ELSEVIER

Sleep Medicine 5 (2004) 351–357

SLEEP MEDICINE

www.elsevier.com/locate/sleep

Original article

A stepped approach for prediction of obstructive sleep apnea in overtly asymptomatic obese subjects: a hospital based study

S.K. Sharma[a,*], S. Kurian[a], V. Malik[a], A. Mohan[a], A. Banga[a], R.M. Pandey[b], K.K. Handa[c], S. Mukhopadhyay[d]

[a]*Division of Pulmonary and Critical Care Medicine, Department of Medicine, All India Institute of Medical Sciences, New Delhi 110029, India*
[b]*Department of Biostatistics, All India Institute of Medical Sciences, New Delhi 110029, India*
[c]*Department of Otorhinolaryngology, All India Institute of Medical Sciences, New Delhi 110 029, India*
[d]*Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi 110 029, India*

Received 23 December 2003; received in revised form 24 February 2004; accepted 25 March 2004

Abstract

Background and purpose: Prevalence of obstructive sleep apnea (OSA) is high in obese subjects, many of whom may not be overtly symptomatic. Polysomnography (PSG) is a costly and time-consuming investigation. Since it is not feasible to subject all obese individuals to PSG, it is useful to define predictors of OSA among these subjects.

Patients and methods: One hundred and eighteen obese subjects [body mass index (BMI) $\geq$ 25 kg/m^2] presenting to the hospital with non-sleep related complaints were included, of which 53 subjects with PSG evidence of OSA [apnea-hypopnea index (AHI) $\geq$ 15/h] were defined as cases and 65 subjects without any evidence of OSA (AHI $<$ 15/h) were defined as controls. Anthropometry, biochemical investigations, blood gas analysis, pulmonary function tests, and PSG were performed for all subjects.

Results: Waist hip ratio (WHR) (as percentage of a standard) [odds ratio (95% CI): 1.07 (1.00–1.14); $P = 0.049$], male gender [odds ratio (95% CI): 3.97 (0.99–15.81); $P = 0.046$] and neck circumference (NC) [odds ratio (95% CI): 1.23 (1.03–1.47); $P = 0.023$] were found to be independent predictors of OSA. Overnight oxygen desaturation data were evaluated in patients selected as having OSA on the basis of these clinical markers, and the best cut-off for level of desaturation (10%) was defined. The stepped approach had a specificity, sensitivity, positive and negative predictive value of 89.2, 88.5, 86.8 and 90.6%, respectively, for the diagnosis of OSA.

Conclusions: Male gender, WHR and NC are independent predictors of OSA in overtly asymptomatic obese subjects. A stepped approach to diagnose OSA should be used, as it is accurate and cost-effective.

Keywords: Predictors; Sleep disordered breathing; Obesity; Obstructive sleep apnea; Polysomnography

1. Inroduction

Sleep related breathing disorders have been recognized as an important cause of morbidity and mortality. In the United States, nearly 12 million people between 30–60 years of age have obstructive sleep apnea (OSA) [1], and almost 38,000 are estimated to die each year from cardiovascular disease attributable to sleep related breathing disorders [2,3]. Patients with OSA are often found to be obese [4]. The precise relationship of OSA to obesity remains unknown. However, potential putative mechanisms include alterations in the upper airway structure and function, alteration in the balance between ventilatory drive and the load, and obesity induced hypoxemia. Excessive fat deposition in the neck and abdomen has been reported to be associated with the occurrence of OSA in obese persons [5]. Neck circumference (NC) [6], skin-fold thickness [7], waist hip ratio (WHR) [8] and distribution of fat in the neck and the abdomen [9] have been reported to be important predictors of OSA in obese subjects. Furthermore, available evidence suggests that OSA is more prevalent in the presence of visceral obesity [10]. Significant weight loss has been reported to result in varying degrees of improvement in sleep apnea, oxygen saturation, sleep architecture and daytime performance [11].

* Corresponding author. Tel.: +91-11-2659-4415; fax: +91-11-2658-9898.
E-mail address: sksharma@aiims.ac.in (S.K. Sharma).

1389-9457/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.sleep.2004.03.004

However, it is unclear why all obese individuals do not develop OSA.

Worldwide data suggest an increasing prevalence of obesity. In the United States, National Health and Nutrition Examination Survey III data show an increase in the prevalence of obesity from 15% in 1980 to 27% in 1999 [12]. In India, data from studies conducted in north India reveal the prevalence of obesity ranging from 15 to 27.8% [13,14]. High prevalence of obesity in this part of the country has been attributed to a considerable shift in the lifestyle and dietary profile of the population, with higher consumption of saturated fat and low intake of fiber. Obesity is an important risk factor for OSA [15] and is present in approximately 70% of patients with OSA [16]. In obese individuals, the severe adiposity not only predisposes to the respiratory abnormalities in OSA, but may also directly contribute to the increased cardiovascular risk associated with OSA.

Obese subjects who do not have overt symptoms of OSA may escape medical attention and present only after long-term complications related to OSA have developed. It is useful to detect these patients early so that timely intervention can be made, but not feasible to subject all these individuals to polysomnography (PSG). Therefore it is important to determine simple, cheap, widely available and easily reproducible markers and predictors of OSA that can be used for evaluation of a large number of subjects. The objective of this study was to determine the predictors for OSA among north Indian obese subjects without overt symptoms related to OSA. An attempt was also made to derive an algorithm with the help of these parameters so that a score could be computed to define the subjects at risk for OSA.

2. Material and methods

2.1. Study population

Obese subjects (BMI $\geq$ 25 kg/m^2) attending the medical outpatient department or the chest clinic of the All India Institute of Medical Sciences Hospital, New Delhi (one of the largest tertiary referral hospitals in northern India), from March 1998 to December 2000, were eligible for inclusion in the study. Subjects reporting to the hospital with non-specific, primarily non-sleep related complaints such as heartburn, headache and backache, as well as for routine medical check-ups, were screened. None had significant OSA related symptoms (habitual snoring, choking spells, sleep fragmentation or daytime somnolence). Patients with a history of alcohol abuse, chronic anxiolytic/sedative use, associated respiratory, renal, hepatic and congestive cardiac failure or hypothyroidism were excluded, as well as those who were pregnant or unconscious. A thorough ENT examination was done to exclude causes of OSA secondary to upper airway obstruction (e.g. enlarged tonsils, adenoids and macroglossia).

Initially, 188 obese subjects with trivial, non-sleep related complaints were screened, of which 40 were excluded on the basis of various exclusion criteria. The remaining 148 subjects were informed of the OSA risk associated with their obesity and the likelihood of many patients suffering from 'silent disease.' All these patients were offered overnight PSG. Thirty patients refused the investigation, leaving us with a cohort of 118 patients.

2.2. Anthropometric profile

Body weight (to the nearest 0.5 kg) and height (H) (to the nearest 1 cm) were recorded in all subjects without shoes and wearing only light indoor clothes. The BMI was calculated as body weight (kg)/height^2 (m^2). The NC (cm) was measured at the level of cricothyroid membrane. The neck length (NL) (cm) was measured from occipital tubercle to the vertebra prominens. A height-corrected measure for NC (percentage of predicted neck circumference (PPNC)) was computed using the formula: $PPNC = \{(1000 \times NC)/(0.55 \times H + 310)\}$ [17]. The waist circumference (cm) was measured midway between the lower rib margin and the anterior superior iliac spine. The hip circumference (cm) was measured at the maximum circumference of the buttocks, the subject standing with feet placed together, and the mean of three readings of each circumference was taken for the calculation of WHR. Triceps skin-fold thickness was measured using Lange skin-fold calipers (Beta Technology Inc., Santa Cruz, CA, USA). Thickness was measured to the nearest 1 mm, midway between the acromion process of the scapula and the olecranon process, and a mean of three readings was recorded.

2.3. Pulmonary functions

Lung volumes and their subdivisions were measured using a constant volume variable pressure body plethysmograph (P.K. Morgan Chatham, Kent, UK), as described previously [18].

2.4. Polysomnography

Polysomnography was performed as described previously [19]. Briefly, subjects reported to the Sleep Laboratory at 8:00 p.m. on the day of their appointment. The patients were hooked to Alice 3 PSG machine (Health dyne Technologies, USA) by standard gold cups, after cleansing the area of attachment with spirit followed by Omni prep,® and requested to sleep at around 21:00 h. Recording was started after ensuring that the impedance of recording electrodes was set to zero. Various parameters monitored included electroencephalogram, electro-oculogram, electrocardiogram, chin and leg

electromyogram (EMG), nasal airflow, tracheal breath sounds, thoracic wall and abdominal movements, transcutaneous oxygen saturation, body position and continuous positive airway pressure (CPAP) titration, where required. Recorded sleep data were manually scored for sleep stages, apneas, and hypopneas by an experienced laboratory technician, blinded to clinical data. Apnea was defined as cessation of oronasal airflow for ≥ 10 s. Obstructive apneas were scored when airflow was absent but respiratory efforts were present. Hypopnoea was defined as a discernible reduction in respiratory airflow for ≥ 10 s during a preceding period of normal breathing, accompanied by a decrease of 4% or more in oxyhemoglobin saturation during sleep. Apnea-hypopnea index (AHI) was calculated based on the following formula: AHI = (total no. of obstructive apneas + total no. of hypopneas)/total sleep time (h).

Subjects with PSG evidence of AHI $\geq$ 15/h were defined as 'cases' and subjects with AHI $<$ 15/h were defined as 'controls'.

3. Statistical analysis

Data were recorded on a pre-designed data sheet and managed on an 'Excel' spreadsheet. Anthropometric measurements and PSG findings in cases and controls were compared using Student's *t*-test. Chi-square test was used to study the association between the outcome variable (AHI) and various ordinal variables. Variables showing statistically significant association at $P < 0.2$ in univariate analysis were considered as candidate predictors to be used in multivariate analysis. Stepwise multiple logistic regression analysis was used to identify the significant independent predictors for OSA. Once these parameters were derived, an equation was constructed using the adjusted odds ratio to develop a scoring system. Receiver operator characteristics (ROC) curve was drawn to assess the diagnostic capability. A cut-off level that resulted in high sensitivity ($>$90%) was chosen to categorize the subjects into high (OSA present) and low score (OSA absent) categories. ROC curve was then plotted for the various levels of maximum oxygen desaturation (from the baseline) in the group of patients with high scores. We chose a cut-off for the level of desaturation that had a high specificity but acceptable sensitivity. Patients showing a level of desaturation above the derived cut-off were designated as having OSA and the rest as without OSA. Cross-tabs were then constructed for the whole group together and Chi-square test applied to study the strength of association.

Statistical analysis was performed using statistical software package 'STATA version 7.0' [(intercooled version), Stata Corporation, Houston, TX, USA]. In this study, $P < 0.05$ was considered as statistically significant.

4. Results

The overnight PSG studies of 118 subjects were analyzed. There were 53 cases and 65 controls. The age (years) of the cases and controls was statistically similar (47 ± 10 vs. 45 ± 11; P = NS). Forty-eight out of 68 males (70%) had AHI $\geq$ 15/h as compared to 5 out of 50 females (10%) ($\chi^2 = 42.7$, $P < 0.001$). The anthropometric profile of subjects is shown in Table 1. The subjects in the case and control groups had comparable BMI (kg/m^2) (34.1 ± 5.3 vs. 33.9 ± 6.4; P = NS). Compared to controls, the cases had higher NC (cm) ($P < 0.001$), PPNC (%) ($P < 0.001$) and WHR ($P < 0.001$) (Table 1). There was no significant difference between the pulmonary function parameters in the two groups (data not provided).

The PSG findings in cases and controls are shown in Table 2. The total sleep time (min) was statistically comparable in cases and controls (390.6 ± 60.3 vs. 388.5 ± 71.3, P = NS). Compared to controls, the cases had significantly lower basal arterial oxygen saturation (%) (93.7 ± 4.3 vs. 96.7 ± 2.2; $P < 0.001$) and percentage of rapid eye movement (REM) sleep (%) (7.6 ± 6.1 vs. 16.4 ± 14.5; $P < 0.001$). For the whole group, the mean oxygen desaturation from baseline was more during REM sleep as compared to NREM sleep (%) (24 ± 10 vs. 19 ± 8). A significant positive correlation of AHI was observed with NC ($r = 0.542$, $P < 0.001$), PPNC ($r = 0.536$, $P < 0.001$) and WHR ($r = 0.378$, $P < 0.001$), and negative correlation with percentage of REM sleep ($r = -0.307$, $P < 0.001$) and baseline oxygen saturation ($r = -0.339$, $P < 0.001$). A strong positive correlation was also found between AHI and level of desaturation ($r = 0.708$, $P < 0.001$).

In the bivariate analysis, gender, NC, PPNC, WHR, baseline PaO_2, $PaCO_2$ and baseline oxygen saturation were found as significant explanatory variables (at $P < 0.2$). Using stepwise multiple logistic regression analysis with

Table 1
Characteristics of cases and controls

Characteristics	Cases (AHI ≥ 15/h) ($n = 53$)	Controls (AHI < 15/h) ($n = 65$)
Age (years)	47 (10)	45 (11)
Male gender	48 (90)	20 (31)*
Body-mass index (kg/m^2)	34.1 (5.3)	33.9 (6.4)
Neck circumference (cm)	42.1 (3.3)	37.6 (3.4)*
Percentage predicted neck circumference (%)[a]	105.0 (7.8)	94.6 (8.0)*
Waist-hip ratio	1.06 (0.08)	0.96 (0.08)*
Mid-arm circumference (cm)	35.9 (4.5)	35.0 (4.6)
Triceps skin-fold thickness (mm)	26.3 (10.0)	24.5 (5.6)

Data are presented as mean (SD) except gender data, which is expressed as number (percentage), AHI, Apnea- hypopnea index; * $P < 0.001$.

[a] Percentage predicted neck circumference = 1000 × neck circumference (cm)/0.55 × height (cm) + 310.

Table 2
Polysomnography parameters in cases and controls

Variables	Cases (AHI ≥ 15/h) ($n = 53$)	Controls (AHI < 15/h) ($n = 65$)
Total duration of polysomnographic study (min)	495.4 (44.8)	499.4 (46.5)
Total sleep time (min)	390.6 (60.3)	388.5 (71.3)
REM sleep (%)	7.6 (6.1)	16.4 (14.5)*
Baseline oxygen saturation (%)	93.7 (4.3)	96.7 (2.2)*
Maximum desaturation during poly- somnographic study (%)	33.7 (12.6)	11.6 (10.0)*

Data are presented as mean (SD), *$P < 0.001$; AHI, Apnea-hypopnea Index.

OSA as the binary dependent variable and the variables found statistically significant at $P < 0.2$ as potential predictor variables, WHR (as a percentage of normal, taken as 0.85) [odds ratio {95% confidence interval (CI)}: 1.066 (1.00–1.137); $P = 0.049$], male gender [odds ratio (95% CI): 3.97 (0.99–15.81); $P = 0.046$] and NC [odds ratio (95% CI): 1.23 (1.03–1.47); $P = 0.023$] were found to be independent predictors of OSA. The scoring equation was computed as follows: score = [1.378 × (gender)] + [0.064 × (WHR)] + [0.21 × (NC)], where (gender: 0 = female; 1 = male; WHR: percentage of normal WHR taken as 0.85; NC: actual NC of the subject). The model had an area under the ROC curve of 87.4% (95% CI: 81.2–93.6%) (Fig. 1). Using ROC curve analysis, the following diagnostic rule was defined: those with scores >16.62 will have OSA, and those with scores ≤16.62 will not. This scoring algorithm had a sensitivity of 90.4%; specificity of 69.8%; positive predictive value (PPV) of 71.2%; and negative predictive value (NPV) of 89.8%. That is, more than 90% of the patients with OSA are likely

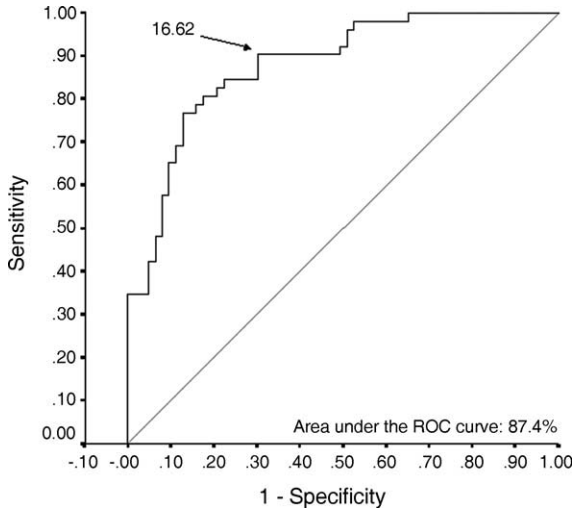


Fig. 1. Receiver–operator characteristics curve plotted for the equation derived from gender, neck circumference and waist hip ratio, to evaluate its utility in prediction of OSA.

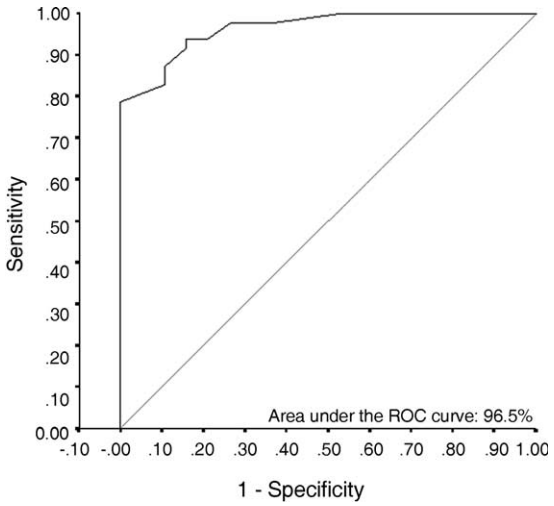


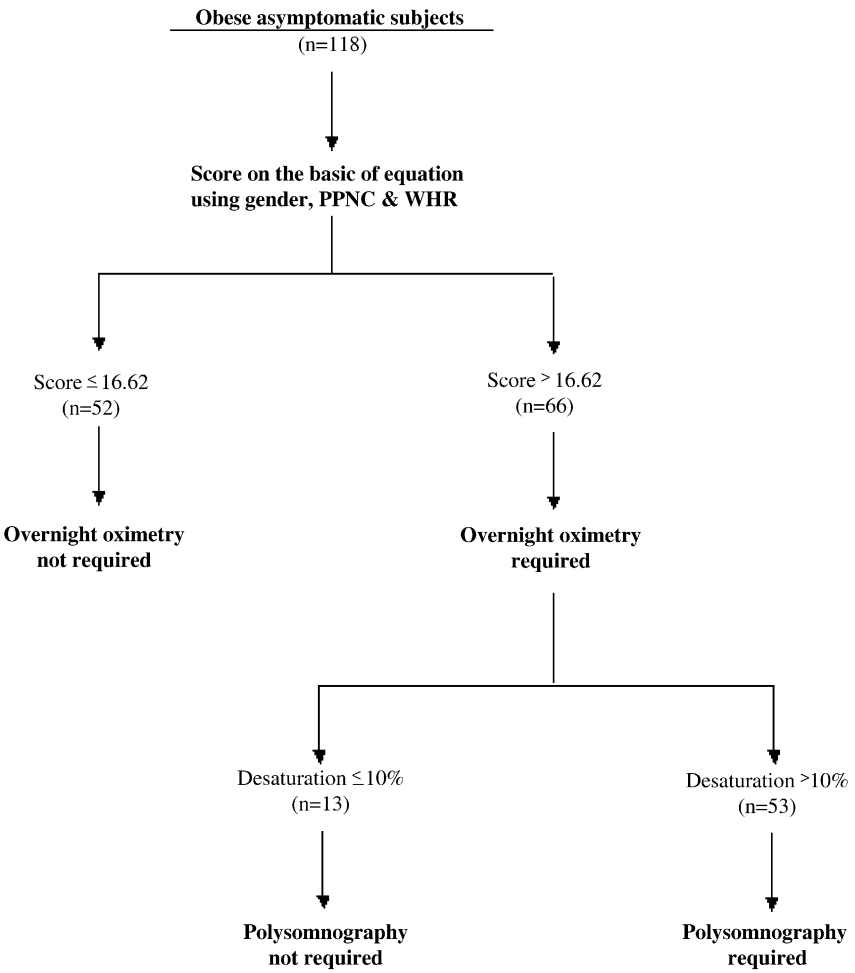
Fig. 2. Receiver-operator characteristics curve plotted for the level of desaturation in patients with a score above 16.62 on the equation, derived by estimation of gender, neck circumference and waist hip ratio, for prediction of OSA.

to be detected by this score, but more than 30% of patients selected will not have OSA (due to the specificity of 69.8%). Patients found to have a high score ($n = 66$) were evaluated for the level of oxygen desaturation during sleep. ROC curve was plotted for various levels of desaturation in these patients, with OSA as a binary variable. ROC curve had an AUC value of 96.5% (95% CI: 92.7–99.8%) (Fig. 2). We chose a cut-off for the level of desaturation that had high specificity for diagnosis of OSA. With a cut-off of 10%, the specificity, sensitivity, PPV and NPV for diagnosis of OSA for the whole group were 89.2, 88.5, 86.8 and 90.6%, respectively. Fig. 3 shows the details of the stepped approach as a flow chart.

5. Discussion

Obesity appears to be attaining epidemic proportions, both in the developed and developing world [12–14]. Although OSA may be seen in non-obese subjects [16], a strong link has been demonstrated between obesity and OSA. It is therefore important that physicians who care for obese subjects should suspect the presence of OSA. PSG, the current standard for the evaluation of sleep-disordered breathing (SDB), is expensive, time-consuming, and in most developing nations, like India, remains inaccessible to a large segment of population, making it essential to prioritize patients for this procedure. The above-mentioned predictors can be useful to identify non-symptomatic, obese individuals before PSG is performed.

In the present study, AHI ≥ 15/h was used as the cut-off for defining OSA, as it is often above this level that the risk of various complications increases and an aggressive treatment is indicated. It is the commonly used cut-off point for SDB of clinical importance, recommended by



Number of patients classified as having OSA on the basis of the stepped approach: 53
Actual number of patients having OSA: 53
Number of patients classified as not having OSA on the basis of the stepped approach: 65
Actual number of patients not having OSA: 65
Specificity, sensitivity, PPV and NPV for diagnosis of OSA: 89.2%, 88.5%, 86.8% and 90.6%

Fig. 3. Algorithm for evaluation of overtly asymptomatic obese subjects.

an international task force on standardization of SDB definition [20]. It was also observed that the independent predictors of OSA in the multivariate model remained the same for the AHI cut-off of $\geq$10/h or $\geq$5/h. The relative contribution of various explanatory variables showed insignificant change. We therefore preferred AHI $\geq$ 15/h as the cut-off, since it reflects the form of apnea that warrants immediate treatment.

Thermistors were used for airflow monitoring. We would like to caution here that hypopnea episodes might have been underestimated in some patients, as thermistors do not tend to have a truly linear relationship with airflow. When the study was initiated in 1998, thermistors were the standard equipment for measurement of airflow; we decided to use the same equipment to evaluate all the subjects for the sake of homogeneity. As expected, the cases had a lower percentage of REM sleep compared to controls because repeated arousals caused by OSA led to sleep fragmentation, with sleep restricted to NREM sleep stage I and II.

As per the proposed reclassification of obesity in adult Asians by the World Health Organization [21], BMI $\geq$25 kg/m^2 was used as the cut-off for obesity. The prevalence of OSA was found to be 45%, which appears to be high considering the fact that most patients were overtly asymptomatic. This finding has important implications. It seems likely that many of these patients, who appeared to be asymptomatic and denied a history of symptoms (e.g. fragmented sleep, loud snoring, choking, daytime somnolence), were suffering from 'silent' OSA. The vague symptoms, such as headache, dizziness and heartburn, reported by these patients may in fact be related

to underlying OSA. Hence, a history of typical, OSA-related symptoms alone may not be sufficiently sensitive to screen many apparently asymptomatic subjects for 'silent disease.'

Both case and control groups had comparable BMI, ensuring no confounding effect on the determination of other predictors of OSA. The strong predictive utility of NC is consistent with previous studies [4,6] and suggests fat accumulation in the neck as an important cause of OSA in obese individuals. Davies and Stradling [18], in a study of 66 patients, reported that the relationship between generalized obesity and sleep apnea was fully explained by variation in neck size. Katz et al. and Hoffstein and Mateika reported similar results, where NC and BMI were found to be the most important predictors of OSA [4,22]. WHR (actual value) was also an important explanatory variable of OSA, an indication of the relation between lower body fat distribution and sleep apnea. However, the usual WHR cut-off used for segregating patients (0.85) does not seem to be useful in predicting OSA. Grunstein and co-workers [8], who also found WHR to be a strong predictor of OSA, reported that the best predictive cut-off was 0.94. In the present study, WHR was analyzed as a continuous variable (by taking its actual value as percentage of a standard), rather than an ordinal variable, by defining a cut-off level for normalcy. As an ordinal variable, WHR with a cut-off of 0.85 or 0.94 was not found to be an independent predictor of OSA, but when used as a continuous variable it emerged as an independent predictor. Since the primary objective of this study was to suggest a diagnostic rule for evaluation of asymptomatic obese individuals, an equation with superior predictive capability was desired. The significantly better predictive capability of an equation based the actual value of WHR supports the possibility that the risk of OSA rises continuously with the rise in WHR, further suggested by the highly significant correlation between WHR and the level of AHI.

The other independent predictor of OSA was male gender. Obese males were found to have almost four-fold higher odds of having OSA than obese females. Community based studies have also reported gender difference in the prevalence of OSA, with male to female ratio of 2:1 or 3:1 [1]. The reason for the lower prevalence of OSA in women is far from clear. Although the influence of sex hormones has been considered, their exact role remains to be defined. The greater central body fat distribution and larger neck dimensions of men may partially account for sex differences in prevalence of OSA [23]. Men have a greater tendency to android fat distribution than women, resulting in a larger neck size. Gender prevalence may also result from differences in upper airway muscle function during sleep. During wakefulness, women have greater genioglossal activity than men [24], and persistence in NREM sleep could prevent upper airway collapse in women.

Once the equation based on gender, NC and WHR was defined, a cut-off with a high sensitivity was determined (to keep false negatives low). However, more than 30% of patients were false positives using this cut-off (specificity with this cut-off was 69.8%), and performing PSG for OSA based solely on this prediction would not be cost-effective. Level of desaturation during PSG is known to be a good marker of OSA [25,26]. The correlation between the level of AHI and desaturation is also high, but in most settings with limited resources it may not be feasible to subject all asymptomatic obese subjects to overnight oximetry, and it would not be ideal as a first-line approach for screening. Keeping these facts in mind, desaturation data derived from overnight oximetry were obtained only for patients designated as having OSA risk based on the initial equation (derived from gender, NC and WHR). This resulted in an approach that had remarkable predictive capability. When the whole study group was analyzed together by drawing cross-tabs for patients diagnosed with OSA on the basis of PSG and those diagnosed on the basis of the proposed stepped approach, specificity as well as PPV were found to be above 86%. Such an approach ensures that false positives among patients selected for PSG remain low. Consequently, use of the proposed approach would result in significant reduction of costs.

On the basis of these results it is suggested that, where PSG facilities are limited, as is the present case in the majority of developing nations, all obese subjects with minimal symptoms attributable to OSA should be scored using the equation derived from gender, NC and WHR. If a particular score is more than 16.62, overnight oximetry should be offered. If the level of desaturation on overnight oximetry is more than 10%, the subject should be a candidate for PSG. In such cases, the chances of subjects having OSA would be near 90% and rest would be false positives. Similarly, if the initial equation score is below 16.62, the patient can be reassured with a high degree of confidence that OSA is not present, and overnight oximetry avoided.

It should be stressed that the results of this study are not applicable for patients with florid symptoms of OSA. In fact, the application of this stepped approach is intended for preventative screening of overtly asymptomatic obese subjects. Prevalence of OSA in these subjects is high, and complications may have developed by the time symptoms appear. Subjects identified by this approach as having a high likelihood of OSA can be evaluated by PSG.

To conclude, findings of the present study suggest that male gender, NC and WHR are all independent predictors of OSA among overtly asymptomatic obese subjects. The proposed equation helps to identify a large majority of those likely to be suffering from OSA. As this equation lacks specificity, selected subjects should undergo overnight oximetry. Based on desaturation data, patients with a high likelihood of OSA are ideal candidates for PSG. This stepped approach appears to be an accurate and cost-effective modality for work-ups of overtly asymptomatic obese subjects.

Acknowledgements

The authors express their appreciation for the staff members of polysomnography laboratory in the Department of Medicine, All India Institute of Medical Sciences, New Delhi (Mr Jitendra Kumar and Mr Jitendra Sharma) for the numerous sleepless nights they spent in performing the sleep studies. The authors also thank all study subjects who voluntarily consented to participate in the study.

References

[1] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
[2] Roux F, D'Ambrosio C, Mohsenin V. Sleep-related breathing disorders and cardiovascular disease. Am J Med 2000;108:396–402.
[3] Sharma SK, Mohan A. Sleep disordered breathing and hypertension: time to wake up! Indian. J Chest Dis Allied Sci 2001;43:77–9.
[4] Katz I, Stradling J, Slutsky AS, Zamel N, Hoffstein V. Do patients with obstructive sleep apnea have thick necks? Am Rev Respir Dis 1990;141:1228–31.
[5] Horner RL, Mohiaddin RH, Lowell DG, Shea SA, Burman ED, Longmore DB, Guz A. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnea and weight matched controls. Eur Respir J 1989;2:613–22.
[6] Davies RJ, Ali NJ, Stradling JR. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnea syndrome. Thorax 1992;47:101–5.
[7] Levinson PD, McGarvey ST, Carlisle CC, Eveloff SE, Herbert PN, Millman RP. Adiposity and cardiovascular risk factors in men with obstructive sleep apnea. Chest 1993;103:1336–42.
[8] Grunstein R, Wilcox I, Yang TS, Gould Y, Hedner J. Snoring and sleep apnea in men: association with central obesity and hypertension. Int J Obes Relat Metab Disord 1993;17:533–40.
[9] Mortimore IL, Marshall I, Wraith PK, Sellar RJ, Douglas NJ. Neck and total body fat deposition in nonobese and obese patients with sleep apnea compared with that in control subjects. Am J Respir Crit Care Med 1998;157:280–3.
[10] Shinohara E, Kihara S, Yamashita S, Yamane M, Nishida M, Arai T, Kotani K, Nakamura T, Takemura K, Matsuzawa Y. Visceral fat accumulation as an important risk factor for obstructive sleep apnea syndrome in obese subjects. J Intern Med 1997;241:11–18.
[11] Harman EM, Wynne JW, Block AJ. The effect of weight loss on sleep-disordered breathing and oxygen desaturation in morbidly obese men. Chest 1982;82:291–4.
[12] National Health and Nutrition Examination Survey (NHANES), National Center for Health Statistics. Prevalence of overweight and obesity among adults: United States Centers for Disease Control and Prevention, Atlanta; 1999.
[13] Gopinath N, Chadha SL, Jain P, Shekhawat S, Tandon R. An epidemiological study of obesity in adults in the urban population of Delhi. J Assoc Physicians India 1994;42:212–5.
[14] Misra A, Pandey RM, Devi JR, Sharma R, Vikram NK, Khanna N. High prevalence of diabetes, obesity and dyslipedemia in urban slum population in Northern India. Int J Obes Relat Metab Disord 2001;25: 1722–9.
[15] Lloyd JE. Saturday conference: Sleep apnea syndrome. South Med J 1983;76:1417–20.
[16] Strobel RJ, Rosen RC. Obesity and weight loss in obstructive sleep apnea: a critical review. Sleep 1996;19:104–15.
[17] Davies RJ, Stradling JR. The relationship b0etween neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnea syndrome. Eur Respir J 1990;3:509–14.
[18] Sharma SK, Pande JN, Singh YN, Verma K, Kathait SS, Khare S, Malaviya AN. Pulmonary function and immunolgical abnormalities in miliary tuberculosis. Am Rev Respir Dis 1992;145:1167–71.
[19] Sharma SK, Reddy TS, Mohan A, Handa KK, Mukhopadhyay S, Pande JN. Sleep disordered breathing in patients with chronic obstructive pulmonary disease: a prospective study. Indian J Chest Dis Allied Sci 2002;44:99–105.
[20] American Academy of Sleep Medicine Task Force, Sleep related breathing disorders in adults: recommendations for syndrome definitions and measurement techniques in clinical research. Sleep 1999;22:667–89.
[21] World Health Organization, The Asia-Pacific Perspective. Redifining Obesity and its Treatment International Diabetes Institute, Health Communications Australia Pty Ltd; 2000.
[22] Hoffstein V, Mateika S. Differences in abdominal and neck circumferences in patients with and without obstructive sleep apnea. Eur Respir J 1992;5:377–81.
[23] Millman RP, Carlisle CC, Mc Garvey ST, Eveloff SE, Levinson PD. Body fat distribution and sleep apnea severity in women. Chest 1995; 107:362–6.
[24] Popovic RM, White D. Influence of gender on waking genioglossal electromyogram and upper airway resistance. Am J Respir Crit Care Med 1995;152:725–31.
[25] Chiner E, Signes-Costa J, Arriero JM, Marco J, Fuentes I, Sergado A. Nocturnal oximetry for the diagnosis of the sleep apnea hypopnea syndrome: A method to reduce the number of polysomnographies. Thorax 1999;54:958–9.
[26] Vazquez JC, Tsai WH, Flemons WW, Masuda A, Brant R, Hajduk E, Whitelaw WA, Remmas JE. Automated analysis of digital oximetry in diagnosis of OSA. Thorax 2000;55:302–7.