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Risk of obstructive sleep apnoea is associated with glycaemia status in South Asian men and women in the United States

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ABSTRACT

Aims: To examine the association between glycaemia status and the risk for obstructive sleep apnoea (OSA) in a cohort of South Asians living in the United States.

Methods: A secondary analysis of a community based cohort of 899 participants from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. The Berlin Questionnaire was used to screen for OSA.

Results: Almost one in four (24%) South Asians was at high risk for OSA. Compared to the normal glucose tolerance group (18%), high risk of OSA was significantly more likely in the prediabetes (24%) and diabetes (32%) groups ($p = 0.007$). More men (28%) than women (18%) were at high risk of OSA. Risk for OSA was also associated with higher haemoglobin A1c values, hypertension, large waist circumference, and BMI > 27.5 kg/m^2. In a multivariate regression analysis, sleep disordered breathing (SDB) remained significantly associated with higher haemoglobin A1c values, even after controlling for waist circumference and other demographic and clinical factors.

Conclusions: The risk for SDB and OSA was high among South Asian men and women. Given the association between dysglycaemia and risk for OSA, these health issues require simultaneous clinical assessment. Future studies using objective sleep measures such as polysomnography are warranted in the diagnosis and treatment of OSA in the South Asian adult population already at high risk for dysglycaemia.

1. Introduction

With the epidemic of obesity in the United States (USA), sleep disordered breathing (SDB) is a growing medical problem. Obstructive sleep apnoea (OSA) is the most serious end of the spectrum of SDB, and is characterised by loud snoring with repeated upper airway occlusions during sleep that result in specific physiological changes, including frequent arousals from sleep in response to each hypoxic event, and chronic sleep loss that manifests as excessive daytime sleepiness. Sleep loss can alter fat and glucose metabolism and together these changes lead to a cascade of events that increase risk for cardiovascular disease, hypertension, metabolic syndrome and Type 2 diabetes (Peppard et al., 2000; Punjabi et al., 2009; Young et al., 2008).

In the USA, it is estimated that 10–17% of men and 3–9% of women between 30 and 70 years of age have moderate to severe OSA (Peppard et al., 2013). Furthermore, results from several large studies suggest that OSA is an independent risk factor for development of Type 2 diabetes, and that as many as 15–30% of patients with OSA have Type 2 diabetes (Pamidi and Tasali, 2012). As the severity of SDB increases, so does the likelihood of worsening glycaemia status (Peppard et al., 2000; Marin et al., 2005; Mehra et al., 2006; Yaggi et al., 2005; Gottlieb et al., 2010; Kent et al., 2014).

South Asians (persons of Indian, Pakistani, Bangladeshi, Sri Lankan, or Nepali origin) have a high prevalence of Type 2 diabetes and dyslipidaemia (McKeigue et al., 1989; Palaniappan et al., 2004). The prevalence of Type 2 diabetes in South Asian adults is reportedly between 16 and 18%. (Karter et al., 2013; Venkataraman et al., 2004; Misra et al., 2010), yet there is limited research on SDB and its association with type 2 diabetes or glycaemia in older adults. Considering the potential link between SDB and Type 2 diabetes, the purpose of this secondary analysis was to describe SDB and the risk for OSA associated with haemoglobin A1c (HbA1c) in a cohort of South Asian men and women previously categorised with normal glucose tolerance, prediabetes or diabetes.

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2. Material and methods

2.1. Design

We conducted a cross-sectional analysis of data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. There were 906 participants enrolled from October 2010 through March 2013 and primary findings on prevalence of the glucose tolerance categories have been reported elsewhere (Kanaya et al., 2014; Shah et al., 2015).

2.2. Sample

The sample for this analysis included 899 South Asian men and women from the San Francisco Bay area and from the greater Chicago metropolitan area who had complete data for glycaemic status. The institutional review board at the University of California, San Francisco and Northwestern University, Chicago approved the study protocol. All participants provided written informed consent. To be included in the study, participants were: 1) of South Asian ancestry (defined as at least three grandparents born in either India, Pakistan, Bangladesh, Nepal, or Sri Lanka); 2) 40–84 years of age; and 3) able to speak and/or read English, Hindi, or Urdu.

Potential participants were excluded if there was: 1) physician-diagnosed MI, stroke or TIA, HF, angina, use of nitroglycerin; 2) history of a cardiovascular procedure such as CABG, angioplasty, valve replacement, pacemaker/defibrillator; 3) current atrial fibrillation; 4) active treatment for cancer; 5) impaired cognitive ability; 6) less than 5-year life expectancy; 7) potential to be out of the study geographic region within 5 years of enrolling; 8) in nursing home residence or on waiting list for nursing home residency; and 7) body weight greater than 136 kg (due to CT scanner limitation).

2.3. Measures

Demographic data were obtained from a detailed socio-demographic questionnaire that included items on age, sex, smoking status, alcohol intake per week, geographic location (Illinois or California), and years living in the USA. Clinical measures included height and weight to calculate BMI (kg/m^2), waist circumference (cm), systolic and diastolic blood pressure (mm/Hg). After a requested-12 h fast, fasting blood samples for HbA1c levels and fasting plasma glucose were obtained and a 2-h oral glucose tolerance test (OGTT) was conducted for participants who were not known to have diabetes. The Berlin Questionnaire, developed at the 1966 Berlin Conference on Sleep in Primary Care, was used to screen for SDB and risk of OSA (Netzer et al., 1999).

2.3.1. Glycaemia status

Based on American Diabetes Association criteria, participants were categorised into one of the three groups: 1) normal, defined as having a fasting plasma glucose (FPG) $<$ 100 mg/dL and 2-h OGTT $<$ 140 mg/dL; 2) prediabetes, defined as having a FPG between 100 and 125 mg/dL or a 2-h OGTT between 140 and 199 mg/dL; or 3) diabetes, defined as having a FPG $\geq$ 126 mg/dL, having a 2-h OGTT $\geq$ 200 mg/dL, or using medication for Type 2 diabetes (American Diabetes Association, 2008).

2.3.2. Sleep disordered breathing and risk of obstructive sleep apnoea

The Berlin Questionnaire (BQ) was used to screen for SDB and risk of OSA. The BQ consists of ten questions in three categories. The first category addresses SDB and consists of an initial question about snoring, (yes, no, or don't know). If the response is yes, there are four follow up questions about their snoring. This SDB category is scored as positive if the participant is symptomatic more than 3–4 times a week with two or more of the four follow up questions. The second category consists of three items on daytime sleepiness and is scored positive if the participant is symptomatic 3–4 times a week on at least two of the three questions. The third category has two questions on history of HTN and BMI $\geq$30 kg/m^2 and is scored positive if either condition is reported (Netzer et al., 1999). Having two positive categories on the BQ indicates a high probability of OSA. In addition to the BMI 30 kg/m^2 criterion for obesity as specified in BQ Category 3, we used current recommendations for the Asian population to classify obesity as BMI $>$ 27.5 kg/m^2 (World Health Organization, 2004).

Regardless of the responses in the first category about SDB, a high risk of OSA on the BQ is identified by any two of the three categories being positive. The BQ has 78.6% sensitivity and 50.5% specificity for detecting moderate or severe OSA (Chung et al., 2012). Each BQ category was included to assess their unique associations with HbA1c and glycaemic status.

2.4. Statistical analysis

Means and standard deviations (SD) were used to describe measures of central tendency, and comparisons were tested with independent sample *t*-tests. Frequencies and percentages (%) were used to describe categorical data. Chi square (X^2) analyses were used to test associations between glycaemia status (normal, prediabetes or diabetes) and each of the three BQ risk categories. To describe the rate of SDB and risk for OSA in South Asians, we evaluated the association between the three BQ categories and categorical variables (sex, geographic location, education, income, smoking status, alcohol use) using X^2. We compared the prevalence of SBD and risk for OSA using the standard BMI category ($>$ 30 kg/m^2) for obesity and the lower BMI category for obesity ($>$ 27.5 kg/m^2) recommended for Asians (World Health Organization, 2004).

To determine the strength of the association between dysglycaemia and OSA risk, a linear multiple regression analysis was performed with HbA1c as the dependent variable. Square root transformation was sufficient to normalise the distribution of HbA1c values. To account for the variance in HbA1c, each BQ OSA risk category was examined while controlling for demographic and clinical variables. Demographic variables included age, sex, geographic research site, years in the USA, income and education. Clinical variables included smoking, alcohol use, waist circumference, systolic blood pressure, diastolic blood pressure, and BMI. SPSS (version 23) was used for all analyses and statistical significance was set at $p < 0.05$.

3. Results

3.1. Sample characteristics, glycaemia status, and OSA risk

Demographic and clinical characteristics are detailed in Table 1 by glycaemia status group, and are similar to the characteristics previously reported for the entire sample (Shah et al., 2015). Ages ranged from 40 to 83 years (mean 55 $\pm$ 9 years), 46% were women, and residence in the USA ranged 2–58 years (mean 27 $\pm$ 11 years). A little more than half the sample (55%) lived in California. Participants had an average BMI of 26 $\pm$ 4.3 kg/m^2, and only 13.5% had a BMI $>$ 30 kg/m^2 (Table 1). Overall, 28% of the participants had a BMI $>$ 27.5 kg/m^2; 23% in the normal glucose tolerance group were classified as obese using this lower cutpoint, compared to 36% in the prediabetes group, and 32% in the diabetes group (Table 2).

HbA1c values ranged from 4.7 to 13.7%, [28–126 mmol/mol] with a mean of 6.06 $\pm$ 0.86% [42 $\pm$ 9.4 mmol/mol] and a median of 5.8 [40 mmol/mol]. There were 42% with normal glucose tolerance, 33% with prediabetes and 25% with diabetes. Men were significantly more likely to be in the diabetes category and women were more likely to be in the normal glucose tolerance category (Table 1).

Overall, 213 (24%) South Asians were at high risk for OSA (positive in 2 or more BQ categories) and the risk was significantly higher for

Table 1
Characteristics of the MASALA study participants, 2010–2013, by glucose tolerance groups (N = 229).

Participant Characteristic	Normal glucose tolerance (n = 375)	Prediabetes (n = 295)	Diabetes (n = 229)	Statistic (*p* value)
Age (yr) (mean ± SD)	53.4 ± 9.2	55.8 ± 9.6	57.7 ± 8.7	$F_{[2,898]}$ = 16.1 (< 0.001)
Residence in USA (yr) (mean ± SD)	26.5 ± 10.1	27.0 ± 11.3	27.9 ± 11.4	$F_{[2,\ 879]}$ = 1.14 (0.32)
Geographic location (n (%))				
Illinois	130 (35%)	168 (57%)	111 (48%)	$X^2_{[2]}$ = 34.2 (< 0.001)
California	240 (65%)	127 (43%)	118 (52%)	
Sex (n (%))				
Men	174 (46%)	170 (58%)	139 (61%)	$X^2_{[2]}$ = 14.4 (≤0.001)
Women	201 (54%)	125 (42%)	90 (39%)	
Income Category (n (%))				
< $40,000	29 (8%)	42 (14%)	44 (20%)	$X^2_{[6]}$ = 26.5 (< 0.001)
$40,000 – $75,000	39 (11%)	42 (14%)	38 (17%)	
$75,000 - $100,000	38 (11%)	27 (9%)	23 (10%)	
> $100,000	254 (70%)	180 (62%)	117 (53%)	
Income not answered	15	4	7	
College Degree Education (n (%))	339 (90%)	261 (88%)	190 (83%)	$X^2_{[2]}$ = 7.5 (0.023)
Alcohol 1 + serving/week (n (%))	121 (32%)	105 (35%)	72 (31%)	$X^2_{[2]}$ = 1.2 (0.541)
Smoking (n (%))				
Non-smoking	320 (85%)	241 (82%)	183 (80%)	$X^2_{[4]}$ = 4.1 (0.397)
Past smoking	42 (11%)	45 (15%)	37 (16%)	
Current nmoking	13 (4%)	9 (3%)	9 (4%)	
Systolic blood pressure (mmHg) (mean ± SD)	121 ± 15	126 ± 17	129 ± 15	$F_{[2,898]}$ = 18.2 (< 0.001)
Diastolic blood pressure (mmHg) (mean ± SD)	72 ± 10	74 ± 10	75 ± 9	$F_{[2,898]}$ = 5.2 (0.006)
BMI (kg/m^2) (mean ± SD)	25.2 ± 3.9	26.4 ± 4.1	26.8 ± 4.2	$F_{[2,895]}$ = 13.7 (< 0.001)
Waist circumference (cm) (mean ± SD)	90.0 ± 9.7	94.0 ± 10.2	95.8 ± 10.4	$F_{[2,895]}$ = 26.5 (< 0.001)
HbA1c (mean ± SD): %	5.67 ± 0.30	5.82 ± 0.34	7.00 ± 1.19	$F_{[2,892]}$ = 312.3 (< 0.001)
HbA1c (mmol/mol)	38 ± 3.3	40 ± 3.7	53 ± 13.1	

men than for women (Table 3). Substituting a BMI > 27.5 kg/m^2 in BQ category 3 increased the risk from 24% to 28%. High OSA risk was significantly different across glycaemia status categories; 18% in the normal glucose tolerance group, 24% in the prediabetes group, and 32% in the diabetes group (Table 2). HbA1c values were also significantly associated with risk for OSA. The participants who were at high risk for OSA (positive for 2 or 3 BQ categories) had significantly (t = 4.5, p < 0.001) higher HbA1c values (6.23 ± 1.04% [45 ± 11.4 mmol/mol]) compared to participants who were low risk for OSA (5.98 ± 0.77% [42 ± 8.4 mmol/mol]).

3.2. BQ category 1: sleep disordered breathing (SDB)

When each item in BQ Category 1 was analyzed, 15% of the participants did not know if they snored, 30% participants responded that they did not snore, and 55% said they snored (Table 3). Compared to participants who did not snore or did not know if they snored, participants who endorsed snoring were more likely to be men, and more likely to have higher HbA1c, BMI, waist circumference, and systolic and diastolic blood pressure.

Of the 499 participants who answered “yes” to the habitual snoring question and continued to answer the remaining questions about their snoring, 375 (75%) met criteria for SDB (positive for Category 1). The participants who were positive for BQ Category 1 also had significantly (t = 3.5, p = 0.001) higher HbA1c values (6.18 ± 1.01% [44 ± 11.0 mmol/mol]) compared to participants who were negative for BQ Category 1 (5.98 ± 0.73% [42 ± 8.0 mmol/mol]). Participants who had SDB were significantly more likely to have prediabetes (43%) or diabetes (45%) compared to participants who did not have SDB. Participants with SDB were more likely to be men, have a history of HTN, have large waist circumference, be past or current smokers, or drink alcohol at least once per week. For participants with BMI > 27.5 kg/m^2, 64% indicated that they snored and half (50%) were positive for BQ Category 1.

Table 2
Berlin Questionnaire comparisons by glucose tolerance group (N = 229).

Berlin Questionnaire	Normal glucose tolerance (n = 375)	Prediabetes (n = 295)	Diabetes (n = 229)	Statistic (*p* value)
Category 1: Sleep Disordered Breathing	n (%)	n (%)	n (%)	
Habitual snoring: No	118 (32%)	89 (30%)	60 (26%)	$X^2_{[4]}$ = 8.8 (0.07)
Don't know	65 (17%)	32 (11%)	40 (17%)	
Yes	192 (51%)	174 (59%)	129 (56%)	
Positive Category 1	143 (38%)	126 (43%)	104 (45%)	$X^2_{[2]}$ = 3.4 (0.19)
Category 2: Excessive Sleepiness				
Positive Category 2	55 (15%)	32 (11%)	22 (10%)	$X^2_{[2]}$ = 4.0 (0.13)
Category 3: Clinical Comorbidities				
BMI > 27.5 kg/m^2	86 (23%)	97 (33%)	86 (38%)	$X^2_{[2]}$ > 15 (< 0.001)
BMI > 30.0 kg/m^2	30 (8%)	44 (15%)	45 (20%)	$X^2_{[2]}$ > 15 (< 0.001)
HTN (> 140/90 mmHg)	71 (19%)	100 (34%)	120 (52%)	$X^2_{[2]}$ > 15 (< 0.001)
HTN or BMI > 27.5 kg/m^2	140 (37%)	157 (53%)	159 (69%)	$X^2_{[2]}$ > 15 (< 0.001)
Positive Category 3 HTN or BMI > 30 kg/m^2	94 (25%)	122 (41%)	139 (61%)	$X^2_{[2]}$ > 15 (< 0.001)
High Risk for OSA (positive 2 or 3 categories)				
if HTN or BMI > 30.0	68 (18%)	71 (24%)	73 (32%)	$X^2_{[2]}$ > 15 (< 0.001)
if HTN or BMI > 27.5	87 (23%)	87 (29%)	80 (35%)	$X^2_{[2]}$ = 10 (0.007)

Note: HTN = hypertension.

Table 3
BQ Category 1: Habitual snoring and sleep disordered breathing (N = 229).

Participant Characteristic	No Snoring n = 270	Don't Know n = 137	Snores n = 499	Statistic, (p value)
Age (yr) (mean ± SD)	55.5 ± 9.9	54.6 ± 9.6	55.4 ± 9.1	$F_{[2,902]}$ = 0.52 NS
Residence in USA (yr) (mean ± SD)	27.2 ± 11.2	26.8 ± 10.6	27.0 ± 10.8	$F_{[2,902]}$ = 0.06 NS
Geographic location (n(%))				
Illinois	128 (47%)	53 (39%)	229 (46%)	$X^2_{[2]}$ = 2.97 NS
California	142 (53%)	84 (61%)	270 (54%)	
Sex (n (%))				
Men	118 (44%)	52 (38%)	316 (63%)	$X^2_{[2]}$ = 43.1 (< 0.001)
Women	152 (56%)	85 (62%)	183 (37%)	
Income (n (%))				
< $40,000	30 (11%)	18 (14%)	67 (14%)	$X^2_{[6]}$ = 3.2 NS
$40,000 – $75,000	41 (16%)	20 (15%)	59 (12%)	
$75,000 - $100,000	24 (9%)	13 (10%)	52 (11%)	
> $100,000	170 (64%)	80 (61%)	306 (63%)	
Income not answered	5	6	15	
College Degree (n (%)):	239 (89%)	115 (84%)	442 89 (%)	$X^2_{[2]}$ = 2.3 NS
Alcohol (1+/week): (n (%)):	78 (29%)	29 (21%)	192 (39%)	$X^2_{[2]}$ = 17.5 (< 0.001)
Smoking (n (%))				
Non-smoker	238 (88%)	119 (87%)	394 (79%)	$X^2_{[4]}$ = 17.5 (0.002)
Past smoker	24 (9%)	11 (8%)	89 (18%)	
Current smoker	8 (3%)	7 (5%)	16 (3%)	
Hypertension history (n (%)):	73 (27%)	45 (33%)	173 (35%)	$X^2_{[2]}$ = 4.7 (0.094)
Systolic blood pressure (mmHg) (mean ± SD)	122 ± 16	124 ± 15	126 ± 16	$F_{[2,905]}$ = 4.9 (0.007)
Diastolic blood pressure (mmHg) (mean ± SD)	71 ± 10	72 ± 9	75 ± 10	$F_{[2,905]}$ = 15.3 (< 0.001)
BMI (kg/m^2) (mean ± SD)	24.5 ± 3.43	26.1 ± 3.95	26.8 ± 4.59	$F_{[2,902]}$ = 26.3 (< 0.001)
BMI > 30.0 kg/m^2 (n (%)):	15 (12%)	24 (19%)	84 (68%)	$X^2_{[2]}$ = 17.5 (< 0.001)
BMI > 27.5 kg/m^2 (n (%)):	48 (18%)	48 (35%)	174 (35%)	$X^2_{[2]}$ = 26.6 (< 0.001)
Waist circumference (cm) (mean ± SD)	89.4 ± 9.2	92.5 ± 10.9	94.7 ± 10.3	$F_{[2,902]}$ = 23.8 (< 0.001)
HbA1c (mean ± SD): %	5.9 ± 0.7	6.0 ± 0.8	6.1 ± 0.9	$F_{[2,897]}$ = 4.7 (0.009)
HbA1c (mmol/mol)	41 ± 7.7	42 ± 8.7	43 ± 9.8	
BQ Sleep disordered breathing (Category1) (n (%))	–	–	376 (75%)	–
BQ Excessive Daytime Sleepiness (Category 2) (n (%))	32 (12%)	18 (13%)	60 (12%)	$X^2_{[2]}$ = 0.15 (NS)
High risk for OSA (2 or 3 BQ categories) (n (%))	8 (3%)	8 (6%)	197 (40%)	$X^2_{[1]}$ = 119.5 (< 0.001)

Note: NS = not significant (p > 0.10).

Table 4
Multivariate linear regression model with HbA1c as the dependent outcome.

	Unstandardised Coefficients		Standardised Coefficients	t	Sig.	Correlations		
	B	Std. Error	Beta			Zero-order	Partial	Part
DEMOGRAPHIC FACTORS								
Age (yrs)	0.001	0.001	0.078	1.686	0.092	0.184	0.058	0.055
Sex (male = 0, female = 1)	−0.011	0.014	−0.036	−0.832	0.405	−0.113	−0.029	−0.027
Residence in USA (yrs)	0.000	0.001	0.013	0.328	0.743	0.072	0.011	0.011
Geographic site (IL = 1, CA = 2)	0.030	0.011	0.095	2.844	0.005	0.070	0.098	0.092
College degree (no = 0, yes = 1)	−0.018	0.017	−0.038	−1.074	0.283	−0.100	−0.037	−0.035
Income	−0.013	0.005	−0.095	−2.509	0.012	−0.160	−0.086	−0.081
CLINICAL FACTORS								
Body Mass Index (kg/m^2)	−0.002	0.002	−0.058	−1.011	0.312	0.143	−0.035	−0.033
Systolic bp (mmHg)	0.001	0.000	0.091	1.938	0.053	0.182	0.067	0.063
Diastolic bp (mmHg)	−0.001	0.001	−0.035	−0.756	0.450	0.057	−0.026	−0.024
Smoke cigarettes (no = 0, past = 1, yes = 2)	0.016	0.011	0.050	1.424	0.155	0.085	0.049	0.046
Alcohol (1 + drinks/wk)	−0.019	0.012	−0.056	−1.587	0.113	−0.023	−0.055	−0.051
Waist circumference (cm)	0.002	0.001	0.162	2.806	0.005	0.227	0.097	0.091
BERLIN QUESTIONNAIRE RISK CATEGORIES								
Category 1 (SDB): 2 + criteria met (items 1–5)	0.022	0.011	0.071	2.059	0.040	0.122	0.071	0.067
Category 2 (EDS): 2 + criteria met (items 6–8)	−0.005	0.016	−0.011	−0.334	0.738	0.001	−0.012	−0.011
Category 3: HTN or BMI > 27.5 (kg/m^2)	0.034	0.012	0.108	2.704	0.007	0.210	0.093	0.088

Note: Dependent Variable: HbA1c (square-root transformation).
15 variables accounted for 12.5% of the variance in HbA1c (R^2 = 0.125; $F_{[15,850]}$ = 7.9, p < 0.001).

3.3. BQ category 2: excessive daytime sleepiness (EDS)

There was no significant difference in HbA1c values or glycaemia status group for BQ Category 2 (EDS). Participants who were positive for EDS were younger, had higher BMI and waist circumference, and were more likely to be women (p = 0.04) or have a history of HTN (p < 0.05, data not shown).

3.4. BQ category 3: comorbidities of hypertension (HTN) and obesity

Participants who were positive for BQ Category 3 (comorbidities of HTN or BMI > 30 kg/m^2) had significantly (t = 6.6, p < 0.001) higher HbA1c values (6.3 ± 1.02% [45 ± 11.1 mmol/mol]) compared to participants who were negative for Category 3 (5.9 ± 0.70% [41 ± 7.7 mmol/mol]). The 356 participants who were positive for BQ Category 3 with either HTN (> 140/90) or obesity (> 30 kg/m^2) were

significantly ($p < 0.001$) more likely to have prediabetes (41%) or diabetes (61%) than the normal glucose tolerance group (25%). As seen in Table 2, rates were even higher for each glycaemia status group when obesity was categorised as BMI > 27.5 kg/m^2 (53%, 69%, and 37%, respectively). Men (45%) were significantly more likely than women (33%) to be positive for BQ Category 3.

3.5. Multivariate analysis

Income and education differed by research study location, and these demographic variables significantly differed for glycaemia status groups (Table 1), but not for SDB categories (Table 3). Compared to women, the men in this sample were more likely to be in the diabetes category, have higher HbA1c values, and have a higher rate of SDB, yet more women reported excessive daytime sleepiness compared to men. To control for these demographic and clinical characteristics related to both OSA and dysglycaemia, a linear regression analysis with HbA1c as the outcome variable was performed to determine additional contributions of each of the three BQ categories to dysglycaemia.

As seen in Table 4, controlling for all other variables in the model, geographic location and income were the only significant demographic variables, and waist circumference was the only clinical variable, that significantly accounted for the variance in HbA1c. BQ Category 2 (EDS) was not significant, but BQ Category 1 (SDB) and BQ Category 3 (Comorbidities of HTN or BMI) were significant (Table 4) even after controlling for absolute BMI and blood pressure values. The overall model accounted for 12.5% of the variance in HbA1c ($F_{[15,850]} = 7.9$, $p < 0.001$). A similar logistic regression model with the three glycaemia status groups as the outcome of interest yielded similar results (data not shown).

4. Discussion

In this community-based sample of adults with South Asian heritage, HbA1c values were significantly higher for participants who said they snored compared to participants who said they did not snore. In addition, risk of OSA was significantly more likely in the prediabetes group (24–29%) and diabetes group (32–35%) compared to the normal glucose tolerance group (18–23%). These rates varied slightly depending on whether BMI of 27.5 kg/m^2 (28%) or 30.0 kg/m^2 (24%) was used for the obesity comorbidity in BQ Category 3.

Our overall prevalence rate for risk of OSA was somewhat higher than rates reported by others, but prevalence did vary by glycaemia status. When Heffner and colleagues (Heffner et al., 2012) examined medical records of over 16,000 patients with diabetes, 18% had also been diagnosed with OSA, and 23% were diagnosed with OSA if they were also obese. Our bivariate results (Table 2) support their multivariate model findings that HbA1c, sex and BMI were significant predictors of OSA (Heffner et al., 2012). However, in our multivariate model with HbA1c as the outcome of interest, waist circumference was a significant predictor while sex and BMI were no longer significant. In other studies of South Asians, waist circumference has also been a stronger predictor of dysglycaemia than BMI (Venkataraman et al., 2004; Misra et al., 2010).

Both BQ Category 1 (SDB) and Category 3 (HTN and BMI) were significant in accounting for the variance in HbA1c values, even when demographic and clinical variables were included in the model. The other significant variables were geographic location, low income, and high waist circumference. Income was not associated with SDB or risk of OSA, and the link between low income and dysglycaemia may reflect a lack of access to health care, poor nutrition or inadequate time for physical activity (Pamidi and Tasali, 2012; Gangwisch et al., 2007). Waist circumference is a risk factor common to both OSA and dysglycaemia (Peppard et al., 2013; Pamidi and Tasali, 2012; Heffner et al., 2012; Gangwisch et al., 2007), and its significance remained strong in the multivariate model. While BMI may be easier for clinicians to obtain than waist circumference, reducing waist circumference may be an even more effective strategy than weight loss *per se* for the goal of lowering HbA1c. Given that both the normal glucose tolerance group (Table 1) and the non-snoring group (Table 3) of South Asians in this sample had a mean waist circumference of 90 cm or less, perhaps the sensitivity and specificity of the BQ would improve by including waist circumference > 90 cm as an additional comorbid risk factor in Category 3.

In our sample, dysglycaemia and risk of OSA were more prevalent in men, and were also associated with older age, HTN, larger waist circumference, and obesity. These bivariate relationships support findings reported by Gangwisch and colleagues (Gangwisch et al., 2007) as well as Peppard and colleagues (Peppard et al., 2013) who also reported higher prevalence of OSA in men (10–17%) than women (3–9%). Their prevalence of actual OSA was based on objective polysomnography results, however, while our higher prevalence of risk for OSA (men 28%; women 18%) was estimated from the BQ screening questionnaire. Age was also significant in bivariate associations with both OSA risk and dysglycaemia in our sample, supporting findings from Young and colleagues (Young et al., 2002) in the Sleep Heart Health Study regarding a two to eight times higher prevalence of OSA among participants over 60 years of age compared to adults under 60 years of age. However, the average age of our sample was under 60 years, and age did not reach statistical significance ($p = 0.09$) when controlling for other demographic and clinical variables in our multivariate model.

Obesity was associated with OSA as well as dysglycaemia, regardless of whether we used BMI of > 30 kg/m^2 or current recommendations of BMI > 27.5 kg/m^2 for South Asians (World Health Organization, 2004). Previous studies indicate that as many as 70% of patients with OSA are obese (Shimura et al., 2005). Our findings suggest that using BMI > 27.5 kg/m^2 to screen for risk of OSA in South Asian adults would yield a similar percentage, but this lower BMI may reflect OSA risk at an earlier point in the downhill trajectory of dysglycaemia and OSA. Nevertheless, it was waist circumference that was more influential than BMI in accounting for the variance in HbA1c values.

HbA1c values were significantly higher in the participants who snored compared to non-snorers (Table 3). In addition, even with controlling for demographic and clinical characteristics, BQ Category 1 SDB explained a significant amount of the variance in HbA1c values. Previous studies report that 50–70% of patients with OSA also have diabetes (Einhorn et al., 2007). In a sample of Japanese adults (27 men and 13 women) with uncontrolled Type 2 diabetes, an overnight sleep study using polysomnography revealed that 31 (78%) had SDB (Kashine et al., 2010). The risk of SDB and OSA was lower in the diabetes group in our sample, suggesting that perhaps risk of OSA is underestimated in South Asians who have Type 2 diabetes, particularly if they are unaware of their habitual snoring (Heffner et al., 2012).

As reflected in the three BQ categories, OSA typically presents with habitual snoring and SDB that, if left untreated, can lead to EDS as well as comorbidities of obesity and hypertension. Dysglycaemia was associated with SDB even after controlling for BMI and systolic and diastolic blood pressure. Hence, a history of snoring and a positive endorsement of BQ Category 1 (SDB) in patients with dysglycaemia should be followed up with a more thorough clinical assessment regardless of having EDS.

Our study has some limitations to consider. First, the cohort may adequately represent South Asians living in Chicago and the San Francisco Bay Area, but our differences in demographic and clinical variables by research site call attention to the limited generalizability to all South Asians in the USA or other countries. While two sites provided more variability in socioeconomic status, the Chicago site included adults with a higher rate of dysglycaemia and lower income and education relative to the California site. Second, the cross-sectional design of this study precludes determination of directionality or causality, yet attention to simultaneously assessing and treating both OSA and

dysglycaemia could more effectively improve clinical management of both conditions. Third, the BQ provides a self-reported estimate of high risk for OSA and requires at least two of the three categories to be positive regardless of responses about snoring. Yet EDS was not associated with dysglycaemia. Hence, sensitivity and specificity of the BQ is overly dependent on EDS and on self-report of habitual snoring, and diagnosis of OSA can only by confirmed by overnight polysomnography. In BQ Category 1, there were 137 participants who did not know if they snored. If the patient is unaware of habitual snoring, there should be an opportunity to ask a bed partner, or audio-record a night's sleep to improve low-cost screening for OSA.

Lastly, we used HbA1c, a conventional metric for determining dysglycaemia and the severity of Type 2 diabetes. Additional correlates and metrics to estimate diabetes severity and risk for OSA are needed, as our multivariate model only explained 12% of the variance in HbA1c. Waist circumference, as an estimate of fat deposition in the abdomen, was a more significant anthropometric characteristic than BMI in accounting for the variance in HbA1c. Based on our findings, waist circumference > 90 cm may improve the sensitivity and specificity of the BQ in evaluating the risk of OSA in South Asians. To further evaluate risk for OSA, clinicians and researchers should also consider measures of neck circumference to estimate fat deposition in the region of the upper airway.

In summary, this large cohort of South Asians in the USA was at high risk for SDB and OSA. OSA is a chronic sleep disorder that can complicate the medical management of other chronic conditions such as diabetes, HTN and obesity (Shaikh et al., 2010; Cappuccio et al., 2010). Findings from this study are important to clinicians because screening South Asians who may need treatment for OSA could also be relevant to the management of dysglycaemia. While the BQ uses BMI > 30 kg/m^2 as an indicator of obesity, current guidelines (BMI > 27.5 kg/m^2) should be substituted for use in screening South Asians for OSA risk (World Health Organization, 2004). Our findings also suggest that waist circumference > 90 cm be included with comorbidities of HTN and obesity in BQ Category 3. Finally, efforts should be made to obtain a patient's history of snoring and SDB. If a patient, regardless of age or sex, screens positive on the BQ for either SDB (Category 1) or comorbidities of HTN or obesity (Category 3), a more intensive overnight polysomnography to diagnose and treat OSA would be warranted regardless of EDS, and may help in the prevention and treatment of dysglycaemia.

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