

The Risk of Obstructive Sleep Apnea among Patients with Type 2 Diabetes Mellitus

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Abstract

Context/Aims: Obstructive sleep apnea (OSA) and Type 2 diabetes mellitus share obesity as a common risk factor. The presence of OSA may contribute to increased morbidity and mortality of diabetes. Despite their close association, OSA is not routinely evaluated in diabetic patients. This study was conducted to determine the risk of OSA among Type 2 diabetes mellitus patients. **Methods:** Type 2 diabetic patients attending a tertiary hospital in Nigeria were evaluated for OSA risk using the Berlin Questionnaire. Other parameters measured included anthropometry and blood pressure (BP). **Results:** Three hundred and twenty-seven patients participated in this survey: 177 (54.1%) were female and 150 (45.9%) were male. The average age of the patients was 56.2 ± 9.3 years. Seventy-eight (44.8%) females were obese compared to 30 (20.0%) males, $P < 0.001$. Two hundred and one (61.5%) patients were previously known hypertensives with only 48 (23.9%; 95% confidence interval [CI]: 18.2–30.4) of them having good BP control. One hundred and sixty-two (49.5%, 95% CI: 44.0–55.1) patients had a high risk for OSA: 96 (54.2%; 95% CI: 44.6–61.7) females and 66 (44.0%; 95% CI: 35.9–52.3) males. The strongest predictor for a high risk of OSA was poorly controlled BP with an odds ratio of 2.6 (95% CI: 1.6–4.3). **Conclusion:** This study has demonstrated that there is a high risk of OSA among Type 2 diabetic patients and that OSA risk is significantly associated with poor BP control and obesity. We recommend that diabetic patients should be assessed for OSA risk as part of their routine evaluation.

Keywords: Diabetes mellitus, hypertension, obstructive sleep apnea

INTRODUCTION

Sleep-disordered breathing (SDB) is a common disorder characterized by repetitive apneas and hypopneas. This is usually accompanied by fragmentation of sleep, arousals, and a drop in oxygen saturation.¹ SDB can be obstructive, central, or both. Obstructive sleep apnea (OSA) is characterized by apnea and or hypopnea despite continued respiratory efforts.² OSA has shown a strong association with cardiovascular risk factors, with hypertension being the most common cardiovascular comorbidity.³ About half of OSA patients have hypertension,⁴ with 30%–40% of hypertensives having OSA.⁵ Resistant hypertension has an even stronger association with OSA.^{6,7}

Type 2 diabetes mellitus is an endocrine disorder characterized by impairment in glucose metabolism due to defective insulin secretion, defective insulin action, or both. It is diagnosed by a persistent fasting plasma glucose ≥ 7.0 mmol/L or 2 h postprandial plasma glucose ≥ 11.1 mmol/L.⁸ Recently, there is mounting evidence to suggest an association between OSA and Type 2 diabetes, these conditions occurring with

increasing frequency in patients with obesity.⁹ Available data suggest that long-term exposure to intermittent hypoxia and sleep fragmentation which occurs in OSA initiates a cascade of events contributing to insulin resistance and disorders of glucose metabolism.^{10,11} Alternatively, some studies proposed that insulin resistance and chronic hyperglycemia might contribute to the development of OSA.¹²⁻¹⁴

The prevalence of obesity and diabetes has steadily been on the rise in Nigeria due to an increase in income and increasing adoption of Western lifestyles.¹⁵ The identification and management of modifiable risk factors such as obesity, hypertension, dyslipidemia, and OSA are important to reduce morbidity and mortality associated with Type 2 diabetes mellitus. This study was

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undertaken to determine OSA risk and its association with blood pressure (BP) control among Type 2 diabetic patients.

METHODS

Study design

This was a cross-sectional study designed to determine the risk of OSA among Type 2 diabetes mellitus patients. The risk of OSA was evaluated using the Berlin Questionnaire.¹⁶ The Berlin Questionnaire is a simple and useful tool developed by Netzer *et al.* for screening OSA risk in the general population.¹⁷ The questionnaire consists of three categories related to the risk of having OSA. The first category scores participant's snoring; the second category assesses daytime somnolence and fatigue; and the third category assesses participants' medical history, demography, and anthropometric parameters. Patients can be classified into high risk or low risk based on their responses to the individual items and their overall scores in the symptom categories. A high risk for OSA occurs when there are two or more categories with positive scores, whereas a low risk is occurs if one or no category has positive score.^{16,18} The questionnaire was administered by a trained interviewer.

Poor BP was defined as a systolic BP >140 mmHg or diastolic BP >90 mmHg. The body mass index (BMI) was calculated using the formula weight divided by the square of the height in meters.

Study area and participants

This study was conducted in the endocrine and metabolic diseases clinic of University of Uyo Teaching Hospital. This is a public hospital located in the capital of Akwa Ibom State in the southeastern part of Nigeria. The hospital provides primary, secondary, and tertiary health-care services for the people of Akwa Ibom and the neighboring states. The clinic receives referrals from the outpatient clinics within the hospital as well as from other primary and secondary health-care facilities within and around the state. There are about two thousand patients on the clinic register who visit regularly.

The sample size was determined using Fisher's formula:¹⁹

$$n = z^2pq/d^2$$

where, n = desired sample size (when population is >10,000). z = the standard normal deviate, set at 1.96 for a 95% confidence interval (CI). Using a prevalence of 27% for OSA risk from a previous local study²⁰ gives a sample size of 302. Because the exact number of source population of respondents is <10,000, we used correction formula of $nf = ni/(1 + ni/N)$ where nf = corrected sample size, ni = uncorrected sample size, and N = total number of all the source population. This gives a sample size of 262. With an expected attrition rate of 10%, the minimum sample size was adjusted to 289.

The sample size was about one-sixth of the diabetic patients on the clinic register; every sixth patient was recruited until the sample size was achieved. The first patient was selected by casting lots.

Inclusion criteria, apart from being a Type 2 diabetic, included being accompanied by a spouse or a room/bed partner and his/her willingness to corroborate some of the patient's responses to the questionnaire. Informed consent was obtained from every patient before recruitment for the study.

Statistical analysis

Categorical variables were reported as frequencies and percentages with CIs, whereas continuous variables were reported as means with standard deviation. The association between the risk for OSA and some traditional risk factors was evaluated using the Pearson's Chi-square for categorical variables and Student's *t*-test for continuous variables. Risk factors with significant association with OSA risk were further evaluated for their independent contribution by multivariate analysis using logistic regression. The model was constructed using independent variables with significant association with the dependent variable under univariate analysis as well as some traditional risk factors with $P > 0.05$ but < 0.1 . The predictor variables were introduced into the model in a hierarchical order.

RESULTS

Three hundred and twenty-seven patients participated in this survey: 177 (54.1%) females and 150 (45.9%) males. The average age of the patients was 56.2 ± 9.3 years. The youngest participant was 35 years whereas the oldest was 82 years, giving a range of 47 years. The males were older than the females (57.6 ± 9.8 vs. 54.9 ± 8.5 years, $P = 0.008$). About 75% of the patients were middle aged whereas only three subjects were above 75 years. Most of the patients were educated up to tertiary level whereas only 21 (6.4%) (all being females) had no formal education. There were more unemployed women than men, 33 (18.6%) versus 6 (4.0%), whereas there were more men engaged in the public service than women, 63 (42.0%) versus 48 (27.1%); $P < 0.001$. Only 18.5% of the patients consumed alcohol. There were more obese women than men, 78 (44.8%) versus 30 (20.0%); $P < 0.001$. Truncal obesity was more common among the women compared to the men, 147 (83.1%) versus 33 (22.0%); $P < 0.001$. Two hundred and one (61.5%) patients were previously known hypertensives with only 48 (23.9%; 95% CI: 18.2–30.4) of them having good BP control. One hundred and sixty-two (49.5%; 95% CI: 44.0–55.1) patients had a high risk for OSA: 96 (54.2%; 95% CI: 44.6–61.7) females and 66 (44.0%; 95% CI: 35.9–52.3) males [Table 1].

For categorical variables, hypertension, poor control of BP, and obesity had a significant positive association with OSA risk, whereas there was no significant association between gender, alcohol consumption, marital status, education, and occupation with OSA risk. For continuous variables, increasing age, BMI, waist circumference, and neck circumference were significantly associated with OSA risk, whereas duration of diabetes was not significantly associated with OSA risk [Table 2].

Binary logistic regression was performed to assess the impact of some patient characteristics on the likelihood that a patient

Table 1: Demographic and physical characteristics of study participants

Parameter	Gender		Total	Significant (<i>P</i>)
	Female, <i>n</i> (%)	Male, <i>n</i> (%)		
Age (years)	54.9±8.5	57.6±9.8	56.16±9.2	0.08
≤45	24 (13.6)	21 (14.0)	45 (13.8)	0.02
46-55	69 (39.9)	39 (26.0)	108 (33.0)	
56-65	72 (40.7)	66 (44.0)	138 (42.2)	
66-75	9 (5.1)	21 (14.0)	30 (9.2)	
>75	3 (1.7)	3 (2.0)	6 (1.8)	
Marital status				
Married	129 (72.9)	144 (96.0)	273 (83.5)	<0.001
Widowed	45 (25.4)	6 (4.0)	51 (15.6)	
Divorced	3 (1.7)	0 (0.0)	3 (0.9)	
Education				
None	21 (11.9)	0 (0.0)	21 (6.4)	<0.001
Primary	63 (35.6)	36 (24.0)	99 (30.30)	
Secondary	27 (15.3)	24 (16.0)	51 (15.6)	
Tertiary	66 (37.3)	90 (60.0)	156 (47.7)	
Occupation				
Unemployed	33 (18.6)	6 (4.0)	39 (11.6)	<0.001
Retired	39 (22.0)	39 (26.0)	78 (23.9)	
Unskilled workers	48 (27.1)	18 (12.0)	66 (20.2)	
Semi-skilled workers	9 (5.1)	9 (6.0)	18 (5.5)	
Public servants	48 (27.1)	63 (42.0)	111 (33.9)	
Business/politics	0 (0.0)	15 (10.0)	15 (4.6)	
High risk for OSA	96 (54.2)	66 (44.0)	162 (49.5)	0.065
Alcohol use	21 (12.1)	39 (26.0)	60 (18.5)	0.001
Hypertension	126 (71.2)	75 (50.0)	201 (61.5)	<0.001
Poorly controlled BP	108 (61.0)	84 (56.0)	192 (58.7)	0.359
Obesity	78 (44.8)	30 (20.0)	108 (33.3)	<0.001
Truncal obesity	147 (83.1)	33 (22.0)	180 (55.0)	<i>P</i> <0.001
Duration of diabetes (years)	8.47±4.8	8.00±5.8	8.26±5.25	0.424
BMI (kg/m ²)	29.00±3.5	26.3±5.8	27.76±4.2	<0.001
Waist circumference (cm)	96.94±7.9	94.10±11.0	95.62±9.55	<0.001
Neck circumference (cm)	34.9±2.2.	38.6±3.1	36.6±3.3	<0.001

OSA – Obstructive sleep apnea; BP – Blood pressure; BMI – Body mass index

would be categorized as having a high risk for OSA. The model contained six variables: age, male gender, alcohol consumption, BMI, poor BP control, and neck circumference. The model containing all the predictors was statistically significant Chi-square (6, *N* = 327) =58.48; *P* < 0.001. The model explained up to 22% (Nagelkerke's *R*²) of the variance in OSA risk and correctly classified 63.3% of the patients. Only BMI and poorly controlled BP made unique significant contributions to the model. The strongest predictor for a high risk of OSA was poorly controlled BP with an odds ratio (OR) of 2.6 (95% CI: 1.6–4.3) [Table 3].

DISCUSSION

The main objective of this study was to determine the risk for OSA among Type 2 diabetic patients using the Berlin Questionnaire. In this study, 162 (49.5%) patients had high risk for OSA. Previous studies have documented similar findings. Cass *et al.*²¹ using the Berlin Questionnaire to determine the

risk of OSA among Type 2 DM patients in a university-based family medicine center observed that 124 (48.6%) patients without a prior diagnosis of OSA were classified as high risk for OSA. Similarly, West *et al.*²² in a survey conducted among Type 2 diabetics men in the UK using a self-administered Berlin Questionnaire observed a high prevalence of OSA risk of 56.2% out of 938 men sampled. A similar survey conducted by Aljabr *et al.*²³ using the Berlin Questionnaire in the King Fahad hospital diabetes center documented a frequency of 45 patients with a high risk for OSA out of 147 patients (30.6%). Similarly, a high frequency of OSA risk was observed by Obaseki *et al.*²⁰ in Ile Ife, South-West Nigeria, among Type 2 diabetics attending the outpatient clinic in a university hospital. The study reported a frequency of 27% for OSA risk using the Berlin Questionnaire. These investigators and other studies suggest that the risk of OSA is higher among patients with Type 2 diabetes than in the general population.^{16,24} Apart from being more common among Type 2 diabetic patients, OSA is usually more severe among Type 2 diabetics than nondiabetic patients.²⁵

Table 2: The association between obstructive sleep apnea and patient characteristics

Parameter	OSAS		P
	Low risk, n (%/SD)	High risk, n (%/SD)	
Education			
Primary	9 (42.9)	12 (57.1)	0.131
Secondary	45 (45.5)	54 (54.5)	
Tertiary	78 (50.0)	78 (50.0)	
Marital status			
Married	141 (51.6)	132 (48.4)	0.63
Widowed	21 (41.2)	30 (58.8)	
Divorced/separated	3 (100.0)	0.0 (0.0)	
Occupation			
Unemployed	21 (53.8)	18 (46.2)	0.21
Retired	45 (57.7)	33 (42.3)	
Unskilled	36 (54.5)	30 (45.5)	
Semi-skilled	6 (33.3)	12 (66.7)	
Public servants	48 (43.2)	63 (56.8)	
Business/politician	9 (60.0)	6 (40.0)	
Alcohol	24 (40.0)	36 (60.0)	0.08
Hypertension	72 (35.8)	129 (64.2)	<0.001
Truncal obesity	78 (43.3)	102 (56.7)	0.004
Obesity	39 (36.1)	69 (63.9)	<0.001
Poor BP control	81 (42.2)	111 (57.8)	<0.001
Gender			
Male	84 (56.0)	66 (44.0)	0.065
Female	81 (45.8)	96 (54.2)	
Age (years)	57.2 (10.1)	55.1 (8.2)	0.039
Duration of DM (years)	8.0 (4.5)	8.52 (5.8)	0.374
BMI (kg/m ²)	26.59 (3.5)	28.97 (4.3)	<0.001
Waist circumference (cm)	93.7 (9.1)	97.5 (9.6)	0.001
Neck circumference (cm)	36.17 (2.7)	37.05 (3.7)	0.016

OSAS – Obstructive sleep apnea syndrome; BP – Blood pressure; BMI – Body mass index; DM – Diabetes mellitus; SD – Standard deviation

Table 3: Predictors of obstructive sleep apnea risk

Parameters	B	Significant	OR	95% CI	
				Lower	Upper
Age	-0.11	0.43	0.98	0.96	1.02
Gender	-0.64	0.13	0.52	0.23	1.19
Alcohol	0.38	0.24	1.46	0.77	2.76
BMI	0.17	0.001	1.2	1.06	1.32
Poor BP control	0.95	<0.001	2.6	1.6	4.3
Neck circumference	0.8	0.167	1.08	0.097	1.21
Truncal obesity	-0.57	0.18	0.56	0.24	1.3

BP – Blood pressure; BMI – Body mass index; OR – Odds ratio; CI – Confidence interval

The risk for OSA is also higher for obese diabetics than the general population; 63.9% of obese patients had a high risk for OSA. This finding has been corroborated by previous studies. Obaseki *et al.*²⁰ documented a high risk for OSA of 51.7% among diabetic patients with BMI above 30 Kg/m². Foster *et al.* observed in the sleep ahead study that BMI was

the only significant predictor of severe OSA (OR: 1.1; 95% CI: 1.0–1.2; $P < 0.05$). Independent of other variables and that a 1 unit increase in BMI was associated with a 10% increase in the predicted odds of severe OSA.²⁶

This study demonstrated a strong association between hypertension and OSA risk. Of 201 hypertensive patients, 129 (64.1%) had a high risk for OSA. Several cross-sectional studies have described a significant association between OSA and hypertension.^{5,27} Studies have also reported an increasing prevalence of hypertension with increased severity of OSA.⁴ OSA has also been shown to increase the risk for hypertension. A previous study in Spain by Marin *et al.*²⁸ involving 1889 participants over a 12-year period reported an increased rate of new hypertension among OSA patients compared with controls, and this relationship remained significant after controlling for age and obesity.

Among patients who were previously known hypertensives, BP control was very poor, and this had a significant association with OSA risk after controlling for the impact of age, gender, neck circumference, and obesity. In a previous study to determine the association between sleep apnea and resistant hypertension, Calhoun *et al.*²⁹ reported that OSA risk was significantly associated with difficult to control BP. Similarly, in a case-control study to evaluate the risk factors associated with resistant hypertension by Gus *et al.*,³⁰ the investigators found a strong and significant association between a high OSA risk and resistant hypertension after controlling for the effects of age, gender, BMI, and duration of hypertension. This association between OSA and resistant hypertension had been confirmed by Pratt-Ubunama *et al.*,³¹ who showed that OSA diagnosed by polysomnography was present in 85% of patients with resistant hypertension presenting to their facility.

CONCLUSION

This study has demonstrated that there is a high risk of OSA among type 2 diabetic patients and that the OSA risk is significantly associated with poor BP control and obesity. Therefore, we suggest that diabetic patients should be evaluated for OSA risk as part of their routine evaluation using the Berlin Questionnaire or other similarly validated instrument.

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Conflicts of interest

There are no conflicts of interest.

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