ORIGINAL ARTICLE

Associations between Obstructive Sleep Apnea, Sleep Duration, and Abnormal Fasting Glucose

The Multi-Ethnic Study of Atherosclerosis

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Abstract

Rationale: No data exist as to the role of ethnicity in the associations between obstructive sleep apnea (OSA), sleep duration, and metabolic dysfunction.

Objectives: To examine links between OSA, objectively measured habitual sleep duration, and fasting glucose in U.S. ethnic groups.

Methods: The Multi-Ethnic Study of Atherosclerosis is a multisite community-based study that conducted polysomnography and wrist actigraphy. In 2,151 subjects (1,839 in fully adjusted models), the apnea–hypopnea index was used to classify OSA as none (0–4.9/h), mild (5–14.9/h), or moderate to severe (≥15/h). Actigraphic sleep duration was classified as short (≤5 h/night), intermediate (>5 and <8 h/night), or long (≥8 h/night). Subjects were classified as having normal fasting glucose (<100 mg/dl and no hypoglycemic medication use) or abnormal fasting glucose (≥100 mg/dl and/or hypoglycemic medication use).

Measurements and Main Results: The sample was 45.8% male, age 68.5 ± 9.2 (mean ± SD) years, and 27.3% African American, 37.2% white, 11.8% Chinese, and 23.8% Hispanic. The prevalence of abnormal fasting glucose was 40.2%. Relative to subjects without apnea, moderate-to-severe OSA was significantly associated with abnormal fasting glucose in African Americans (odds ratio, 2.14; 95% confidence interval, 1.12–4.08) and white participants (odds ratio, 2.85; 95% confidence interval, 1.20–6.75), but not among Chinese or Hispanic subjects, after adjusting for site, age, sex, waist circumference, and sleep duration ($P = 0.06$ for ethnicity-by-OSA severity interaction). In contrast, sleep duration was not significantly associated with abnormal fasting glucose after considering the influence of OSA.

Conclusions: This large multiethnic study confirmed previous reports of an independent association between OSA and metabolic dysfunction, and suggested that this association may vary by ethnicity.

Keywords: obstructive sleep apnea; type 2 diabetes mellitus; insulin resistance; ethnicity

The prevalence of type 2 diabetes mellitus (T2DM) in the United States has increased markedly in recent decades, particularly among ethnic minorities (1), and it has been suggested that insufficient sleep and/or sleep disorders may play an important role in the development of impaired glycemic control. Obstructive sleep apnea (OSA) has been identified as an independent risk factor for T2DM (2–6); potential mechanisms include sympathetic activation, oxidative stress, inflammation, and/or hypothalamic–pituitary–adrenal axis dysfunction. Extremes of habitual sleep duration, both short and long, also have been identified as predictors of T2DM (7, 8), whereas short-term sleep deprivation and fragmentation experiments induce insulin resistance (9, 10). Several limitations in prior work preclude a complete understanding of the association between sleep exposures and glucose homeostasis.

First, all but one study have relied on self-reported sleep duration (11), and it is known that subjective and objective measurements of sleep correlate only moderately (12). Second, studies

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At a Glance Commentary

Scientific Knowledge on the Subject: Prior studies have shown significant associations between obstructive sleep apnea and self-reported sleep duration with glycemic status; however, these studies have primarily focused on white populations and have not evaluated these relationships in minority populations at highest risk for diabetes.

What This Study Adds to the Field: Our study found that independent of obesity and sleep duration, moderate-to-severe obstructive sleep apnea is associated with abnormal fasting glucose in African Americans, and this association is of similar magnitude to that observed in white participants. In contrast, this association was much weaker in the Hispanic and Chinese subgroups. Actigraphic sleep duration was not independently associated with abnormal fasting glucose in any group.

investigating the influence of OSA have not adequately controlled for sleep duration, and vice versa; thus, the independent effects of OSA and sleep duration are unknown. Finally, although international studies have been performed (13–15), the aforementioned U.S.-based studies linking T2DM with OSA and either short or long sleep duration have recruited predominantly white populations, so whether these relationships exist in other ethnic groups is also unknown. The prevalence of T2DM in the United States is higher among minority populations compared with white populations (16–20). Age-adjusted National Health Interview Survey data from 2007–2009 indicates T2DM prevalence of 7.1% in white individuals, 8.4% in Asian Americans, 11.8% in Hispanics, and 12.6% in African Americans (21). Glycemic control among minority patients with T2DM is also worse than in white patients (22, 23), and thus minorities seem to suffer from a greater burden of T2DM, which may be explained in part by increased prevalence and severity of OSA (24–29) and a greater prevalence of extremes in sleep duration in these groups (30–32).

We therefore sought to examine the role of ethnicity in moderating the associations between fasting glycemic status and OSA and habitual sleep duration using data from the Multi-Ethnic Study of Atherosclerosis (MESA), a large prospective cohort study designed to investigate the prevalence and progression of subclinical cardiovascular disease.

Methods

Study Design

MESA is a prospective study designed to evaluate ethnic heterogeneity in cardiovascular risk factors. During 2000–2002, 6,814 subjects free of clinically apparent cardiovascular disease, aged 45–84, who identified as African American, white, Chinese, or Hispanic were recruited from six sites in the United States. The study was approved by the institutional review board of each site, and written informed consent was obtained from all subjects. Full methodology has been published (33).

At MESA Exam 5 (2010–2013), participants underwent fasting phlebotomy assayed for plasma glucose, and completed a questionnaire including use of insulin or oral medications for diabetes in the past 2 weeks, regular alcohol consumption (yes/no), smoking status (never/former/current), annual household income (<$20,000/$20,000–$39,999/≥$40,000), and current employment status (yes/no). Participants also completed a food frequency questionnaire, which was used to calculate the Healthy Eating Index (34, 35). All Mesa Exam 5 participants other than those reporting regular use of positive airway pressure, oral appliances, nocturnal oxygen, or living too far away were invited to participate in the MESA Sleep Ancillary Study. The median time from Exam 5 to the sleep examination was 301 days (range, 0–1,024 d).

Polysomnography and Actigraphy

Details regarding MESA polysomnography (PSG) and actigraphy methodology have been published (36). In brief, 15-channel home-PSG was conducted using the Somte device (Compumedics, Victoria, Australia). The primary apnea–hypopnea index (AHI) used in this paper was based on the 2007 American Academy of Sleep Medicine (AASM) alternative hypopnea criteria (37). An apnea was defined as a greater than or equal to 90% reduction in airflow for greater than or equal to 10 seconds; a hypopnea was defined as a greater than or equal to 50% reduction in airflow associated with an arousal and/or a 3% oxygen saturation as measured by pulse oximetry (Sp_{O_2}) desaturation. As sensitivity analyses, models were repeated using the AHI based on the 2007 AASM-recommended hypopnea scoring criteria (≥50% reduction in airflow associated with a 4% Sp_{O_2} desaturation), and using the percentage of sleep time spent with Sp_{O_2} less than 90%. Inter-scorer and intrascorer reliability was assessed; intraclass correlation coefficients for AHI exceeded 0.95. Participants were excluded from analyses if the central apnea index was greater than or equal to five events per hour. The AHI was used to categorize OSA as none (0–4.9 events/h), mild (5–14.9 events/h), or moderate to severe (≥15 events/h).

Subjects were asked to wear the Actiwatch Spectrum (Respironics, Murrysville, PA) on the nondominant wrist for 7 consecutive days. A minimum of 4 weekdays and 1 weekend day were required for analysis. Actigraphic data were scored in 30-second epochs as sleep or wake using Actiware-Sleep version 5.59 software as previously described (36). Sleep duration was calculated as the sum of epochs scored as sleep in each main sleep interval (manually identified based on a self-actuated event marker, sleep diary, and light sensor) averaged over all days of valid recording. Inter-scorer and intrascorer reliability was assessed; intraclass correlation coefficients for sleep duration exceeded 0.90. Sleep duration was categorized as short (≤5 h/night), intermediate (>5 and <8 h/night), or long (≥8 h/night). Average activity counts per minute of wakefulness were calculated as a measure of physical activity.

Glycemic Status

Subjects were classified as having normal fasting glucose (<100 mg/dl and no hypoglycemic medication use) or abnormal fasting glucose (≥100 mg/dl and/or hypoglycemic medication use) (38). We conducted secondary analyses where subjects were classified as having normal fasting glucose, impaired fasting glucose (≥100 and <126 mg/dl, and no

hypoglycemic medication use), or T2DM (glucose ⩾126 mg/dl and/or hypoglycemic medication use).

Statistical Analyses

Statistical analysis was performed using SAS version 9.3 (Cary, NC). Differences between groups were compared using *t* tests, analysis of variance, or chi-squared tests as appropriate. Multivariable logistic regression was used to assess the association between OSA severity and sleep duration (in categories) with abnormal fasting glucose. For analyses of OSA, the reference group was no OSA (AHI <5 events/h); for analyses of sleep duration, the reference group was intermediate sleep (>5 and <8 h/night). Secondary analyses considered AHI as a continuous independent variable. Effect modification by ethnicity was assessed by including ethnicity-by-OSA severity and ethnicity-by-sleep duration interaction terms. Multinomial logistic regression was used for investigation of the three-category dependent variable (normal fasting glucose, impaired fasting glucose, T2DM).

Results

Study Sample

Of 4,077 MESA Exam 5 participants approached, 147 were ineligible, and 141 participants lived too far away to participate. Of the remaining 3,789 participants, 2,261 participated in the MESA Sleep ancillary study (59.7%). PSG was performed in 2,166, of which 2,060 met minimum quality criteria for determining the AHI. Actigraphy was performed in 2,211, of which 2,156 met minimum quality criteria for determining habitual sleep duration.

In our analysis, 43 participants were excluded for having incomplete fasting glucose data and a further 43 for having a central apnea index greater than or equal to five events per hour. Our total sample was n = 2,151; for the fully adjusted regression models, our effective sample size was 1,839. The analytic sample participating in the MESA Sleep ancillary study differed slightly from the overall MESA Exam 5 cohort. Those included in this analysis were 2.6 years younger on average ($P < 0.01$), had 0.6 kg/m^2 greater mean body mass index (BMI) ($P < 0.01$), and were less likely to be white (37.2% vs. 43.9%; $P < 0.01$).

Our sample included 984 males (45.8%), the mean ± SD age was 68.5 ± 9.2 years, and on average the sample was overweight with mean BMI 28.8 ± 5.6 kg/m^2 and mean waist circumference 99.6 ± 14.6 cm (Table 1). The prevalence of abnormal fasting glucose was high (n = 865; 40.2%), which included 410 with T2DM. The ethnic breakdown was 27.3%

Table 1. Demographic and Sleep Data by Fasting Glucose Level

	Combined Sample	Normal Fasting Glucose	Abnormal Fasting Glucose	*P* Value, Normal vs. Abnormal
Descriptive information	n = 2,151	n = 1,286	n = 865	
Age, yr	68.5 ± 9.2	67.9 ± 9.2	69.4 ± 9.0	<0.01
Male sex, n (%)	984 (45.8)	529 (41.1)	455 (52.6)	<0.01
Ethnicity				
African American, n (%)	587 (27.3)	344 (26.8)	243 (28.1)	<0.01
Chinese, n (%)	254 (11.8)	138 (10.7)	116 (13.4)	
White, n (%)	799 (37.2)	553 (43.0)	246 (28.4)	
Hispanic, n (%)	511 (23.8)	251 (19.5)	260 (30.1)	
Waist circumference, cm	99.6 ± 14.6	96.3 ± 13.5	104.5 ± 14.9	<0.01
Body mass index, kg/m^2	28.8 ± 5.6	27.7 ± 5.2	30.4 ± 5.9	<0.01
Systolic blood pressure, mm Hg	122.9 ± 20.4	121.6 ± 20.6	124.7 ± 19.9	<0.01
Diastolic blood pressure, mm Hg	68.1 ± 10.0	68.2 ± 10.0	68.0 ± 10.1	0.71
Fasting glucose, mg/dl	102.1 ± 28.1	89.6 ± 6.0	120.8 ± 36.5	<0.01
Polysomnography data	n = 1,924	n = 1,161	n = 763	
Total sleep time, min	360.5 ± 82.2	366.6 ± 79.8	351.4 ± 85.0	<0.01
Sleep time with Sp_{O_2} < 90%, %	3.7 ± 8.8	3.0 ± 7.9	4.9 ± 9.9	<0.01
AHI, events/h	23.0 ± 18.8	20.4 ± 17.4	27.0 ± 20.3	<0.01
OSA severity categories				
No OSA				<0.01
n (%)	217 (11.3)	163 (14.0)	54 (7.1)	
AHI in this group, events/h	2.7 ± 1.4	2.7 ± 1.4	2.7 ± 1.3	
Mild OSA				
n (%)	599 (31.1)	393 (33.9)	206 (27.0)	
AHI in this group, events/h	9.8 ± 2.9	9.7 ± 2.9	10.0 ± 3.0	
Moderate-to-severe OSA				
n (%)	1,108 (57.6)	605 (52.1)	503 (65.9)	
AHI in this group, events/h	34.1 ± 17.7	32.2 ± 16.6	36.5 ± 18.6	
Actigraphy data	n = 2,043	n = 1,231	n = 812	
Average sleep duration, h	6.5 ± 1.4	6.6 ± 1.3	6.4 ± 1.5	<0.01
Sleep duration categories				
⩽5 h/night, n (%)	263 (12.9)	124 (10.1)	139 (17.1)	<0.01
>5 and <8 h/night, n (%)	1,545 (75.6)	965 (78.4)	580 (71.4)	
⩾8 h/night, n (%)	235 (11.5)	142 (11.5)	93 (11.5)	

Definition of abbreviations: AHI = apnea–hypopnea index; OSA = obstructive sleep apnea; Sp_{O_2} = oxygen saturation as measured by pulse oximetry.

African American, 37.2% white, 11.8% Chinese, and 23.8% Hispanic. Demographic characteristics are presented by ethnic group in Table 2.

OSA Severity and Abnormal Fasting Glucose

In unadjusted analyses, the AHI was significantly higher among those with abnormal fasting glucose (27.0 ± 20.3 vs. 20.4 ± 17.4 events/h; $P < 0.01$). After adjusting for site, age, sex, and ethnicity, subjects with mild or moderate-to-severe OSA had a higher prevalence of abnormal fasting glucose compared with those with no OSA (Table 3, Model 1). After additionally adjusting for waist circumference as a measure of central obesity, only moderate-to-severe OSA was associated with abnormal fasting glucose (odds ratio [OR] with reference to no OSA, 1.45; 95% confidence interval [CI], 1.01–2.08) (Table 3, Model 2). Findings were very similar when BMI was used to adjust for adiposity instead of waist circumference (data not shown). Additional adjustment for actigraphy-measured average sleep duration minimally changed this relationship (OR for moderate-to-severe OSA with reference to no OSA, 1.57; 95% CI, 1.07–2.29) (Table 3, Model 3). After additional adjustment for diet, physical activity, smoking, alcohol consumption, income, and employment, the ORs for both mild OSA (1.39; 95% CI, 0.93–2.06) and moderate-to-severe OSA (1.51; 95% CI, 1.02–2.24) remained consistent. Modeling AHI as a continuous variable, the OR for abnormal fasting glucose per 10-unit increase in AHI was 1.07 (95% CI, 1.01–1.13) after adjusting for site, age, sex, ethnicity, waist circumference, and sleep duration.

The association between OSA overall and abnormal fasting glucose was significant in white participants ($P = 0.048$), borderline significant in African Americans ($P = 0.065$), and nonsignificant in both Chinese and Hispanic subjects ($P = 0.75$ and 0.42, respectively). Table 4 presents the model adjusted for site, age, sex, waist circumference, and sleep duration stratified by ethnic group. Moderate-to-severe OSA (compared with no OSA) was significantly associated with higher risk for abnormal fasting glucose in both African Americans and white participants; the ORs for these associations were similar in these groups (2.14; 95% CI, 1.12–4.08 and 2.85; 95% CI, 1.20–6.75, respectively). In contrast, the ORs were smaller and not statistically significant in Chinese subjects (1.37; 95% CI, 0.50–3.75) and Hispanics (0.78; 95% CI, 0.36–1.70). Mild OSA seems to be associated with an elevated risk for abnormal fasting glucose in African Americans and white participants, although the pairwise comparison between mild OSA and no OSA, excluding those with moderate-to-severe OSA, did not reach statistical significance (OR, 1.72; 95% CI, 0.88–3.37 in African Americans) (OR, 2.25; 95% CI, 0.93–5.44 in white participants). Formal testing for an ethnicity by OSA severity interaction on abnormal fasting glucose was of borderline significance ($P = 0.06$).

When all OSA models were repeated using a 4% desaturation level to define hypopneas, the patterns of association did not change substantially (*see*

Table 2. Demographic and Sleep Data by Ethnicity

	African American	Chinese	White	Hispanic	*P* Value across Groups
Descriptive information	n = 587	n = 254	n = 799	n = 511	
Age, yr	68.6 ± 9.0	67.3 ± 8.9	68.8 ± 9.2	68.5 ± 9.4	0.18
Male sex, n (%)	256 (43.6)	128 (50.4)	368 (46.1)	232 (45.4)	0.34
Waist circumference, cm	102.9 ± 14.1	88.6 ± 9.8	99.2 ± 15.3	101.8 ± 13.3	<0.01
Body mass index, kg/m^2	30.4 ± 5.6	24.2 ± 3.3	28.1 ± 5.4	30.2 ± 5.5	<0.01
Systolic blood pressure, mm Hg	127.7 ± 20.7	121.1 ± 20.0	119.6 ± 19.5	123.3 ± 20.5	<0.01
Diastolic blood pressure, mm Hg	70.0 ± 10.0	68.7 ± 9.4	66.6 ± 9.7	68.0 ± 10.4	<0.01
Fasting glucose, mg/dl	102.4 ± 32.3	102.2 ± 22.0	97.9 ± 22.2	108.3 ± 32.5	<0.01
Polysomnography data	n = 533	n = 230	n = 697	n = 464	
Total sleep time, min	350.5 ± 86.6	357.5 ± 82.9	373.7 ± 76.7	353.9 ± 82.4	<0.01
Sleep time with Sp_{O_2} < 90%, (%)	3.7 ± 8.9	2.0 ± 4.0	4.3 ± 10.7	3.7 ± 7.1	<0.01
AHI, events/h	21.7 ± 19.2	22.8 ± 18.2	22.6 ± 18.7	25.2 ± 18.7	0.03
OSA severity categories					
No OSA					
n (%)	75 (14.1)	26 (11.3)	75 (10.8)	41 (8.8)	0.02
AHI in this group, events/h	2.6 ± 1.4	2.3 ± 1.4	2.8 ± 1.3	3.1 ± 1.3	
Mild OSA					
n (%)	173 (32.5)	70 (30.4)	232 (33.3)	124 (26.7)	
AHI in this group, events/h	9.9 ± 2.9	9.0 ± 3.0	9.9 ± 2.9	10.0 ± 2.9	
Moderate-to-severe OSA					
n (%)	285 (53.5)	134 (58.3)	390 (56.0)	299 (64.4)	
AHI in this group, events/h	34.0 ± 18.8	34.0 ± 16.0	34.0 ± 17.9	34.6 ± 17.0	
Actigraphy data	n = 566	n = 227	n = 766	n = 484	
Average sleep duration, h	6.1 ± 1.4	6.3 ± 1.4	6.8 ± 1.2	6.6 ± 1.4	<0.01
Sleep duration categories					
≤5 h/night, n (%)	115 (20.3)	37 (16.3)	58 (7.6)	53 (11.0)	<0.01
>5 and <8 h/night, n (%)	411 (72.6)	171 (75.3)	597 (77.9)	366 (75.6)	
≥8 h/night, n (%)	40 (7.1)	19 (8.4)	111 (14.5)	65 (13.4)	

Definition of abbreviations: AHI = apnea–hypopnea index; OSA = obstructive sleep apnea; Sp_{O_2} = oxygen saturation as measured by pulse oximetry.

Table 3. Associations between OSA and Abnormal Fasting Glucose

	Number (% of OSA Severity Group) with Abnormal Fasting Glucose	Abnormal Fasting Glucose Odds Ratio (95% CI)
All subjects (n = 1,843), Model 1		
No OSA	48 (23.2)	1.00
Mild OSA	194 (34.1)	**1.59 (1.11–2.28)**
Moderate-to-severe OSA	481 (45.1)	**2.28 (1.62–3.21)**
All subjects (n = 1,839), Model 2		
No OSA	48 (23.20	1.00
Mild OSA	194 (34.1)	1.33 (0.91–1.93)
Moderate-to-severe OSA	479 (45.1)	**1.45 (1.01–2.08)**
All subjects (n = 1,839), Model 3		
No OSA	48 (23.2)	1.00
Mild OSA	194 (34.1)	1.45 (0.98–2.14)
Moderate-to-severe OSA	479 (45.2)	**1.57 (1.07–2.29)**

Definition of abbreviations: CI = confidence interval; OSA = obstructive sleep apnea.
Results presented are from logistic regression analyses, with the dependent variable fasting glucose status. No OSA was the reference group; that is, odds ratios are presented for mild OSA versus no OSA, and for moderate-to-severe OSA versus no OSA. Bold entries indicate statistical significance ($P < 0.05$).
Model 1 adjusts for study site, age, sex, and ethnicity. Model 2 additionally adjusts for waist circumference. Model 3 additionally adjusts for sleep duration (in three categories).

Tables E1–E3 in the online supplement). When the percentage of sleep time spent with Sp_{O_2} less than 90% (continuous variable) was used in place of the AHI, the associations in African Americans and white participants were of borderline significance (*see* Table E4).

Multinomial Glycemic Models

Additional sensitivity models were performed to assess separately the association between OSA severity with impaired fasting glucose and T2DM (*see* Table E5). These results demonstrate a similar pattern of association: moderate-to-severe OSA was more strongly associated with both impaired fasting glucose and T2DM among African American and white participants than Chinese participants, and there was no evidence of any association in Hispanics.

Table 4. Associations between OSA and Abnormal Fasting Glucose by Ethnicity

	Number (% of OSA Severity Group) with Abnormal Fasting Glucose	Abnormal Fasting Glucose Odds Ratio (95% CI)
African American (n = 516)		
No OSA	17 (23.6)	1.00
Mild OSA	58 (35.2)	1.72 (0.88–3.37)
Moderate-to-severe OSA	134 (48.0)	**2.14 (1.12–4.08)**
Chinese (n = 209)		
No OSA	9 (39.1)	1.00
Mild OSA	26 (41.3)	1.10 (0.40–3.01)
Moderate-to-severe OSA	58 (47.2)	1.37 (0.50–3.75)
White (n = 672)		
No OSA	7 (9.60	1.00
Mild OSA	51 (23.2)	2.25 (0.93–5.44)
Moderate-to-severe OSA	143 (37.7)	**2.85 (1.20–6.75)**
Hispanic (n = 442)		
No OSA	15 (38.5)	1.00
Mild OSA	59 (48.8)	1.07 (0.48–2.39)
Moderate-to-severe OSA	144 (51.1)	0.78 (0.36–1.70)

Definition of abbreviations: CI = confidence interval; OSA = obstructive sleep apnea.
Results presented are from logistic regression analyses, with the dependent variable fasting glucose status. No OSA was the reference group; that is, odds ratios are presented for mild OSA versus no OSA, and for moderate-to-severe OSA versus no OSA. Bold entries indicate statistical significance ($P < 0.05$).
Model adjusts for study site, age, sex, waist circumference, and sleep duration (in three categories).

Sleep Duration and Abnormal Fasting Glucose

The sleep duration for subjects with abnormal fasting glucose was shorter than that for subjects with normoglycemia (6.4 ± 1.5 vs. 6.6 ± 1.3 h/night; $P < 0.01$). After adjusting for site, age, sex, and ethnicity, we found a significant association between short sleep duration and abnormal fasting glucose (Table 5, Model 1); this relationship remained statistically significant after additional adjustment for waist circumference (Table 5, Model 2). After adjusting for AHI, however, this relationship was no longer statistically significant (OR for short sleep duration with reference to intermediate sleep duration, 1.33; 95% CI, 0.98–1.80) (Table 5, Model 3). The OR for long sleep duration was 1.04 (95% CI, 0.75–1.46) with reference to intermediate sleep duration. In stratified analyses, no clear relationship between sleep duration and abnormal fasting glucose was observed in any of the four ethnic groups (Table 6). In addition, there was no evidence of an ethnicity by sleep duration interaction ($P = 0.75$).

Discussion

In this large-scale study of adults recruited from the community, we have demonstrated for the first time that increasingly severe OSA is independently associated with abnormal fasting glucose in a multiethnic sample, controlling for age, sex, ethnicity, central obesity, and objectively determined habitual sleep duration. In the combined sample, the odds of having abnormal fasting glucose were almost 60% greater in those with moderate-to-severe OSA compared with those without OSA. We also found evidence for ethnicity-specific differences in these associations as supported by interaction testing and our stratified analyses, suggesting that ethnicity may modify the effect of OSA on abnormal fasting glucose. We demonstrated similarly increased odds of abnormal fasting glucose with

Table 5. Associations between Sleep Duration and Abnormal Fasting Glucose

	Number (% of Sleep Duration Group) with Abnormal Fasting Glucose	Abnormal Fasting Glucose Odds Ratio (95% CI)
All subjects (n = 2,043), Model 1		
Short sleep duration: ⩽5 h	139 (52.9)	**1.63 (1.24–2.14)**
Intermediate sleep duration: >5, <8 h	580 (37.5)	1.00
Long sleep duration: ⩾8 h	93 (39.6)	1.08 (0.81–1.45)
All subjects (n = 2,039), Model 2		
Short sleep duration: ⩽5 h	139 (52.9)	**1.44 (1.08 –1.91)**
Intermediate sleep duration: >5, <8 h	580 (37.6)	1.00
Long sleep duration: ⩾8 h	91 (39.1)	1.08 (0.80–1.47)
All subjects (n = 1,839), Model 3		
Short sleep duration: ⩽5 h	123 (51.9)	1.33 (0.98–1.80)
Intermediate sleep duration: >5, <8 h	525 (37.4)	1.00
Long sleep duration: ⩾8 h	73 (36.9)	1.04 (0.75–1.46)

Definition of abbreviation: CI = confidence interval.
Results presented are from logistic regression analyses, with the dependent variable fasting glucose status. Intermediate sleep duration was the reference group; that is, odds ratios are presented for short sleep duration versus intermediate sleep duration, and for long sleep duration versus intermediate sleep duration. Bold entries indicate statistical significance ($P < 0.05$).
Model 1 adjusts for study site, age, sex, and ethnicity. Model 2 additionally adjusts for waist circumference. Model 3 additionally adjusts for apnea–hypopnea index (continuous variable).

moderate-to-severe OSA among African American and white subjects, supporting prior studies that have recruited predominantly white samples (2–5). Among Chinese and Hispanic individuals, however, the association was weaker and nonsignificant. Our stratified analyses controlling for waist circumference suggest that the ethnic differences shown here are not driven solely by obesity, despite the fact that the average BMI in the Chinese group was lower than the other three ethnic groups. Although not statistically significant, the odds of abnormal fasting glucose in African American and white participants with mild OSA were intermediate between those without OSA and with moderate-to-severe OSA suggesting a continuous dose–response relationship. When AHI was modeled continuously, it was significantly associated with abnormal fasting glucose, suggesting that mild OSA may still be associated with impairment of glucose metabolism.

Table 6. Associations between Sleep Duration and Abnormal Fasting Glucose by Ethnicity

	Number (% of Sleep Duration Group) with Abnormal Fasting Glucose	Abnormal Fasting Glucose Odds Ratio (95% CI)
African American (n = 516)		
Short sleep duration: ⩽5 h	56 (53.8)	1.46 (0.91–2.35)
Intermediate sleep duration: >5, <8 h	141 (37.3)	1.00
Long sleep duration: ⩾8 h	12 (35.3)	0.76 (0.35–1.66)
Chinese (n = 209)		
Short sleep duration: ⩽5 h	17 (47.2)	1.17 (0.55–2.47)
Intermediate sleep duration: >5, <8 h	67 (42.7)	1.00
Long sleep duration: ⩾8 h	9 (56.3)	1.60 (0.55–4.62)
White (n = 672)		
Short sleep duration: ⩽5 h	23 (46.0)	1.43 (0.74–2.75)
Intermediate sleep duration: >5, <8 h	155 (29.1)	1.00
Long sleep duration: ⩾8 h	23 (25.8)	0.97 (0.55–1.72)
Hispanic (n = 442)		
Short sleep duration: ⩽5 h	27 (57.4)	1.17 (0.60–2.28)
Intermediate sleep duration: >5, <8 h	162 (48.2)	1.00
Long sleep duration: ⩾8 h	29 (49.2)	1.23 (0.67–2.28)

Definition of abbreviation: CI = confidence interval.
Results presented are from logistic regression analyses, with the dependent variable fasting glucose status. Intermediate sleep duration was the reference group; that is, odds ratios are presented for short sleep duration versus intermediate sleep duration, and for long sleep duration versus intermediate sleep duration.
Model adjusts for study site, age, sex, waist circumference, and apnea–hypopnea index (continuous variable).

Few studies have assessed the relationship between OSA and glucose levels in nonwhite populations. The Hispanic Community Health Study/Study of Latinos (39) did report an association between OSA and T2DM in a younger more diverse Hispanic population but unlike our cohort, this study was unable to compare the strength of this association in Hispanics versus other ethnic groups. In addition, that study used a limited channel home monitor as compared with full PSG. Hispanic Community Health Study/Study of Latinos also had a greater representation of Puerto Ricans and Dominicans, populations with greater African admixture, as compared with individuals of Mexican heritage, which were the largest Hispanic group in MESA. No prior studies have evaluated the impact of OSA on glucose metabolism among Chinese Americans; however, data from China suggest that although OSA is associated with impaired glucose tolerance, these differences are attenuated after adjustment for BMI (40).

There is some evidence that Hispanics have higher levels of inflammatory biomarkers, such as C-reactive protein, IL-6, and fibrinogen, compared with white and African American individuals (41–43); it is therefore possible that the additional presence of OSA may not increase risk for abnormal fasting glucose and T2DM as strongly in this group because of competing risk factors, especially in a cohort of predominantly older individuals. Among Chinese subjects there may be a weaker association of OSA on glycemia, because prior studies have shown a smaller degree of hypoxemia

associated with sleep-disordered breathing events in Asians caused by less obesity (44). In our own data, the mean proportion of time spent with oxygen saturation below 90% was lower among the Chinese despite a similar AHI to the other groups. In contrast, there is evidence of a stronger association between OSA symptoms and hypertension in African Americans compared with Hispanic and white individuals after controlling for obesity (45), suggesting a heightened sensitivity to hypoxemia and potentially elevated sympathetic response to apneic events that may translate to greater elevations in insulin resistance. Candidate genes associated with the insulin response to glucose and glucose homeostasis seem to vary across ethnic groups and so may provide additional mechanisms for heterogeneity in susceptibility to the metabolic effects of OSA (46, 47).

We also found that although objectively measured short sleep duration was associated with abnormal fasting glucose after controlling for many potential confounders, this association became nonsignificant after controlling for AHI. These results suggest that OSA may be a confounder of the sleep duration–glycemia relationship not adequately accounted for in prior studies, or alternatively may reflect a loss of power from the increased number of model covariates. The associations between short sleep duration and abnormal fasting glucose were positive in all ethnic groups, consistent with a true effect of short sleep duration. However, the only other study incorporating actigraphic-measured sleep duration found no association with fasting glycemia (11). Several prior studies have found significant associations between self-reported long and short sleep duration and markers of T2DM (7, 8), including analyses of Hispanic (48) and African American populations (49). It is possible that other factors influencing self-reported sleep (e.g., sleep quality) may be more important in impacting glucose levels than sleep duration; if so, our use of objectively measured sleep duration, which has only moderate correlation with self-reported sleep duration, would not capture this.

In our primary analyses of OSA, we chose to score hypopneas associated with a 3% desaturation or arousal because there is evidence that Sp_{O_2} desaturation events between 2% and 4% are associated with abnormal fasting glucose (50). The alternative AASM scoring criteria has been proposed to capture the potential contributions of both intermittent hypoxia (at 3% desaturation) and sleep fragmentation. The literature suggests that both of these characteristics of OSA may be on the causal pathway to metabolic dysfunction and cardiovascular disease (4, 5, 51). Importantly, our findings were similar when our data were reanalyzed using hypopneas scored based solely on being associated with a 4% desaturation, and when we used the percentage of sleep time spent with Sp_{O_2} less than 90% in place of the AHI.

Prior studies of the associations between OSA, sleep duration, and T2DM have lacked generalizability because of the absence of multiethnic samples. We have addressed this gap by studying a sample including three U.S. minority groups (African American, Chinese, and Hispanic) that suffer a greater burden of T2DM in the community. The availability of actigraphy data also meant that we were able to control for differences in habitual sleep duration in the OSA analyses, whereas previous studies have relied on either self-reported sleep duration or the sleep duration recorded during PSG, neither of which are an accurate reflection of usual sleep habits (e.g., in our study the correlation between actigraphy-measured sleep duration and sleep duration during the PSG was only moderate, at $r = 0.34$). Similarly, we were able to control for the presence of OSA in our sleep duration analyses, an important potential confounder not addressed in previous studies.

Our study has some limitations. The cross-sectional nature of data collection means that we are unable to draw causal inferences from our results. Participants using treatment for OSA were not invited to participate in the MESA Sleep ancillary study; this may have resulted in some bias by excluding those with more severe OSA. Given the ethnic and socioeconomic barriers to OSA diagnosis and treatment, this bias may have impacted the four ethnic groups differently. However, a very small number were excluded for this reason (n = 13 using positive airway pressure and n = 7 using an oral appliance). Finally, we chose to combine impaired fasting glucose and T2DM and relied on a single fasting plasma glucose measurement to categorize patients as abnormal versus normal. Our choice to define abnormal fasting glucose in this way was based on the fact that this is an important clinical endpoint, particularly because it is possible that the effects of OSA on metabolic function may be irreversible once T2DM is established (52); however, the relationships between OSA and impaired fasting glucose and T2DM may be very different. Reassuringly, when we modeled impaired fasting glucose and T2DM separately, the aforementioned differences across ethnic groups remained consistent.

In conclusion, we found that although objectively measured short sleep duration was associated with abnormal fasting glucose after controlling for common confounders, we have demonstrated for the first time that this association is weakened when the presence of OSA is accounted for. Furthermore, our data indicate that there are comparable associations of OSA with abnormal fasting glucose and T2DM in African American and white adults. These associations were not statistically significant among our sample of predominantly older Asians and Hispanics, an observation that requires replication in further research. Our data add to the growing literature supporting the need to investigate the role of OSA as a potentially reversible contributor to abnormal glucose metabolism. Furthermore, this study highlights the potential variability in associations across ethnic groups, and thus suggests the need to include multiethnic samples in future evaluations of OSA and glucose metabolism. ■

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