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Chapter 4

Obstructive Sleep Apnea: Beyond Obesity

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Abstract

Sleep disorders are of growing concern and are a major public health problem. The obstructive sleep apnea (OSA) is the most common among different sleep-related breathing disorders (SRBDs). Obesity is a known associated risk factor for the OSA but is not limited to them. OSA is also recognized in nonobese population. The description of OSA in non obese patients in the literature is sparse. The clinical presentation is similar as in obese but has few differences as far as pathophysiology and polysomnographic features are concerned. The severity of OSA in nonobese has less severe manifestations thus requires early recognition and different treatment strategy to prevent mismanagement of these patients.

Keywords: OSA, UARS, nonobese

1. Introduction

Sleep disorders are of growing concern and has become a major public health problem. Sleep disorders involve difficulty in breathing during sleep and are grouped under sleep-related breathing disorders (SRBDs). SRBDs are commonly classified as central sleep apnea syndrome, obstructive sleep apnea syndrome, hypoventilation/hypoxia syndrome, nonspecific/undefined sleep disorder [1]. Among SRBDs, obstructive sleep apnea (OSA) is the most common. OSA has characteristically been associated with obesity and lack of awareness and ignorance has contributed more to its increasing prevalence. OSA escaped the thought of many doctors till it was first described by Gastaut in a *Neurology journal* in 1965. Although it was first observed and mentioned in a book of Charles Dickens, an English book writer, in 1936 about a character of a person by name Joe (fat boy) in his book, *The Pickwick Papers* [2]. According to Dacal Quintas et al. [3], frequency and severity of OSA in normal

weight patients was lower than overweight and obese patients. They reported frequency of 70.52 and 22% OSA in obese and normal weight patients, respectively. Normal weight group patients were mainly women, snorers, nonsmokers, nondrinkers and were significantly younger and with a smaller neck and waist circumference. The exact and recent data regarding prevalence of OSA in nonobese are not available. However, the recent studies have shown a wide scope for the evaluation of the OSA among nonobese patients globally and in India. Physicians noticed that the clinical presentations of OSA are not only limited in obese but also found in nonobese [4]. The common clinical presentation in obese and nonobese is the outcome of the basic underlying pathophysiological change that is airway narrowing or collapse during the sleep which may have different determinants that are being addressed in this chapter.

2. Pathophysiology of airway obstruction

OSA is a major public health problem affecting sizeable population. The patho physiological mechanism of OSA is not thoroughly understood and it appears to be of multifactorial origin which majorly involves interaction between anatomical (static), functional (dynamic), and systemic factors. Although these factors form the basis of OSA in nonobese and obese persons, their contribution may differ in the two groups of people.

3. Mechanism of airway obstruction during sleep

Pharynx is the only collapsible segment of the respiratory tract (except nares and small airways), and it is also the site for upper airway closure or narrowing during sleep. The patency of the pharynx is maintained by two counteracting forces, i.e. upper airway muscles (dilates and stiffens the pharynx) and negative intraluminal pressure (tends to narrow the pharynx). The imbalance between these two is the basis for OSA. Retropalatal and retroglossal areas of oropharynx are the commonly involved site in the narrowing of airways in OSA [5, 6].

The reasons for narrowing in OSA are different in nonobese and obese patients in comparison with normal individual [7]. In OSA, upper airway soft tissue enlargement may play a more important role in obese patients, whereas bony structure discrepancies may be the dominant contributing factors among nonobese patients. The various factors responsible for OSA in nonobese are mentioned below (**Figure 1**).

3.1. Anatomical (Static) factors in upper airway structure

(1) Edema: Negative pressure due to airway closure and repeated apnea may lead to edema of soft tissues particularly uvula and genioglossus [8–10].

(2) Muscle injury: Repeated fatigue of upper airway muscles in sleep apnea leads to myopathy which in turn results in remodeling of muscles [11, 12].

(3) Gender: Upper airway size and neck size are smaller in women than in men, thus the size of soft tissue structures is also smaller in women than in men. Fat deposition in men is primarily seen in upper body and trunk, whereas in women fat is deposited more commonly in lower body and extremities [13–15].

The above factors contribute to the development of OSA in both obese and nonobese. Obesity is a major risk factor for OSA, where there is decrease in pharyngeal airway size and increases airway collapsibility. Increase in neck size associated with an increase in BMI, seen in OSA patients, is a good predictor of sleep apnea. Weight gain is associated with generalized fat deposition, which contributes to the increase in the oropharyngeal muscle mass responsible for its malfunctioning and thus airway collapsibility [16–18].

3.2. Physiological (dynamic) factors in upper airway structure

The data indicate that the upper airway collapsibility during apneic events occurs at the end of expiration in addition to collapse during inspiration [19, 20]. During wakefulness, the

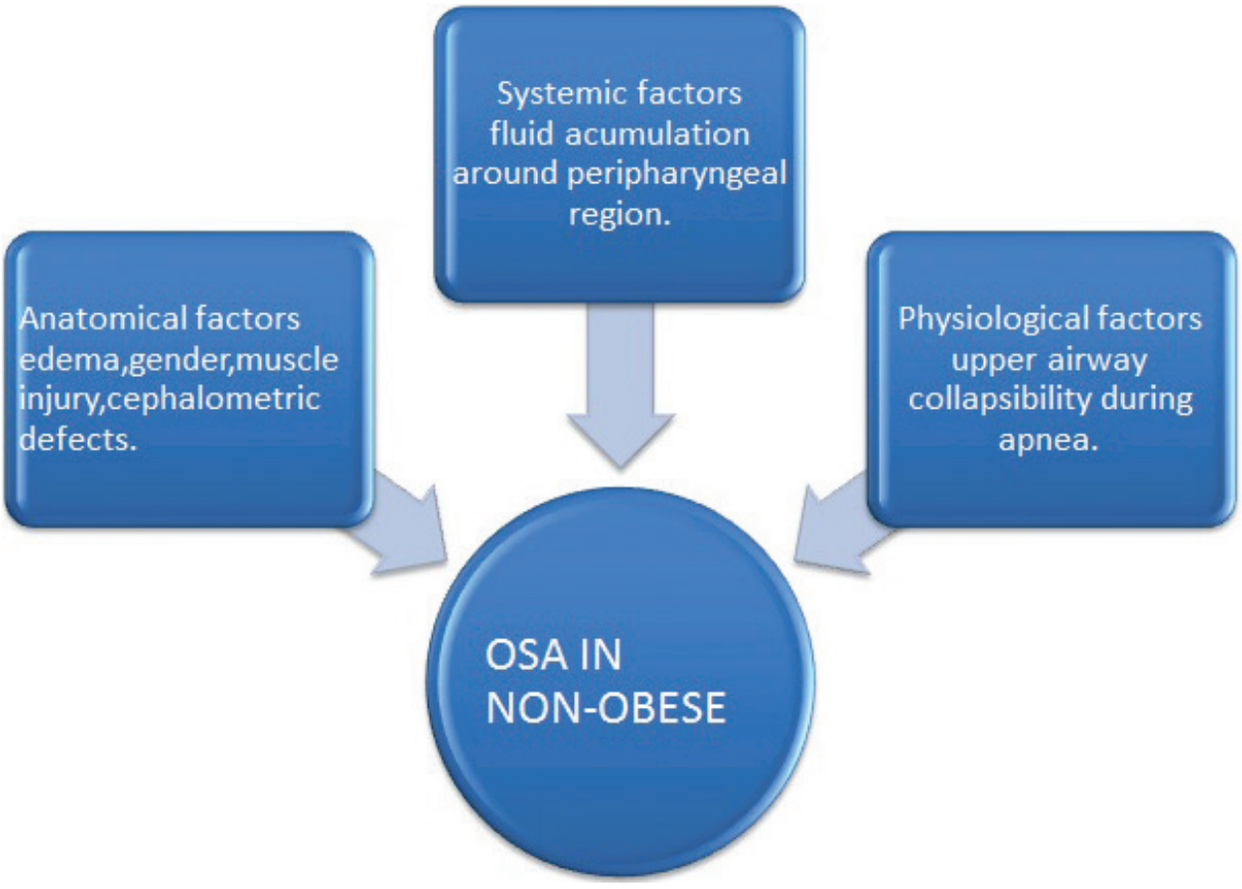

Figure 1. Factors responsible for OSA in nonobese.

balance between the upper airway dilator muscles and negative intraluminal pressure leads to a constant upper airway caliber [21, 22]. During sleep (in normal subject), it is associated with narrowing of pharyngeal luminal area due to decrease in upper airway muscle activity and a persistence of subatmospheric luminal pressure during inspiration. When the severity of this narrowing increases along with the anatomical impairment, this may lead to the development of OSA during sleep.

3.3. Systemic factors affecting upper airway structure

Accumulated fluid in the leg has a tendency to suffer overnight rostral displacement to the parapharyngeal region. Additionally, this rostral fluid displacement further interacts with the displacement of subcutaneous tissue, thus compromising the pharyngeal airway lumen. Few published articles, all in nonobese subjects, confirmed overnight increase in neck circumference resulting from shift of fluid from the legs [23–25]. This has further been proved by experimental studies using medical antishock trousers (MAST) [26, 27]. Organ failures such as heart failure [28], renal failure [29], and other disease conditions such as hypertension [30–32], stroke [33, 34], pulmonary arterial hypertension [35], and other conditions with potential for fluid retention are associated with OSA.

3.4. Other factors

Upper airway resistance syndrome (UARS) can be considered as the other factor, though the debate has been in existence since Guilleminault et al. first described UARS in 1993 [36]. The UARS has clinical presentations similar to OSA but certain differences are found in OSA and UARS. Many authors have tried to differentiate these two entities but only could reach to a very thin line of demarcation [37, 38]. The fact remains that UARS is commonly seen in nonobese, with body mass index (BMI) ≤25 kg/m^2 [39, 40]. Patients are frequently younger than patients with OSAS. UARS is more common in males but the female to male ratio seems to be highest in UARS group compared to OSA [41]. Frequent arousals due to increased respiratory effort also known as respiratory effort-related arousals (RERAs) in UARS are associated with daytime sleepiness, functional symptoms, cardiovascular, and cognitive disturbances. These RERAs are the classical features of UARS [42]. Unfortunately, many UARS patients are still under diagnosed as these patients are not subjected to polysomnographic studies as belief that patients must be obese or at least overweight with a large neck and these patients are usually labeled as fibromyalgia, chronic fatigue syndrome, or as psychiatric disorders, such as attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) [43].

The pathophysiology of UARS appears to be similar to OSA despite subtle differences in them. In UARS, pharyngeal reflexes are preserved compared to impaired reflexes in OSA [44]. Nocturnal polysomnography in UARS does not show apneas or hypopneas, which are the main features of obstructive sleep apnea syndrome (OSAS). Even though UARS does not have apneas/hypopneas, RERAs are associated with significant disturbances in sleep leading to impairment of daily routine of individuals. So ICSD II recommends that UARS should be considered as a part of OSA and not as a separate entity [45].

4. Causes for OSA in nonobese patients

Along with UARS and organ failure, causes for OSA in nonobese patients are mainly limited to several cephalometric defects compared with their BMI matched normal controls [7].

Nonobese OSA patients tend to present the following anatomical craniofacial characteristics, such as caudal hyoid, increased soft palate dimensions, and consequent anterior-posterior reductions of the airways at the soft palate level, reduction of anterior-posterior region of nasopharynx and oropharynx [7].

It has been suggested that the discrepancy in these cephalometric measurements may also depend on sex, age, and race [46–49]. OSA in Asian men has been found more frequently in the nonobese patients, despite the presence of severe illness, when compared with white male patients with OSAS [50].

Garg et al. [4] reported that nonobese subjects were more likely in habit of taking sedatives for sleeping when compared to obese counterpart, which was in concordance with other study conducted by Ghanem and Mahmood on 102 patients with OSA [51].

5. Clinical manifestations

There is no much difference between the clinical features of OSA in obese and nonobese as the pathophysiology of OSA is same in both obese and nonobese patients. Point of differentiation comes at severity of symptoms and management. Frequency and severity of OSA in nonobese is comparatively less than OSA in obese [3].

According to the study conducted by the author, the obese group had a significance with regard to lower minimal oxygen saturation (68.47 ± 13.00 vs. 80.25 ± 7.40, $P < 0.001$), higher average desaturation index (48.32 ± 13.08 vs. 30.63 ± 15.63, $P < 0.001$), and higher arousal index (28.42 ± 4.99 mm vs. 17.84 ± 5.07 mm, $P < 0.001$). Although there were a large number of obese patients than nonobese in the study (25/45 vs. 14/36) having minimum oxygen saturation <90%, the percentage of nonobese patients showing similar findings was not less (55.6 vs. 38.9, $P = 0.37$). The rest of the polysomnographic parameters were comparable [4].

6. Diagnosis

Diagnosis of OSA should be made after a comprehensive work up on the basis of history, examination, polysomnography, limited channel testing, split-night testing, and oximetry.

Since in most of these patients anatomical factors contribute to their problem, thus the emphasis should be to assess the airway thoroughly.

Airway may be assessed with the help of a number of imaging modalities such as acoustic reflexion, fluoroscopy, nasopharyngoscopy, and cephalometry (**Figures 2** and **3**; **Table 1**),

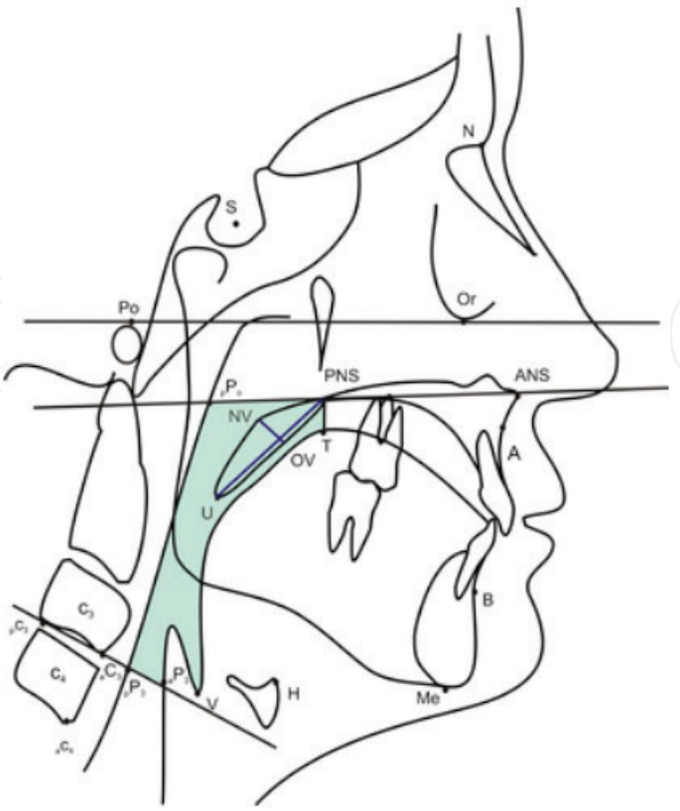

Figure 2. Cephalometric landmarks A.

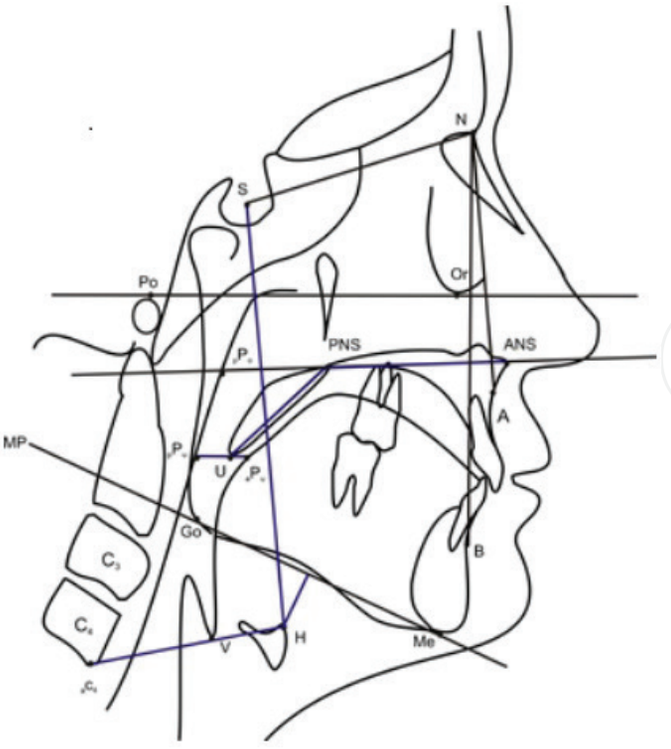

Figure 3. Cephalometric landmarks B.

S	Center of sella turcica
N	Nasion, the deepest point concavity of nasofrontal suture
ANS	Anterior nasal spine
PNS	Posterior nasal spine
Point A	The deepest point in the concavity of the anterior maxilla between the anterior nasal spine and the alveolar crest
Point B	The deepest point in the concavity of the anterior mandible between the alveolar crest and pogonion
Go	Gonion, the most posteroinferior point on angle of mandible
Me	The most inferior point on bony chin
U	The tip of uvula
OV	Intersection point between line on maximal diameter of velum in oronasal direction and oral surface of velum
NV	Intersection point between line of maximal diameter of velum in oronasal direction and nasal surface of velum
T	Intersection point between dorsal surface of tongue and line perpendicular to maxillary plane at PNS
H	The most superior and anterior point on the body of hyoid bone
${}_{a}C_{3}$	Anteroinferior point on corpus of third cervical vertebrae (C3)
${}_{p}C_{3}$	Posteroinferior point on corpus of third cervical vertebrae (C3)
${}_{a}C_{4}$	Anteroinferior point on corpus of fourth cervical vertebrae (C4)
${}_{a}P_{u}$	Intersection point between anterior pharyngeal wall and line passing through point 'U' parallel to maxillary plane
${}_{p}P_{u}$	Intersection point between posterior pharyngeal wall and line passing through point 'U' parallel to maxillary plane
${}_{p}P_{o}$	Intersection point between nasal line and posterior pharyngeal wall
${}_{p}P_{3}$	Intersection point between line connecting points, ${}_{p}C_{3}$ and ${}_{a}C_{3}$ and posterior pharyngeal wall
ANS-PNS	Maxillary plane
Go-Me	Mandibular plane (MP); line tangent to lower border of body of mandible through gnathion
H-MP	Distance between H and mandibular plane
S-H	Distance between S and H
${}_{a}C_{4}$-H	Distance between H and ${}_{a}C_{4}$
PNS-U	Soft palate length
NV-OV	Soft palate thickness
ANS-PNS-U	Soft palate (SP) angle, angle between maxillary plane and soft palate
R	Radius of curvature of nasal surface of soft palate $r = \frac{(\text{NV to OV distance})}{2} + \frac{(\text{PNS to U distance})^2}{8(\text{NV to OV distance})}$
${}_{a}P_{u} - {}_{p}P_{u}$	Anteroposterior dimension of oropharynx at U
PNS-${}_{p}P_{0}$-${}_{p}P_{3}$-${}_{a}P_{3}$-L	Total pharyngeal area

Table 1. Cephalometric landmarks and reference lines used.

MR imaging, and both conventional and electron-beam CT scanning. MR imaging is probably the best imaging modality, although still not ideal [52].

7. Treatment

Possible treatment options for adult patients with OSA should be based on the severity of the sleep disorder, preference of the patient, the patient's general health, and the preference and experience of the team members. Treatment approach for OSA should be holistic and multimodality. Positive airway pressure (PAP) is universally accepted as the treatment of choice for mild, moderate, and severe OSA and thus should be offered to all patients as the first option. Side effects and adverse events are mainly minor and reversible with CPAP and BPAP therapy [53]. It may be delivered in continuous (CPAP), bilevel (BPAP), or autotitrating (APAP) modes. CPAP is indicated for the treatment of moderate-to-severe OSA [53]. Treatment of mild OSA could be optional other than PAP therapy. The American Academy of Sleep Medicine (AAOSM) has recommended the use of oral appliances (OAs) in patients with primary snoring and mild-to-moderate OSA [52]. Oral appliances are not as efficacious as CPAP. They are indicated for use in patients with mild-to-moderate OSA who prefer OAs to CPAP, or who do not respond to CPAP, are not appropriate candidates for CPAP, or who fail CPAP and are not fit candidate for surgery [54]. Oral appliances can also achieve satisfactory outcomes in UARS [55]. If surgical measures are predicted (severe obstructing anatomy that is surgically correctible) to be highly effective in treating sleep apnea, upper airway surgery (including tonsillectomy and adenoidectomy, craniofacial operations, and tracheostomy) may also supersede use of OAs. Surgical procedures may also be considered as a secondary treatment for OSA when the patient is intolerant of PAP, or PAP therapy is unable to eliminate OSA [56]. There are no widely effective pharmacotherapies for OSA. Topical nasal corticosteroids may improve the AHI in patients with OSA and concurrent rhinitis, and thus may be a useful adjunct to primary therapies for OSA. However, short-acting nasal decongestants are not recommended for treatment of OSA [56]. Oxygen supplementation has no role as a primary treatment for OSA [57]. Modafinil is recommended for the treatment as an add-on therapy of residual excessive daytime sleepiness in OSA patients who have sleepiness despite effective PAP treatment and who are lacking any other identifiable and correctable cause for their sleepiness [57]. We suggest that CPAP and Bi level is not the only modality of treatment. Any patient with systemic disorder requires treatment of primary disorder before application of these devices.

8. Conclusion

The severity of OSA in nonobese has less severe manifestation and requires different treatment strategy according to the contributory factor playing in its causation. Patients also require thorough clinical evaluation and confirmation by means of polysomnographic studies as many patients showing features of daytime sleepiness and fatigue may be erroneously managed as psychological symptoms.

The OSA in nonobese can be missed in elderly patients who have comorbidities like cardiovascular and neurological disease along with weak oropharyngeal muscles leading to easy collapsibility of airway along with obstruction. Correction of OSA in nonobese person is a multimodality approach. Assessment of upper airway anatomical variation from normalcy is a crucial step of management. Besides maintenance of sleep hygiene, patient could be subjected to many different modality of treatment as a holistic approach.

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