ORIGINAL ARTICLE

Pattern of sleep disordered breathing in obese Indians

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Abstract

Introduction: Obesity has become a major health problem worldwide due to high co-morbidity and an increasing prevalence. It is the greatest risk factor for obstructive sleep apnea (OSA). Owing to lack of data on the association of obesity and OSA within the country, the present study was designed to evaluate the pattern of sleep disordered breathing (SDB) among obese Indian subjects.

Material and Method: The study was prospectively carried out in Sleep Laboratory of LRS Institute of Tuberculosis and Respiratory Diseases, New Delhi. 30 obese [having body mass index BMI > 27.5 kg/m^2] and 10 non-obese (having BMI < 27.5 kg/m^2) subjects were consecutively enrolled into the study (obesity) and the control (non-obese) groups respectively as per the World Health Organization (WHO) Criteria of Obesity for Asians. Detailed clinical history including that of sleep was taken, a physical examination along with anthropometric measurements like neck circumference (NC), waist circumference (WC) and hip circumference (HC) was done and laboratory investigations were performed in all subjects, who thereafter, underwent an overnight polysomnography (PSG) on Compumedics E-Series sleep software. Sleep was staged as per Rechtshaffen and Kales (R & K) rules and SDB evaluated as per standard criteria. Data was subjected to statistical analysis.

Results: There were 16 obese, 8 severely obese & 6 morbidly obese subjects. Respective characteristics of the obesity and the control group subjects showed a mean age of 47.73 and 40.90 years, a male-female ratio of 19: 11 and 7:3, and a mean BMI of 33.46 and 23.73 kg/m^2. Mean Apnoea-Hypopnoea Index (AHI) was significantly higher among the subjects of the obesity group as compared to the controls. Similarly, mean AHI was significantly higher among the obese males, those having NC between 35 to < 45 cms, symptomatics, those having 4 to 6 number of symptoms, and those having co-morbidities as compared to the respective non-obese counterparts. Mean value of sleep latency was higher, while that of Total Sleep Time (TST) & sleep efficiency lower in the obesity than the control group. Oxygen De-saturation Index (ODI) and indices of arousal, Periodic Limb Movement (PLM) in Sleep (PLMS) & PLM with arousals were significantly higher in the obesity as compared to the control group respectively. No significant differences were noticed between the groups with regard to sleep stage percentages.

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SDB was present in 86.6% (26/30) of obesity subjects, of whom 80% (24/30) had mild, moderate and severe OSA (with 2/3rd having moderate to severe OSA and more than half having severe OSA), and 6.6% (2/30) had Upper Airway Resistance Syndrome (UARS) or Respiratory Effort Related Arousal (RERA). Obesity Hypoventilation Syndrome (OHS) co-existed in 37.5% (9/24) of subjects with OSA constituting one-third of total cases. PLMS co-existed in 7 subjects with OSA. All 6 morbidly obese subjects had some form of SDB with OSA in 5 and RERA in 1 of them.

Among the control subjects, 50% had a normal sleep study and others had only mild (40%; 4/10) and moderate OSA (10%; 1/10), while none had severe OSA. Further, OSA co-existed with PLMS in only 1 subject.

Conclusions: Mean AHI is higher among the subjects of obesity group as compared to non-obese subjects. Mean AHI is also higher among the obese males, those having NC between 35 to < 45 cms, symptomatics, those having 4 to 6 number of symptoms, and those having co-morbidities in comparison to the respective non-obese subjects. The obese subjects sleep for less time taking longer time to sleep, have higher number of arousals and PLMS per hour, and have greater nocturnal oxygen de-saturation (NOD) than the non-obese. OSA is present in 80% of subjects with obesity and SDB exists in all morbidly obese subjects. A need exists for all obese subjects to undergo a thorough clinical assessment with inclusion of a sleep history, a polysomnographic evaluation and an arterial blood gas analysis to detect and manage SDB early.

Keywords: Obese, SDB, AHI, polysomnography, India

Introduction

Obesity, an abnormal accumulation of body fat in proportion to body size, is commonly determined by the BMI that is calculated as weight in kilograms divided by the square of height in meters. It has been observed that the greater the BMI, the greater is the risk of co-morbidities like diabetes mellitus, hypertension, cardiovascular disease, dyslipidemia, OSA, many cancers, and overall mortality.(1) Overweight and obesity are estimated to have involved 1.7 billion people worldwide (2), and that by 2015, are likely to affect 75% of adults in United States.(3) Thus, with a high co-morbidity and an increasing global prevalence, obesity has become a major health problem.

The obese have compromised respiratory functions in awake state that worsen during sleep. Obesity has been reported as the greatest risk factor for OSA (4) that increases the risk by approximately 10 folds from the range of 2-4% in general adult population to up to 20-40% in those with BMI > 30kg/m^2.(5) OSA has been found in 55% of moderate to severe (6) and in 98% of morbidly obese patients.(7) An Indian study has observed the prevalence of SDB (AHI $\geq$ 5/ hour) in healthy middle aged urban men to be 19.5% and that of SDB with Excessive Daytime Sleepiness (EDS) as 7.5%.(8) The data in respect of SDB is scarce for the obese patients within country. The present study was, thus, designed to evaluate the pattern of SDB among obese Indian subjects.

Material and Method

The study was prospectively carried out in the Sleep Laboratory of LRS Institute of TB and Respiratory Diseases, New Delhi over the 2-year period from March 2006 to February 2008. The case enrollment was done into two groups, namely the study (obesity) group and the control (non-obese) group. The obesity group comprised of thirty obese subjects with BMI > 27.5 kg/m^2, who were consecutively enrolled as per the WHO Criteria of Obesity for Asians and subdivided into obese (with BMI between 27.5 to < 32.5 kg/m^2), severely obese (with BMI between 32.5 to < 37.5 kg/m^2) and morbidly obese (with BMI $\geq$ 37.5 kg/m^2) categories.(9) The control group comprised of ten consecutively enrolled non-obese subjects with BMI < 27.5 kg/m^2. Enrolled subjects in either group comprised of those attending the out-patient department (OPD) / admitted in the hospital, their attendants or the hospital staff irrespective of age, sex, co-morbidity and sleep complaints. However, subjects having age > 80 years, tuberculosis, chronic obstructive pulmonary disease (COPD), pregnancy, uncontrolled congestive heart failure

(CHF), chronic renal failure (CRF) and neurological disorders were excluded from the study.

An informed consent was taken from all the enrolled subjects after imparting them health education. Their clinical details comprising of symptoms (like snoring, EDS, choking, frequent awakening, un-refreshing sleep, fatigability, impaired concentration, morning headache, leg movements, leg twitching, sleep attack, sleep paralysis and night mares), co-morbidities (apart from the excluded ones), findings of physical examination and results of routine laboratory investigations including arterial blood gas analysis (in awake state, as well as, immediately after a sleep study), pulmonary function tests, electrocardiograms and chest skiagrams were recorded in a sleep questionnaire. Epworth Sleepiness Scale (ESS) was used in the subjective assessment of excessive daytime sleepiness.(10) The anthropometric measurements like NC, WC and HC were respectively made at the level of cricothyroid membrane, at the level midway between the lower rib margin and the anterior superior iliac spine, and at the level of greater trochanter, and recorded in the questionnaire. Necessary instructions were given prior to the conduct of sleep studies.

All subjects underwent an overnight PSG in the Sleep Laboratory on Compumedics E-Series software. Two channels each were used for the measurement of the parameters like electro-encephalogram (EEG), electro-oculogram (EOG), chin electro-myogram (EMG) and electro-cardiogram (ECG). Oro-nasal airflow was recorded over nose and mouth by a thermistor, while respiratory effort was obtained by thoracic and abdominal sensors. Snoring was recorded by a microphone secured over the vocal cords. Arterial oxygen saturation was measured through pulse oximetry, while leg movements were recorded by leg sensors in form of anterior tibialis EMG. The study was started at a time, which coincided with the normal sleeping time of the subjects.

All sleep studies were manually analysed before reporting. Staging of sleep was based on the R and K Rules of 1968 and classified into Awake, Non Rapid Eye Movement (NREM) Sleep with Stages I, II, III and IV, and Rapid Eye Movement (REM) sleep.(11) Sleep latency, sleep efficiency, Total Sleep Time (TST), REM latency, REM duration and Arousal Index (AI) were also noted for each study.

Polysomnographic evaluation of SDB was done according to the standard criteria. Apnea was defined as the cessation of airflow for $\geq$ 10 seconds. Hypopnea was defined as a recognizable, transient reduction, but not a complete cessation of breathing for $\geq$ 10 seconds with a decrease in airflow amplitude by $\geq$ 50% of a validated measure of breathing or a < 50% amplitude reduction associated with either an oxygen desaturation of $\geq$ 3% or an EEG arousal. (12) Obstructive apnoeas and hypopnoeas were distinguished from central events by the detection of respiratory efforts during the event. AHI was defined as the sum of apneas and hypopneas per hour of sleep time. AHI value of < 5 was taken as normal, 5 to < 15 as Mild OSA, 15 to < 30 as Moderate OSA and $\geq$ 30 as Severe OSA. Upper airway resistance syndrome was diagnosed by episodes of increased respiratory effort resulting in an arousal index (i.e. total number of EEG arousals per hour of sleep) of >10, occurring in absence of OSA but associated with clinical complaint of EDS.(13,14) Sleep Hypoventilation Syndrome (SHVS) was diagnosed by the fulfillment of criteria 'A' that required presence of one or more out of cor pulmonale, pulmonary hypertension, un-explained EDS, erythrocytosis and awake hypercapnia (PaCO2 > 45 mmHg) and 'B' that mandated presence of one or both of the following in overnight study: (i) an increase in PaCO2 during sleep > 10 mmHg from awake supine value and (ii) an oxygen desaturation during sleep not explained by apneas or hypopneas.(15) Obesity hypoventilation syndrome was defined as the presence of obesity, awake hypercapnia in absence of other known causes of hypoventilation and an associated sleep disorder like OSA, SHVS or both (16), with the consideration of obesity based on the Asian BMI criteria. Nocturnal oxygen de-saturation was defined as either spending $\geq$ 30% of sleep recording time with a trans-cutaneous SaO_2 < 90% (17) or an ODI (number of events with oxygen de-saturation of 4% per hour in bed) $\geq$ 15.(18).

Standard PSG criteria for PLMs included their occurrence in a series of 4 or more movements spaced by intervals of 5 to 90 seconds (onset to onset) with EMG burst durations of 0.5 to 5 seconds that rose to 1/4 of the EMG bio-calibration amplitude.(19,20) Periodic Limb Movement Index (PLMI) referred to the number of PLMS per hour of sleep.(20) A PLMI value of < 5 was taken as normal, while its severity was graded from 5 to < 25 as mild, 25 to < 50 as moderate and $\geq$ 50 as severe.(21,22) Since only limb movements associated with arousals were assumed to be clinically significant with regard to sleep disruption, Periodic Limb Movement

Arousal Index (PLMAI) was also calculated which indicated the number of PLMS per hour of sleep associated with an arousal on polysomnography. A PLMAI value >5 was considered to be abnormal. (21)

Results are presented as mean ± standard deviation (SD) unless otherwise indicated. Data was analysed for statistical significance by application of standard tests. Differences between two groups of variables were tested by two-sided unpaired Student *t*- test or by Mann-Whitney U test as appropriate. More than two groups were assessed for differences between them with analysis of variance (ANOVA) test. Variables were assessed for correlation using the Pearson's correlation coefficient. A p value < 0.05 was considered statistically significant.

Results

Out of 30 subjects in the obesity group, 16 (53.3%) were obese, 8 (26.7%) were severe obese and 6 (20%) were morbidly obese. Their respective mean BMIs were 30.03 ± 1.37, 34.62 ± 1.55 and 41.05 ± 4.81 with a highly significant difference (P<0.001). The mean BMI of the subjects in the obesity group was observed to be significantly higher than that of the subjects in the control group (Table 1). The male and female subjects of the obesity group also had significantly higher mean BMIs as compared to their counterparts (33.33±5.37 vs 23.46±4.42, p<0.001 and 33.68±4.28 vs 24.37±2.04, p=0.004 respectively).

A further comparison of the group characteristics (Table 1) shows that both the obesity and the control groups had subjects with a mean age of more than 40 years and a pre-dominance of males. Mean values of NC, WC and HC were respectively higher in the obesity as compared to those in the control group. While majority (70%) of the subjects in both groups had a NC between 35 to < 45 cms, a greater proportion of those in the obesity group had a WC between 100 to < 120 cms and a HC between 110 to < 130 cms when compared to the control group (Table 2).

Mean value of ESS was higher amongst the subjects of the obesity than the control group, although the difference was not statistically significant (Table1). Majority of the subjects in both groups had mild sleepiness with an ESS between 8 to 12 (Table 3).

The symptomatics (having any number of symptoms like snoring, EDS, choking, frequent awakening, un-refreshing sleep, fatigability, impaired concentration, morning headache, leg movements, leg twitching, sleep attack, sleep paralysis or night mares) constituted the majority in both the obesity and the control groups when compared to asymptomatics (27/30 and 7/10 vs 3/30 and 3/10 respectively). When a comparison was made in respect of the number of symptoms, the majority of subjects in both groups had 4 to 6 symptoms (15/30 and 6/

Table1: Group characteristics of subjects

Parameter	Obesity Group (n=30)		Control Group (n=10)		P value
	Mean ± SD	Range ± SD	Mean	Range	
BMI (Kg/m^2)	33.46± 4.93	27.7-50.39	23.73± 3.76	15.2-27.34	<0.001
Age (in years)	47.73± 11.396	32-72	40.90± 18.38	18-61	0.291
Sex*					
Male	19 (63.3%)	- -	7- (70%)	- -	-
Female	11 (36.7%)	- -	3- (30%)	- -	-
NC (cms.)	38.55± 4.94	28-50	35.20± 5.30	26-40	0.076
WC (cms.)	109.38± 12.23	80-130	93.0± 12.87	72-112	0.001
HC (cms.)	111.08± 10.31	93-140	93.0 ± 13.59	69-114	<0.001
ESS	10.16± 4.92	0-21	8.8± 4.82	0-16	0.450

**Values indicate number (%) of subjects*

Table 2: Subject distribution according to circumference

Circumference (cms)	Obesity Group Number (%) (n=30)	Control Group Number (%) (n=10)
Neck		
< 35	5 (16.67%)	3 (30%)
35 - < 45	21 (70%)	7 (70%)
≥ 45	4 (13.3%)	0
Waist		
<100	6(20%)	6(60%)
100-<120	16(53.33%)	4(40%)
≥ 120	8(26.67%)	0
Hip		
<100	11(36.67%)	9(90%)
100-<120	17(56.67%)	1(10%)
≥ 120	2(6.67%)	0

Table 3: Subject distribution according to ESS

ESS	Obesity Group Number (%) (n=30)	Control Group Number (%) (n=10)
< 8	9 (30%)	3 (30%)
8 – 12	11 (36.67%)	5 (50%)
13 – 16	7 (23.33%)	2 (20%)
> 16	3 (10%)	0

10 respectively) than those with 1 to 3 (11/30 and 0/10 respectively) or > 6 symptoms (1/30 and 1/10 respectively).

The co-morbidities present in the obesity group comprised of hypertension in 10, diabetes mellitus in 5, bronchial asthma in 2, hypothyroidism in 1, old coronary artery disease in 1, sinusitis in 1 and polycystic ovarian disease in 1, while those in control group included hypertension in 3 subjects, each of whom had either diabetes mellitus, hypothyroidism or bronchial asthma. Two subjects of obesity group were taking an anti-anxiolytic and 12 had history of alcohol intake, while 3 controls were taking an anti-depressant and 1 had history of alcohol intake. The number of co-morbidities present in any subject varied from 1 to 3. An overall number of 17 (56.7%) subjects had co-morbidities in the obesity group against 3 (30%) in the control group. Four out of 6 (66.6%) of the morbidly obese subjects had at least one co-morbidity.

Mean AHI of subjects in the obesity group was 37.82± 33.19 that was significantly higher than 5.77± 5.46 of those in the control group ($p<0.001$). Further, mean AHIs of the severely and the morbidly obese subjects were respectively higher than that of the obese subjects, although their statistical differences were not significant (53.34± 38.68, $p=0.065$ and 43.05± 41.45 vs 28.11± 24.88, $p=0.309$ respectively).

As seen from Table 4 (showing the inter-group comparison of mean AHIs according to characteristics), AHI increased with a rise in the sub-category of age in both groups. Unlike the subjects of obesity group, the non-obese showed a significant increase of mean AHI with the rise of age sub-category ($p=0.827$ for obesity group and $p=0.026$ for control group). In all the comparable sub-categories of age, the subjects in the obesity group had a respectively higher AHI than that of the control subjects. However, the differences were not statistically significant except for those in the sub-category of > 50 years.

The male subjects of the obesity group had a significantly ($p<0.001$) higher AHI as compared to that of their male

Table 4: Comparison of mean AHIs between groups according to characteristics

Characteristic	Mean AHI		P value
	Obesity Group (n=30)	Control Group (n=10)	
Age (in years)			
Up to 30	31.75± 40.37	1.475 ± 1.096	
30 – 40	32.91± 41.75	-	
41 – 50	35.20 ± 32.89	4.50 ± 3.95	
> 50	46.75 ± 27.92	10.70 ± 4.99	
Sex			
Male	43.95 ± 31.21	5.5 ± 4.16	<0.001
Female	27.24 ± 35.31	6.4 ± 9.02	<0.343
NC (cms)			
< 35	24.48± 23.60	1.63± 1.28	0.156
35 - < 45	36.90 ± 32.60	7.543± 5.65	0.001
≥ 45	59.35 ± 43.31	-	-
WC (cms)			
<100	24.03 ± 43.18	3.316 ± 2.738	0.293
100-<120	31.238 ± 22.96	9.45 ± 6.846	0.082
≥ 120	61.358 ± 34.76	-	-
HC (cms)			
<100	20.47 ± 22.10	5.6 ± 5.76	0.054
100-<120	48.62 ± 36.78	7.3	0.291
≥ 120	41.55 ± 9.6	-	-
ESS			
<8	22.16 ± 15.43	1.73 ± 1.18	-
8-12	33.21 ± 29.03	7.82 ± 5.52	-
13-16	46.42 ± 32.13	6.7±8.49	-
>16	69.57 ± 55.66	-	-
Symptoms			
Symptomatics	40.65 ± 33.63	7.50 ± 5.71	<0.001
Asymptomatics	12.36 ± 13.82	1.73 ± 1.18	0.255
No. of Symptoms			
0	12.36 ± 13.82	1.73 ± 1.18	-
4-6	49.39 ± 37.57	8.46 ± 5.59	0.001
>6	60.60	1.70	-
Co-morbidities			
Present	50. 07 ± 35.33	11.83 ± 5.45	0.001
Absent	21.81 ± 22.54	3.17 ± 2.94	0.012

counterparts of the control group, while the female subjects of the obesity group had an insignificantly higher AHI ($p=0.343$) than that of the female counterparts of the control group (Table 4). A higher mean AHI was observed among the male as compared to the female subjects in the obesity group, but the difference was not found to be statistically significant ($p=0.189$). Similarly, no significant difference ($p=0.827$) was found between the mean AHIs of the male and female subjects in control group also.

In contrast to the control group, subjects in the obesity group had higher mean AHIs for all the respectively comparable categories of NC, WC and HC (table 4). However, only the subjects of obesity group with NC between 35 to < 45 cms had a significantly (p=0.001) higher mean AHI than the control subjects. No significant differences in mean AHI were noted within either group for the increase in the sub-category of NC, WC or HC (p=0.121, p=0.079 and p=0.787 for the controls, and p=0.295, p=0.053 and p=0.086 for the obesity group respectively).

The respective values of mean AHIs were found to be higher in the obesity as compared to the control group for all the comparable categories of ESS but the differences were not statistically significant (Table 4). Further, mean AHI increased insignificantly with the rise of ESS within the obesity group (p=0.089).

Both symptomatic and asymptomatic subjects of the obesity group had higher mean AHIs in comparison to those of the corresponding control subjects (Table 4). However, the difference was significantly higher only for symptomatics. Further, the symptomatic subjects of the obesity group having 4 to 6 symptoms had a significantly hjgher mean AHI than their corresponding control subjects.

The subjects of the obesity group with and without co-morbidities had significantly higher mean AHIs than those of the corresponding control subjects (Table 4). Further, the subjects of the obesity and the control groups having co-morbidities had significantly higher mean AHIs than those of the corresponding subjects without co-morbidities (p=0.018 and p=0.010 respectively).

A comparison of the mean values of the sleep parameters of the subjects of the two groups showed that AI, PLMI, PLMAI, ODI and snoring index were significantly higher in the obesity than the control group. No significant changes were observed in the mean values of sleep latencies, TSTs, sleep efficiencies and sleep stages (Table 5).

A further comparison of the mean values of the sleep parameters of the obese, severely obese and morbidly obese subjects of the obesity group showed significantly increasing sleep latency, decreasing TST and sleep efficiency and an increasing AI with the corresponding increase in the severity of obesity. The sleep stages, PLMI, PLMAI, snoring index and ODI, however, did not show significant changes (Table 6). NOD was present in 60% (18/30) of subjects in the obesity group against 10% (1/10) of control subjects. A greater proportion of the severely (75%; 6/8) and morbidly (67%; 4/6) obese subjects had NOD as compared to the obese (50%; 8/16) subjects.

Table 5: Comparison of sleep parameters between groups

Sleep Parameter	Obesity Group	Control Group	P value
Sleep Latency (Min.)	14.71 ± 26.70	12.85 ± 18.99	0.840
Total Sleep Time (Min.)	328.95 ± 98.17	339.360 ± 69.21	0.002
Sleep Efficiency (%)	80.15 ± 16.69	85.51 ± 11.48	0.420
REM (%)	3.69 ± 6.49	2.23 ± 4.52	0.512
NREM Stage 1 (%)	19.85 ± 15.18	13.64 ± 10.51	0.239
NREM Stage 2 (%)	50.11 ± 19.47	54.0 ± 14.16	0.566
NREM Stage 3 (%)	14.96 ± 11.39	14.70 ± 4.30	0.916
NREM Stage 4 (%)	11.37 ± 11.88	15.42 ± 13.61	0.374
PLM Index	34.63 ± 34.03	7.37 ± 8.59	< 0.001
PLM Arousal Index	3.98 ± 5.35	2.12 ± 5.57	0.031
Arousal Index	20.50 ± 20.81	8.77 ± 7.03	0.011
Snoring Index	770.91 ± 799.69	144.04 ± 138.64	<0.001
ODI	30.46 ± 31.37	5.98 ± 4.54	<0.001

No significant correlation was found between AHI and the parameters mentioned in (Table 7) other than age in the control group, and WC, ESS and no. of symptoms in the obesity group. Similarly, no significant correlation was observed between BMI and the sleep parameters mentioned in (Table 8) in either group except a significant positive correlation with sleep latency and ODI, and a significant negative correlation with sleep efficiency in the obesity group.

OSA was found in 80% of subjects in the obesity group in contrast to 50% of the control subjects. Further, within the obesity group, OSA was observed in a greater proportion of the severely (87.5%; 7/8) and morbidly (83.3%; 5/6) obese as compared to the obese (75%; 12/16) subjects (Table 9).

Table 6: Comparison of sleep parameters with grade of obesity

Sleep Parameter	Obese	Severely Obese	Morbidly Obese	P value
Sleep Latency (Min.)	5.18 ± 7.50	11.56 ± 13.34	44.33 ± 48.56	0.005
Total SleepTime (Min.)	366.01 ± 69.06	340.52 ± 114.03	214.72±55.87	0.002
Sleep Efficiency (%)	88.51 ± 6.50	76.58 ± 22.28	62.63 ± 13.47	0.002
REM (%)	5.35 ± 7.89	1.81 ± 4.68	1.78 ± 2.06	0.334
NREM Stage 1 (%)	16.41 ± 10.10	27.85 ± 21.81	18.38 ± 14.93	0.218
NREM Stage 2 (%)	46.05 ± 17.15	50.63 ± 23.52	60.23 ± 19.15	0.325
NREM Stage 3 (%)	17.71 ± 12.83	10.77 ± 9.28	12.20 ± 9.05	0.352
NREM Stage 4 (%)	14.46 ± 10.95	8.90 ± 14.71	6.43 ± 9.3	0.302
PLM Index	30.65 ± 30.21	50.93 ± 43.09	23.50 ± 27.49	0.268
PLM Arousal Index	2.13 ± 2.35	6.0 ± 8.20	6.21 ± 5.67	0.130
Arousal Index	15.57 ± 15.02	16.45 ± 15.01	39.05 ± 31.68	0.045
Snoring Index	684.38± 815.55	872.0 ± 818.43	866.88±851.23	0.828
ODI	22.18 ± 19.47	42.80 ± 41.75	36.09 ± 40.35	0.289

Table 7: Correlation between AHI and BMI, Age, ESS, No. of Symptoms and Anthropometric Parameters

Parameters	AHI	
	Obesity Group r	Control Group r
BMI	0.356*	0.430*
Age (in years)	0.201*	0.743**
NC (cms)	0.330*	0.622*
WC (cms)	0.486***	0.466*
HC (cms)	0.360*	0.449*
ESS	0.376**	0.433*
No. of Symptoms	0.398**	0.458*

**p>0.05; ** p<0.05; ***p<0.01*

The pattern of observed sleep disorders amongst the subjects showed that severe OSA was present in more than half of them in the obesity group, while it was non-existent in the control group that had 50% of the subjects with no abnormality and only 40% with mild OSA. Sleep disordered breathing was detected in an overall 87% of the subjects in the obesity group against 50% in the control group. A co-existence of OHS was seen in 9 and PLMS in 7 cases of OSA in the obesity group while only one case had PLMS in the control group (Table 10).

Table 8: Correlation between BMI and Sleep Parameters

Parameters	BMI	
	Obesity Group r	Control Group r
Sleep Latency (Min.)	0.671***	-0.212*
TST (Min.)	-0.189*	-0.516*
Sleep Efficiency (%)	-0.505***	-0.262*
REM (%)	-0.219*	-0.091*
NREM Stage 1 (%)	0.134*	0.177*
NREM Stage 2 (%)	0.074*	0.300*
NREM Stage 3 (%)	-0.028*	-0.180*
NREM Stage 4 (%)	-0.146*	-0.359*
PLM Index	0.031*	-0.471*
PLM Arousal Index	0.339*	-0.082*
Arousal Index	0.268*	-0.140*
Snoring Index	0.088*	0.496*
ODI	0.375**	0.342*

** p>0.05; ** p<0.05; ***p<0.01*

Discussion

In present study, the mean values of BMI and AHI were found to be significantly higher among the subjects of the obesity group than those of the control group respectively, suggesting the association between obesity and sleep apnoea in them.

Table 9 : Distribution of OSA in the groups

OSA	Control Group Number (%) (n=10)	Obesity Group (n=30)			
		Obese Number (%) (n=16)	Severely Obese Number (%) (n=8)	Morbidly Obese Number (%) (n=6)	Total Number (%) (n=30)
Absent	5 (50)	4 (25)	1 (12.5)	1 (16.7)	6 (20)
Present	5 (50)	12 (75)	7 (87.5)	5 (83.3)	24 (80)

Table 10 : Pattern of sleep disorders in the groups

Sleep Disorders	Control Group Number (%) (n=10)	Obesity Group (n=30)			
		Obese Number (%) (n=16)	Severely Obese Number (%) (n=8)	Morbidly Obese Number (%) (n=6)	Total Number (%) (n=30)
Mild OSA	4 (40)	3 (18.8)	1 (12.5)	0	4 (13.3)
Moderate OSA	1 (10)	2 (12.5)	1 (12.5)	1 (16.7)	4 (13.3)
Severe OSA	0	7 (43.7)	5 (62.5)	4 (66.6)	16(53.3)
RERA*	0	1 (6.2)	0	1 (16.7)	2 (6.7)
OHS**	-	5	3	1	9
PLMS***	1	1	3	3	7
Normal	5 (50)	3 (18.8)	1 (12.5)	0	4 (13.4)
Total	10 (100)	16 (100)	8 (100)	6 (100)	30 (100)

** The diagnosis based upon polysomnographic criteria without performing oesophageal manometry.*

*** Co-existent OHS was seen in one case of mild OSA, one of moderate OSA and seven of severe OSA. Of these, five belonged to obese, three to severe obese and one to morbid obese category.*

**** Six cases of severe OSA and one case of moderate OSA had co-existing PLMS in obesity group. One case of PLMS was found in control group which was associated with moderate OSA.*

Similar results have been reported in studies from America (23, 24, 25), Italy (26) and Japan (27). Further, respective mean AHIs of the severely and the morbidly obese subjects were found to be insignificantly higher than that of the obese subjects. However, studies from Australia (4), America (24), Italy (26) and Poland (28) have shown significant increase of AHI or Respiratory Disturbance Index (RDI) with the increase of obesity. Our results need to be validated in a larger Indian population.

An increasing severity of AHI has been associated with a significant increase of body weight, BMI, NC, WC and HC (4, 26), and the NC found to be the best simple clinical measure of increased risk of OSA. (4) We observed higher mean AHIs of the subjects in obesity than control group in all the comparable sub-categories of measured anthropometric parameters, but found a significantly higher mean AHI in the obesity group with NC sub-category between 35 to < 45 cms than the corresponding controls. Possibly an increased fat distribution in the area of the upper airway might have predisposed the obese subjects to the development of OSA.

Aging may result in a change in BMI, body fat distribution, tissue elasticity, ventilatory control, pulmonary and cardio-respiratory functions, and is associated with more co-morbidities that may enhance the risk of OSA. (29) Age more than 40 years is a useful feature in determining the probability of SDB. (30) Older age has been reported to independently predict AHI in the severely obese. (4) Our subjects also had a mean age of more than 40 years in both groups and showed an increase of mean AHI with a rise in the sub-category of age. However, unlike the obesity group, only the non-obese showed a significant increase of mean AHI with the rise of age sub-category, as well as, a significant positive correlation between age and AHI. These findings are consistent with the observation of The Sleep Heart Health Study that noted a poor prediction of SDB in older people by higher BMI. The decreased importance of body habitus as a predictor of SDB in older people could be due to age differences in how well current measures reflected the past status of weight and other body habitus measures that would be relevant to the onset of SDB. (31)

Male gender is a risk factor for OSA. (32,33) The relative influence of both obesity and gender for increasing the risk of OSA in males is probably due to the action of sex hormones. Androgenic pattern of body fat distribution favours fat deposition centrally including the neck area. In addition, sex hormones may modulate respiratory and upper airway neuromuscular activities. (32) We found a significantly higher mean AHI in the male subjects of the obesity group as compared to that of the control subjects highlighting the possible association of obesity, gender and OSA in them. However, we did not find a significant difference in the mean AHIs of the male as compared to the female subjects in either group requiring the conduct of a larger Indian study to better define the role of gender in the causation of OSA.

Excessive daytime sleepiness is an important symptom of OSA that is subjectively assessed by Epworth Sleepiness Scale. A higher score indicates greater chance of sleepiness. A study from Italy found significantly higher mean

ESS scores respectively in non-apnoeic obese (RDI < 10) than non-obese (control) and in severely apnoeic obese (RDI ≥ 30) than non-apnoeic obese subjects. The scores were not significantly different between the non-apnoeic and moderately apnoeic (RDI between 10 and 29) obese subjects. (26) Other studies did not find a correlation between ESS and AHI. (4, 34) We observed a higher mean AHI in subjects of obesity than control group in various sub-categories of ESS with no significant difference and noted an insignificantly higher mean AHI with the rise of ESS score. A significant correlation was found between them in obesity but not in control group. Thus, our findings are not in agreement with those reported in previous studies. The etiology of EDS in patients with SDB is not well defined. However, AHI, nocturnal hypoxemia and sleep fragmentation have been shown to independently contribute to an increased risk of daytime sleepiness in obese patients with SDB. (35)

Apart from EDS, other symptoms of sleep disordered breathing that may be seen in both obese and non-obese subjects are habitual snoring, choking, witnessed apnoeas, frequent awakening, un-refreshing sleep, fatigability, sleep attacks, impaired concentration, morning headache, leg movements, nocturia, sleep paralysis and night mares. Patients with a history of habitual snoring, EDS, a body mass index greater than 35 and witnessed apnoeas have a greater than 70% probability of having sleep apnoea. (36) We found that symptomatics constituted the majority (90% in obesity and 70% in control group) in our study. The symptomatics among the obesity group had a significantly higher mean AHI than those of the control group. A previous study has similarly shown significantly higher RDI in symptomatic obese subjects when compared to non-obese with similar symptoms. (26) It was further observed in our study that the subjects of obesity group with increasing number of symptoms had higher mean AHI values and those with 4 to 6 symptoms had a significantly higher mean AHI than the respective controls. A significant correlation was also noted between number of symptoms and AHI. A past study on severely obese subjects has similarly reported earlier that when the total number of symptoms was added, those comprising of greater number of symptoms had a higher AHI. (4) Thus, obese symptomatics and those with 4 to 6 symptoms could be at risk of having higher AHI than their respective controls.

Studies have shown a variable prevalence of SDB in hypertension (37, 38), cardiovascular disease (39, 40), diabetes mellitus (41), COPD (42, 43), polycystic ovarian disease (44) and other illnesses. It has been observed that the risk of a co-morbidity increases as the degree of obesity increases. (45) Approximately three fourths of extremely or morbidly obese adults are reported to have at least one obesity-related medical co-morbidity. (46) In present study, we found a number of co-morbidities like hypertension, diabetes mellitus, bronchial asthma, hypothyroidism, polycystic ovarian disease etc. amongst 56.7% of the obesity and 30% of the control subjects (despite excluding those with tuberculosis, COPD, uncontrolled CHF, CRF, pregnancy and neurological disorders as per the study criteria) with 4 out of 6 (66.6%) morbidly obese subjects displaying at least one co-morbidity. The subjects of obesity group with co-morbidities exhibited a significantly higher mean AHI as compared to those without co-morbidities and to non-obese with co-morbidities suggesting a contribution of both obesity and co-morbidity in the observation of high AHIs in them. Previous studies have similarly reported a high prevalence of OSA in the obese subjects with co-morbidities. (47, 48) Further, our control subjects with co-morbidities also had a significantly higher mean AHI than those without them highlighting the role of underlying medical illness. Thus, there is a need for all the subjects with co-morbidities irrespective of obesity to undergo a polysomnographic evaluation so as to detect and manage SDB early.

Past studies have shown that mean value of sleep latency is significantly higher and that of sleep time percentage significantly lower in obesity than control group (23, 49), and mean sleep efficiency decreases significantly with the rise of BMI. (4) The mean sleep latency in our study was insignificantly higher in obesity than in control group, but increased significantly with the severity of obesity, indicating that in case of a more severe grade of obesity, the subjects took longer time to sleep. Mean values of TST and sleep efficiency were insignificantly less in obesity than in control group, but decreased significantly with the increase in severity of obesity. A significant positive correlation of sleep latency and a significant negative correlation of sleep efficiency were observed with BMI. Thus, our results were in broad agreement with the findings of previous studies, suggesting that the obese subjects slept late and for less time with increasing severity of obesity. Presence of anxiety or depression in these subjects could have contributed though only 2 of them were actually taking an anti-anxiolytic. In addition, the significantly increased number of arousals/awakenings in the obesity than in the control subjects, as observed in a past study (23) and also noted in the present study, in the form of spontaneous, respiratory effort related or PLM associated arousals, may have caused sleep

fragmentation and led to decreased sleep time and sleep efficiency in them. However, the exact cause for these observations needs further exploration.

A comparison of the sleep stages in previous studies has shown that percentage of stage 1 sleep increases significantly and of REM sleep decreases significantly in obese as compared to non-obese (23) and higher BMI was associated with a significantly lower REM sleep percentage. (4) The present study also found increased stage 1 sleep and lowered REM sleep percentage in subjects of obesity than control group, but the differences were not statistically significant. A note was, however, made of a decreased REM sleep percentage in the control subjects too for unclear reasons. This aberration may have been related to the fact that 60% (6/10) of our control subjects were overweight, who have been previously reported to have a significantly low REM sleep as compared to the normal weight subjects (50). Moreover, if the overweight group was viewed in the light of the recent obesity guidelines released for the Indians with a reduced cut-off of obesity as 25 or more (51), the subjects would be actually classified as obese, and could show a lowered REM sleep percentage in a manner similar to the obese. Factors such as sleep fragmentation, medications (like tri-cyclic anti-depressants, mono-amine oxidase inhibitors, anti-cholinergics, alcohol etc.), age and environmental disturbances are known to play a role in resulting of a low REM sleep. (52) Increased PLMS have also been associated with REM sleep disruption. (53) In our study, 40% of the obesity and 10% of the control group subjects had history of an alcohol intake, while 30% of the controls were taking an anti-depressant as well. Sleep fragmentation was evident from the raised arousal and snoring indices in obesity group and the raised PLMS indices in both groups. However, exact disturbances of sleep stages in obese subjects and their underlying etiologic mechanisms need to be further explored.

Researchers have used one or more parameters like NOD, ODI, minimum oxygen saturation, nocturnal hypoventilation etc. to measure nocturnal hypoxaemia in obese subjects. ODI has been reported to be significantly increased in obese than non-obese subjects. (54) Minimum oxygen saturation has been shown to decrease in obese and severely obese as compared to non-obese subjects. (55) Nocturnal hypoventilation has been found to be present in 29% of a severe obese population, in which BMI directly correlated with TST with a oxy-haemoglobin saturation < 90%. (26) Morbidly obese subjects have been reported to have an extended time of nocturnal oxygen de-saturation SaO_2 < 65%. (7) Our study found a significantly higher mean ODI in obesity as compared to control group and about two-third of the morbidly obese subjects had NOD. We also observed a significant correlation between BMI and ODI. These results were in agreement with the findings of previous studies. Further, we observed a high concurrence of both parameters (NOD and ODI) in demonstrating nocturnal hypoxaemia in obese subjects as 17 out of 18 subjects with NOD simultaneously had a high ODI more than 15 per hour. A possible reason for the existence of nocturnal de-saturation in obese subjects could be that obesity led to alteration in upper airway structure, function, balance between ventilatory drive / load and obesity induced hypoventilation which led to hypoxemia. (7)

Obese have been found to have a higher prevalence of SDB than non-obese subjects. A study has reported the presence of SDB in 41.2% of obese as compared to that in 9% of control subjects (23), while the respective figures in another study were 54.5% and 30.8%. (56) Similarly, obese have been shown to have a higher prevalence of SDB in comparison to the overweight individuals (74.5% vs 60% respectively). (28) Since we found SDB in 86.7% of the subjects in obesity group against 50% in control group, our results were consistent with the findings of previous studies. Obesity is responsible for increasing the upper airway collapsibility and the risk of SDB through several mechanisms. These include reduced pharyngeal lumen size due to fatty tissue within the airway or in its lateral walls, decreased upper airway dilator muscle protective force due to fatty deposits in the muscle, and reduced upper airway size secondary to mass effect of the large abdomen on the chest wall and tracheal traction. (57) Changes in upper airway function and modifications in central mechanisms regulating airway tone or ventilatory control stability have also been implicated. (28)

A variable prevalence and pattern of SDB have been noted in obesity studies from Western countries. While one American study reported sleep apnoea in 41.2% (103/250) of the obese subjects (23), another found a prevalence of SDB in 54.5% (1036/1909) of overweight/ obese subjects. (56) An Italian study showed 51.5% (83/ 161) of the obese subjects to be having moderate (26.7%; 43/161) or severe (24.8%; 40/161) sleep apnea with another 5% demonstrating nocturnal hypoventilation as a unique breathing alteration that was otherwise seen in 29% of the entire obese group. (26) A Polish study found 74.5% (38/51) of the obese subjects with mild (9.8%; 5/51), moderate (29.4%; 15/51) or severe OSAS (35.3%; 18/51). (28) We observed SDB in 86.7% (26/30) of the subjects in obesity group, of whom 80% (24/30) had mild, moderate or severe OSA and 6.7% (2/30) had RERA, while OHS and PLMS respectively co-existed in 9 and 7 cases of OSA. Further, two third of the subjects in obesity group had moderate to severe OSA and more than half had severe OSA. Thus, we found a much higher prevalence of

SDB in our subjects with obesity as compared to those from the West. Similarly, a greater percentage (50%) of our controls too showed OSA (with mild OSA in 40% and moderate OSA in 10%) when compared to the reported figures of prevalence in Western studies. (23, 56) SDB has also been earlier reported in 19.5% of the healthy urban middle aged male population of Bombay (8). The possible reason for a higher observation of SDB in Indians could be their craniofacial anatomy pre-disposing this race to OSA (58) as observed in a study from Singapore comparing them with the two other ethnic populations (Malays and Chinese) living there (4.5% vs 3.7% and 1.6% respectively) (59). Another reason could be the presence of co-morbidities in both obese and non-obese subjects pre-disposing them to SDB as discussed earlier. Yet another probable reason for the higher observed SDB in control group could be the fact that majority (60%) of our subjects were overweight, in whom too, an OSA prevalence of 60% (33/55) has been reported (28), and who could be classified as obese according to the recent Obesity Guidelines for Indians. (51) However, it is desirable to analyse the data from different regions of our country and to make a relevant comparison at the global level prior to arriving at definite conclusions about the pre-disposition of the Indian race for SDB.

Morbidly obese subjects have been reported to have high prevalence of SDB of severe type. A study from USA has detected obstructive sleep related breathing disorders in 88% of the severely obese patients being evaluated for bariatric surgery who showed OSA in 71% (29/41) and UARS in 17% (7/41). (60) Another study from Mexico found OSA in 98% of morbidly obese subjects, of whom, one-third had severe OSA. (8) All morbidly obese subjects in our study were seen to have some form of SDB with 83.7% having OSA and 16.7% having RERA. Two-third of them had severe OSA. Our findings are consistent with those of previous workers and are likely to have resulted owing to the enhancement of the previously mentioned effects of obesity.

The prevalence of OHS among patients with OSA has been reported between 10 to 20% and is likely to be higher in the subgroup of patients with extreme obesity. (61) Using the Asian criteria of obesity (BMI $\geq$ 27.5 kg/m2), we found 37.5% (9/24) of OSA cases having co-existent OHS, amounting to about one third of total cases (9/30). It is possible that cephalometric differences between the Asians and the Western population may have played a role in the higher occurrence of OHS in our subjects. The exact mechanisms need better understanding. However, the hypoventilation can result due to chronic exposure to hypoxemia and sleep fragmentation that leads to a diminished ventilatory drive. A need exists, therefore, to perform arterial blood gas analysis in all obese subjects to rule out hypercapnia.

Although, we did not study effects of weight loss, it has been shown to significantly improve sleep abnormalities (62) and predicted to decrease AHI by 26% with a 10% loss of weight. (24) We also did not perform an Ear, Nose and Throat (ENT) evaluation of the subjects in order to assess the upper airway narrowing that may have caused SDB in them. The smaller sample size of both groups was another limiting factor of the study, which may not have given statistically significant results despite providing valuable data regarding the existing trends of SDB in the Indian population with or without obesity.

In conclusion, mean AHI is higher among the subjects of the obesity group as compared to the controls. Similarly, mean AHI is higher among the obese males, those having NC between 35 to < 45 cms, symptomatics, those having 4 to 6 number of symptoms, and those having co-morbidities as compared to their respective non-obese counterparts. The obese subjects sleep for less time taking longer time to sleep, have higher number of arousals and PLMS per hour, and have greater nocturnal oxygen de-saturation than the non-obese. OSA is present in 80% of subjects with obesity, while some form of SDB exists in all morbidly obese subjects. Therefore, a need exists for all obese subjects to undergo a thorough clinical assessment with the inclusion of a sleep history. They should be subjected to a polysomnographic evaluation, as well as, an arterial blood gas analysis so as to detect and manage any sleep related breathing disorder early. It is also desirable to carry out larger community based prevalence studies to further validate and to draw definite conclusions about the observed prevalence and the pattern of SDB among the obese and the non-obese population of our country.

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