**Review Article**

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# Obstructive sleep apnoea: Definitions, epidemiology & natural history

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**Obstructive sleep apnoea (OSA) is increasingly being recognized as an important health issue in the last two to three decades. It is characterized by frequent episodes of upper airway collapse during sleep, causing recurrent arousals, intermittent hypoxaemia, sleep fragmentation and poor sleep quality. There is accumulating evidence that OSA is being considered as an independent risk factor for hypertension, glucose intolerance / diabetes mellitus, cardiovascular diseases and stroke, leading to increased cardiometabolic morbidity and mortality. The prevalence rates of OSA have been estimated in the range of 2 to 10 per cent worldwide, and the risk factors for obstructive sleep apnoea include advanced age, male sex, obesity, family history, craniofacial abnormalities, smoking and alcohol consumption. The common clinical presenting symptoms are heavy snoring, witnessed apnoeas and daytime hypersomnolence, which would help to identify the affected individuals. With increasing awareness of this disease entity and associated complications in our society, there have been increased referrals to sleep physicians or expertise for further investigations and diagnostic evaluation. Early recognition and treatment of obstructive sleep apnoea may prevent from adverse health consequences. Some of the epidemiological aspects of obstructive sleep apnoea in adults are reviewed.**

**Key words** CPAP - epidemiology - obesity - obstructive sleep apnoea - risk factors,

## Introduction

Obstructive sleep apnoea (OSA) is a prevalent condition in close association with obesity epidemic globally, and it is characterized by repetitive, partial or complete collapse of the upper airway during sleep, causing impaired gaseous exchange and sleep disturbance. It is the most common form of sleep-disordered breathing (SDB) worldwide as shown in different epidemiological studies. There is increasing evidence that OSA is an independent risk factor for an adverse cardiometabolic profile[1], and it has been associated with increased cardiovascular and cerebrovascular morbidity and mortality, although much of the causal role and mechanisms are still poorly understood[2]. The hypothesized link between OSA and cardiovascular disease is complex, and the underlying interactions of pathophysiologic mechanisms in SDB involve the interactions of various metabolic risk factors. Other health consequences from OSA are also

significant: excessive daytime sleepiness, cognitive dysfunction, impaired work performance, anxiety, difficulties in personal relations, and an increased risk of fatal and non fatal automobile accidents which lead to loss of human life and huge economical burden in our modern world[3].

Despite the recent advances in diagnostic technology in the field of sleep medicine and increased awareness of OSA in the public, a majority of those affected are still undiagnosed[4]. Therefore, it is important for primary care physicians and specialists to be competent to recognise and identify those affected subjects for early and appropriate treatments. This review article explores some of the epidemiological aspects of OSA in adults.

**Definitions and diagnosis**

The gold standard diagnostic test for OSA is the overnight in-laboratory polysomnography. It involves multi-channel continuous polygraphic recording from surface leads for electroencephalography, electro-oculography, electromyography, electrocardiography, nasal pressure transducer (supplemented by thermistor) for nasal airflow, thoracic and abdominal impedance belts for respiratory effort, pulse oximetry, tracheal microphone for snoring, and sensors for leg and sleep position. These recordings will identify different types of apnoeas and hyponoeas during sleep. An apnoea is defined as the complete cessation of airflow for at least 10 sec. There are three types of apnoeas: obstructive, central and mixed. In obstructive sleep apnoea, respiratory effort is maintained but ventilation decreases or disappears because of partial or total occlusion in the upper airway. Central sleep apnoea is defined as reduced respiratory effort resulting in reduced or absent ventilation. Mixed apnoea is often characterized by starting with central apnoeas and ending with obstructive events. A hypopnoea is defined as a reduction in airflow (30-50%) that is followed by an arousal from sleep or a decrease in oxyhaemoglobin saturation (3-4%)[5,6]. Sleep apnoea severity is assessed with apnoea-hypopnoea index (AHI), which is the number of apnoeas and hypopnoeas per hour of sleep. According to the American Academy of Sleep Medicine recommendations, OSA is defined with AHI $\geq$5, and it is classified as mild OSA with AHI of 5 to 15; moderate OSA with AHI of 16 to 30; and severe OSA with AHI > 30[5].

Overnight sleep study requires an overnight stay in the hospital with trained staff who are capable of monitoring and interpreting the real-time complicated physiologic data throughout the night. This process is expensive, labour intensive and time consuming. In view of limited resources and the increasing demand, many researchers have explored the use of clinical predictors or questionnaires that may help to identify high risk patients. Screening devices have also been introduced and may represent an alternative method to diagnose OSA[7].

Home unattended polysomnography is a viable option for evaluating patients with moderate to high clinical suspicion for sleep-disordered breathing. Nevertheless, patients with failed or equivocal home studies and those with negative studies but persistent symptoms should undergo a standard polysomnography[8,9]. It has also been reported that a continuous positive airway pressure (CPAP) trial is the first diagnostic tool as well as a treatment modality for patients with sleep apnoea at the same time. The authors believed that patients who suffered from OSA would continue to use CPAP if their symptoms improved[10]. For patients with a high probability of OSA, it has been shown that standard polysomonography confers no advantage over the ambulatory approach in terms of diagnosis and CPAP titration[11]. When access to polysomnography is inadequate, the ambulatory approach can be used to expedite management of patients most in need of treatment.

**Prevalence**

The adult prevalence rates of sleep disordered breathing are now available in many different countries[12-23] after having large-scale epidemiological studies being conducted (Table). For an overall estimation across different countries, it is approximately 3 to 7 per cent for adult men and 2-5 per cent for adult women in the general population[24]. Thus, OSA is more common in men, approximately 2 to 3 times that of women. Besides, the prevalence of OSA is similar in both Caucasians and Asians, this indicates that OSA is not only common in developed but also in developing countries. However, the disease prevalence is higher in the subgroups with overweight or obese subjects, elderly people and those of different ethnic origins. Inter-ethnic studies suggest that African-American ethnicity may also be a significant risk factor for OSA. The increased prevalences of OSA among American Indians and Hispanic adults, and increased severity among Pacific Islanders and Maoris, were mainly explained by the increased obesity indices[25].

**Table.** Recent studies on the prevalence of obstructive sleep apnoea in different ethnic groups

| Reference | Study population | Age, yr | Prevalence (%) |
|---|---|---|---|
| Young *et al* 1993[12] | American men and women | 30-60 | Men: 4*-25# Women: 2*-19# |
| Bixler *et al* 1998[15] | American men | 20-100 | 17# |
| Bixler *et al* 2001[16] | American men and women | 20-100 | Men: 3.9* Women: 1.2* |
| Duran *et al* 2001[17] | Spanish men and women | 30-70 | Men: 14*-26# Women: 7*-28# |
| Ip *et al* 2001[18] | Chinese men | 30-60 | 4.1*-8.8# |
| Ip *et al* 2004[19] | Chinese women | 30-60 | 2.1*-3.7# |
| Kim *et al* 2004[20] | Korean men and women | 40-69 | Men: 4.5*-27# Women: 3.2*-16# |
| Udwadia *et al* 2004[21] | Indian men | 25-65 | 7.5*-19.5# |
| Sharma *et al* 2006[22] | Indian men and women | 30-60 | Men: 4.9*-19.7# Women: 2.1*-7.4# |

*Obstructive sleep apnoea syndrome is defined as apnoea-hypopnoea index ≥ 5 with excessive daytime sleepiness; # Obstructive sleep apnoea is defined as apnoea-hypopnoea index ≥ 5. All these prevalence studies were assessed with standard polysomnography

## Risk factors

The major risk factors for OSA include advanced age, male sex and obesity, although the underlying mechanisms remain unclear. It has been proposed that the pathophysiological pathways linking these risk factors for OSA can be explained by anatomical abnormalities, increased pharyngeal dilator muscle dysfunction, lowered arousal threshold, increased ventilatory control instability, and / or reduced lung volume[26].

*Age*: The increased prevalence of SDB breathing in the elderly appears to plateau after 65 yr [27], it is estimated to be 10 per cent. However, when the prevalence is controlled for body mass index, the severity appears to decrease with age[12]. Several studies have attempted to address the cause of age-related impact on sleep apnoea but no conclusions have been reached. Mechanisms proposed for the increased prevalence of sleep apnoea in the elderly include increased deposition of fat in the parapharyngeal area, lengthening of the soft palate, and changes in body structures surrounding the pharynx[28].

*Sex*: It is not clear why OSA is more common in men than women. It can be attributed to anatomical and functional properties of the upper airway and in the ventilatory response to the arousals from sleep[29]. Imaging studies have revealed that men have increased fat deposition around pharyngeal airway as compared with women[30]. Besides, hormonal differences may play a role in the predisposition to abnormal breathing during sleep[31]. Pre-menopausal women are relatively protected from OSA even if they have other known risk factors for OSA. In a cross-sectional prevalence study, it shows a four-fold higher prevalence of at least moderate OSA in post-menopausal women as compared with pre-menopausal women[16]. And interestingly, in post-menopausal women taking hormonal replacement therapy, the prevalence of OSA is similar to premenopausal women[16]. It would be of great interests to understand why female hormonal status may protect against the development of OSA in premenopausal women.

*Obesity*: Obesity / visceral obesity is the major risk factor for the development of OSA, it is thought to be associated with anatomic alterations that predispose to upper airway obstruction during sleep, by increasing adiposity around the pharynx and body. Central obesity has been associated with reduction in lung volume, which leads to a loss of caudal traction on the upper airway, and hence, an increase in pharyngeal collapsibility[32]. A number of previous epidemiological studies have investigated the associations between sleep apnoea and obesity. In a community-based cohort of middle-aged Caucasian subjects, a 1-SD increase in body mass index was associated with a four-fold rise in the prevalence of sleep apnoea[12], and 40 per cent of subjects from the community with OSA were moderately overweight but otherwise healthy[33]. In addition, subjects with severe obesity, BMI of >40, the prevalence of sleep apnoea was markedly increased to 40-90 per cent[34]. It was well demonstrated that a 10 per cent body weight reduction was associated with a parallel 26 per cent decrement in AHI[35]. Thus, weight reduction is an important conservative treatment for sleep apnoea.

*Family history and genetic predisposition*: Familial aggregation and genetics factors are thought to play a role in the development of OSA. First degree relatives of those with OSA increases the relative risk compared to those without OSA by 1.5 -2.0, and familial susceptibility to OSA increases directly with the number of affected relatives[36,37]. Obesity is closely associated with OSA and itself aggregates in families, so it is possible that familial aggregation of OSA is related to the genetics of obesity. Besides, apolipoprotein E (APOE) 4 is particularly associated with OSA in younger subjects, the odds ratio for

subjects with this allele who are < 65 yr of having an AHI > 15 is 3.1[38]. Craniofacial morphology represents another mechanism by which genetics may influence the development of OSA, the bony and soft tissue structures that are seen from one generation to another in different families, including specific craniofacial disorders, for example, Pierre-Robin syndrome, these patients have micrognathia, glossoptosis, and cleft palate, the tongue tends to prolapse backward, leading to airway obstruction, and hence, they are more prone to suffer from OSA[39]. Further research is warranted to define the genetic basis in OSA.

*Craniofacial abnormalities*: The structural factors in the upper airway may alter its mechanical properties. Differences in craniofacial morphology may explain some of the variation in risk for OSA in different ethnic groups. Previous studies have shown that craniofacial abnormalities are important in the pathogenesis of OSA, particularly in non obese patients[40]. Our study of computerized tomography of cephalometric analysis on 92 subjects with AHI ranging from normal to severe OSA, confirmed that Chinese subjects had inferiorly positioned hyoid bone and a retropositioned maxilla, contributing to a more severe degree of sleep-disordered breathing[40]. Furthermore, in an inter-ethnic study evaluated anthropometric parameters and craniofacial structures in 239 consecutive Chinese and Caucasian subjects from two different centres in Hong Kong and Canada, Chinese subjects had more crowded upper airways and relative retrognathia than the Canadians after controlling for body mass index and neck circumference[40].

*Smoking and alcohol consumption*: Cigarette smoking and alcohol have been shown to be risk factors for OSA. Smoking is associated with a higher prevalence of snoring and sleep-disordered breathing[41,42]. In Winconsin Sleep Cohort Study, current smokers had a much greater risk of moderate or worse degree of OSA (odds ratio, 4.44) compared with never smokers[43]. It can well be explained by the cigarette-induced airway inflammation and damage which could change the structural and functional properties of the upper airway, and increasing the risk of collapsibility during sleep. Alcohol relaxes upper airway dilator muscles, increases upper airway resistance and may induce OSA in susceptible subjects. Therefore, alcohol intake can prolong apnoea duration, suppress arousals, increase frequency of occlusive episodes and worsen the severity of hypoxaemia[44], however, the underlying mechanisms are not well understood.

**Natural history**

Obstructive sleep apnoea is a chronic condition with multiple potential associations with cardiometabolic sequelae. There is increasing awareness and recognition of OSA in our society today, because of the accumulating evidence of its contribution to atheroslerosis[45]. It has been considered as a systemic problem or a clinical manifestation of the metabolic syndrome, comprising a cluster of cardiometabolic risk factors, namely, hypertension, insulin resistance, dyslipidaemia and obesity[46]. Early observational studies in the 1980s, looked for the prevalence of OSA in different ethnic populations, and some longitudinal studies became more informative in time to define the natural history and associated risk factors with an increased prevalence in different subsets of the population. The 4-year Wisconsin Sleep Cohort Study[35] and the recent Sleep Heart Health Study[47] were the landmark studies of the impact of body weight changes on the severity of sleep apnoea. The overall incidence of moderate to severe OSA over a 5-year period was 11.1 per cent in men and 4.9 in per cent women. Men with >10 kg weight gain over the follow up period had five-fold risk of increasing their AHI by > 15. In contrast, for the same amount of weight gain, women had two and half fold risk of a similar increment in their severity of sleep apnoea[47]. Given the epidemic of obesity, and different cohorts of the effects of body weight changes on OSA, OSA patients are likely to be overweight or obese at presentation[48]. Hence, obesity does have a major impact on the evolution of sleep apnoea.

There have been increasing interest in the research on OSA and its cardiometabolic complications during the last 10 years. OSA is considered to be a long-standing illness and the associated complications seem to impose an economic burden in our society, affecting both developing and developed countries all over the world. There is evidence that OSA is associated with ischaemic heart disease, hypertension, stroke, arrhythmia, coagulability, diabetes mellitus, endothelial dysfunction and inflammation[49], and the implications of future research in these areas are highly encouraged in order to look into the general public health burden.

**Conclusions**

Sleep medicine is obviously a challenging field, evolving with new technology. There have been major new discoveries and growing evidence in clinical research studies, however, a number of key questions remain unanswered. The mechanisms by which sleep

apnoea contributes to increased cardiovascular risk are should be a focus for future basic and clinical research.

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