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Prevalence of Sleep Disordered Breathing in an Ambulatory Bariatric Population

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Abstract

Aims

Rising global obesity trends suggest that the prevalence of sleep disordered breathing is under-represented. We aim to characterise the prevalence obstructive sleep apnoea (OSA) and obesity hypoventilation syndrome (OHS) in a population with ambulatory severe obesity (body mass index (BMI) ≥35 kg/m2).

Methods

Patients were recruited for this cross-sectional study between October 2017 and October 2018 from a weight management service for respiratory and sleep assessment.

Results

81 patients underwent full assessment. The mean age was 47 years and mean BMI was 53 kg/m2. OSA was prevalent in 92.6% (n=75), moderate-to-severe OSA in 70.4% (n=57) and OHS in 17.2% (n=14) of the total population. The risk of moderate to severe OSA increased significantly above a BMI of 50 kg/m2. The risk of daytime hypoventilation increased significantly above a BMI of 60 kg/m2. There was no significant difference in daytime sleepiness across obesity severity. Obesity and sleep disorder severity were significantly correlated, especially for females.

Conclusions

OSA is the most common obesity-related co-morbidity in a population with severe obesity. Patients with BMI ≥60 kg/m2 are at particular risk of OHS. The presence of a BMI ≥50 kg/m2 alone should indicate referral for sleep assessment.

Abbreviations

AASM	American Academy of Sleep Medicine	NIV	Non-invasive ventilation
ABG	Arterial blood gas	ODI	Oxygen desaturation index
AHI	Apnoea-hypopnoea index	OHS	Obesity hypoventilation syndrome
ANOVA	Analysis of variance	OSA	Obstructive sleep apnoea
BMI	Body mass index	OSAS	Obstructive sleep apnoea syndrome
CPAP	Continuous positive airway pressure	PaCO2	Arterial carbon dioxide tension
ESS	Epworth sleepiness scale	PAP	Positive airway pressure
HCO3	Bicarbonate	SpO2	Oxyhaemoglobin saturations
HSAT	Home sleep apnoea test	T<90	Time spent below oxygen saturations of 90%
IQR	Interquartile range	WMS	Weight management service

Introduction

The presence of severe obesity (BMI ≥40 kg/m^2) is rising globally, with obesity-related disease projected to increase in all European countries by 2030[1]. In Ireland, about 25% of males and females classify as having obesity (BMI ≥30 kg/m^2)[2], and if current obesity trends continue, it is estimated that by 2030, this will increase to 48% of men and 57% of women[3].

Obesity's effects on the respiratory system include obstructive sleep apnoea (OSA) and obesity hypoventilation syndrome (OHS)[4,5]. Obesity and sleep-disordered breathing have a synergistic metabolic effect on the body and are associated with hypertension and glucose intolerance[6,7]. OHS is associated with a higher risk of cardiopulmonary morbidity and mortality[5], although outcomes can be mitigated with the use of nocturnal positive airway pressure (PAP) therapy[8].

Sleep disordered breathing prevalence is increasing along with obesity trends, with the Swiss Hypnolaus study finding moderate-to-severe OSA in up to 50% of the general population[9]. Within a population with obesity, OSA prevalence increases up to 87%[10] and OHS prevalence is up to 20%[5]. However, data regarding disease trends in so-called 'super' (BMI ≥50 kg/m^2) and 'super-super' (BMI ≥60 kg/m^2) obesity is lacking as this group remains under-represented in current literature, notable because evidence suggests a dose-response relationship[11].

We aimed to assess up-to-date sleep disordered breathing prevalence in an ambulatory cohort with severe obesity in the context of rising obesity trends.

Methods

This was a prospective, cross-sectional study of adult patients with a BMI ≥40 kg/m2, or a BMI ≥35 kg/m2 with one or more obesity-related co-morbidities, attending an ambulatory weight management service (WMS), St. Columcille's Hospital, Dublin, Ireland. The St. Vincent's University Hospital Ethics and Medical Research Committee approved this study (e-Appendix 1). Exclusion criteria included an antecedent diagnosis of sleep disordered breathing.

Baseline information included demographics, anthropometrics including BMI and neck circumference and medical co-morbidities. Waist circumference was not measured due to limited measurement reliability and predictive power of disease in subjects with severe obesity[12].

Subjects were referred for a single-night level 3 cardiorespiratory home sleep apnoea test (HSAT)[13] using the Embletta Portable Diagnostic Study (Embletta PDS, Resmed PEI, Dublin, Ireland). Data was analysed in accordance with AASM scoring guidelines[14]. Data collected included apnoea-hypopnoea index (AHI), oxygen desaturation index (ODI), nocturnal oxygen saturation (SpO2) nadir, and time spent below oxygen saturations of 90% (percent of study (T<90)). OSA was defined as an AHI ≥5 events per hour. Obstructive sleep apnoea syndrome (OSAS) was defined as AHI ≥5/hr with daytime somnolence. OHS was defined as (1) BMI ≥30 kg/m2 and (2) arterial hypercapnia ≥6 kPa without an alternative cause for hypoventilation.

Subjects attended respiratory assessment including an interview, physical examination and arterial blood gas (ABG) analysis. The Epworth Sleepiness Scale (ESS) was used to assess subjects' daytime sleepiness, with a score above 10 indicative of excessive daytime sleepiness[15]. Subjects were asked whether the HSAT study night reflected a subjectively typical night of sleep. ABG sampled the radial artery at the wrist directly into a heparinised blood gas syringe and analysed on either the ABL90 Flex (Radiometer Medical ApS, Denmark), or ABL800 Flex (Radiometer Medical ApS, Denmark) machines, regularly calibrated as per local hospital protocol.

The primary outcome was to characterise the prevalence of sleep disordered breathing in this population with severe obesity. Secondary outcomes included evaluating correlation between parameters of sleep disordered breathing and obesity severity.

Subjects were stratified by obesity severity into three subgroups: BMI of 35-50 kg/m2, 50-60 kg/m2, or ≥60 kg/m2. Results across groups were compared using analysis of variance (ANOVA) with post hoc Tukey analysis, Kruskal–Wallis with Dunn's multiple comparison, and Chi-squared tests for parametric, nonparametric, and categorical variables, respectively. Correlative statistics were performed using Spearman's or Pearson's correlation coefficients for continuous variables, according to distribution, or a Fisher's exact test for categorical variables.

Main-effects logistic regression was performed and reported as odds ratios to assess the dependent variables of OHS or moderate to severe OSA (AHI ≥15/hr) against predictors age, sex, hypertension, neck circumference, diuretic use, and BMI as a continuous variable (model 1), and categorically over 50 kg/m2 (model 2) and over 60 kg/m2 (model 3). AHI was included as an independent variable in the analysis for OHS.

All statistics were calculated using IBM SPSS version 24 (IBM Corporation, New York, USA) and Prism version 6 (GraphPad Software, San Diego, California, USA). P-values of ≤0.05 were considered statistically significant. Missing data was not included in the analysis.

Results

A total of 210 patients were screened. 85 patients were excluded due to an antecedent diagnosis of sleep disordered breathing and 44 patients refused to participate. Two patients did not attend for follow up. A total of 81 patients were included in the OSA analysis. Nine patients with missing ABG data were not included in the OHS analysis.

The baseline characteristics of the study population are displayed in Table 1. There was a two-thirds female predominance, the mean age was 47 years and the mean BMI was 53 kg/m2. Patients with a BMI 50-60 kg/m2 were found to be significantly younger than those with BMI <50 kg/m2 (p<0.001).

	Obesity Class (kg/m2)								
	<50 (n=27)		50-60 (n=36)		>60 (n=18)		Total (n=81)		p-value
Female (%)	16	(59.3)	25	(69.4)	13	(72.2)	54	(66.7)	0.594
Age, years	53	(11)	43	(10)	47	(8)	47	(11)	<0.001
Weight, kg	124.74	[21]	155.58	[19]	182.29	[32]	151.24	[31]	<0.001
BMI, kg/m2	45.2	[8.0]	53.3	[6.0]	64.0	[2.0]	53.0	[11.5]	<0.001
Neck circumference, cm	44.5	(5)	45.9	(5)	47.3	(5)	45.7	(5)	0.314
Hypertension (%)	16	(59.3)	13	(36.1)	10	(55.6)	39	(48.1)	0.148
T2DM (%)	11	(40.7)	9	(25.0)	5	(27.8)	25	(30.9)	0.388
Dyslipidaemia (%)	17	(63.0)	8	(22.2)	3	(16.7)	28	(34.6)	0.001
CRP, mg/L	5	[4]	10	[8]	10	[14]	8	[8]	0.031
HbA1c, mmol/mol	39.0	[14]	38.0	[10]	43.5	[9]	40.5	[12.5]	0.095
Diuretics (%)	5	(18.5)	3	(8.3)	2	(11.1)	10	(12.3)	0.470
COPD (%)	4	(14.8)	0	(0.0)	1	(5.6)	5	(6.2)	0.053
Asthma (%)	3	(11.1)	9	(25.0)	4	(22.2)	16	(19.8)	0.374
Smoking history (%)	14	(51.9)	19	(52.8)	5	(29.4)	38	(46.9)	0.526
Pack years	0.5	[45]	1.0	[16]	0	[33]	0.0	[12.5]	0.353

Table 1: *Baseline characteristics of bariatric population stratified by obesity severity.*

Data are presented as mean (standard deviation) or median [interquartile range], unless otherwise indicated. BMI = body mass index. T2DM = type 2 diabetes mellitus. CRP = c-reactive protein. HbA1c = glycosylated haemoglobin. COPD = chronic obstructive pulmonary disease.

OSA (AHI ≥5/hr) was seen in 75 subjects (92.6%; 95% CI 84.6 – 97.2), including 25 males and 50 females (92.6%; 95% CI 75.7 – 99.9 and 92.6%; 95% CI 82.1 – 97.9, respectively, p=0.999). Moderate to severe OSA (AHI ≥15/hr) was seen in 57 subjects (70.4%; 95% CI 59.2 – 80), including 22 males and 35 females (81.5%; 61.9 – 93.7 and 64.8%; 50.6 – 77.3, p=0.196). OHS was seen in 14 subjects (17.3%; 95% CI 9.8 – 27.3), including six males and eight females (22.2%; 95% CI 8.6 – 42.3 and 14.8%; 95% CI 6.6 – 27.1, p=0.534). The prevalence of moderate-to-severe OSA (AHI ≥15/hr) and OHS increased significantly with obesity severity (p=0.021 and p<0.001, respectively). There was no significant increase in OSAS prevalence across obesity severity groups (Figure 1).

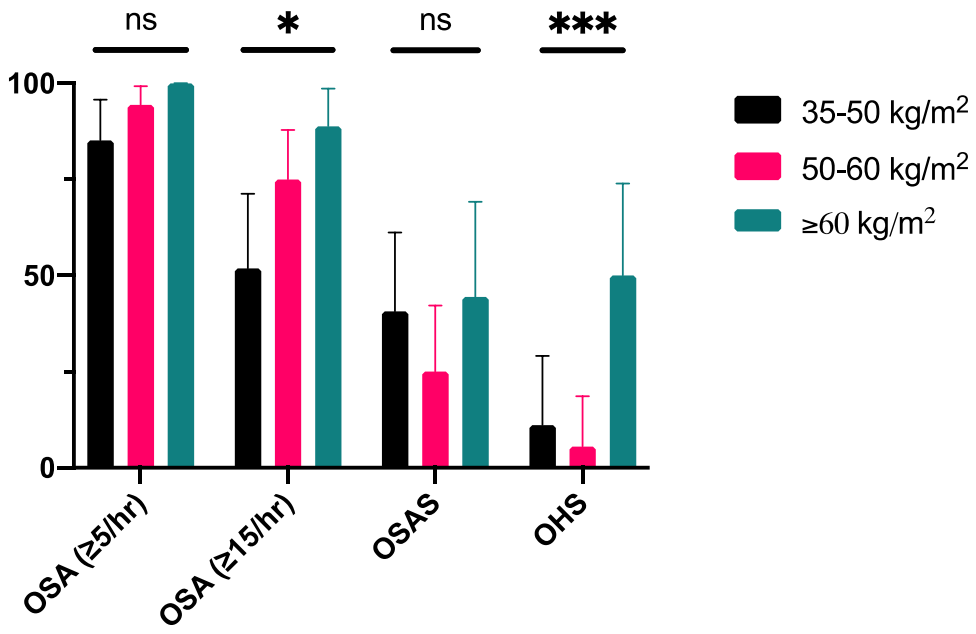

Figure 1: *Sleep disordered breathing prevalence stratified by obesity severity.*

OSA = obstructive sleep apnoea. OSAS = obstructive sleep apnoea syndrome. OHS = obesity hypoventilation syndrome.

Increasing obesity severity was significantly associated with OSA severity as measured by AHI, ODI and oxygen saturation nadir (Table 2). BMI also significantly correlated with markers of daytime hypoventilation in PaCO2 and HCO3 (Table 2).

AHI and BMI maintained a significant correlation in females but not males, despite a similar trend (Table 2). However, a significant correlation persisted in both sexes between BMI and both arterial carbon dioxide (PaCO2) and bicarbonate (HCO3) (Table 2).

		r	95% CI	p-value
AHI	Total	0.312	0.094 – 0.502	0.005
	Males	0.311	-0.091 – 0.625	0.115
	Females	0.340	0.072 – 0.563	0.012
4% ODI	Total	0.278	0.057 – 0.473	0.012
	Males	0.202	-0.204 – 0.549	0.312
	Females	0.336	0.067 – 0.560	0.013
Mean SpO2	Total	-0.116	-0.332 – 0.112	0.303
	Males	-0.115	-0.483 – 0.288	0.569
	Females	-0.167	-0.423 – 0.114	0.228
T<90 (%)	Total	0.133	-0.094 – 0.347	0.237
	Males	-0.037	-0.421 – 0.358	0.854
	Females	0.265	-0.014 – 0.506	0.055
Nadir SpO2	Total	-0.342	-0.526 – -0.127	0.002
	Males	-0.205	-0.551 – 0.201	0.305
	Females	-0.458	-0.651 – -0.209	<0.001
PaO2	Total	-0.108	-0.346 – 0.143	0.385
	Males	-0.034	-0.460 – 0.405	0.882
	Females	-0.169	-0.448 – 0.140	0.266
PaCO2	Total	0.356	0.135 – 0.543	0.002
	Males	0.416	0.012 – 0.703	0.039
	Females	0.340	0.059 – 0.572	0.019
HCO3	Total	0.400	0.186 – 0.578	<0.001
	Males	0.575	0.221 – 0.795	0.003
	Females	0.357	0.077 – 0.584	0.014

Table 2: *Correlation between BMI and parameters of sleep disordered breathing.*

AHI = apnoea-hypopnoea index. 4% ODI = oxygen desaturation index by 4%. SpO2 = oxygen saturations. T<90 (%) = time spent below oxygen saturations of 90% (% of the total recording time). PaO2 = arterial oxygen tension. PaCO2 = arterial carbon dioxide tension. HCO3 = arterial bicarbonate.

In a logistic regression model, BMI as a continuous variable was the significant predictor for moderate to severe OSA (OR 1.102, 95% CI 1.010 – 1.223, p=0.046) against non-significant predictors of age, sex, neck circumference, hypertension and diuretic use (Table 3). A BMI ≥50 kg/m2 increased the odds ratio of moderate to severe OSA (OR 6.804, 95% CI 1.754 – 31.240, p=0.008).

BMI was also a significant predictor for OHS (OR 1.144, 95% CI 1.057 – 1.269, p=0.003) along with age (OR 1.115, 95% CI 1.022 to 1.242, p=0.026) against non-significant predictors of sex, hypertension and AHI (Table 3). A BMI ≥60 kg/m2 significantly increased the odds ratio of OHS (OR 5.692, 95% CI 1.443 to 25.190, p=0.015).

(A) Moderate to severe OSA		Odds ratios	95% Confidence intervals	p-value
Model 1	**Age (years)**	1.003	0.941 to 1.068	0.930
	Male	2.467	0.367 to 18.500	0.355
	BMI	1.102	1.010 to 1.223	0.046
	Neck circumference	1.014	0.851 to 1.223	0.881
	Hypertension	1.304	0.344 to 5.149	0.696
	Diuretic use	3.862	0.456 to 89.520	0.278
Model 2	**Age (years)**	1.016	0.948 to 1.090	0.657
	Male	2.069	0.306 to 14.920	0.454
	BMI ≥50 kg/m2	6.804	1.754 to 31.240	0.008
	Neck circumference	1.024	0.860 to 1.242	0.792
	Hypertension	1.562	0.383 to 6.812	0.537
	Diuretic use	3.743	0.448 to 83.840	0.282
Model 3	**Age (years)**	0.986	0.926 to 1.046	0.632
	Male	1.827	0.283 to 12.670	0.525
	BMI ≥60 kg/m2	2.519	0.518 to 18.760	0.292
	Neck circumference	1.041	0.880 to 1.250	0.648
	Hypertension	1.080	0.293 to 4.021	0.907
	Diuretic use	4.305	0.558 to 93.450	0.224
(B) Obesity hypoventilation syndrome				
Model 1	**Age (years)**	1.115	1.022 to 1.242	0.026
	Male	1.507	0.320 to 7.277	0.599
	BMI	1.144	1.057 to 1.269	0.003
	Hypertension	0.805	0.127 to 3.963	0.788
	AHI	1.016	0.997 to 1.038	0.107
Model 2	**Age (years)**	1.082	1.005 to 1.182	0.052
	Male	1.223	0.320 to 4.513	0.763
	BMI ≥50 kg/m2	2.766	0.539 to 18.380	0.248
	Hypertension	1.250	0.316 to 5.117	0.750
	AHI	1.017	0.999 to 1.037	0.069
Model 3	**Age (years)**	1.072	0.996 to 1.167	0.079
	Male	0.871	0.207 to 3.381	0.844
	BMI ≥60 kg/m2	5.692	1.443 to 25.190	0.015
	Hypertension	1.172	0.271 to 5.200	0.830
	AHI	1.024	1.005 to 1.046	0.016

***Table 3**: **(A)** Multiple logistic regression to assess association of predictors of moderate to severe obstructive sleep apnoea (Model 1: Tjur's R2=0·134, adjusted R2=0·064; Model 2: Tjur's R2=0.186, adjusted R2=0.120; Model 3: Tjur's R2=0.085, adjusted R2=0.011). **(B)** Multiple logistic regression to assess association of predictors of obesity hypoventilation syndrome (Model 1: Tjur's R2=0.328, adjusted R2=0·277; Model 2: Tjur's R2=0.128, adjusted R2=0.062; Model 3: Tjur's R2=0.190, adjusted R2=0.129)*

Discussion

In our ambulatory bariatric cohort, we found a high prevalence of OSA (92.6%) and OHS (17.2%). Correlation between AHI and BMI was stronger and more significant for females rather than males, suggestive of possible physiological sex differences apart from BMI contributing to OSA severity in males. However, BMI remained the significant predictor for AHI against potential confounders of age, sex, neck circumference, hypertension, and diuretic use. The risk of moderate to severe OSA increased significantly above a BMI of 50 kg/m2. The risk of daytime hypoventilation increased significantly above a BMI of 60 kg/m2. We did not find an increase in reported OSAS despite increasing sleep disordered breathing prevalence.

Our methodology differed from existing literature by recruiting all-comers to a bariatric service, as opposed to recruitment from sleep clinics[11] or emergency departments[16,17]. We may have underestimated the prevalence of sleep disordered breathing in this population by not including patients with antecedent sleep diagnoses or those who refused to participate, although including these may have in fact over-estimated the burden of disease and not reflect an ambulatory population.

OSAS prevalence in our population was higher than the general population (33.3% versus up to 18%). The lack of a significant difference in OSAS prevalence across obesity severity raises questions regarding the utility of screening questionnaires in this population. The ESS is often used as a single tool by physicians to screen for daytime somnolence, but our data suggests that in a population with severe obesity, daytime symptoms do not change significantly even in the presence of more severe disease.

Our data suggests 'tipping points', whereby the risk of moderate-to-severe OSA significant rises with a BMI >50 kg/m^2, and the risk of OHS with a BMI ≥60 kg/m^2. This may be due to reduced functional lung volumes in severe obesity, as reported by Marillier, et al[18], worsening ventilation/perfusion mismatch or right to left shunting, reducing alveolar gas stores and prolonging nocturnal hypercapnia altering the daytime ventilatory response[19]. In addition, increased leptin resistance in severe obesity may blunt daytime ventilation[20].

In our study, obesity correlated more significantly with desaturation (SpO2 nadir) in females than males. Why females displayed more desaturation is unclear. Men tend to develop more severe OSA for a given level of obesity, likely due to differences in adiposity distribution[21]. Pre-menopausal oestrogen and progesterone levels in females reduce upper airway collapsibility, although this increases post-menopause[22] (the mean age for females in our cohort was 46 years). We did not measure waist circumference due to its limited measurement reliability and ability to predict disease in the context of severe obesity[12]. However, more detailed anthropometric measurement may help account for the sex differences seen here.

Our BMI groups were not matched for age; it is possible that patients who are younger with more severe obesity are more likely to seek help. Our regression analysis did not find age or sex to be significant predictors of OSA severity as compared to BMI; age predicted for OHS, which may reflect age-related leptin resistance[23].

Our study's main strength was the recruitment of unselected ambulatory patients with severe obesity who had not yet been diagnosed with sleep disordered breathing. Our study population demographics largely reflects published data from tier 3 weight management services. A systematic review of obesity services published in 2019 described a mean population BMI below that of our cohort (range 34.1 to 49.4 compared to 53 kg/m2) suggesting that obesity is continues to trend upwards in severity, as shown in our cohort[24]. However, recruiting from a weight management service may have introduced a self-selection bias of patients who are symptomatic and/or interesting in seeking medical care.

Performing limited sleep studies instead of polysomnography was a pragmatic choice that allowed for a high volume of patients to be screened in accordance with clinical guidelines[13]. However, without hypnogram monitoring, indices are calculated for total study time rather than total sleep time and may be underestimated. Nor did we control for co-morbid sleep complaints such as insomnia or sleep medication use, although commonly used 'z-drugs' do not affect OSA severity[25]. We also note that limited HSAT have not been specifically validated for use in the severely obese population in a published clinical trial.

We did not exclude patients with a smoking history or a diagnosis of COPD, although OHS diagnostic criteria requires excluding alternate causes for hypoventilation. As there was no significant difference in smoking history between obesity groups, we do not feel that our results were significantly affected in this regard, and our inclusive criteria are reflective of ambulatory service attendees.

Finally, we did not perform any pre- or post-menopausal subgroup analysis, and the Caucasian predominance of our study population also limits international generalisability of our results.

Our findings show that in subjects with severe obesity, OSA prevalence is higher than any other single metabolic co-morbidity, and the risk of significant sleep disordered breathing increases after thresholds of BMI ≥50 kg/m2 for moderate-to-severe OSA and ≥60 kg/m2 for OHS. The presence of so-called 'super' obesity alone (BMI ≥50 kg/m2) should trigger early sleep assessment to identify patients at risk of increased cardiopulmonary morbidity and mortality.

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