

#### Study Design

This was a retrospective study in which we reviewed the records of 1008 consecutive patients who had polysomnography in the Sleep Science Center at the University of Illinois at

**Table 1**—Characteristics of the Patient Population

CHARACTERISTICS	AHI < 5 (n = 263)	AHI ≥ 5 (n = 745)	p value for difference b/w means or proportions
Age (years)	45 ± 14.6	51.5 ± 12.8	< 0.0001
Gender			
Male	75 (28.5%)	393 (52.8%)	< 0.0001
Female	188 (71.5%)	352 (47.2%)	
Race*			
Caucasian	47 (18.2%)	121 (16.5%)	0.02
Hispanic	39 (15.1%)	109 (14.8%)	
African American	165 (63.7%)	500 (68%)	
Asian	8 (3.1%)	5 (0.7%)	
BMI (kg/m <sup>2</sup> )	37.0 ± 10	42.0 ± 11	< 0.0001
Neck (inches)**	15.5 ± 1.6	17 ± 1.9	< 0.0001
Smoking current	49 (21.9%)	235 (37%)	< 0.0001
Lowest oxygen saturation	84.2 ± 6.7	74.9 ± 10.7	< 0.0001
Time with oxygen saturation more than 90%	96.1%	85.6%	< 0.0001

Student's *t*-test was used to compare continuous variables and chi-square test to compare categorical variables between the OSA and control groups. *p*-value ≤ 0.05 or less indicates statistical significance. \*Information was missing on 14 subjects for race. \*\*Information on the neck size was available for 593 subjects only. AHI, apnea-hypopnea index; BMI, body mass index (weight in kg/ height in m<sup>2</sup>).

Chicago Medical Center (UICMC) from June 2004 to February 2006. This research was approved by the Institutional Review Board (IRB) at the University of Illinois at Chicago (UIC). The patients were referred to the Sleep Science Center for evaluation of snoring, witnessed apnea episodes while asleep, unrefreshing sleep, or excessive daytime somnolence. Exclusion criteria were age < 18 years, pregnancy, or diagnosed neuromuscular disease.

## Methods

Comprehensive nocturnal polysomnography was performed in the Sleep Science Center with recording of electroencephalography, electro-oculography, oro-nasal airflow, snoring, chest and abdominal respiratory movements, chin and bilateral leg electromyography, body position, electrocardiography, and finger pulse-oximeter. Obstructive apnea was identified as cessation of airflow ≥ 10 sec, with continued chest and abdominal movement. Hypopnea was identified as ≥ 30% reduction in airflow accompanied by 4% decrease in oxygen saturation and/or followed by an arousal, with continued chest and abdominal movement. Obstructive apnea-hypopnea index (AHI) was defined as the number of obstructive apneas or hypopneas per hour of sleep.

Subjects who had an AHI ≥ 5/h were defined as having obstructive sleep apnea (OSA). Subjects who had an AHI < 5/h were included in the non-OSA group. REM AHI was defined as the number of obstructive apneas or hypopneas per hour of REM sleep. REM AHI ≥ 10/h was considered REM related OSA. The presence or absence of type 2 DM was determined by reviewing medical records, patient self-report, or the use of anti-diabetic medications. Patients with type 1 DM, as determined by the patients' physician notes and medications, were not included in the analysis.

## Statistical Analysis

SAS version 8.2 (by SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis. Student's *t*-test was used to compare continuous variables and chi-square test to compare

categorical variables between the OSA and non-OSA groups. Multivariate logistic regression analysis was used to evaluate the association of type 2 DM (primary outcome) with different covariates and risk factors, including obstructive sleep apnea, age, gender, race, body mass index (BMI), neck size, smoking, alcohol and drug abuse, oxygen nadir, and duration of oxygen desaturation during polysomnography. Some of the major risk factors for type 2 DM, such as levels of physical activity and family history, were not accurately available in the charts, and hence, were not utilized. A 2-tailed *p* value ≤ 0.05 was considered to indicate statistical significance.

## RESULTS

The characteristics and comorbidities of the study population are summarized in Table 1. A total of 1008 consecutive subjects were included in the study. There were 66.9% African Americans, 16.9% Caucasians, 14.9% Hispanics, and 1.3% Asians. OSA was diagnosed in 745 individuals (74%) while 263 individuals in the non-OSA group (26%) served as the control. The subjects in the OSA group were, on average, 6.5 years older than the non-OSA group. There were 52.8% males in OSA group while only 28.5% in the non-OSA group. As expected, the patients with OSA had a higher BMI (42 kg/m<sup>2</sup> vs. 37 kg/m<sup>2</sup>) and a bigger neck size (17 vs. 15.5 inches) than the non-OSA group. Overall, 37% of the patients in OSA group were current smokers compared to 21.9% in non-OSA group.

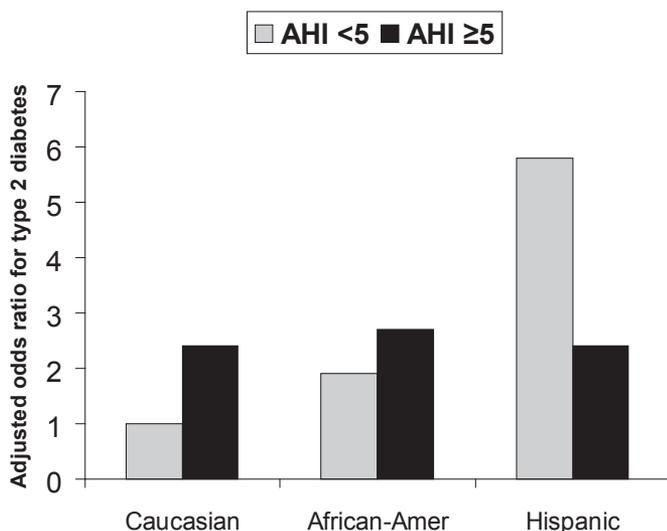
As detailed in Table 2, the prevalence of type 2 DM was 30.1% in the group with OSA compared to 18.6% in the non-OSA group (unadjusted OR 1.8, 95% CI 1.3–2.6; *p* = 0.0012). Among diabetics, the mean hemoglobin A1c was higher in patients with OSA than those without OSA (mean HbA1c 6.8 versus 6.5, respectively; *p* = 0.08). In addition, patients with OSA had a higher prevalence of hypertension (58.7% vs. 37.8%) and CHF (7.9% vs. 3%) than those without OSA.

Univariate logistic regression analysis (Table 3, model 1) showed a significant association between the primary outcome of type 2 DM and presence of OSA, with an odds ratio of 1.8 (95% CI 1.3–2.6; *p* = 0.0012). We assessed for potential con-

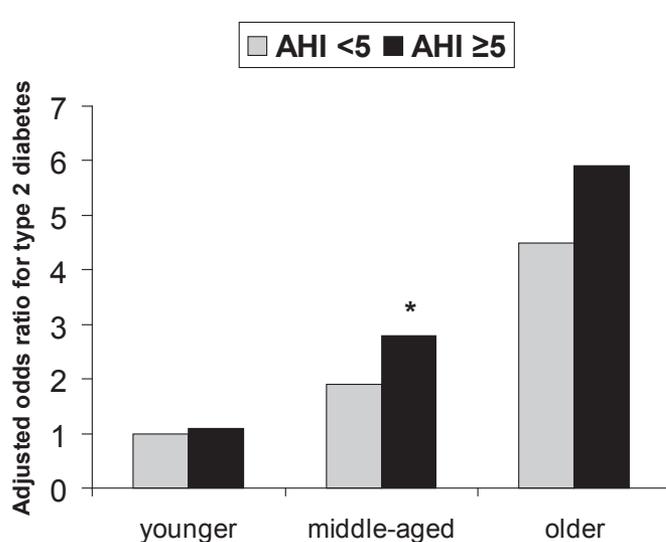
**Table 2**—Comorbidities of the Patient Population

COMORBIDITY	AHI < 5 (n = 263)	AHI ≥ 5 (n = 745)	p value for difference b/w means or proportions
Type 2 DM	49 (18.6%)	224 (30.1%)	0.0003*
HbA1c	Mean: 6.5	Mean: 6.8	0.08
Alcohol use	32 (14.5%)	103 (16.9%)	0.42
Drug abuse	7 (3.2%)	28 (4.6%)	0.39
CAD	16 (6.1%)	63 (8.5%)	0.22
Hypertension	99 (37.8%)	437 (58.7%)	< 0.0001*
CHF	8 (3.0%)	59 (7.9%)	0.006*
Hyperlipidemia	46 (17.5%)	150 (20.1%)	0.35
Asthma	64 (24.3%)	129 (17.3%)	0.01*
COPD	15 (5.4%)	45 (6.1%)	0.49
Liver disease	10 (3.6%)	19 (2.6%)	0.37
AIDS	3 (1.1%)	5 (0.7%)	0.51
ESRD	4 (1.4%)	17 (2.3%)	0.4
Hypothyroidism	17 (6.2%)	39 (5.3%)	0.58
Depression	48 (18.3%)	99 (13.3%)	0.05*

Student's *t*-test was used to compare continuous variables and chi-square test to compare categorical variables between the OSA and control groups. P-value ≤ 0.05 indicates statistical significance (\*). DM, diabetes mellitus; HbA1c, glycosylated hemoglobin; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; AIDS, acquired immunodeficiency syndrome; ESRD, end-stage renal disease.



**Figure 1**—Adjusted odds ratio for type 2 diabetes in racial subgroups stratified according to presence or absence of obstructive sleep apnea, controlling for BMI, gender, and age.



**Figure 2**—Adjusted odds ratio for type 2 diabetes mellitus in age subgroups stratified according to presence or absence of obstructive sleep apnea, controlling for BMI, gender and race. \*Statistically significant compared to younger subjects without OSA and/or middle aged subjects without OSA. Younger 18-40 years, Middle-aged > 40-60 years, Older > 60 years

finding effects of BMI, age, gender, race, neck size, smoking, oxygen nadir, and duration of oxygen desaturation. Among these, only BMI and age were found statistically to be potential confounders. Multivariate logistic regression analysis was used to further examine the relationship between type 2 diabetes and AHI, while controlling for potentially important clinical covariates and confounders including BMI, age, gender, race, oxygen nadir and duration with oxygen saturation > 90% (Table 3, model 1). In multiple logistic regression analysis, the odds ratio for type 2 DM in patients with OSA compared to those without OSA was 1.3 (95 % confidence interval, 0.9–2.0;  $p = 0.15$ ) after controlling for covariates. We also found a direct and dose-dependent association of type 2 DM with age and BMI. In addition current smoking, alcohol abuse or neck size did not have a statistically significant relationship to type 2 diabetes (information not shown).

The severity of OSA was categorized as mild, moderate, and severe, based on AHI of 5 to 14.9, 15 to 29.9, and ≥ 30, respectively. The odds for type 2 DM were high in all the categories of OSA in crude analysis compared to patients without OSA (Table 4, model 2). However, when controlling for covariates, the results were not statistically significant (Table 4, model 2).

We examined the association of type 2 DM and OSA in the different ethnic and age subgroups. We did not find any significant association in Caucasian or African-American subgroups. However, Hispanics had high prevalence of type 2 DM and OSA did not affect this relationship (Figure 1). The middle-aged group with OSA had higher odds of having type 2 diabetes mellitus than younger or middle-aged participants without OSA (odds ratio 2.8,

**Table 3**—(Model 1): Results of Logistic Regression Analysis with Type 2 DM as the Dependent Variable and OSA (AHI ≥ 5) with Other Covariates as Independent Variables

Covariates	Odds Ratio	95% Confidence Interval	p-value
<b>Unadjusted</b>			
AHI ≥ 5	1.8	1.3-2.6	0.0012
<b>Adjusted</b>			
AHI ≥ 5	1.3	0.9-2.0	0.15
Age, years			
18-40	1.0 (Reference)		
40-60	2.3	1.5-3.6	< 0.0001
> 60	5.0	3.1-8.2	< 0.0001
BMI, kg/m <sup>2</sup>			
20-30	1.0 (Reference)		
30-40	2.6	1.4-4.6	0.0014
40-50	2.9	1.6-5.4	0.0005
> 50	5.2	2.7-10.1	< 0.0001
Male gender	0.9	0.6-1.2	0.63
Race/Ethnicity			
White	1.0 (Reference)		
Hispanic	2.0	1.2-3.4	0.01
Black	1.2	0.8-1.9	0.41
Oxygen nadir			
> 90%	1.0 (Reference)		
75-90%	0.5	0.2-1.4	0.20
< 75%	0.5	0.2-1.5	0.21
Time (oxygen saturation above 90%)			
> 90%	1.0 (Reference)		
75-90%	1.3	0.8-2.0	0.25
< 75%	1.2	0.7-1.8	0.53

AHI, apnea-hypopnea index; BMI, body mass index

95% confidence interval 1.4–5.6; p = 0.003), after adjusting for BMI, gender, and race (Figure 2). There was a high prevalence of type 2 DM in older patients, with or without OSA.

**Relationship of REM AHI and Type 2 Diabetes**

Subjects with REM AHI ≥ 10/h had significantly higher odds of type 2 diabetes than subjects with REM AHI < 10/h, with odds ratio of 2.7 (95% CI, 1.8–3.9; p < 0.0001, Table 5, model 3). BMI and age were found to be possible confounders. However, the relationship remained statistically significant (odds ratio 2.1, 95% CI 1.3–3.3; p = 0.001), even after controlling for confounders and covariates of clinical interest like BMI, age, race, gender, and oxygenation parameters as described in model 3 (Table 5).

**DISCUSSION**

We found that the prevalence of type 2 diabetes was 30.1% in patients with OSA, compared to 18.6% in patients without OSA. Our result is similar to that reported by Meslier et al,<sup>3</sup> who found a prevalence of type 2 diabetes of 30% in OSA patients and 13.9% in non-OSA patients in a cross-sectional analysis.

In our study, the unadjusted odds ratio for the risk of type 2 diabetes in subjects with OSA was statistically significant. However, the association became non-significant when we controlled for BMI, age and other covariates of potential interest like race and gender.

**Table 4**—(Model 2): Results of Logistic Regression Analysis with Type 2 DM as the Dependent Variable and OSA Severity Categories with Other Covariates as Independent Variables

Covariates	Odds Ratio	95% Confidence Interval	p-value
<b>Unadjusted</b>			
OSA severity			
None	1.0 (Reference)		
Mild	1.8	1.2-2.8	0.005
Moderate	1.5	0.95-2.5	0.07
Severe	1.9	1.3-2.8	0.001
<b>Adjusted</b>			
OSA severity			
None	1.0 (Reference)		
Mild	1.5	0.9-2.4	0.06
Moderate	1.1	0.7-1.9	0.61
Severe	1.2	0.7-1.9	0.44
Age, years			
18-40	1.0 (Reference)		
40-60	2.4	1.5-3.6	< 0.0001
> 60	5.1	3.1-8.3	< 0.0001
BMI, kg/m <sup>2</sup>			
20-30	1.0 (Reference)		
30-40	2.6	1.5-4.7	0.0013
40-50	3.0	1.6-5.6	0.0004
> 50	5.4	2.8-10.4	< 0.0001
Male gender	0.9	0.7-1.3	0.78
Race/Ethnicity			
White	1.0 (Reference)		
Hispanic	2.0	1.2-3.5	0.01
Black	1.2	0.8-1.9	0.39
Oxygen nadir			
> 90%	1.0 (Reference)		
75-90%	0.5	0.2-1.6	0.20
< 75%	0.5	0.2-1.4	0.24
Time (oxygen saturation above 90%)			
> 90%	1.0 (Reference)		
75-90%	1.4	0.9-2.2	0.18
< 75%	1.2	0.7-1.9	0.46

OSA severity, none: AHI < 5, mild: AHI 5-14.9, moderate: AHI 15-29.9, severe: AHI ≥ 30. AHI, apnea-hypopnea index; BMI, body mass index

Our results are consistent with several studies on the association of sleep disordered breathing with glucose tolerance, insulin resistance and type 2 diabetes. Glucose intolerance and insulin resistance are considered known risk factors and possible precursors to type 2 DM. In cross-sectional studies, AHI and hypoxemia have been shown to be associated with glucose intolerance and insulin resistance, independent of BMI, age, gender and other confounders. Most of these studies were done on predominantly Caucasian or Asian samples, and the effect of race was not evaluated.<sup>3,4,7-10</sup> Punjabi et al. reported in 2,656 predominantly Caucasian subjects included in the Sleep Heart Health Study Cohort that subjects with mild SDB (AHI 5-14.9) and moderate to severe SDB (AHI ≥ 15) had increased odds of glucose intolerance; adjusted odds ratios of 1.27 (95% CI 0.98–1.64) and 1.46 (95% CI 1.09–1.97), respectively. Hypoxemia during sleep was also associated with glucose intolerance, independent of age, BMI, waist circumference and gender.<sup>4</sup> A recent study suggested that mild oxyhemoglobin desaturation

of less than 4% during sleep may predispose to fasting hyperglycemia.<sup>10</sup> Few prospective studies have concluded that habitual snoring may independently increase the risk of type 2 diabetes.<sup>11,12</sup> The Wisconsin Sleep Cohort study examined the prevalence and incidence of type 2 diabetes in 1,387 patients, mostly Caucasians, and observed an odds ratio of 2.3 for type 2 diabetes with an AHI of 15 or greater compared to an AHI of less than 5 (95% CI 1.28–4.11), after adjusting for age, gender and body habitus but AHI was not predictive of *developing* diabetes within 4 years.<sup>5</sup> Several studies have addressed the efficacy of CPAP in treatment of glucose intolerance and diabetes but the results have not been conclusive.<sup>13–15</sup>

There are several possible mechanisms by which OSA could be associated with glucose intolerance and type 2 DM. Severe OSA results in an increased neurogenic sympathetic activity and circulating levels of norepinephrine,<sup>4,16,17</sup> which could result in increased glycogenolysis, lipolysis, and insulin resistance. It is also possible that SDB leads to release of cortisol resulting in higher glucose concentration and excessive insulin secretion.<sup>18,19</sup> Yet another possibility is that adipocyte-derived inflammatory mediators, such as IL-6, TNF- $\alpha$ , and leptin, which are released as a result of cyclic hypoxia, contribute to insulin resistance and hyperglycemia.<sup>20–25</sup> Sleep loss and poor sleep quality have been associated with the risk of type 2 diabetes in several studies as well.<sup>26–29</sup>

When examining the relationship of type 2 DM and OSA in different ethnic and age subgroups, Hispanics had a high prevalence of type 2 DM, irrespective of OSA. We also observed that the odds of type 2 DM in middle aged patients with OSA were 2.8 times as high as odds for younger or middle aged participants without OSA. The older participants had higher odds of type 2 DM regardless of OSA status. These ethnic and age related differences would be interesting to explore in prospective fashion.

REM related SDB is more common in mild to moderate cases of OSA, especially in women and in patients younger than 55 years of age.<sup>30–32</sup> We found a strong and independent association of REM AHI with type 2 diabetes. This relationship may be explained on the premise that there may be more pronounced neurohormonal perturbations and cytokine release during REM sleep caused by apnea and hypopnea, as compared to NREM sleep.<sup>33–36</sup> This may increase the risk of insulin resistance and type 2 diabetes. Another reason for high REM AHI may be sleep fragmentation leading to reduced REM sleep time, as has been described in OSA. Even if a high REM AHI is secondary to sleep fragmentation, it could still serve as an important marker for the prevalence of type 2 diabetes.

The current investigation has several strengths. To the best of our knowledge, this study is the first to examine the relationship between OSA and type 2 DM in a sample composed predominantly of African Americans and Hispanics. Though there is a paucity of studies in sleep disordered breathing directed towards this population,<sup>37</sup> there are numerous investigations of outcomes including DM, hypertension, coronary artery disease, etc., indicating the increased vulnerability of these ethnic groups. Several studies have reported that after controlling for obesity, socioeconomic status, and health care access, Hispanics and African Americans had worse glycemic control than Caucasians, based on data from the National Health and Nutrition Examination

**Table 5**—(Model 3): Results of Logistic Regression Analysis with Type 2 DM as the Dependent Variable and REM Related OSA with Other Covariates as Independent Variables

Covariates	Odds Ratio	95% Confidence Interval	p-value
<i>Unadjusted</i>			
REM AHI $\geq 10$ /hr	2.7	1.8-3.9	< 0.0001
<i>Adjusted</i>			
REM AHI $\geq 10$ /hr	2.1	1.3-3.3	0.001
Age, years			
18-40	1.0 (Reference)		
40-60	2.0	1.3-3.3	0.004
> 60	3.9	2.2-6.9	< 0.0001
BMI, kg/m <sup>2</sup>			
20-30	1.0 (Reference)		
30-40	2.4	1.2-4.6	0.009
40-50	2.5	1.3-5.1	0.009
> 50	5.5	2.6-11.7	< 0.0001
Male gender	1.0	0.7-1.5	0.83
Race/Ethnicity			
White	1.0 (Reference)		
Hispanic	1.8	0.9-3.5	0.07
Black	1.0	0.6-1.7	0.97
Oxygen nadir			
> 90%	1.0 (Reference)		
75-90%	0.4	0.1-1.4	0.15
< 75%	0.3	0.1-1.4	0.13
Time (oxygen saturation above 90%)			
> 90%	1.0 (Reference)		
75-90%	1.2	0.7-2.1	0.42
< 75%	1.0	0.6-1.8	0.99

AHI, apnea-hypopnea index; BMI, body mass index

Surveys (NHANES).<sup>38</sup> In addition, it has been shown that socioeconomic risk factors might not fully explain the high cardiovascular disease mortality in African Americans compared to Caucasians.<sup>39</sup> The CDC has also recently reported that the prevalence of obesity is higher in African American and Hispanic women than Caucasian women.<sup>40</sup> It is possible that the prevalence of OSA may be higher in African Americans and Hispanics than the traditional data generally quoted from Caucasians, and it may contribute to the poor metabolic and cardiovascular outcomes.

Other strengths of our study include the large sample size of 1008 subjects, with a wide range of age, BMI, and AHI, and inclusion of both genders. Furthermore, all of our patients were evaluated with comprehensive overnight polysomnography. This study has a number of weaknesses that should be considered. It is cross-sectional and retrospective in design and, therefore, cannot establish the temporal association of diabetes with OSA or with REM AHI. In addition, the study relied on existing medical records for data collection including the diagnosis of type 2 DM. It is possible that we may have missed some cases of undiagnosed type 2 DM, and some of the important risk factors for diabetes like family history and physical activity could not be accurately determined. However, several other epidemiologic studies have relied on an established diagnosis of diabetes.<sup>4</sup> Another limitation of this study is that it used a patient sample referred to a sleep disorders center, instead of a general

population sample. There were several differences between the OSA and control groups, including BMI, age, gender, neck size, and smoking, which might have influenced the results of our study. However many of our associations persisted even after adjusting for confounding variables.

In summary, our study shows that obstructive sleep apnea is not independently associated with type 2 diabetes in a predominantly African American and Hispanic sample. However, the relationship of REM related OSA with type 2 diabetes may be statistically significant in this population. These findings are preliminary and prospective studies are needed to further examine this hypothesis.

### ABBREVIATIONS

AHI = apnea-hypopnea index  
 BMI = body mass index  
 CDC = Centers for Disease Control and Prevention  
 DM = diabetes mellitus  
 NHANES = National Health and Nutrition Examination Surveys  
 OSA = obstructive sleep apnea  
 REM = rapid eye movement

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**Institution where work was performed:** Department of Medicine, Section of Pulmonary, Critical Care and Sleep Medicine, University of Illinois at Chicago, Chicago IL

### DISCLOSURE STATEMENT

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