STUDY OF THE CLINICAL PREDICTORS OF OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME (OSAHS) IN BANGLADESHI ADULT POPULATION

Submitted by:
Dr AKM Mosharraf Hossain
Assoc. Prof. of Medicine (Respiratory Diseases)
Respiratory Wing, Department of Medicine
Bangabandhu Sheikh Mujib Medical University
Registration no: 143/2006-2007

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Declaration

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another neither person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of any university or institute of higher learning.

Dr AKM Mosharraf Hossain
Assoc Prof Respiratory Diseases
Department of Medicine, BSMMU

Forward

Certified that DR AKM MOSHARRAF HOSSAIN carried out this research titled 'Study of the Clinical Predictors of Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) in Bangladeshi adult population' and prepared this thesis under my direct supervision. I have found the work and the thesis submitted for the degree of Doctor of Philosophy in the Faculty of Postgraduate Medical Science and Research, Dhaka University is up to my full satisfaction.

Professor Md. Tahir
Ex-VC and Chairman
Deptt. of Medicine, BSMMU.

Dedication

This thesis is dedicated to
My wonderful parents who have raised me to be the person I am today
My wife who believe in the richness of learning
My children who made me keen on learning

Acknowledgment

Most of all thanks to the Almighty, the Allah who continues to make the impossible possible and granted me breath thus far to complete my thesis. .

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Abstract

Background: Obstructive sleep apnea hypopnea syndrome (OSAHS) is a recently appreciated contributor to morbidity and mortality in Bangladesh. Physicians are still not aware enough about the risk factors of OSAHS. This study was aimed to identify clinical and anthropometric risk factors of OSAHS in Bangladeshi adult population.

Methods: This is a case-control study. The study was performed from July 1, 2007 to June 30, 2009. A total of 190 subjects were included in the study following inclusion and exclusion criteria. Subjects who were diagnosed as obstructive sleep apnea hypopnea syndrome (OSAHS), were included in case group (n=65) and those non-OSAHS subjects were included in the control group (n=125).

Results: The mean (± SD) age of the study population was 42.97 ± 8.34 years, with 123 male (64.7%) participants. The subjects had a mean body mass index (BMI) of 25.63 ± 5.28 kg/m^2 (range, 18.30 to 39.81 kg/m^2). Habitual snoring and excessive daytime somnolence (EDS) were present in all OSAHS cases. Symptoms including witness apnea (81.5%), choking or gasping (61.5%), brief awakening from sleep (57.8%), feeling unrefreshed after sleep (79.6%), dry mouth during sleep (56.3%), morning headache (40.60%) and impotence (47.6%) were found more frequently in the OSAHS group and showed statistically significant differences between two groups ($P<.05$). Obesity as defined by BMI $\geq$ 25 kg/m^2 and other parameters of obesity were defined as Waist circumference (WC) > 102 cm in men and > 88 cm in women, Waist-hip ratio (WHR) of > 0.95 in men and > 0.8 in women, and Neck circumference (NC)>40 cm in men and >38 cm in women. These obesity parameters were compared between OSAHS and control groups and showed statistically significant differences ($P<.05$). In this study, ESS score

was used to quantify the degree of sleepiness and a cut off score ≥11 was labeled as sleepy. In this study, mean ESS (Epworth sleepiness scale) score in the OSAHS group was significantly higher than the non-OSAHS group (P <.001). The prevalence of hypertension (HTN) and diabetes mellitus (DM) were greater in OSAHS subjects, though the difference was significant statistically in HTN (P=.001). In this study, odd ratio for HTN was 2.91. Stepwise multiple logistic regression analysis revealed age≥46 (OR 6.00, 95% CI 1.45 to 25.46), obesity defined as waist circumference (WC) > 102 cm in men and > 88 cm in women (OR 25.15, 95%CI 5.20 to 121.24), higher education(OR 8.88, 95%CI 1.93 to 40.82), witnessed apnea (OR 125.12, 95%CI 19.75 to 792.71) and choking (OR 39.17, 95%CI 6.34 to 242.06) as risk factors of OSAHS in this study subjects.

Conclusion: Increased age, obesity parameter WC, higher education, witnessed apnea and choking were found to be independent predictors of OSAHS. These results strongly suggest that obesity is very important risk factor for OSASH in our study population. In addition, craniofacial features which were significant in OSAHS including macroglossia, retrognathia that reflect structural narrowing of the upper airway are readily identified and should prioritise patients for polysomnography of suspected OSAHS cases. Further large population based study will illuminate more in this emerging health problem.

Acronyms

AASM	American Academy of Sleep Medicine
AHI	Apnea-hypopnea index
ANOVA	Analysis of variance
ArI	Arousal index
BMI	Body mass index
CAD	Coronary artery disease
CPAP	Continuous positive airway pressure
COPD	Chronic obstructive pulmonary disease
DM	Diabetes mellitus
EDS	Excessive daytime sleepiness
EEG	Electro-encephalogram
EMG	Electromyography
EOG	Electro-oculography
ESS	Epworth Sleepiness Scale
GABA	Gamma amino butyric acid
GERD	Gastroesophageal reflux disease
HTN	Hypertension
ICSD-2	International classification of sleep disorders, version 2
M	Mean
MONICA	Monitoring trends and determinants in cardiovascular disease
MR	Magnetic resonance

MS	Mallampiti score
NC	Neck-circumference
NPSG	Nocturnal polysomnography
NREM	Non-rapid eye movement
OHS	Obesity hypoventilation syndrome
OR	Odd ratio
OSA	Obstructive sleep apnea
OSAHS	Obstructive sleep apnea hypopnea syndrome
P	Probability
PaCO2	Arterial carbon dioxide tension
PLMS	Periodic limb movement of sleep
PM	Portable monitoring
POCS	Polycystic ovary syndrome
PSG	Polysomnography
RDI	Respiratory disturbance Index
REM	Rapid eye movement
RG	Retroglossal
RERA	Respiratory effort related arousal
ROC	Receiver operating characteristic curve
RP	Retropalatal
SD	Standard deviation
SFT	Skinfold thickness
SF-36	Short form of the Medical Outcomes Study

SpO_2	Arterial oxyhemoglobin saturation
SPSS	Statistical Package for Social Science
SWS	Slow wave sleep
TMA	Thyromental angle
TMD	Thyromental distance
UARS	Upper Airway Resistance Syndrome
WC	Waist circumference
WHR	Waist/hip ratio

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1. Introduction

Sleep related breathing disorders are common, present in all age groups and result in significant morbidity and mortality. Eighty percent of patients presenting to sleep disorders centers have some kind of sleep related breathing disorders.[1] According to International classification of sleep disorders, version 2 (ICSD-2), the term obstructive sleep apnea (OSA) include those sleep related breathing disorders in which there is an obstruction in the airway resulting in increased breathing effort and inadequate ventilation.[2] The term OSA syndrome has been introduced initially to describe this condition with its central feature of daytime hypersomnolence and polysomnographically proven obstructive apneas.[3] After hypopnea has been described as respiratory events of shallow breathing causing oxygen desatuaration,[4] the OSA syndrome has been referred to as obstructive sleep apnea hypopnea syndrome (OSAHS).[5] So, OSAHS is characterized by recurrent episodes of complete or partial upper airway obstruction during sleep, in conjunction with excessive daytime sleepiness (EDS) and OSA also termed as sleep apnea hypopnea (OSAH) is defined by respiratory events as measured by polysomnography (PSG) criteria[5]. Sleep physicians already began to learn much about epidemiology of OSA from large prospective community based studies especially in western countries. The OSAHS is a highly prevalent disease, affecting middle aged 4% of men and 2% of women in United states.[6] In Asia, the prevalence of symptomatic OSA in middle aged men and women is 4.1–7.5% and 2.1–3.2% respectively, almost similar to those reported in Caucasian populations.[7] The prevalence of OSA among Korean adult was 27% and 16% in men and women and OSAHS was 4.5% and 3.2% in men and women respectively.[8] The population based studies in Hong Kong showed that 4.1% of

men and 2.1% of women of middle aged Chinese suffered from OSAHS.[9,10] In a recent study among 30-60 yrs aged semi-urban Indian showed prevalence rates of OSA and OSAHS were 13.74% and 3.57% respectively.[11] Significant clinical consequences of the disorder cover a wide spectrum including daytime hypersomnolence,[12] neurocognitive dysfunction,[13] cardiovascular disease (hypertension, stroke, myocardial infarction, heart failure),[14,15]metabolic dysfunction,[16] respiratory failure, and cor pulmonale.[17]

A number of risk factors have been found to be associated with OSA in different studies. Obesity has been identified as a strong risk factor and a number of parameters such as body mass index (BMI),[18-8] waist circumference (WC),[9,10] waist/hip ratio (WHR), neck-circumference (NC),[10,21] percentage of body fat and skinfold thickness (SFT)[20] have been studied to determine its association with OSA in several studies. Male gender,[10] age,[9] smoking and alcohol intake [21] have been found to be independent correlates of the apnea-hypopnea index (AHI) in some studies. Logistic regression analyses showed that sex, body mass index, and hypertension were closely associated with the risk of OSA among Asian Korean adult [8]. A recent study[22] among multiracial Singaporeans showed male sex, BMI, NC, ESS and lowest oxygen saturation as significant predictors for increasing severity of OSA based on AHI. Significant familial aggregation of OSA has also been observed in several studies.[23] A positive family history increases the risk of OSA by twofold to fourfold.[5]

Bangladesh is a developing country in south-east Asia where the first single bedded standard PSG laboratory was established at private level on 23rd June, 2005 under the supervision of the investigator. Snoring, daytime sleepiness, wake time tiredness and motor vehicle accidents are not less frequently seen among Bangladeshi population.

Obstructive sleep apnea (OSAHS) is a recently appreciated contributor to morbidity and mortality in Bangladesh. Physicians are still not aware enough about OSAHS. The diagnosis of OSAHS is very often delayed and sometimes difficult to establish for various reasons. Also the gold standard procedure PSG to establish OSAHS is limited, expensive and less feasible in some settings especially in developing nations with limited resources, like Bangladesh. So, selective performance of PSG should be done by appropriate referral using clinical parameters of OSAHS as screening tools in our setting. The investigator failed to find study on OSA and its risk factors among Bangladeshi adults. In a recent study among 30-60 years subjects of Dhanmondi, Dhaka, prevalence rates of OSAH and OSAHS were found to be 12.71 % and 3.75 % respectively.[24] In a questionnaire based pilot study among Bangladeshi adults,[25] [N: 96; sex (male/female): 66/30]; age [(yrs, m ± SD):33 ± 8] using the Berlin questionnaire and Epworth sleepiness scale (ESS) snoring and day time sleepiness was observed in 35% and 46% respectively. Both witness apnea and wake time tiredness was seen in 25%. About 41% subjects showed ESS score ≥11. After establishment of PSG laboratory, in another study,[26] 63 consecutive clinically suspected OSA patients were included. Among them 58 patients [age: (M±SD) 47±11.55 in yrs; sex: (m/f) 42/16] underwent in-laboratory nocturnal polysomnography (NPSG). Epworth sleepiness scale (ESS), sleep efficiency, apnea-hypopnea index (AHI), lowest oxygen saturation and parameters from sleep interview and anthropometric data were compared in OSAHS and non-OSAHS. In that PSG based study snoring, witness apnea, leg movements in sleep, dry throat, nocturia and ESS were shown to have significant relationship with OSAHS. Multiple regression analysis showed BMI, snoring and EDS as independent predictors of OSAHS.

The investigator planned this PSG based study to identify risk factors of OSAHS among Bangladeshi adults. These will be clinical tools to screen OSAHS patients and assist in early and appropriate referral for PSG study.

1.1. Research Questions:

a) What are the clinical risk factors of OSAHS for Bangladeshi adults?

b) What are the anthropometric risk factors of OSAHS for Bangladeshi adults?

1.2. Hypotheses:

Null hypothesis: there is no difference of clinical and anthropometric parameters between OSAHS and non-OSAHS patients among Bangladeshi adults.

Alternate hypothesis: there is difference of clinical and anthropometric parameters between OSAHS and non-OSAHS patients among Bangladeshi adults.

1.3. Aims and Objectives:

General objective: This study was planned to evaluate risk factors of obstructive sleep apnea hypopnea syndrome (OSAHS) in Bangladeshi adults.

Specific objectives: i) to identify clinical and anthropometric risk factors of OSAHS patients among Bangladeshi adults,

ii) to evaluate symptoms of OSAHS patients

iii) to compare symptoms of OSAHS between male and female and

vi) to develop an accessible and less expensive algorithm to approach a case of OSAHS among Bangladeshi adults and assist in appropriate referral for NPSG study.

2. Literature Review

2.1. Overview of Normal Human Sleep: Sleep is a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment.[27] Sleep is a brain process. The body rests but the brain sleeps. This is not to say that body does not require sleep; there are essential body processes that occur only when the brain is asleep. Sleep is not a unitary phenomenon. There are several types of sleep, each with their own particular characteristics, functions and regulatory systems. Because sleep is a brain process, the traditional approach to study sleep began by measuring brain activity. The first great step forward toward the modern understanding of human sleep was taken by Berger who made the first sleep recording and noted that the alpha rhythm disappeared when his subject fell asleep.[28] The second major step occurred within a decade when the first continuous overnight EEG sleep recordings in humans were published in 1937 by Loomis et al and sleep staging was summarized.[29]

Sleep is promoted by neurons in the lower brainstem and upper forebrain that inhibit wake-generating neurons to dampen cortical activation and behavioral arousal.[30] During REM sleep, the cerebral cortex is activated, whereas muscle tone along with behavioral arousal is inhibited. Many of the central activating systems including the brainstem reticular formation are active during this state. Wakefulness is maintained by multiple neural systems that extend from the brainstem reticular formation into the thalamus and through the posterior hypothalamus up to the basal forebrain.

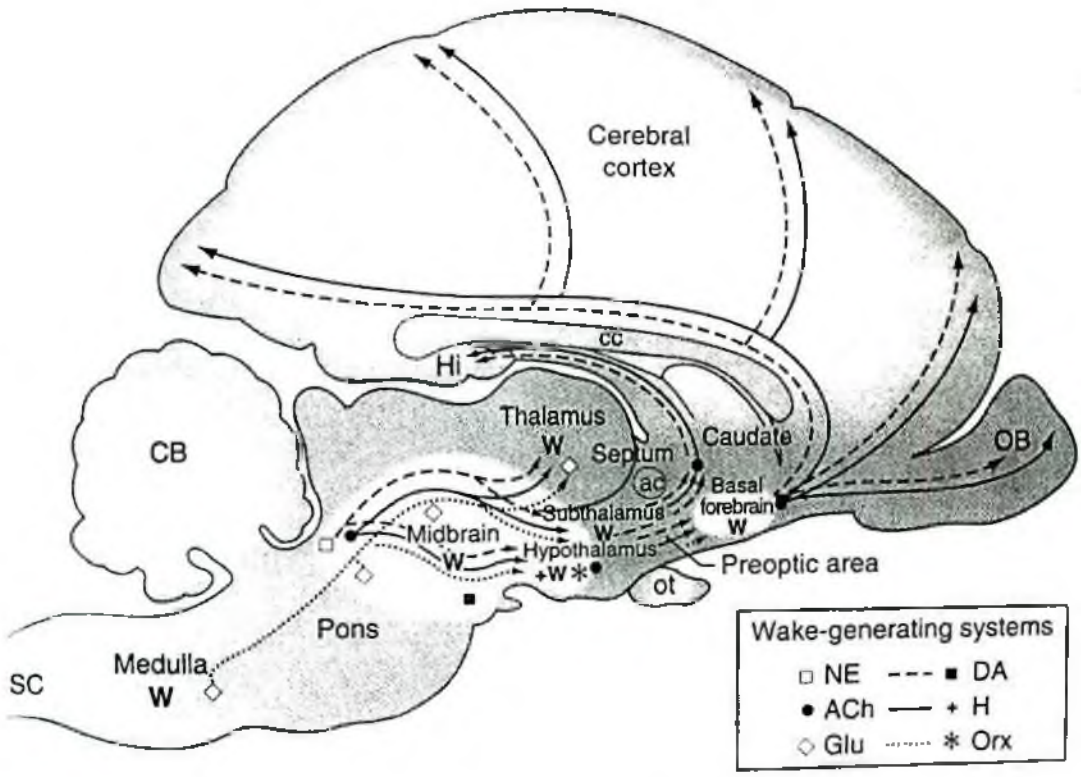

Figure 1: A drawing showing neural systems generating wakefulness. Points marked with 'W'(waking) indicate regions where high frequency electrical stimulation produces cortical activation and arousal. (**ac**, anterior commissure; **•Ach**, acetylcholine—; **CB**, cerebellum; **cc**, corpus callosum; **■DA**, dopamine----; **◊Glu**, glutamate….; **+H**, histamine —; **Hi** hippocampus; **□NE**, norepinephrine----; **OB**, olfactory bulb; **ot**, optic tract; ***Orx**, orexin….; **SC**, spinal cord)

The arousal system involved in wake generation utilizes a number of different neurotransmitters such as glutamate, noradrenaline, acetylcholine, dopamine, glutamic acid, histamine and orexine. Slow wave sleep occurs through the inhibition of the arousal systems. The key neurotransmitters involved in sleep generation are adenosine, GABA, acetylcholine during REM sleep, glycine and some immune modulators.[31]

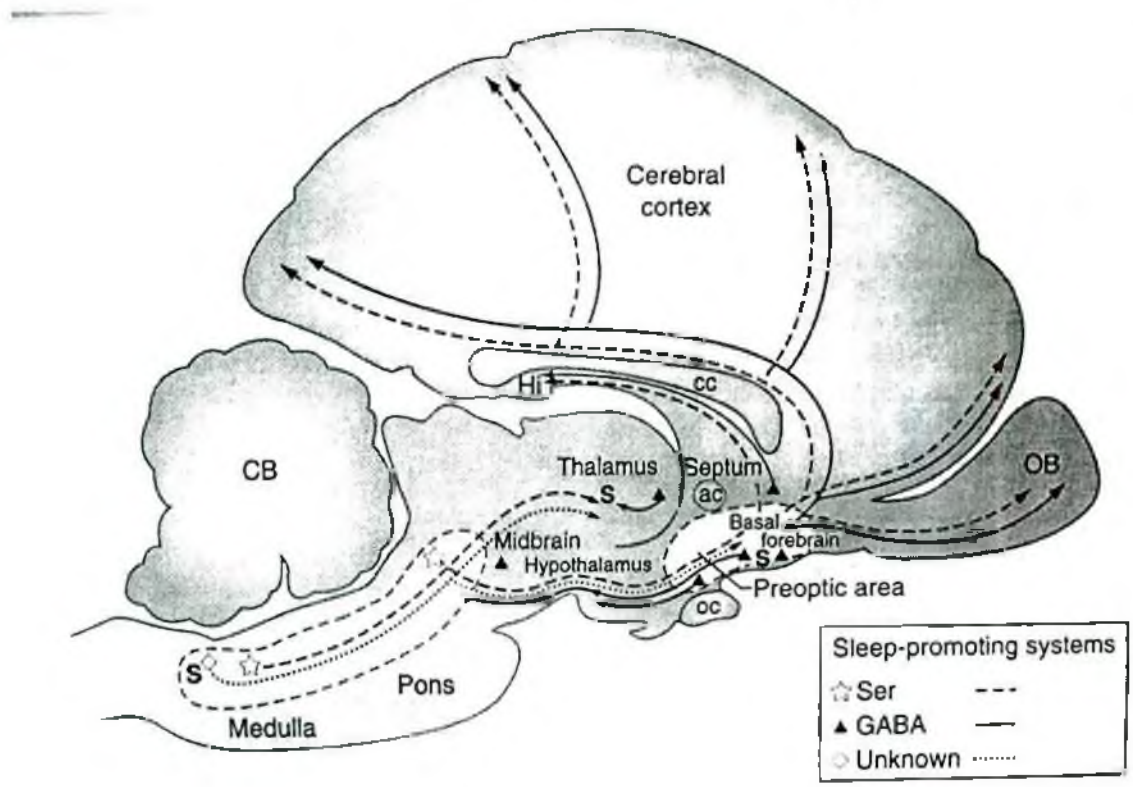

Figure 2: Neural systems promoting slow wave sleep. Points marked with 's' (slow wave sleep) indicate regions where low frequency electrical stimulation produces cortical synchrony and behavioral sleep (ac, anterior commissure; CB, cerebellum; cc, corpus callosum; Hi hippocampus; OB, olfactory bulb; oc, optic chiasma ☆ Ser---; ▲ GABA — ;◇Unknown.....).

2.2. Normal Sleep Architecture:[32] Electro-encephalograph (EEG) and other physiological recordings during sleep define two distinct states of sleep: rapid eye movement (REM) sleep and non-REM (NREM) sleep. The latter is divided into four different stages: stage 1 (light sleep), stage 2 (consolidated sleep), and stages 3 and 4 (deep, or slow wave sleep). Division of sleep into these stages relies on three physiological variables: EEG, electromyography (EMG) and electro-oculography (EOG) as demonstrated in Table 1.

Table1: Physiological characteristics of the various stages of sleep

	EEG	**EMG**	**EOG**
Wake	α, β	Very high	Rapid
Stage 1	Some θ	High	Slow
Stage 2	θ, Spindles	Some	Rare
Stage 3	Moderate δ	Low	Rare
Stage 4	Much δ	Low	Rare
REM	Fast(θ,α)	Absent	Rapid

The length and content of sleep cycles change throughout the night as well as with age. The relative percentage of deep sleep is highest in the first sleep cycle and decreases as the night progresses, whereas the relative length of REM sleep episodes increases throughout the course of the night. When totaling the various sleep stages through the night in normal young adults, stage 1 occupies up to 5% of the night, stage 2 occupies 50%, and REM sleep and slow wave sleep (SWS) 20–25% each. These relative percentages change with age, as does the cycle length. In infants the normal cycle of sleep lasts about an hour, whereas in adults it lasts about 1.5 hours. Table 2 demonstrates the percentages of different sleep stages and sleep length at different ages.

Table 2: Changes in sleep content and length with age

	Sleep Time(h)	**Stage 1-2(%)**	**Stage 3-4(%)**	**REM (%)**
Infants	13–16	10–30	30–40	40–50
Children	8–12	40–60	20–30	20–30
Adults	6–9	45–60	15–25	15–25
Elderly people	5–8	50–80	5–15	15–25

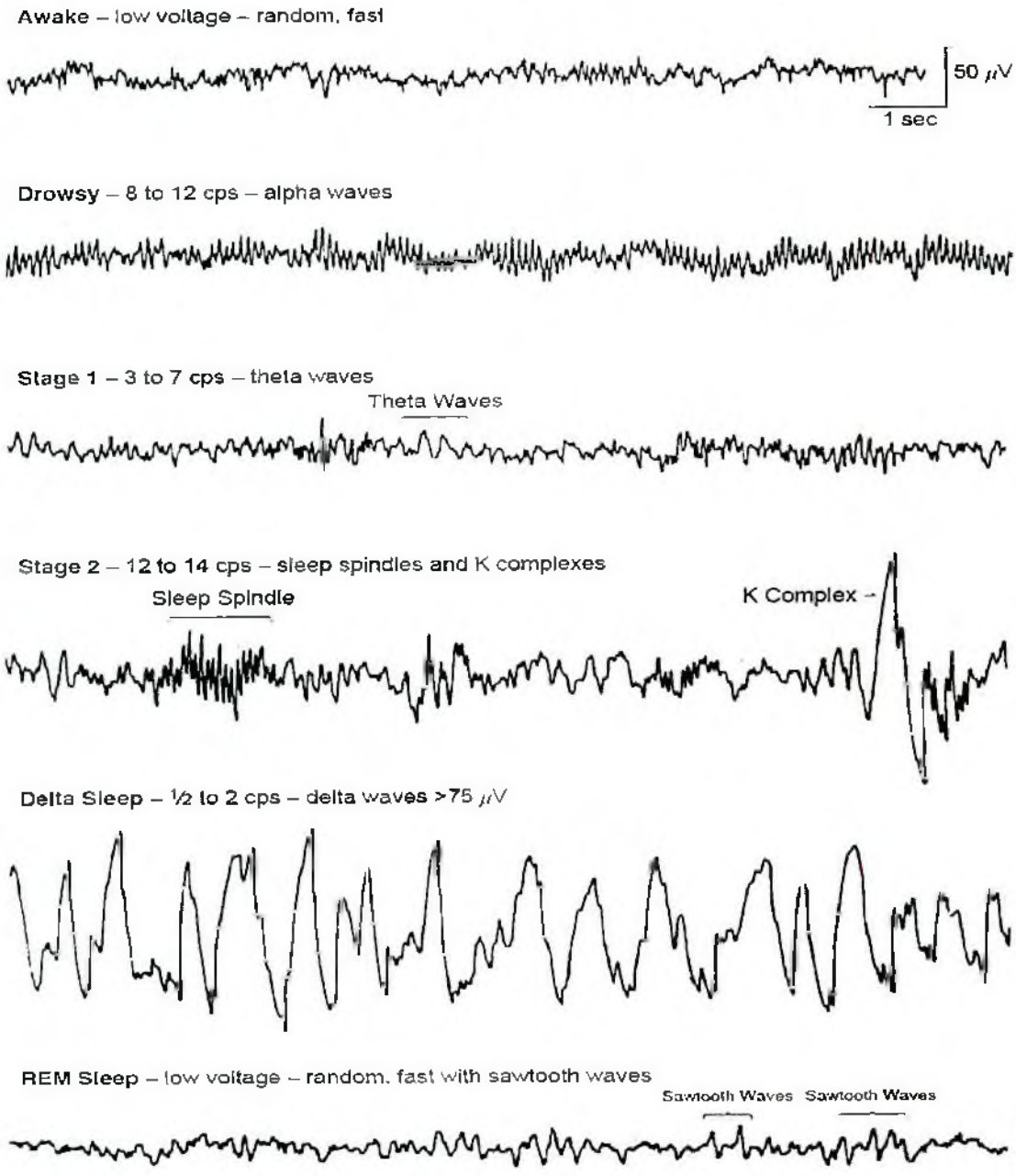

Figure 3: EEG patterns of human sleep states and stages

Stage 1 is characterized by relatively low-amplitude θ (theta) activity intermixed with episodes of α/θ activity. In stage 2 there are K-complexes and sleep spindles, whereas stages 3 and 4 are dominated by increasing amounts of slow-wave high-amplitude δ (delta) activity (Figure 3).

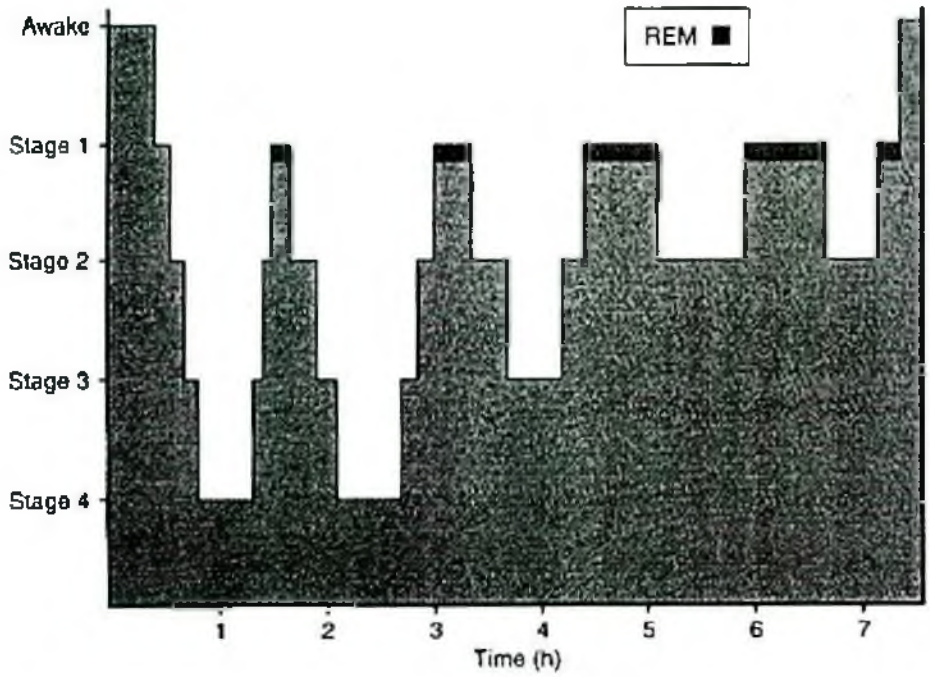

Figure 4: The characteristics of sleep architecture over a 7.5-hour sleep period

2.3. Classification of sleep disorders: The 2nd edition of the International Classification of Sleep Disorders (ICSD-2) was published by the American Academy of Sleep Medicine in 2005.[33] This system classifies sleep disorders into eight major categories including 70 specific diseases:

1. Insomnia,
2. Sleep related breathing disorders,
3. Hypersomnias of central origin,
4. Circadian rhythm sleep disorders,
5. Parasomnias,
6. Sleep related movement disorders,
7. Isolated symptoms and normal variants,
8. Other sleep disorders

2.4. Classification of Sleep Related Breathing Disorders: Sleep related breathing disorders occur in both adults and children.[33] there are three major sleep related breathing disorders:

1. Central sleep apnea syndromes,
2. Obstructive sleep apnea syndromes and,
3. Sleep related hypoventilation/hypoxemia syndromes.

These syndromes are further divided according to their etiology: The central sleep apnea syndromes include i) primary central sleep apnea, ii) central sleep apnea due to Cheyne-Stokes breathing, iii) central sleep apnea due to high altitude periodic breathing, iv) central sleep apnea due to a medical condition, v) central sleep apnea due to drug, medication, or substance use, and vi) primary sleep apnea of infancy.

The obstructive sleep apnea syndromes include i) adult obstructive sleep apnea-hypopnea and ii) pediatric obstructive sleep apnea-hypopnea. The sleep related hypoventilation/hypoxemia syndromes include i) idiopathic sleep related non-obstructive alveolar hypoventilation, ii) congenital central alveolar hypoventilation syndrome, and iii) sleep related hypoventilation/hypoxemia due to a medical condition.

2.5. Sleep Related Breathing Disorders Definitions: Sleep disordered breathing refers to an abnormal respiratory pattern (i.e., apneas, hypopneas, or respiratory effort related arousals) or an abnormal reduction in gas exchange (i.e., hypoventilation) during sleep. It alters sleep duration and architecture if repetitive, which may result in daytime symptoms, signs, or organ system dysfunction. Sleep-disordered breathing is best characterized by polysomnography that has captured one or more periods of rapid eye

movement (REM) sleep because severe perturbations can be common during REM sleep.[34-5]

- **Apnea:** Apnea is the cessation, or near cessation, of airflow. It exists when airflow is less than 20 percent of baseline for at least 10 seconds in adults.[28] In children, the duration criteria are shorter. Three types of apnea may be observed during sleep: a) **Obstructive apnea** — an obstructive apnea occurs when airflow is absent or nearly absent, but ventilatory effort persists. It is caused by complete, or near complete, upper airway obstruction (figure 5), b) **Central apnea — A** central apnea occurs when both airflow and ventilator effort are absent (figure 6), and c) **Mixed apnea** — During a mixed apnea, there is an interval during which there is no respiratory effort (i.e., central apnea pattern) and an interval during which there are obstructed respiratory efforts (figure 7). The central apnea pattern usually precedes the obstructive apnea pattern during mixed apnea.

Obstructive sleep apnea

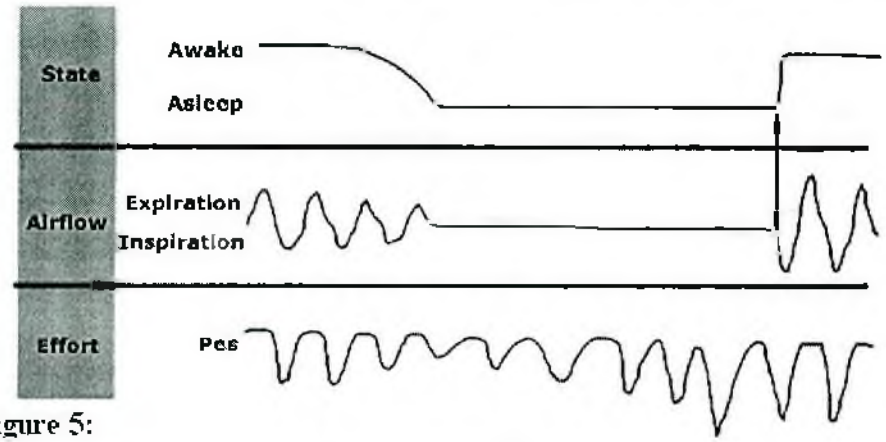

Figure 5:

Obstructive sleep apnea in which there is continuing respiratory effort, as shown by progressively increasing fluctuations in esophageal pressure (Pes) at the time of cessation of airflow. The arrow illustrates that arousal in obstructive apnea occurs simultaneously with the resumption of airflow.

Central sleep apnea

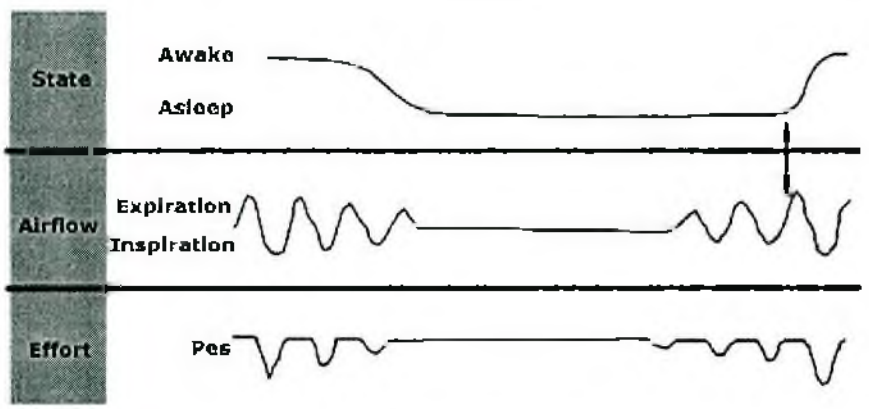

Figure 6:

There is no respiratory effort, as shown by absence of changes in esophageal pressure (Pes), at the time of cessation of airflow. The arrow illustrates that arousal in central apnea typically occurs in the middle of the hyperpneic phase.

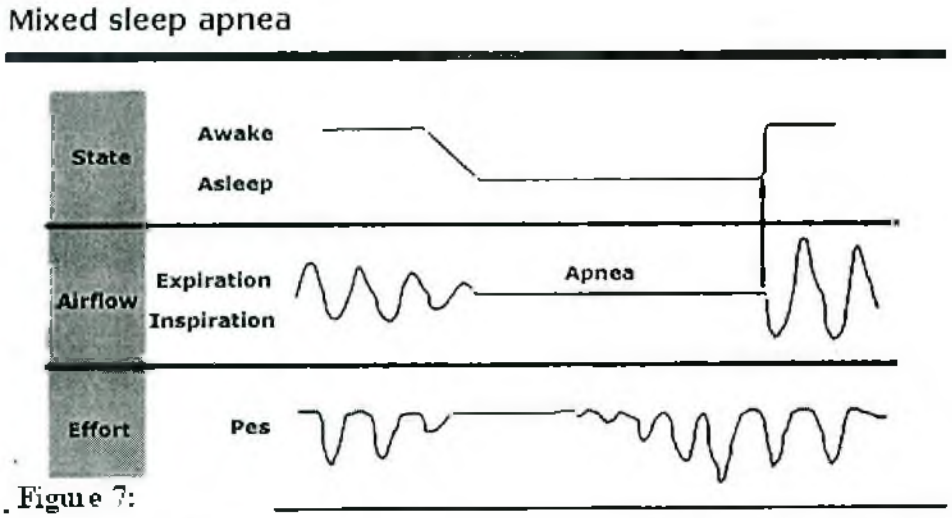

Figure 7:

The apnea initially appears as a central apnea (without respiratory effort as evidenced by the constant esophageal pressure [Pes]). This is followed by a period of obstructive apnea (with respiratory effort as evidenced by changes in esophageal pressure).

- **Hypopnea** — Hypopnea is a reduction of airflow to a degree that is insufficient to meet the criteria for an apnea. A precise deflnition has varied over time, according to technology, expert opinion, and reimbursement guidelines. The most recent definition, endorsed by the American Academy of Sleep Medicine, recommends that hypopnea be scored when all of the following four criteria are met:[34]

1. Airflow decreases at least 30 percent from baseline,
2. There is diminished airflow lasting at least 10 seconds,
3. At least 90 percent of the duration of diminished airflow is spent with airflow that is at least 30 percent less than baseline and,
4. Decreased airflow is accompanied by at least 4 percent oxyhemoglobin desaturation

Alternative scoring criteria are also endorsed as follows:

1. Airflow decreases at least 50 percent from baseline,
2. There is diminished airflow lasting at least 10 seconds,
3. At least 90 percent of the duration of diminished airflow is spent with airflow that is at least 30 percent less than baseline, and
4. Decreased airflow is accompanied by at least 3 percent oxyhemoglobin desaturation or an arousal.

- **Respiratory effort related arousals** — Respiratory effort related arousals (RERAs) exist when there is a sequence of breaths that lasts at least 10 seconds, is characterized by increasing respiratory effort or flattening of the nasal pressure waveform, and leads to an arousal from sleep, but does not meet the criteria of an apnea or hypopnea.[34] The inspiratory airflow or tidal volume is maintained during these episodes, but requires increased respiratory effort.[33-4] RERAs are often accompanied by a terminal snort or an abrupt change in respiratory measures. Daytime sleepiness, fatigue, or inattention can result from microarousals (i.e., electroencephalographic activation lasting three seconds or less), despite the absence of apneas or hypopneas. Snoring may or may not be a prominent complaint. These symptoms are reduced by treatment that alleviates RERAs.
- **Upper airway resistance syndrome (UARS):** RERAs (>5 events per hour) that are associated with daytime sleepiness were previously called upper airway resistance syndrome (UARS), are now termed as obstructive sleep apnea (OSA).[33]

- **Apnea-Hypopnea Index:** The **AHI** is derived from the total number of apneas and hypopneas divided by the total sleep time.
- **Respiratory Disturbance Index (RDI):** The RDI is defined as the number of obstructive apneas, hypopneas, and respiratory event–related arousals (RERAs) per hour. The RDI is preferred over the AHI because it includes flow-limitation events that end with arousals. The RDI is best suited to meet the new AASM diagnostic criteria for OSA.
- **Arousal index:** The arousal index (ArI) is the total number of arousals per hour of sleep. It is generally lower than the AHI or RDI because approximately 20 percent of apneas or hypopneas are not accompanied by arousals that are evident on polysomnography. However, the ArI can be greater than the AHI or RDI if arousals occur due to causes other than apneas or hypopneas. As examples, arousals can be caused by periodic limb movements, noise, and sleep state transitions.
- **Obstructive sleep apnea hypopnea syndrome:** According to American Academy of Sleep Medicine (AASM) task force report[5] an individual must fulfill criterion A or B, plus criterion C to be diagnosed as Obstructive sleep apnea hypopnea syndrome (OSAHS):

A. Excessive daytime sleepiness that is not better explained by other factors;

B. Two or more of the following that are not better explained by other factors:

-choking or gasping during sleep,

-recurrent awakenings from sleep,

-unrefreshing sleep,

-daytime fatigue,

-impaired concentration; and/or

C. Overnight monitoring demonstrates five or more obstructed breathing events per hour during sleep. These events may include any combination of obstructive apneas/hypopneas or respiratory effort related arousals.

- **Obesity Hypoventilation Syndrome (OHS):** OHS also known as the Pickwickian Syndrome is defined as obesity with alveolar hypoventilation (awake arterial carbon dioxide tension [PaCO2] >45 mmHg) that exists in the absence of other conditions known to cause hypoventilation.[36-37] All patients with OHS have sleep disordered breathing with oxyhemoglobin desaturation during sleep and most have OSA.

2.6. Diseases Spectrum:

- **Normal** — Healthy individuals may experience apneas and hypopneas at sleep onset or during rapid eye movement (REM) sleep. Such events are less than ten seconds in duration and are not repetitive. Occasionally, an isolated apnea lasting up to 30 seconds may occur during REM sleep.[38] These episodes are infrequently accompanied by arousals, sleep-state changes, or hypoxemia. There are no known clinical sequelae.
- **Snoring** — Snoring is common and its frequency increases with age. It is estimated that 45 percent of men and 30 percent of women older than 65 years snore.[39] Those individuals who snore on a regular basis, but have an AHI less than five events per hour, are probably at risk for developing OSA. So, treatment for heavy snoring in the absence of OSA is done for social reasons.

- **Symptomatic** — Patients with OSA have an AHI greater than five events per hour. In addition, most have sleep related symptoms and signs, which improve with treatment. Such patients can be classified as having mild, moderate, or severe disease:[40]

    1. **Mild** — Such patients usually have an AHI between 5 and 15 events per hour. The respiratory disturbance index (RDI) may be higher than the AHI because respiratory effort related arousals (RERAs) are often more frequent than apneas and hypopneas.[41] Patients with mild OSA generally have "passive" or sedentary daytime sleepiness, which does not impair daily activity or behavior. The daytime sleepiness may be inapparent to the patient, but recognized by family members. Alternatively, it may become apparent to the patient after treatment of apnea, weight loss, or alcohol abstinence. Systemic hypertension, corpulmonale, or polycythemia are absent, with the oxygen saturation during sleep below 90 percent for less than 5 percent of the total sleep time. Sleep stages and slow wave sleep are preserved. Approximately 30 percent of patients with mild OSA will tolerate and respond to treatment with nasal CPAP, with a reduction in daytime sleepiness and blood pressure.[42]
    2. **Moderate** — Such patients generally have an AHI between 15 and 30 events per hour. Patients with moderate OSA are generally aware of their daytime sleepiness and take steps to avoid falling asleep at inappropriate times (e.g., taking a nap or avoiding driving). Such patients are able to continue their daily activities, but at reduced levels. Patients with

moderate OSA may have an increased incidence of motor vehicle violations or accidents. Hypertension may exist, but daytime signs or symptoms of corpulmonale are usually absent. Sleep fragmentation is observed, but the progression of sleep stages is better conserved than with severe disease. Patients with moderate OSA usually respond to nasal CPAP with an improvement in the daytime sleepiness, quality of life, and blood pressure.

3. **Severe** — these patients generally have more than 30 apneas per hour of sleep and oxygen saturation below 90 percent for more than 20 percent of the total sleep time. Patients with severe OSA have disabling daytime sleepiness that interferes with normal daily activities; in addition, there are signs of cardiopulmonary failure, nocturnal angina, polycythemia, or corpulmonale. Such patients fall asleep during the day, in a sitting posture, and are at risk for accidental injury. Patients with severe OSA benefit from prompt therapeutic intervention.[42] Treatment will improve daytime sleepiness, hypertension, and, possibly, other hypoxemia-related abnormalities, such as polycythemia and corpulmonale.

2.7. Risk Factors of OSAHS: Knowledge of risk factors for obstructive sleep apnea is therefore crucial to properly direct diagnostic attention at those with the highest risk. In the following sections, several of the key risk factors for obstructive sleep apnea are briefly discussed:

1. Age: Epidemiologic surveys reveal that more than 50% of adults over the age of 65 years have some form of chronic sleep-related complaints.[43] Moreover, one of the prevailing characteristics of sleep with advancing age is the significant variability in objective sleep parameters. The age-related variability in subjective and objective sleep parameters is, in part, related to the high prevalence of obstructive sleep apnea with advancing age. In one of the earliest studies, Ancoli-Israel and colleagues,[44] reported that 70% of men and 56% of women between 65 and 99 years of age had obstructive sleep apnea defined as an AHI of at least 10 events per hour. Subsequent studies from several population-based cohorts confirm the high prevalence of SDB in older individuals. In a probability sample from two Pennsylvania counties, obstructive sleep apnea prevalence was shown to progressively increase with age.[45-6] In men, obstructive sleep apnea (AHI ≥ 10 events/h) was present in 3.2%, 11.3%, and 18.1% of the 20- to 44-year, 45- to 64-year, and 61- to 100-year age groups, respectively.[45] Using the youngest group as the reference category, the odds ratio for an AHI greater than or equal to 10 events per hour for those in the 65- to 100-year age group was 6.6 (95% confidence interval, 2.6–16.7). In a separate analyses of women from the same cohort, the prevalence of obstructive sleep apnea (AHI ≥15 events/h) was 0.6%, 2.0%, and 7.0% for the 20- to 44-year, 45- to 64-year, and 61- to 100-year age groups, respectively.[46] Disease prevalence was lowest in pre-menopausal women (0.6%) and intermediate in post-menopausal women on hormone replacement therapy (1.1%). In contrast, the prevalence of obstructive sleep apnea was relatively high (5.5%) in post-menopausal women not on hormone replacement therapy.[46] Data from the community-based Sleep Heart Health Study have shown that disease prevalence increases steadily with age and reaches a plateau after the age of 60 years.[47] Similar trends with

increasing age have also been noted in other cohorts in which the prevalence of moderate to severe obstructive sleep apnea (AHI ≥15–20 events/h) remains relatively constant after the sixth decade of life.[48] Mechanisms proposed for the age-related increase in prevalence include increased deposition of fat in the parapharyngeal area, lengthening of the soft palate, and changes in body structures surrounding the pharynx.[49-50]

2. Excess Body Weight: Excess body weight is a common clinical finding and is present in more than 60% of the patients referred for a diagnostic sleep evaluation.[51] Epidemiologic studies from around the world have consistently identified body weight as the strongest risk factor for obstructive sleep apnea. In the Wisconsin Sleep Cohort study, a one standard deviation difference in body mass index (BMI) was associated with a 4-fold increase in disease prevalence.[7] Other population- and community-based studies conducted in the United States and abroad have since confirmed that excess body weight is uniformly associated with a graded increase in obstructive sleep apnea prevalence.[8,18,19,52] Moreover, longitudinal data from the Sleep Heart Health Study, Wisconsin Sleep Cohort Study, and the Cleveland Family Study show that an increase in body weight over time can certainly accelerate the progression of obstructive sleep apnea or lead to development of moderate to severe disease.[53-55] Although limited by small study samples and the lack of appropriate control groups, the unvarying observation is that weight loss by any means (i.e., surgery or caloric restriction) can improve severity of disease in many patients and may be completely curative in some.[56]

Despite the unquestionable link between obesity and obstructive sleep apnea, controversy remains as to whether specific measures of body habitus (e.g., neck circumference, waist

circumference) that reflect a central versus peripheral distribution of fat are associated with an increased risk for obstructive sleep apnea after controlling for BMI.[57] Nonetheless, cross-sectional analyses of the Sleep Heart Health Study data show that, in middle-aged and older adults, moderate to severe obstructive sleep apnea, as defined as an AHI greater than or equal to 15 events per hour, is independently associated with BMI, neck circumference, and waist circumference.[47] Increases in body weight can alter normal upper airway mechanics during sleep through several distinct mechanisms including: (1) increased parapharyngeal fat deposition resulting in a smaller upper airway, (2) alterations in neural compensatory mechanisms that maintain airway patency, (3) respiratory control system instability, and (4) reduction in functional residual capacity with a resultant decrease in the stabilizing caudal traction on the upper airway.[58]

3. Sex: It has long been recognized that men have greater vulnerability than women toward developing obstructive sleep apnea. Clinic-based studies have shown that, in patients referred for clinical evaluation, the ratio of men to women is in the range from 5 to 8:1.[51] Epidemiologic studies have confirmed the higher prevalence of obstructive sleep apnea in men but report a lower male-to-female ratio in the range 2 to 3:1.[6,46,48] Several explanations exist for the disparity in sex differences between clinic- and population-based studies. First, it is possible that men and women with obstructive sleep apnea have distinct symptom profiles, with women possibly not reporting the classical symptoms, namely loud snoring, nocturnal snorting or gasping, and witnessed apneas.[59] In fact, analyses from different referral centers show that women with obstructive sleep apnea have a greater tendency to report symptoms of fatigue and lack of energy than men.[60-61] Second, differential response of the bed-partner to the symptoms of obstructive breathing

during sleep may also contribute to the clinical under recognition of the disorder in women. Although systematic evaluations of sex differences in the response to snoring and breathing pauses have not been conducted, female bed partners of male patients appear to have a lower threshold for symptom perception and reporting than male bed partners of female patients.[62] Finally, it is also possible that health care providers have a lower index of suspicion for considering obstructive sleep apnea in men than women given the general expectation that the disorder predominantly affects men.

In addition to the differences in prevalence, polysomnographic characteristics of sleep and breathing patterns also differ between women and men. Women tend to have a lower AHI in non–rapid eye movement (non-REM) sleep but have a similar AHI in REM sleep. Moreover, disordered breathing events in women have a shorter duration and are associated with less oxyhemoglobin desaturation than in men.[63] The male predisposition for the disorder has been attributed to sex differences in anatomical and functional properties of the upper airway and in the ventilatory response to arousals from sleep.[64] Hormonal influences are also likely to have an important role in pathogenesis of obstructive sleep apnea, as disease prevalence is higher in post- versus pre-menopausal women.[46] Furthermore, hormone replacement therapy in post-menopausal women has been associated with a lower prevalence in epidemiologic studies.[46,65] Finally, although there are limited controlled data, exogenous androgen therapy in men and women can aggravate obstructive sleep apnea severity.

4. Race: Until recently, most of the population-based studies on the prevalence of obstructive sleep apnea were focused on characterizing disease prevalence in North America, Europe, or Australia. With the increasing appreciation that obstructive sleep

apnea can lead to serious medical sequelae, several studies have been undertaken to characterize the disease burden in countries including China, India, and Korea. These studies show that the prevalence of obstructive sleep apnea in Asians is comparable to that documented in North American and European samples. An interesting and unexpected observation that has emerged is that, while Asians are less obese than whites, disease prevalence in the East is no less than in the West. Moreover, for a given age, sex, and BMI, Asians have greater disease severity than whites.[66-7] Differences in craniofacial features between Asians and whites have been demonstrated and are considered as the etiologic factors for the increased risk and greater severity of obstructive sleep apnea in Asians despite lesser degrees of obesity.[68]

5. Craniofacial Anatomy: Several soft and hard tissue factors can alter the mechanical properties of the upper airway and increase its propensity to collapse during sleep. Static cephalometric analyses using radiography, computerized tomography, and magnetic resonance imaging have revealed a number of skeletal and soft-tissue structural differences between individuals with and without obstructive sleep apnea during wakefulness. Features such as retrognathia, tonsillar hypertrophy, enlarged tongue or soft palate, inferiorly positioned hyoid bone, maxillary and mandibular retroposition, and decreased posterior airway space can narrow upper airway dimensions and promote the occurrence of apneas and hypopneas during sleep.[69] Even in the absence of clinically obvious craniofacial abnormalities, subtle differences in maxillary or mandibular size can increase the vulnerability for obstructive sleep apnea. A meta-analysis of studies investigating the craniofacial risk factors showed that mandibular body length is a craniofacial measure with the strongest association with increased risk.[70] Some recently

investigated clinical parameters of craniofacial profile including (a) thyromental distance (TMD)-the horizontal distance from the thyroid prominence to a perpendicular dropped from the soft tissue mentum, measured with a modified tape measure with a vertical attachment, (b) thyromental angle (TMA)- the angle between the soft tissue plane of the anterior neck and a plane running through the soft tissue mentum and the thyroid prominence, measured from a lateral photograph of the head and neck taken in the natural head position with the patient looking straight ahead were proved to be strong predictor of OSAHS among Asians.[68] Comparisons between Chinese Asians and whites show that Chinese patients with obstructive sleep apnea have a more crowded upper airway and relative retrognathia compared with their white counterparts after controlling for BMI and neck circumference.[68] In addition, Asians have other craniofacial features which increase disease predisposition, including a shorter cranial base and a more acute cranial base flexure.[67] Collectively, such studies confirm that craniofacial abnormalities are important in pathogenesis of obstructive sleep apnea, particularly in non-obese patients. Moreover, given that different racial groups are inclined to develop obstructive sleep apnea at varying degrees of obesity, clinicians should consider the possibility of this disorder particularly in the presence of clinically detectable craniofacial abnormalities.

6. Familial and Genetic Predisposition: Familial aggregation of obstructive sleep apnea was first recognized in the 1970s by Strohl and coworkers in a family with several affected individuals.[71] Since then, several large-scale studies have confirmed a role for inheritance and familial factors in the genesis of obstructive sleep apnea.[72] First-degree relatives of those with the disorder are more likely to be at risk compared with first-degree relatives of those without the disorder. Familial susceptibility to obstructive sleep

apnea increases directly with the number of affected relatives.[73] Genome-wide association scans have identified susceptibility loci for obstructive sleep apnea and show that linkage patterns for the disorder may differ between whites and African Americans.[74] However, some has been argued that confounding factors, such as obesity, prohibit definitive conclusions on genetic underpinnings for obstructive sleep apnea and that additional studies are needed to further define whether the disorder truly has a genetic component.[75]

7. Smoking and Alcohol Consumption: Cigarette smoking and alcohol have been suggested as possible risk factors for obstructive sleep apnea. Epidemiologic investigations show that current smoking is associated with a higher prevalence of snoring and obstructive sleep apnea.[76,77] Even exposure to second-hand smoke has been independently linked with habitual snoring.[78] Because former smokers do not manifest the increased risk for obstructive sleep apnea, airway inflammation and damage due to cigarette smoke could alter the mechanical and neural properties of upper airway and increase its collapsibility during sleep. Ingestion of alcohol before sleep has been shown to increase upper airway collapsibility and the precipitate obstructive apneas and hypopneas during sleep. Alcohol ingestion can induce apneic activity in normal or asymptomatic individuals.[79] Alcohol intake can prolong apnea duration and worsen the severity of associated hypoxemia.[80]

8. Medical Comorbidity: Besides the unfavorable effects on daytime sleep tendency and cognitive performance, OSA is an established cause of secondary hypertension (HTN).[81] It also has been implicated in the etiology of cardiovascular conditions, including coronary artery disease, congestive heart failure, and stroke. Although evidence for causal associations with other medical conditions is likely forthcoming, the lack of such

associations with prevalent health outcomes should not annul the clinical and public health significance of obstructive sleep apnea. For example, the Wisconsin Sleep Cohort Study has shown that obstructive sleep apnea is independently associated with prevalent diabetes mellitus.[82] In that study, obstructive sleep apnea was also associated with incident diabetes mellitus, but the association was not statistically significant after adjusting for BMI and waist circumference. Even if obstructive sleep apnea is eventually found not to be a harbinger of excess metabolic risk, the high prevalence of this condition in those with diabetes mellitus because of underlying obesity cannot be neglected. Identification of obstructive sleep apnea is of clinical significance, as early intervention may directly or indirectly enhance glycemic control. It is possible that intermittent hypoxemia and sleep disruption of obstructive sleep apnea are deleterious to glucose homeostasis and alleviating obstructive breathing during sleep with continuous positive airway pressure therapy has direct effects in improving hyperglycemia. Alternatively, treatment can diminish daytime fatigue, foster increase in physical activity, and thus result in improved metabolic control. Similarly, patients with other comorbid conditions such as coronary artery disease could experience direct and indirect benefits with early identification and treatment of undiagnosed disease. The potential of such improvements emphasizes the fact that in the presence of medical conditions such as uncontrolled hypertension, coronary artery disease, congestive heart failure, stroke, and diabetes mellitus, undiagnosed obstructive sleep apnea should be considered as a possible concomitant problem.

9. Other Risk Factors: There are several conditions that have been associated with an increased prevalence of obstructive sleep apnea. These conditions include polycystic

ovary syndrome, hypothyroidism, and pregnancy. Polycystic ovary syndrome (PCOS) is a clinical syndrome that is diagnosed in the presence of oligomenorrhea and signs of androgen excess. Although limited by small samples, a number of studies have shown a high prevalence (~60–70%) of obstructive sleep apnea in women with PCOS.[83] Visceral adiposity and higher androgen levels may predispose to obstructive sleep apnea by altering upper airway passive mechanical properties and neural control during sleep.[84] OSA is more prevalent in patients with hypothyroidism. Hypothyroidism leads to widespread accumulation of hyaluronic acid in the skin and subcutaneous tissues, which gives rise to myxedematous appearance in these patients. Such deposition of mucoproteins in the upper airway causes enlargement of the tongue and the pharyngeal and laryngeal mucous membranes, thereby increasing the propensity for upper airway collapse during sleep.[85] In addition to these mechanical alterations, there is evidence to suggest that hypothyroidism leads to a decrease in central ventilatory drive.[86]

Pregnancy is also associated with a higher prevalence of snoring particularly in the third trimester.[87] While some of the physiologic changes that accompany pregnancy (e.g., higher progesterone levels, decrease in sleep time in the supine position) may protect against obstructive sleep apnea, gestational weight gain, decrease in pharyngeal luminal size, and alterations in pulmonary physiology increase the tendency for disordered breathing during sleep.[88]

2.8. Pathophysiology of OSAHS: The upper airway extends from the posterior margin of the nasal septum to the larynx (Figure 5). It can be divided anatomically into three regions: a) The nasopharynx (the region between the nasal turbinates and the hard palate),

b) The oropharynx, which can be subdivided into the retropalatal region (also called the velopharynx) and the retroglossal region, and c) The hypopharynx/ laryngopharynx (the region from the base of the tongue to the larynx). The physiologic functions of the upper airway include ventilation, phonation, and deglutition. The evolutionary adaptations necessary to allow for such functional diversity have resulted in a structure that is heavily dependent on muscle activity and intrinsic airway collapsibility to maintain airway patency. The collapsibility of the upper airway represents a balance between opposing forces. The negative intraluminal pressure generated by the diaphragm during inspiration and the positive extraluminal pressure from surrounding tissue constitute the collapsing factors. The action of the upper airway pharyngeal dilator muscles counteracts the collapsing forces. Several surrounding tissue and craniofacial structures contribute to the morphology of the airway.

Normal upper airway

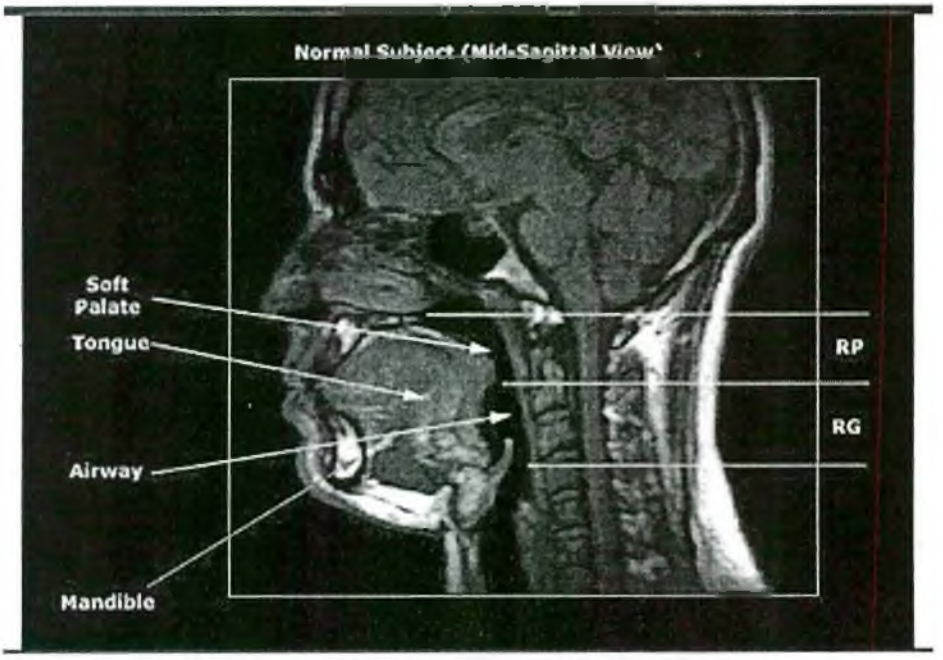

Figure 8 Mid-sagittal MR image in a normal subject demonstrating the anatomic regions of the upper airway and relevant soft tissue structures. The retropalatal (RP) region is defined from the level of the hard palate to the distal margin of the soft palate; the retroglossal (RG) region is defined from the distal margin of the soft palate to the base of the epiglottis. *Courtesy of Richard J Schwab, MD.*

During wakefulness, the upper airway remains patent regardless of size, except in some rare cases. However, the balance between factors to maintain airway patency changes during sleep, and many individuals are at risk for partial or complete upper airway obstruction. Airway narrowing and increased upper airway resistance can occur even in normal, non-snoring individuals during sleep.[89,90] Many investigators believe that a reduction in drive to the dilator muscles of the upper airway out of proportion to the reduction in drive to the chest wall or pump muscles is the primary cause of airway narrowing and obstructive events during sleep. This disproportionate change may be a direct result of a decrease in medullary respiratory activity, particularly in those neurons that have a weak correlation with respiration.[91] Activity of the upper airway muscles can be divided into two components: tonic and phasic. Most of the phasic activity which is

relevant to this discussion is inspiratory. Tonic activity refers to the activity during expiration or the level of activation in muscles without any phasic activity. The tonic component is reduced with the loss of wakefulness. In contrast, phasic upper airway muscle activity shows no change or may even increase during sleep.[92] This activity is maintained by noradrenergic mechanisms.[93] These findings suggest that the loss of tonic, rather than phasic activity, is the important factor which compromises airway patency during sleep.[94] Serotonin has been shown to be excitatory to upper airway motoneurons The decrease in activity of upper airway motoneurons during sleep, particularly during REM sleep, has implicated serotonin as an important factor in the reduction of upper airway patency during sleep.[95] There is substantial evidence that the ability to respond immediately to increases in negative pressure is lost or attenuated with sleep onset. Sleep appears to reduce the magnitude of the genioglossus' response to negative pressure and to increase the latency of the response.[96]During sleep body position plays an important role in the genesis of obstructive events.[97-8] Some individuals with position-dependent OSA obstruct exclusively in the supine position. In supine position, soft structures such as the tongue and soft palate can be drawn into the pharyngeal airway by the effects of gravity and also reduced lung volume cause airway narrowing which can lead to upper airway obstruction.

Airway size falls in supine position

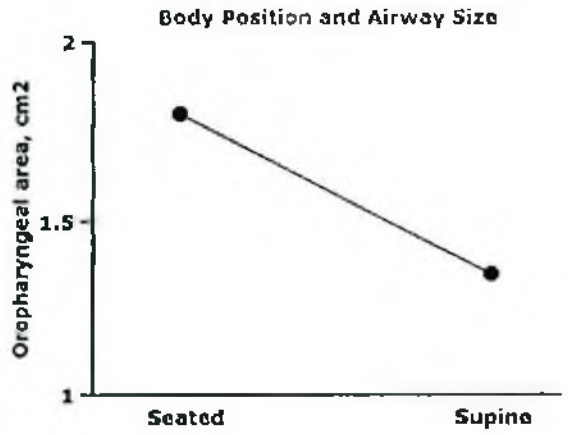

Figure 9:

Oropharyngeal area in the seated and supine positions during wakefulness. *Redrawn from Martin, SE, Marshall, I, Douglas, NJ, Am J Respir Crit Care Med 1995; 152:721.*

Alcohol, benzodiazepines, and other similar agents have been shown to cause or worsen sleep-disordered breathing in non-snorers, snorers, and patients with OSA.[99] These substances may increase sleep-disordered breathing by depressing respiration and/or preferentially inhibiting upper airway muscle activity. It has been demonstrated that the upper airway of the patient with OSA is smaller than the airway of a non-snorer. Thickened lateral pharyngeal walls have been shown to account for most of the narrowing of the upper airway in individuals with OSA.[100] Airway narrowing can also be caused by: nasal congestion, physical obstruction (e.g., tonsillar hypertrophy), conditions which cause macroglossia and facial malformations, obesity and genetic factors affecting upper airway size and tissue volumes.[101] The upper airway is smallest in the oropharynx in both normal subjects and patients with OSA, particularly in the retropalatal region. Airway closure during sleep occurs in the retropalatal region in the majority of patients with OSA.[102]

2.9. Clinical Presentation of OSAHS: Most patients with OSA are males, 18 to 60 years old.[7] Daytime somnolence is a common feature of OSA. However, its presence may go unnoticed or its significance may be underestimated because of its insidious onset and chronicity. The patient may not describe his/her symptom as sleepiness, but may use other terms, such as fatigue.[60] Careful questioning of the patient typically reveals drowsiness in boring, passive, or monotonous situations. As an example, drowsiness often occurs when the patient reads, watches television, or operates a motor vehicle. In addition, embarrassing or inappropriate episodes of sleep (e.g., at morning religious services) may be reported. Reviewing patient behavior away from the workplace is essential, because daytime sleepiness can be masked by activity. A simple questionnaire, the Epworth Sleepiness Scale (ESS), is a rapid screen to reveal the significant subjective sleepiness.[103] It is usually helpful to have the patient's bed partner or a family member present during the interview because they may have greater insight than the patient. Moreover, it is the bed partner who frequently provides the motivation for the patient's first visit to the clinician, complaining about intolerable snoring, snorts, and disconcerting apneas. A small portion of patients with OSA may complain of insomnia rather than daytime sleepiness because they are unable to maintain sleep. This can progress to difficulties initiating sleep. Insomnia with repetitive awakenings should prompt consideration of OSA. Other associated symptoms and historical features include: a) awakening with a sensation of choking, gasping, or smothering, b) restless, fitful sleep, c) episodes of cessation of breathing terminated by loud, resuscitative snoring, d) moodiness, e) lack of concentration, f) morning headaches, g) decreased libido and impotence, h) wakening with angina pectoris, i) nocturia[104] and j) history of hypertension,

cardiovascular disease, cerebrovascular disease, renal disease, type 2 diabetes mellitus, or gastroesophageal reflux disease.

3. Differentials of OSAHS: Following conditions are considered as differential diagnosis of OSA:

- **Periodic limb movements of sleep** — Periodic limb movements of sleep (PLMS) are recurrent jerks of the legs and arms, associated with arousals. Patients become sleep deprived and may snore more heavily because of the sleep deprivation. PLMS is most common in the elderly, but also shows a familial aggregation in younger patients. PLMS is often observed in association with OSA and can further fragment sleep, even after successful therapy for the apneas and hypopneas.
- **Rotating shift workers** — Night-shift workers obtain approximately seven hours less sleep per week compared to non-shift workers. They often revert to a "daytime" schedule on their leisure days, adding to sleep deprivation.
- **Narcolepsy** — Younger patients with symptoms suggestive of OSA may actually have narcolepsy. Narcolepsy is the second most common cause of disabling daytime sleepiness after sleep apnea.[105] Narcolepsy is a clinical syndrome of daytime sleepiness with cataplexy, hypnagogic hallucinations, and sleep paralysis. a) Daytime sleepiness — all patients with narcolepsy have chronic sleepiness. They do not sleep more than normal controls over 24 hours, but they are prone to fall asleep throughout the day, often at inappropriate times, b) Hypnagogic hallucinations — Hypnagogic hallucinations are vivid, often frightening hallucinations that occur just as the patient is falling asleep or upon

awakening. These are not due to psychiatric disease, but probably result from a mixture of REM sleep dreaming and wakefulness, c) Sleep paralysis — Sleep paralysis is a complete inability to move for one or two minutes immediately after awakening. This immobility may be accompanied by hypnagogic hallucinations or a feeling of suffocation, perhaps due to slight reductions in tidal volume. These episodes can be quite frightening, d) Cataplexy — Cataplexy is emotionally-triggered, transient muscle weakness. Most episodes are triggered by strong, generally positive emotions such as laughter, joking, or excitement. However, the episodes may be triggered by anger or grief in some individuals. The weakness is often partial, affecting the face, neck, and knees. Severe episodes can cause bilateral weakness and complete collapse. Only about one-third of patients will have all four of these classical symptoms; thus, the diagnosis of narcolepsy should be considered even in patients with sleepiness alone.

- **Upper airway resistance syndrome** — Upper Airway Resistance Syndrome (UARS) exists when there are arousals from sleep induced by airflow limitation due to increased upper airway resistance. There are few discrete respiratory disturbances (i.e., apneas or hypopneas) or episodes of desaturation. UARS is common in thin women with certain craniofacial abnormalities.[106]
- **Primary snoring** — Patients with primary (habitual or continuous) snoring are typically asymptomatic and present to the office due to complaints from their bed partners. Primary snoring is far more common than OSA; however, many

patients undergo polysomnography to exclude the latter. Strategies to identify these patients before they undergo costly, time-consuming testing are a priority.

- **Respiratory disease** — Respiratory disease can lead to excessive daytime sleepiness either alone or in combination with OSA (i.e., an overlap syndrome). As an example, patients with either chronic obstructive lung disease or restrictive lung disease may suffer from sleep-related desaturation. Atonia of the accessory muscles of respiration causes a drop in functional residual capacity, resulting in rapid desaturations during the transition from non-REM to REM sleep. Sudden awakenings and dyspnea can result, imitating OSA. Poorly controlled asthma is often worse at night, with nocturnal bronchospasm and cough inducing sleep fragmentation and paroxysmal dyspnea.
- **Gastroesophageal reflux disease** — Gastroesophageal reflux disease (GERD) can mimic OSA by producing a choking sensation and dyspnea. In addition, GERD can be exacerbated by OSA. Both GERD and OSA appear to improve with continuous positive airway pressure (CPAP) therapy.[107]
- **Sleep-related laryngospasm** — Sleep-related laryngospasm also induces choking and awakenings. Like OSA, it is most prevalent in middle-aged males. Sleep-choking syndrome is another proposed sleep disorder, although detailed published reports are lacking.
- **Miscellaneous** — Other disorders that can mimic OSA include abnormal swallowing disorders, nocturnal seizures, and psychiatric illness such as panic attacks.

3.1. Diagnostic Tests of OSAHS: Obstructive sleep apnea (OSA) is confirmed in only 50 to 60 percent of those suspected of having the disorder on the basis of history and physical examination.[108] This emphasizes the importance of diagnostic testing in confirming or excluding the diagnosis of OSA. The diagnostic tests for OSA are PSG, unattended portable monitoring, pulse oximetry, and radiography:

- **Polysomnography** — Polysomnography (PSG) is considered the gold-standard diagnostic test for OSA. Traditionally, patients undergo diagnostic PSG lasting a full night, then a second study for continuous positive airway pressure (CPAP) titration. To increase the efficiency of resource utilization, however, many centers now combine diagnostic PSG with CPAP titration, each lasting approximately half of the night.[109-10] Despite its reputation as the gold-standard, negative PSG should be viewed with skepticism if the clinical suspicion of OSA is high, as repeat PSG may become positive- suggesting that PSG can vary significantly from night-to-night.[111] Following are the indications of PSG:[112]

  i) Sleep related breathing disorders- for diagnosis and titration

  ii) Narcolepsy

  iii) Parasomnias and sleep related seizure disorder

  iv) Restless leg syndrome (RLS)

  v) Periodic leg movement disorder (PLMD)

  vi) Depression with insomnia

  vii) Medical conditions- heart failure, coronary artery diseases, stroke

  viii) Preoperative to exclude OSA

- **Portable monitors** — Portable monitoring (PM) refers to the diagnostic evaluation of obstructive sleep apnea outside of a conventional sleep laboratory with acceptable level of accuracy. It has evolved as an alternative to overnight, in-laboratory polysomnography (PSG) because it is convenient, relatively accurate, and less costly. Fewer physiologic variables are measured during PM compared to PSG, but PM does not require a technologist to attend and can be performed in the patient's home or in a hospital room. The devices that can record at least four channels of data (eg, airflow, respiratory effort, oxyhemoglobin saturation, and heart rate) should be used.[113-116]
- **Overnight oximetry** — Overnight pulse oximetry is a widely accepted and important component of both PSG and unattended portable monitoring. However, overnight pulse oximetry alone is not recommended for the diagnostic evaluation of suspected OSA.[115-117]
- **Radiographic imaging** — Routine radiographic imaging of the upper airway has not been helpful in confirming or excluding OSA. As a result, the primary purpose of radiographic imaging is identification of sites of upper airway obstruction to guide surgical intervention. Craniofacial photographic analysis is a promising new technique that has identified anatomical data that may predict OSA.[118]
- **Empiric therapy** — It has been suggested that the diagnosis of OSA can be inferred from a beneficial clinical response to CPAP. In a prospective study, 76 consecutive snorers with excessive daytime sleepiness were administered CPAP for two weeks.[119] Patients who reported that they used the CPAP for two or more

hours per night and wished to continue therapy were considered to have a positive CPAP trial. Among the patients with a positive CPAP trial, 97 percent had OSA confirmed by PSG. Among the patients with a negative CPAP trial, 78 percent had OSA excluded by PSG, suggesting that an empiric CPAP trial may be helpful in confirming, but not in excluding OSA. Although CPAP is a relatively benign therapy with potentially large benefit, we find it difficult to justify institution of a chronic therapy without first confirming the diagnosis of OSA. Thus, we believe that the diagnosis of OSA should be confirmed before CPAP is instituted and that the above approach should only be considered when diagnostic studies are unavailable.

3. 2. Diagnostic Approach: Unfortunately, the clinical features of OSA are nonspecific and the diagnostic accuracy of clinicians' subjective impression is poor,[108] making diagnostic testing essential. Clinicians must select patients for diagnostic testing who are most likely to have OSA because the gold-standard diagnostic modality PSG is expensive, time-consuming, labor intensive, and not always available. Most patients present with a chief complaint of snoring. It is important that the clinician discerns whether daytime sleepiness also exists. If excessive daytime sleepiness exists, we recommend that the patient undergo PSG. In the absence of excessive daytime sleepiness, the clinician should seek alternative symptoms and signs that are suggestive of OSA. We recommend that PSG be performed if two or more of the features are present (Table 3).

Table 3: Clinical features of Obstructive sleep apnea hypopnea syndrome

Daytime sleepiness	Obesity
Nonrestorative sleep	Large neck circumference
Witnessed apneas by bed partner	Systemic hypertension
Awakening with choking	Hypercapnia
Nocturnal restlessness	Cardiovascular disease
Insomnia with frequent awakenings	Cerebrovascular disease
Lack of concentration	Cardiac dysrhythmias
Cognitive deficits	Narrow or "crowded" airway
Changes in mood	Pulmonary hypertension
Morning headaches	Cor pulmonale
Vivid, strange, or threatening dreams	Polycythemia
Gastroesophageal reflux	

In the absence of clinical features of OSA, we suggest that PSG be performed only on patients with "mission-critical" professions (e.g., airline pilots, bus drivers). The role of routine PSG in disorders with high association with sleep apnea, such as stroke and heart failure, remains unclear. However, the threshold for diagnostic testing may need to be lower in these groups given the high prevalence of OSA. Despite its reputation as the gold standard, negative PSG should be viewed with skepticism if the clinical suspicion of OSA is high, and repeat PSG should be considered. Otherwise, we suggest that patients with negative PSG be followed clinically. The approach for diagnosing OSA is shown in the algorithm (figure 10):

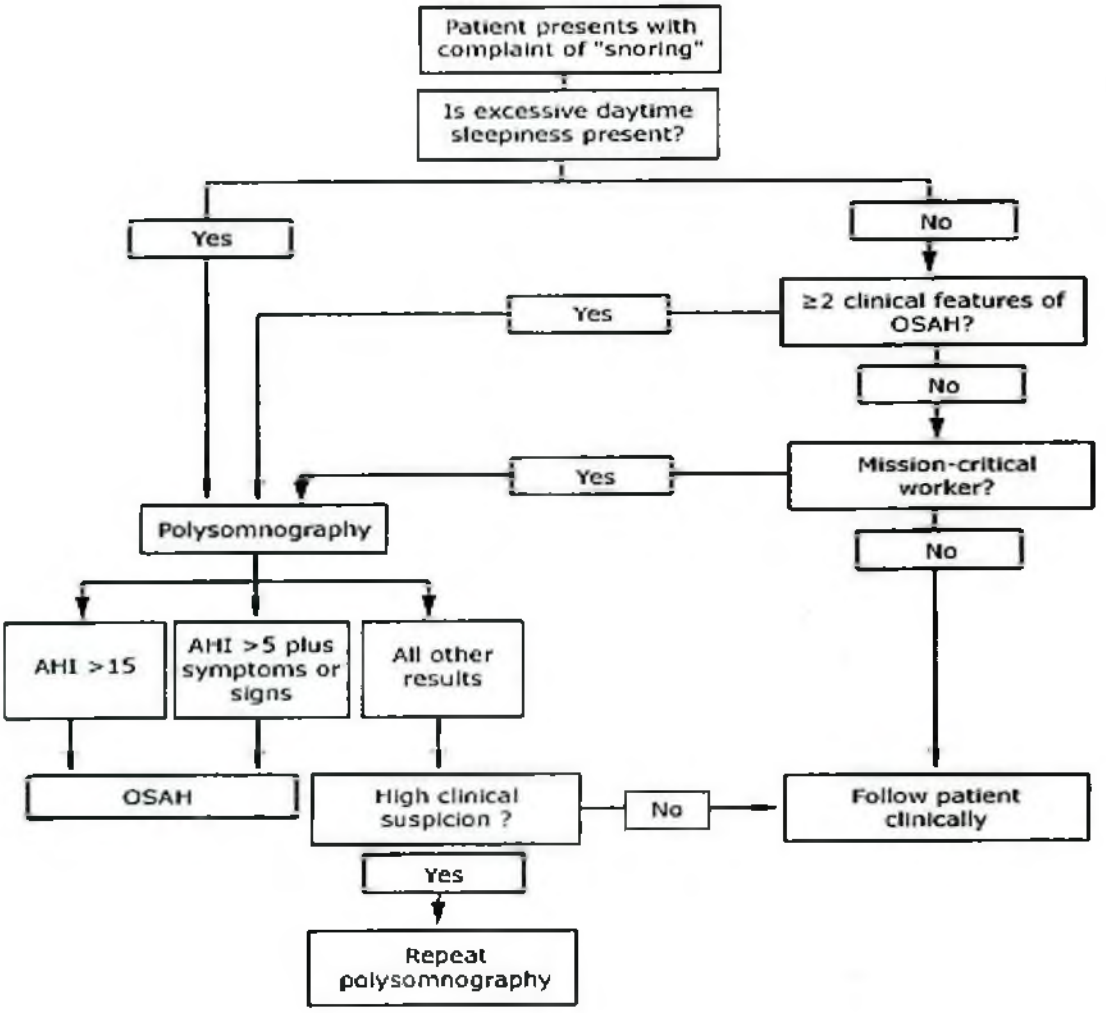

Figure 10: Diagnostic approach of OSA.

3.3. Management: Obstructive sleep apnea (OSA) has multiple risk factors, the most notable being obesity. The optimal approach to patients with OSA requires that the clinician identify and treat any predisposing factors, establish the severity of the OSA, and then match the patient with the most appropriate treatment.[1] There are many compelling reasons to treat patients with OSA, most notably the physiologic improvements and enhanced quality of life that result.[120] The following algorithm (figure 11) shows the common management approach:

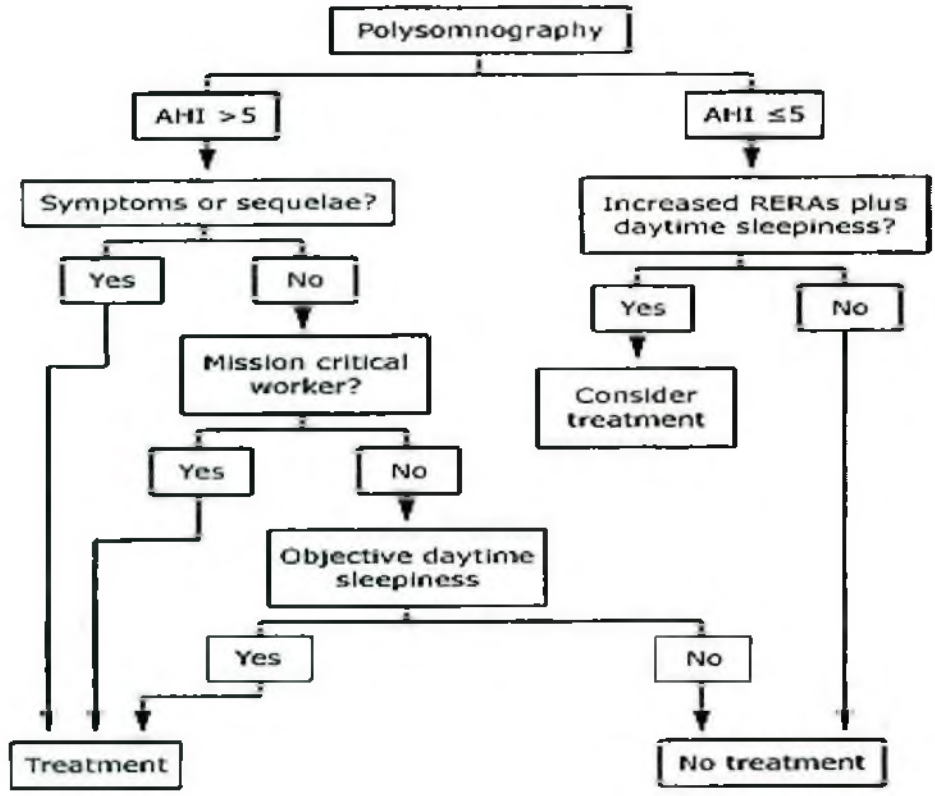

Figure 11: Algorithm to manage OSAHS.

Both continuous positive airway pressure (CPAP) and oral appliances are effective therapies for patients who have mild or moderate disease (i.e., AHI ≤ 30 events/hr).[121] For patients who have severe disease (i.e., AHI >30 events/hr), CPAP therapy rather than alternative therapies is suggested. Choosing surgical therapy and the type of procedure for OSA are controversial because there have been few outcome studies. Surgical therapy should be considered on a case-by-case basis for patients in whom positive airway pressure or oral appliances are not an option or are ineffective.[122] Tracheotomy may be the only treatment option in a small number of patients whose severe, life threatening OSA cannot be controlled by other means.

3. Subjects and Methods

3.1. Study design: The study was designed as a case-control study comparing clinical and anthropometric parameters between two groups: i) OSAHS group (n=65): OSAHS defined as AHI ≥ 5 with presence of EDS were included in that group and designated as 'Cases' and ii) Non-OSAHS group (n=125): subjects unmatched and not diagnosed as OSAHS by NPSG were included in that group and designated as 'Controls.'

3.2. Study setting: The study was carried out in the Respiratory wing, Department of Medicine, Bangabandhu Sheikh Mujib Medical University and NPSG was performed in a private clinic.

3.3. Sample size estimation: Sample size was estimated using following formula:

n = sample size in case group

OR= 3.05

P_1= exposure among cases = 35%

P_2= exposure among controls = 15%

Z_α= 1.96 at 95% confidence level

Z_β= Z value (one tail) of standard normal distribution at definite power

e.g. Z_β= .85 at 80% power

$$P_2 = \frac{P_1}{OR(1-P_1)+P_1}$$

$$n = \frac{\left\{Z_\alpha\sqrt{2\times P_2(1-P_2)} + Z_\beta\sqrt{P_1(1-P_1)+(1-P_2)}\right\}^2}{(P_1-P_2)^2}$$

$$= \frac{\{1.96\sqrt{2\times.15\times.85} + .85\sqrt{.35\times.65+.85}\}^2}{(.35-.15)^2}$$

$$= 59$$

So, the calculated sample size which was case 59 and control 118, with case-control ratio 2:1, at 95% CI , power 80% and calculated at 35 % expected frequency of exposure (witnessed apnea) to case. Considering drop out at different stage of the study, case 65 and control 125 were taken.

3.4. Subjects recruitment process: Subjects were recruited conveniently from a private sleep laboratory. All consecutive subjects diagnosed as OSAHS, 30 to 60 years old, had the opportunity to be included in the study. A subject was excluded from the study if any condition was found in a subject like- i) history of recent myocardial infarction, ii) Severe acute asthma, iii) Severe chronic obstructive pulmonary disease (COPD), iv) upper airway surgery, v) class III/IV congestive heart failure, vi) respiratory failure, vii) pregnancy, viii) hypothyroidism on treatment, ix) acromegaly, x) chronic renal failure, xi) systemic steroid treatment, and xii) hormone replacement therapy, xiii) disorders including craniofacial abnormality like Marfan's syndrome, Down's syndrome, Pierre-Robin syndrome etc.

All subjects attending sleep clinic for the complaints suggestive of OSA, were given the option of nocturnal polysomnography (NPSG) in the laboratory free of charge. Subjects (n=65) who are diagnosed as OSAHS fulfilling the operational definition was included in case group. Afterward, unmatched subjects (n=125), healthy volunteers including clinic staffs, patients relatives were offered free NPSG, those who underwent and not diagnosed as OSAHS were included in control group.

3.5. Polysomnography (PSG): PSG was performed in a private single bedded Sleep Laboratory by the investigator. A fully computerized PSG device (Compumedics, E series) was used with 16 channels recordings and in accordance with standard 10-20-20 electrode placement. Sixteen channels of PSG documented the parameters as follows:

1. 4 channels for electroencephalography (EEG),
2. 2 channels for electro-oculography (EOG),
3. 2 channels for electromyography (EMG),
4. 2 channels for electrocardiography (ECG),
5. 1 channels for thermistors for nasal and oral airflow,
6. 1 channel for tracheal microphone for snoring,
7. 2 channels for thoracic and abdominal impedance belts for respiratory effort,
8. 1 channel for pulse oximetry for arterial oxyhemoglobin saturation (SpO_2),
9. 1 channel for sensors of body position during sleep.

The electroencephalographs using leads C_3/A_2 and O_1/A_2 are shown in figure 12. All the wave forms needed to distinguish sleep stages are well visualized in the central lead; the occipital EEG O_1/A_2 is an adjunct to the central EEG C_3/A_2 for assessing sleep onset or arousal during sleep.

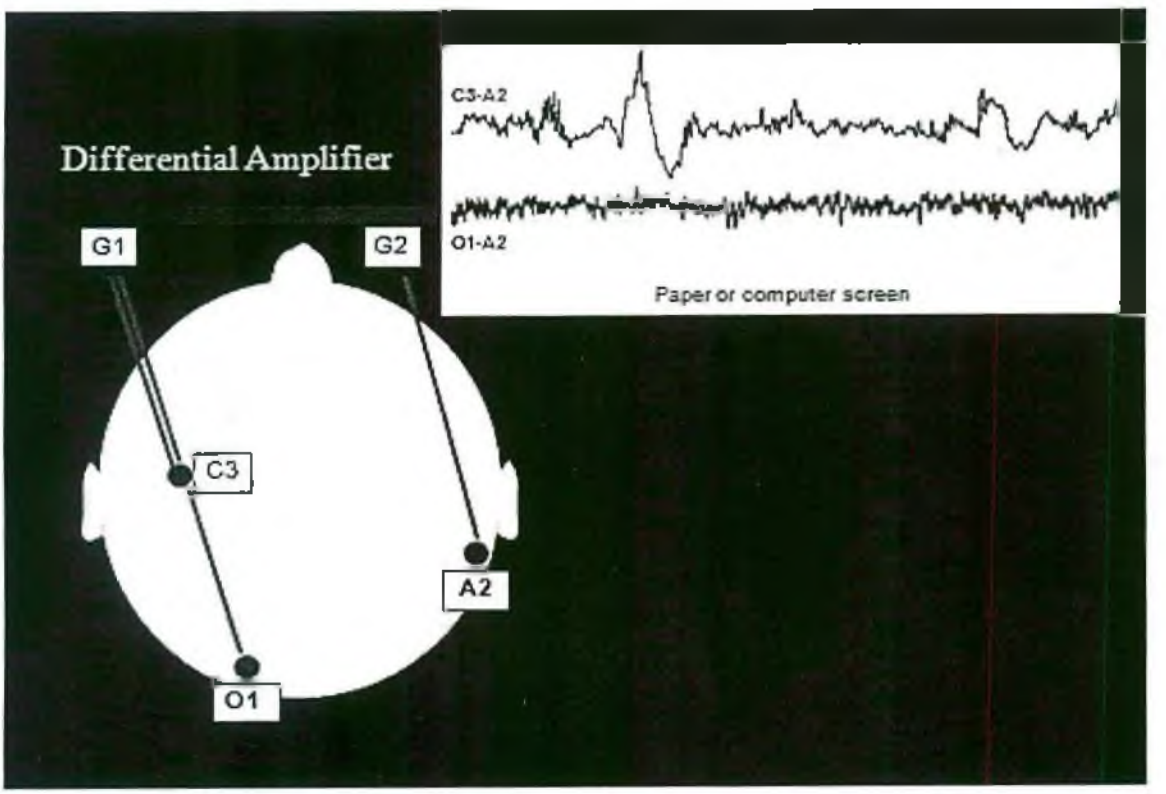

Figure 12: Electroencephalography (EEG)

The Electrooculographs measure the eye movement activity during sleep for two primary reasons- the phasic bursts of rapid eye movements to score REM stage and the slow, rolling eye movements to assess sleep onset. The EOG recordings are based on the small eletropotential difference from the front to the back of the eye. The cornea is positive with respect to the retina. An electrode nearest the cornea registers a positive potential, while nearest the retina registers negative potential. As the eye moves, the positions of the cornea and retina change relative to the fixed position of the electrode and the potential change registers as a pen deflection at the graph.

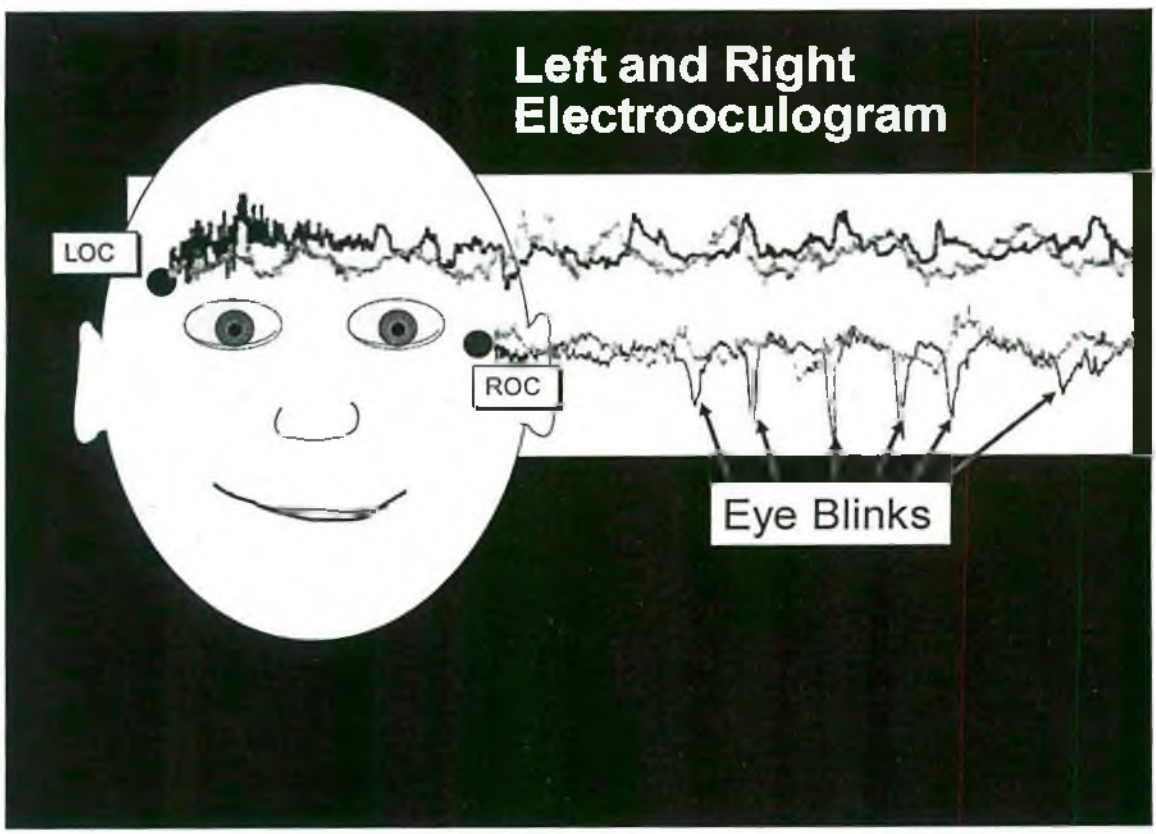

Figure 13: Electrooculograph (EOG)

The EMG from mentalis/submentalis muscles beneath the chin during clenched teeth is shown in figure 14. An atonic electromyogram (EMG) is consistent with inactivity of all voluntary muscles except the extraocular muscles. The atonia of REM sleep is known to result from direct inhibition of alpha motor neurons.

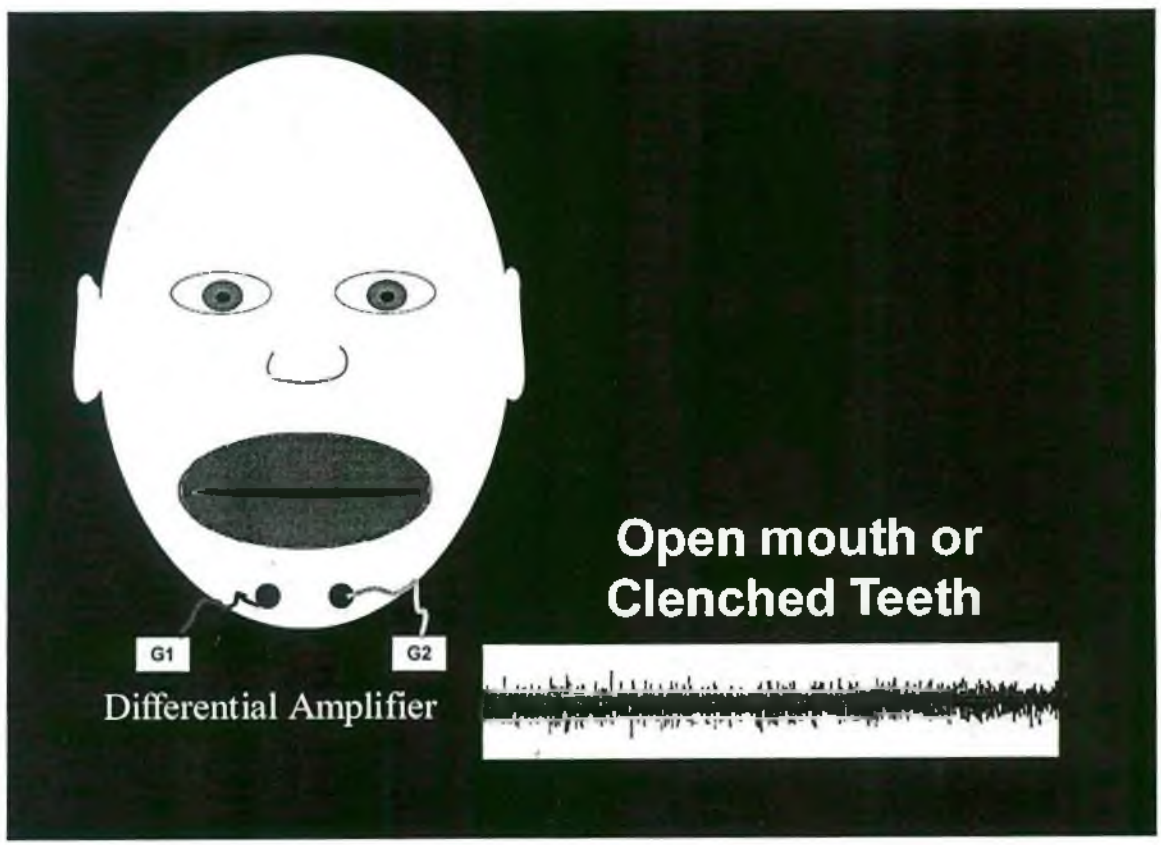

Figure 14: Electromyograph (EMG)

The oronasal airflow is detected by thermistors, a thermally sensitive resistor which senses expiration in front of nose and mouth.

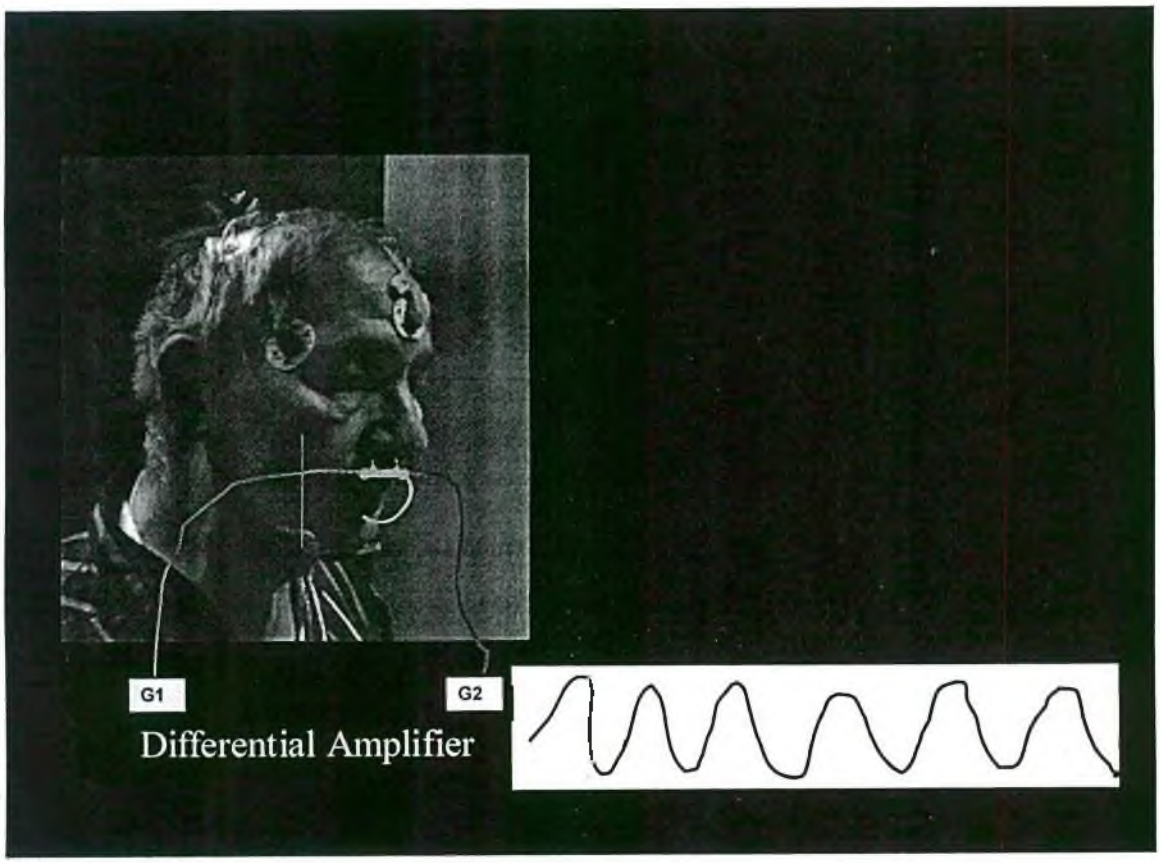

Figure 15: Thermistors detecting oronasal airflow

The graphs of snoring noise, respiratory effort and EMG for anterior tibialis muscle are shown in figure 16. The electrode sensing snoring noise is connected to a microphone placed in front of the trachea. The respiratory effort is measured by transducers-the physiological equivalent of conductors, which assess the changes in the cross sectional area of thorax and abdomen.

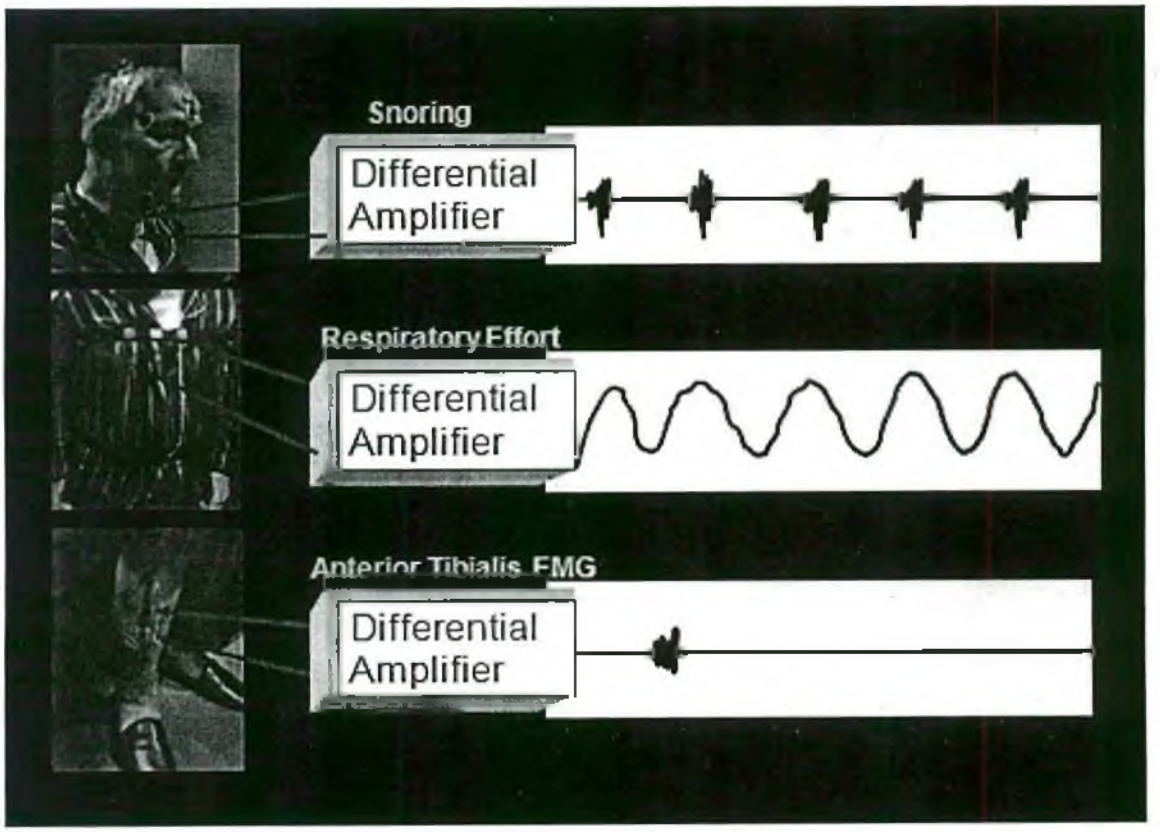

Figure 16: Graphs for snoring, respiratory effort and EMG for tibialis.

3.6. Interpretation of PSG parameters: PSG records were scored manually in a 30 secs epoch by the investigator according to standard Rechtschaffen and Kales criteria:[32] i) an apnea was defined as complete cessation of airflow lasting ≥ 10 s with discernible thoraco-abdominal movement, ii) hyperpnoea was defined as reduction in airflow accompanied by a decrease of ≥ 4% in oxy-hemoglobin saturation, and iii) mixed apnea was defined as an apnea that began as a central apnea and ended as an obstructive apnea and are treated as obstructive apnea. The apnea-hypopnea index (AHI) was calculated as the average number of apnea and hypopnea events per hour of sleep. Arousal was defined according to American sleep disorder association (ASDA) criteria as abrupt shift in EEG frequency of 3 seconds or more in duration with minimum 10 minutes of continuous sleep.[123] In this study, OSAH was defined as AHI ≥ 5 and OSAHS was defined as AHI ≥ 5 with presence of EDS. OSAHS severity was classified in 3 categories on the basis of AHI as follows; mild 5-14.9, moderate 15-29.9 and severe ≥ 30. Figure 17 is a 30-second epoch of PSG showing different parameters of an individual during sleep including stage II, NREM sleep, time during sleep, EEG, EMG, ECG, SpO_2, airflow, respiratory efforts, snoring, leg movements and heart rate.

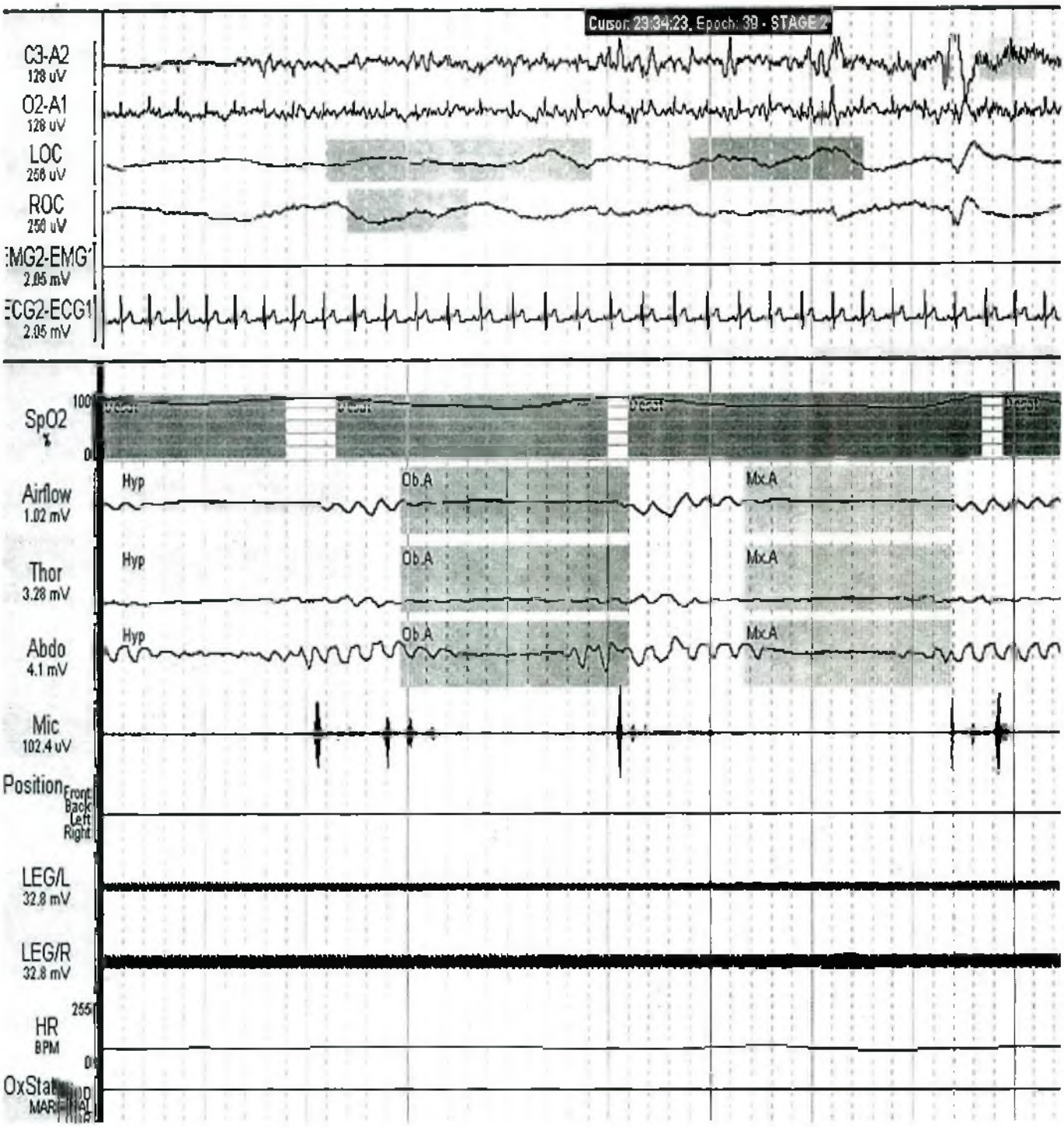

Figure 17: A 30-second epoch of PSG

3.7. Checklists of variables: Following variables were studied.

- Sociodemographic variables were- age, sex, educational status, smoking and alcohol drinking, family history of snoring;
- Sleep variables were- snoring, excessive daytime sleepiness (EDS), witnessed apnea, choking or gasping, brief awakening during sleep, dry mouth, unrefreshed sleep, excessive sweating, nocturia, morning headache, sleep talking, bruxism, memory impairment, impaired cognitive function, loss of libido;
- Anthropometric parameters were- body mass index (BMI), waist circumference (WC), waist hip ratio (WHR), neck circumference (NC),
- Craniofacial variables were- nasal cavity abnormality, dental problem, macroglossia, retrognathia, tonsillar enlargement and posterior oropharyngeal crowding.

3.8. Variables with operational definitions: Sociodemographic variables included in the study were age, sex, educational status, smoking and alcohol drinking habits, family history of snoring. Age was stated by the patient himself. Educational status was classified in three categories- primary, who studied in primary school; secondary, who studied up to higher secondary level and tertiary, who studied in graduation and above. Smoking habit and alcohol habit was taken as positive if a subject smoked everyday for at least three months and if a subject drunk alcohol at least once weekly for at least three months.[9] Sleep variables included in the study were snoring, excessive daytime sleepiness (EDS), witnessed apnea, choking or gasping, brief awakening, dry mouth, unrefreshed sleep, excessive sweating, morning headache, sleep talking, bruxism, memory impairment, loss of libido etc. Snoring was categorized as habitual if the subject or bed partner complained of snoring in four or more nights per week; non-habitual if snoring occurred in three or less nights per week; non-snoring if the subject did not snore at all during sleep.[9] Family history of snoring was taken as positive if presence of snoring was complained in a first degree relation of the subjects. The subjective complaint of excessive daytime sleepiness (EDS) was measured by questionnaire called the Epworth Sleepiness Scale (ESS).[103] The sleep study questionnaire included well validated eight-item sleep questions to rate sleepiness of the subject in different situations. The possible total score ranges from 0 (not sleepy) to 24 (most sleepy). The ESS score $\geq$ 11 were considered as sleepy. The following scale was used for the appropriate number for each situation:

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

Table 4: Questionnaire for Epworth sleepiness scale (ESS)

Sitting and reading	
Watching TV	
Sitting in active in a public place (e.g. a theater or meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the after noon When circumstances permit	
Sitting and talking to some one	
Sitting quietly after a lunch with out alcohol	
In a car while stopped for a few minutes in traffic	
Total	

The complaint of witnessed apnea was considered as present if cessation of breathing during sleep is observed by the bed partner or room mate; choking or gasping during sleep was present if feeling of hindrance in breathing or laboured breathing during sleep was complained by the subject or bed partner or room mate; excessive sweating was present if sweating was observed, especially in the upper chest, or wet bed sheet, not explained by any other condition; abnormal limb movements during sleep or irresistible urge to move limbs before sleep or excessive body movements designated as restless sleep was present it was stated by the subject or room mate; dry mouth during sleep was

present if the subject complains of dry mouth, sometimes needed drinking water during sleep time; sleep talking (somniloquy) during sleep and teeth grinding or clenching (bruxism) during sleep was stated by others, brief awakening from sleep and was stated by subject or room mate; nocturia was considered to be present if two or more times micturition occurred at night unless it was explained otherwise and enuresis or bed wetting during sleep was complained by the subject; unrefreshed sleep was considered to be present when the subject felt unrefreshed in the morning irrespective of time spent in sleep; morning or nocturnal headache was considered to be present when the subject complained of headache during sleep or in the morning when he or she woke up; Impotence or loss of libido was considered to be present if the subject or the partner complains of erection failure or decreased desire for sex not explained otherwise, impaired cognitive function was considered to be present if the patient or his attendant stated difficulty in performing arithmetic calculation for more than five minutes or the performance of the subject in the office was slow and of poor quality; memory impairment in regard to short and long term was assessed by asking the subjects to memorise a telephone number or address and recall immediately and by asking the patient a remote past event, like liberation war; number of automobile accidents in last three years by the subject, if he/she drives was considered.

Regarding comorbidities of OSAHS, HTN and DM were included in the study. Hypertension was considered as present if stated by the subject and evidenced by taking antihypertensive prescribed by the physician or if the subject satisfied the Joint National Committee 7 criteria.[81] DM was considered as present if stated by the subject and evidenced by the documents.

Regarding variables of anthropometric measurements included in the study were body mass index (BMI), waist circumference (WC), waist hip ratio (WHR), neck circumference (NC) and recent weight gain. BMI of a subject was measured by dividing body weight in kilograms by squared value of his height in meter; WC was measured at a level midway between the lower rib margin and iliac crest with the tape all around the body in horizontal position; WHR was calculated as the ratio of waist and hip circumference and hip circumference was measured as the maximal circumference over the buttocks; NC was measured at a point just below the larynx and perpendicular to the long axis of the neck, tape was put as close to horizontal as anatomically feasible and recent weight gain was considered as positive if the subject gained ≥5% of weight of the previous year in one year.

Regarding variables included in the craniofacial features were- nasal cavity abnormality if any one problem like septal deviation or evidence of trauma or rhinitis or polyp was present; dental problem was taken as present, if any one abnormality like dental overjet, a forward extrusion of the upper incisors beyond the lower incisors, or dental malocclusion, or dental overlapping was found in a subject; macroglossia was present when the tongue was larger as compared to normal by the investigator (Figure 18);

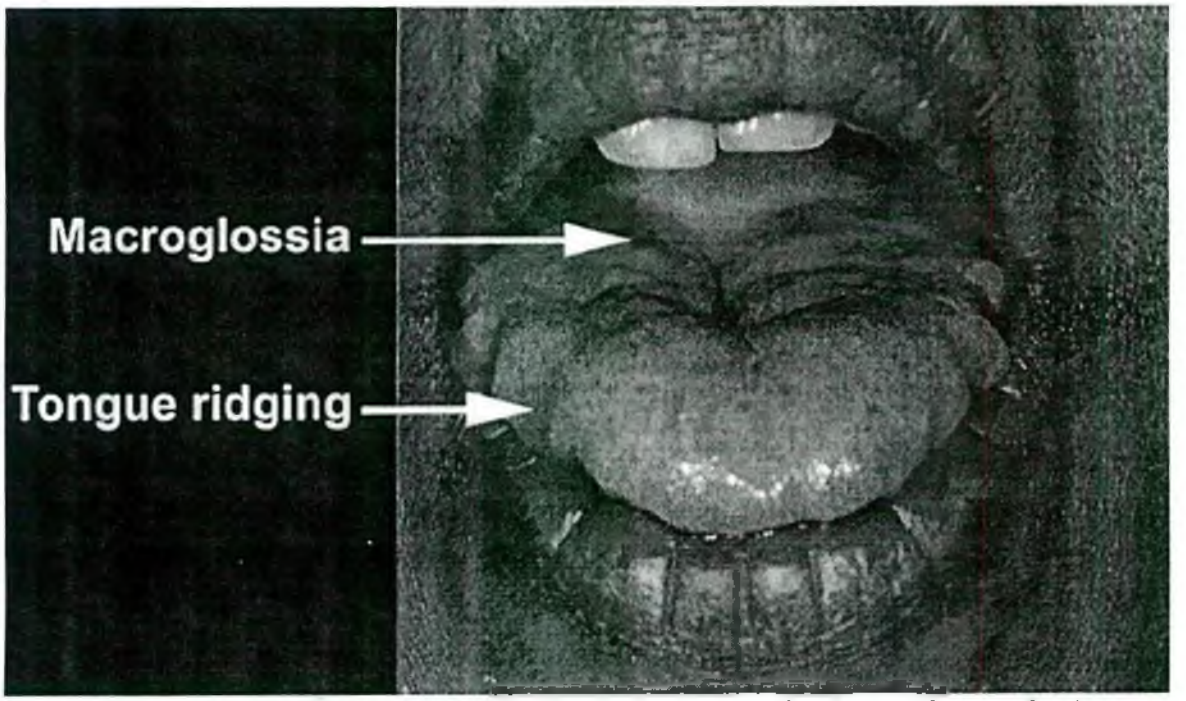

Figure 18: A view of the Macroglossia during a maximal mouth opening/tongue extrusion (Mallampati) maneuver. The tongue is enlarged with its superior aspect well above the level of the mandibular occlusal plane, nearly filling the observable pharyngeal space. Tongue ridging, a common associated finding in macroglossia, is also demonstrated.

retrognathia (Figure 19) was present if the the position of the gnathion is posteriorly displaced as compared with the nasion as observed by the investigator; tonsillar enlargement was classified from grade 0 to grade IV based on the degree of enlargement as follows: grade 0- tonsils were not visible, grade I- tonsils were hidden by the pillars, grade II- tonsils extended past the pillars, grade III- tonsils extended past the pillars, but did not reach midline, and grade IV- tonsils extended past the pillars, and reached midline;[124] the modified Mallampiti classification was used to assess the severity of posterior pharyngeal crowding from I-IV as follows: class I: the entire uvula and tonsils/pillars were visualized, class II: uvula but not the tonsils were visualized, class III: soft palate but not the uvula was visualized, class IV: only the hard palate was visible.[124]

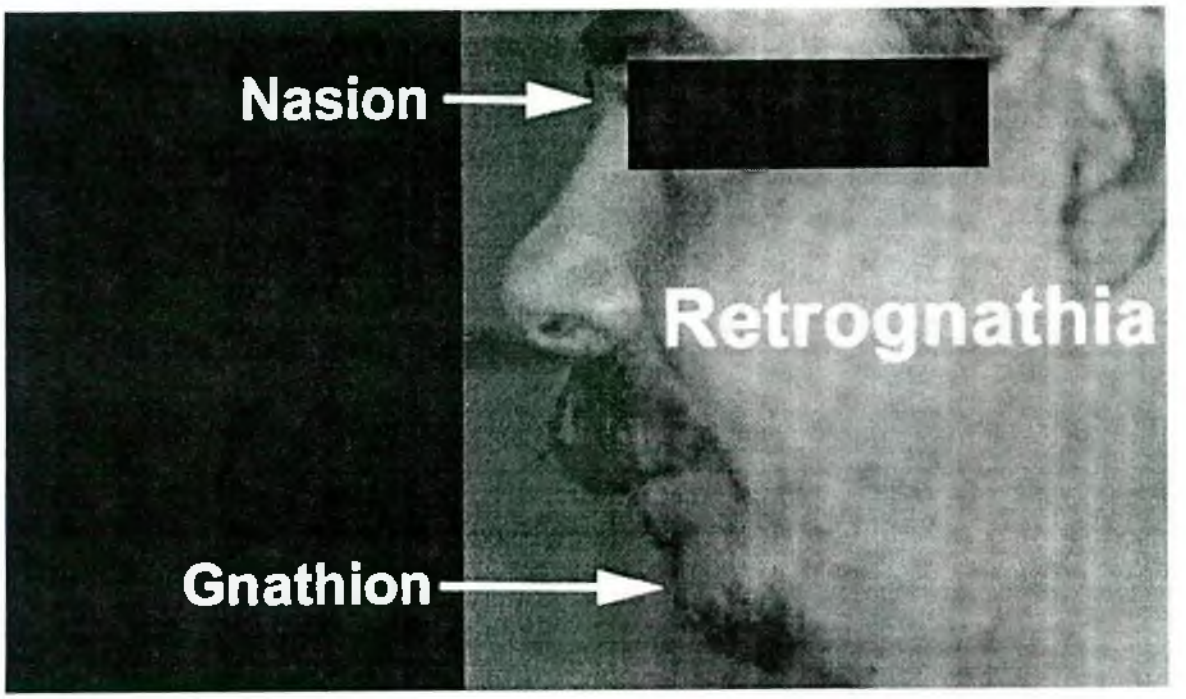

Figure 19: A lateral profile of the entire face demonstrating retrognathia. Retrognathia is observed as the position of the gnathion is posteriorly displaced as compared with the nasion.

3.9. Data collection: Data were collected in a predesigned structured quistionarrie (Appendix-1). A medical graduate was taught about variables of the study and he interviewed the subject and bed partner. After preliminary selection of the subjects, he or she was sent to the interviewer. He was informed about the study and interviewed. Data related to anthropometric measurements, Blood pressure record and oronasal cavity examination was performed by the investigator and was noted in the sleep clinic. Then the patient was given the date for PSG study in the same place. After completion of the PSG, relevant PSG data was noted.

3.10. Statistical analysis: The data were presented as mean ± SD for continuous variables and percentages for categorical variables. Comparison between groups was done with the Student's t test for continuous variables and Chi square test with Yates correction for categorical variables. ANOVA was applied to study average increase in ESS, BMI, NC and age in different OSAH severity. Stepwise multiple logistic regression was applied to identify the independent risk factors of OSAHS among variables that were found to be significant by univariate analysis. All significance tests were two sided, and a value of $p < 0.05$ was considered statistically significant. All analysis was done with statistical software (Statistical Package for Social Science, release 12.0 for Windows; SPSS).

3.11. Ethical issues: Participation in the study was completely on voluntary basis. Prior to enrolment each participant was provided with the consent form. The form stated the study procedure and assured that even if a subject consented to be participant of the study, they would have the right to refuse, to respond to any or all of the interview questions and may decline to continue to participate in the study. The enrolled participant were provided with written assurance that information gathered in course of the study would not be disclosed to any other individual unless authorized by the participant and the information gained would be used in such a way that identity of the participant would not be revealed. No experimental drug or placebo was administered as part of this study. All tests that were planned for the study were non-invasive.

4. Results

A total of 190 PSG studies were performed from July 1, 2007 to June 30, 2009 for adult Bangladeshi subjects. The mean (± SD) age of the study population was 42.97 ± 8.34 years, with 109 male (57.4%) participants. The subjects had a mean BMI of 25.63 ± 5.28 kg/m^2 (range, 18.30 to 39.81 kg/m^2).

Demographic and anthropometric profile: The demographic characteristics of the study population are summarized in Table 5.

Table 5: Demographic profile of the study population (N=190) *

Variables	Values
Age, yrs	42.97 ± 8.34
Male/Female ratio	1.35
Higher education	86 (46.80%)
BMI, kg/m^2	25.63 ± 5.28
Habitual Snoring	100 (52.60%)
Smoking	53 (27.90%)
Drinking	14 (7.40%)

* Values are expressed as mean ± SD or No.(%), unless otherwise indicated.

About 86 (46.80%) subjects were of higher education status, having education above higher secondary level. The percentage of habitual snorers in the study population was 52.60%. The percentage of current smoker was 27.90% and that of alcohol drinking was only 7.40% among study subjects.

The demographic and anthropometric profile of OSAHS and non-OSAHS subjects were compared (Table 6). The OSAHS group had higher mean age of 46.60 ± 9.40 years, compared to 41.08 ± 7.05 years of non-OSAHS or control group (P<0.001). The male gender predominated in OSAHS group compared to control group and OSAHS was

found to be more common in subjects with higher education, these difference were significant statistically (P<0.001). The anthropometric parameters BMI, WC, WHR and NC showed statistically significant difference between OSAHS and control group. Habitual snoring was found in 98.50% of OSAHS group compared to 28.80% of normal subjects (P<0.001). Smoking and drinking alcohol though were common in OSAHS group but not significant statistically (P= 0.125 and P=0.079 respectively).

Table 6: Comparison of demographic and anthropometric profile of OSAHS and non-OSAHS subjects.*

Variables	OSAHS (n=65)	Non-OSAHS (n=125)	P values
Age, yrs	46.60 ± 9.40	41.08 ± 7.05	0 .00
BMI, kg/m^2	31.19 ± 4.69	22.74 ± 2.54	0.00
WC, cms	105.33 ± 12.90	84.02 ± 9.91	0 .00
WHR	0.97 ± 0.08	0.92 ± 0.05	0.00
NC, cms	40.34 ± 3.22	37.73 ± 2.72	0.00
ESS score	15.29± 2.85	6.95± 2.76	0.00
Smoking	23 (35.40%)	30 (24%)	0.125
Drinking	8 (12.30%)	6 (4.80%)	0.079
Habitual Snoring	64 (98.50%)	36 (28.80%)	0.00
DM	18 (28.1%)	24 (19.2%)	0.196

* Values are expressed as mean ± SD or No.(%), unless otherwise indicated.

The age ≥ 45 years, male gender and various parameters of obesity such as BMI > 25 kg/m2, WC > 102 cm in men and > 88 cm in women, WHR of > 0.95 in men and > 0.80 in women, and NC>40 cm in men and >38 cm in women showed statistically significant correlation with OSAHS. The prevalence of hypertension (HTN) and diabetes mellitus (DM) were greater in OSAHS subjects, though the difference was significant statistically in HTN (P=.001).

Table 7: Comparison of demographic and anthropometric profile of OSAHS and non-OSAHS subjects with OR.

Variables	OSAHS (n=65)	Non-OSAHS (n=125)	OR (95%CI)
Age≥ 45 yrs	34 (53.1%)	32 (25.6%)	3.60(1.92- 6.79)
Male/Female ratio	1.60	1.23	1.29(0.70-2.39)
Higher education	40 (61.5%)	49 (39.2%)	2.48(1.34-4.59)
Obese as defined by			
• BMI>25	56 (86.2%)	30 (24.0%)	19.7 (8.72-44.51)
• WC	46 (70.8%)	15 (12.0%)	17.75 (8.31-37.94)
• WHR	49 (75.4%)	24 (19.2%)	12.89 (6.28-26.44)
• NC	45 (69.2%)	33 (26.4%)	6.27 (3.24-12.14)
HTN	34 (53.1%)	35 (28.0%)	2.91 (1.56-5.46)

* Values are expressed as No. (%) and odd ratios (OR) with 95% confidence intervals (95% CI), unless otherwise indicated.

Symptomatic profile: Symptomatic profile between OSAHS and control subjects were compared excluding habitual snoring and EDS, as they were present in all cases. Symptoms including witness apnea, choking or gasping, brief awakening from sleep, feeling unrefreshed after sleep, dry mouth during sleep, morning headache and impotence showed statistically significant differences between two groups (P<0.05). Symptoms like

restlessness during sleep, sleep talking, excess sweating during sleep, nocturia and recent weight gain were not significantly different in both groups.

Table 8: Comparison of symptomatic profile of OSAHS (n=65) and control (n=125) groups with odds ratio (OR).

Variables	OSAHS (n=65)	Control (n=125)	OR (95%CI)
Witness apnea	53 (81.5%)	10 (8.0%)	50.79 (20.65-124.94)
Choking	40 (61.5%)	6 (4.8%)	31.73 (12.15-82.91)
Brief awakening	37 (57.8%)	18 (14.4%)	8.15 (4.03-16.47)
Unrefreshed sleep	51 (79.70%)	52 (41.6%)	5.51 (2.72-11.15)
Dry mouth	36 (56.3%)	15 (12.0%)	9.43(4.53-19.59)
Recent wt gain	42 (65.60%)	78 (62.4%)	1.15 (.61-2.16)
Morning Headache	26 (40.60%)	9 (7.2%)	8.82 (3.80-20.47)
Restless sleep	28 (43.8%)	34 (34.4%)	1.48 (.80-2.75)
Sleep talking	10 (15.4%)	9 (7.2%)	2.34 (.90-6.10)
Sweating	14 (21.5%)	16 (12.8%)	1.87 (.85-4.12)
Nocturia	15 (23.1%)	15 (12%)	2.20 (.99-4.85)
Impotence	30 (47.6%)	33 (26.4%)	2.53 (1.34-4.78)

* Values are expressed as mean ± SD or No. (%), unless otherwise indicated.

Upper airway predictors: Upper airway variables including rhinitis, dental overjet, retrognathia and macroglossia were compared between OSAHS and control subjects. Retrognathia and macroglossia showed significant difference ($P<0.05$).

Table 9: Upper airway predictors compared between OSAHS and control subjects with OR (95% confidence interval).

Variables	OSAHS (n=65)	Control (n=125)	OR (95%CI)
Rhinitis	15 (23.8%)	25 (20.0%)	1.51 (0.75-3.00)
Macroglossia	7 (11.1%)	1(0.8%)	15.50(1.89-128.49)
Retrognathia	27(42.9%)	15(12.0%)	5.50 (2.64-11.47)
Dental overjet	19 (30.2%)	25(20.0%)	1.73(0.86- 3.46)

- Values are expressed as mean ± SD or No. (%), unless otherwise indicated.

The degree of tonsillar enlargement and posterior oropharyngeal crowding assessed by modified Mallampiti score (MS) were compared. MS showed significant difference in two groups (P<0.001).

Table 10: Tonsillar enlargement and posterior pharyngeal crowding were compared between OSAHS and control subjects (N=190).

Variables	OSAHS (n=65)	Non-OSAHS (n=125)	P values
Tonsil enlargement:			
Grade- 0	10(15.4%)	17(13.7%)	
Grade- I	23(35.4%)	49(32.3%)	
Grade-II	20(30.8%)	40(32.3%)	0.94
Grade-III	7(10.8%)	11(8.9%)	
Grade-IV	5(7.7%)	7(5.6%)	
Mallampiti score:			
Class-I	9(13.8%)	113(90.4%)	
Class-II	20(30.8%)	12(4.6%)	0.00
Class-III	18(27.7%)	0	
Class-IV	18(27.7%)	0	

* Values were expressed as No.(%), unless otherwise indicated.

The upper airway narrowing due to tonsillar enlargement was classified from grade 0 to grade IV. The effect of increasing degree of tonsillar enlargement on AHI was analysed by one way analysis of variance (ANOVA), it was not statistically significant (P=0.079).

Table 11: Effect of tonsillar enlargement on AHI (N=190).

Tonsil size	No of Subs	Mean AHI ± SD	P
Gr 0	27	12.54 ± 20.34	
Gr I	72	18.69 ± 31.07	
Gr II	60	18.69 ± 29.97	0.079
Gr III	18	29.33 ± 38.32	
Gr IV	12	40.93 ± 49.80	

- Values are expressed as mean ± SD or No., unless otherwise indicated.

The impact of increasing severity of posterior pharyngeal crowding and its influence on AHI was analysed by one way analysis of variance (ANOVA), it was statistically significant (P=.00). The modified Mallampiti score (MS) was used to assess the severity of posterior pharyngeal crowding from class I to class IV.

Table 12: Effect of Posterior pharyngeal crowding on AHI (N=190).

MS	No of Subs	Mean AHI ± SD	P
Class I	122	2.09 ± 5.03	
Class II	32	22.95 ± 20.77	0.00
Class III	18	62.33 ± 14.59	
Class IV	18	93.89 ± 12.02	

* Values are expressed as mean ± SD or No., unless otherwise indicated.

Figure 20 showed the effect of different grades of tonsillar enlargement on AHI analysed by one way ANOVA (analysis of variance), it was not significant P=0.079).

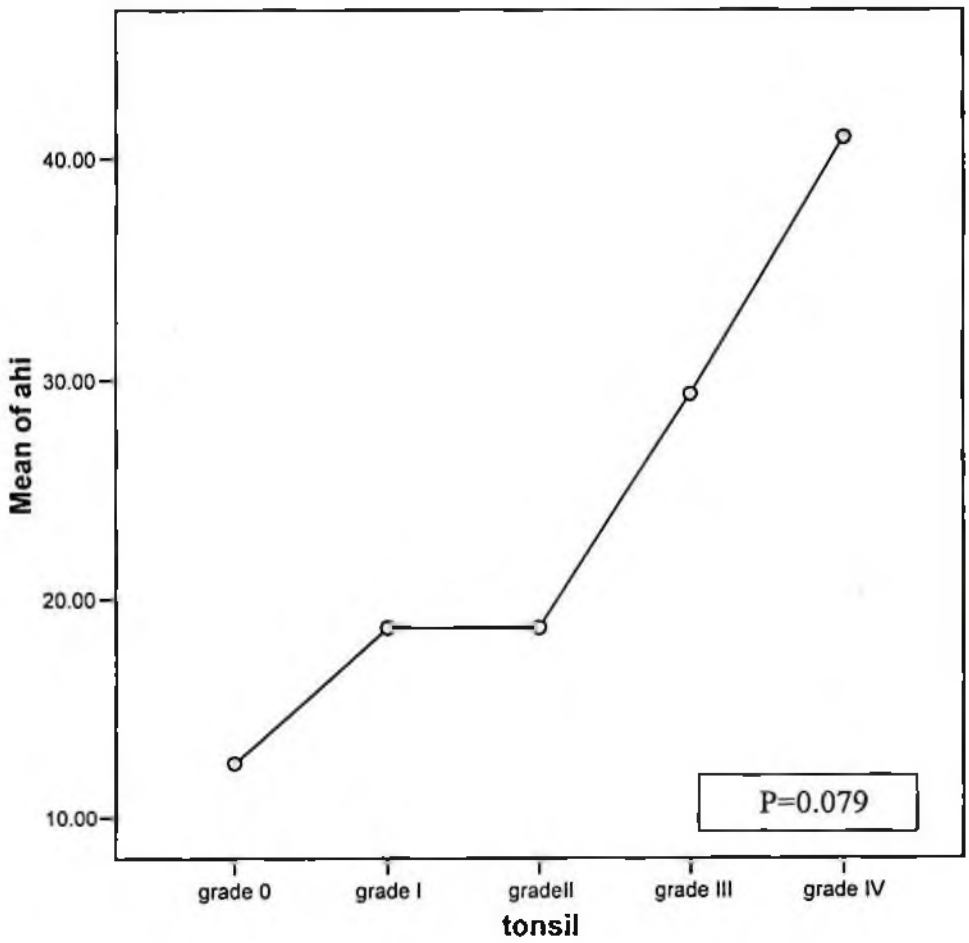

Figure 20: Means plot of the effect of tonsillar enlargement on AHI.

The severity of posterior pharyngeal crowding was assessed by the modified Mallampiti score (MS) and were classified in four groups. The effect of increasing MS on AHI was analysed by one way ANOVA (analysis of variance) and it was significant (P<0.001).

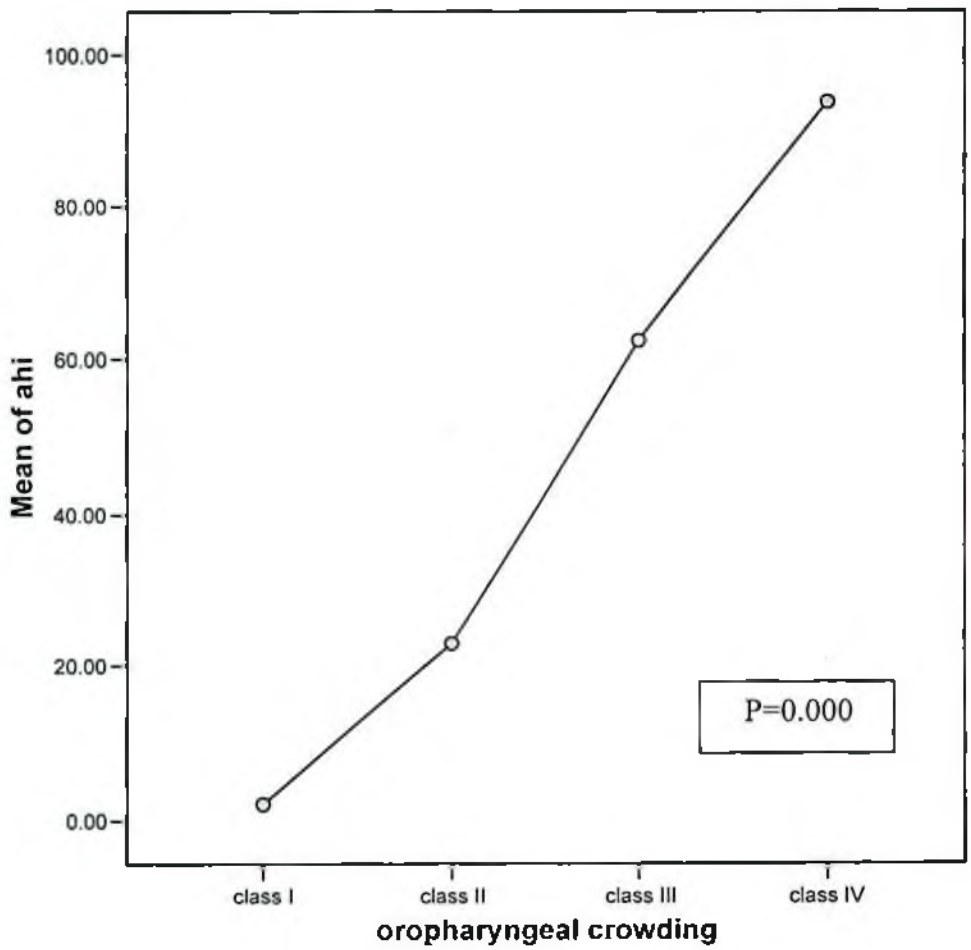

Figure 21: Means plot showing the effect of posterior oropharyngeal crowding (MS score) on AHI .

The variables including age, ESS score, BMI, WC, NC and WHR showed difference in mild, moderate and severe OSAHS. The difference was statistically significant ($P<0.05$) for ESS score, BMI and WC.

Table 13: Relationship of factors age, BMI, ESS score, WC, NC and WHR with OSAHS severity (n=65).

Variables	Mild (n_a=14)	Moderate (n_b=18)	Severe (n_c=33)	P values
Age, yrs	48.50 ± 8.98	46.67 ± 8.60	45.76 ± 10.20	0.665
BMI, kg/m^2	25.75 ± 1.97	29.16 ± 2.87	32.67 ± 3.38	0.00
ESS score	11.21 ± .43	14.33 ± 1.37	17.55 ± 1.48	0.00
WC, cms	98.79 ± 11.58	101.12 ± 11.48	109 ± 12.57	0.01
WHR	0.96 ± 0.04	0.97 ± 0.06	0.98 ± 0.05	0.668
NC, cms	39.62 ± 2.94	40.76 ± 3.85	40.41 ± 3.02	0.540

* Values are expressed as mean ± SD or No.(%), unless otherwise indicated.

PSG parameters were compared in OSAHS and control group. The sleep efficiency was significantly poor in OSAHS patients. Sleep architecture revealed significantly high light stages and low REM stages and low SWS with out significance in OSAHS group. The minimum SpO_2 (oxygen saturation) was significantly low and arousal index was significantly high in OSAHS group.

Table 14: Comparison of PSG parameters in the OSAHS and non-OSAHS subjects (N=190).*

Variables	OSAHS (n=65)	Control (n=125)	P value
Sleep Efficiency (%)	70.36 ± 14.74	79.63 ± 10.06	0.000
Sleep architecture:			
Stage I (%)	17.00 ± 10.54	7.77 ± 3.67	0.000
Stage II (%)	53.49 ± 11.55	46.24 ± 6.64	0.000
SWS (%)	20.74 ± 14.31	23.76 ± 7.14	0.054
REM (%)	8.89 ± 7.69	22.15 ± 4.31	0.000
Minimum O_2 sat (%)	65.31 ± 16.11	92.28 ± 2.11	0.000
SpO_2 <90%, mins	55.79 ± 57.19	.03 ± .14	0.000
Arousal index (%)	35.88 ± 21.39	9.50 ± 6.07	0.000
AHI	50.73 ± 38.33	0.82 ± 0.37	0.000

* Values are expressed as mean ± SD and No.(%), unless otherwise indicated.

The clinical profile of men and women with OSAHS was compared. Age was higher in female OSAHS patients and the difference was significant (P<0.001). The anthropometric measurements and ESS score did not reveal significant gender differences. Among sleep symptoms only morning or nocturnal headache was significantly higher in female (P=0.036). The HTN was shown to be higher significantly in female (P=0.039). Upper airway features showed no gender differences significantly.

Table 15: Differences of clinical profile of men and women with OSAHS (n=65).

Variables	Male (n=40)	Female (n=25)	P values
Age, yrs	41.83 ± 7.30	54.24 ± 7.11	0.00
BMI, kg/m^2	29.95 ± 3.38	30.62 ± 5.00	0.519
WC, cms	105.33 ± 12.90	84.02 ± 9.91	0.746
WHR	.98 ± .03	.96 ± .07	0.33
NC, cms	40.53 ± 3.00	40.06 ± 3.56	0.580
ESS score	15.63 ± 2.85	14.76 ± 2.83	0.238
Witness Apnea	31 (58.5%)	22 (41.5%)	0.235
Choking/Gasping	27 (67.5%)	13 (32.5%)	0.162
Brief awakening	23 (67.6%)	11 (32.4%)	0.318
Unrefreshed Sleep	31 (60.8%)	20 (34.2%)	0.751
Dry Mouth	23 (63.9%)	13 (36.1%)	0.801
Morning Headache	12 (46.2%)	14(53.8%)	0.036
Impotence	19 (63.3%)	11 (36.7%)	1.00
HTN	17 (50%)	17 (50.0%)	0.039
Macroglossia	5 (71.4%)	2 (28.6%)	1.00
Retrognathia	20 (74.1%)	7 (25.9%)	0.187
Pharyngeal crowding:			
Class I	5 (12.5%)	4 (16.0%)	
Class II	12 (30.0%)	8 (32.0%)	0.949
Class III	11 (27.5%)	7 (28.0%)	
Class IV	12 (30.0%)	6 (24.0%)	

* Values are expressed as mean ± SD or No.(%), unless otherwise indicated.

The distribution of OSAHS cases in both male and female in different age groups showed statistically significant (P<0.001) differences.

Table 16: Distribution of OSAHS cases in men and women (n=65).

Age Group	Male	Female	P
30-39.9 y	15 (37.5%)	3 (12.0%)	
40-49.9 y	16 (40.0%)	0 (0.0%)	<0.001
≥ 50 y	9 (22.5%)	22 (88.0%)	
Total	40 (100%)	25 (100%)	

*Values are expressed as mean ± SD or No.(%), unless otherwise indicated.

Receiver operating characteristic (ROC) curves showed comparison of different anthropometric parameters including BMI, WC, NC and WHR as a predictor of OSAHS. The area under curve values were .952, .899, .772 and .724 for BMI, WC, WHR and NC respectively.

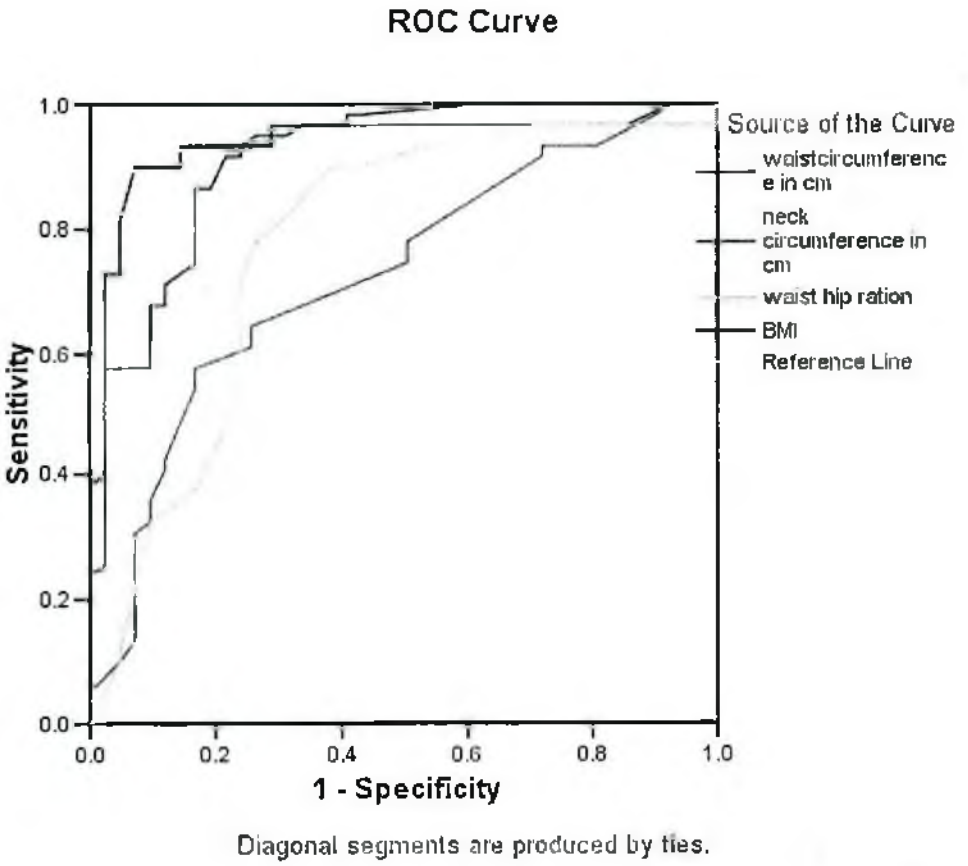

Figure 22: ROC curves showing comparison of different anthropometric parameters.

Variables showing significant association including age ≥ 46, higher education, obesity parameters BMI>25 and WC>102cm in men/WC>88 in women, habitual snoring, witnessed apnea, choking, dry mouth, morning headache, impotence, presence of HTN, macroglossia, retrognathia were analysed using stepwise multiple logistic regression. Age≥46, higher education, WC, witness apnoea and choking were revealed as independent risk factors of OSAHS (Table 17).

Table 17: Predictors of OSAHS in study population (N=190).

Variables	B	SE	OR (95% CI)
Age ≥ 46	1.793	0.737	6.00(1.416-25.468)
Higher education	2.184	0.778	8.88(1.934-40.817)
Witnessed apnea	4.289	0.942	125.119(19.749-792.706)
Choking	3.668	0.929	39.171(6.339-242.063)
Obesity(WC>102/88)	3.224	0.803	25.116(5.203-121.238)

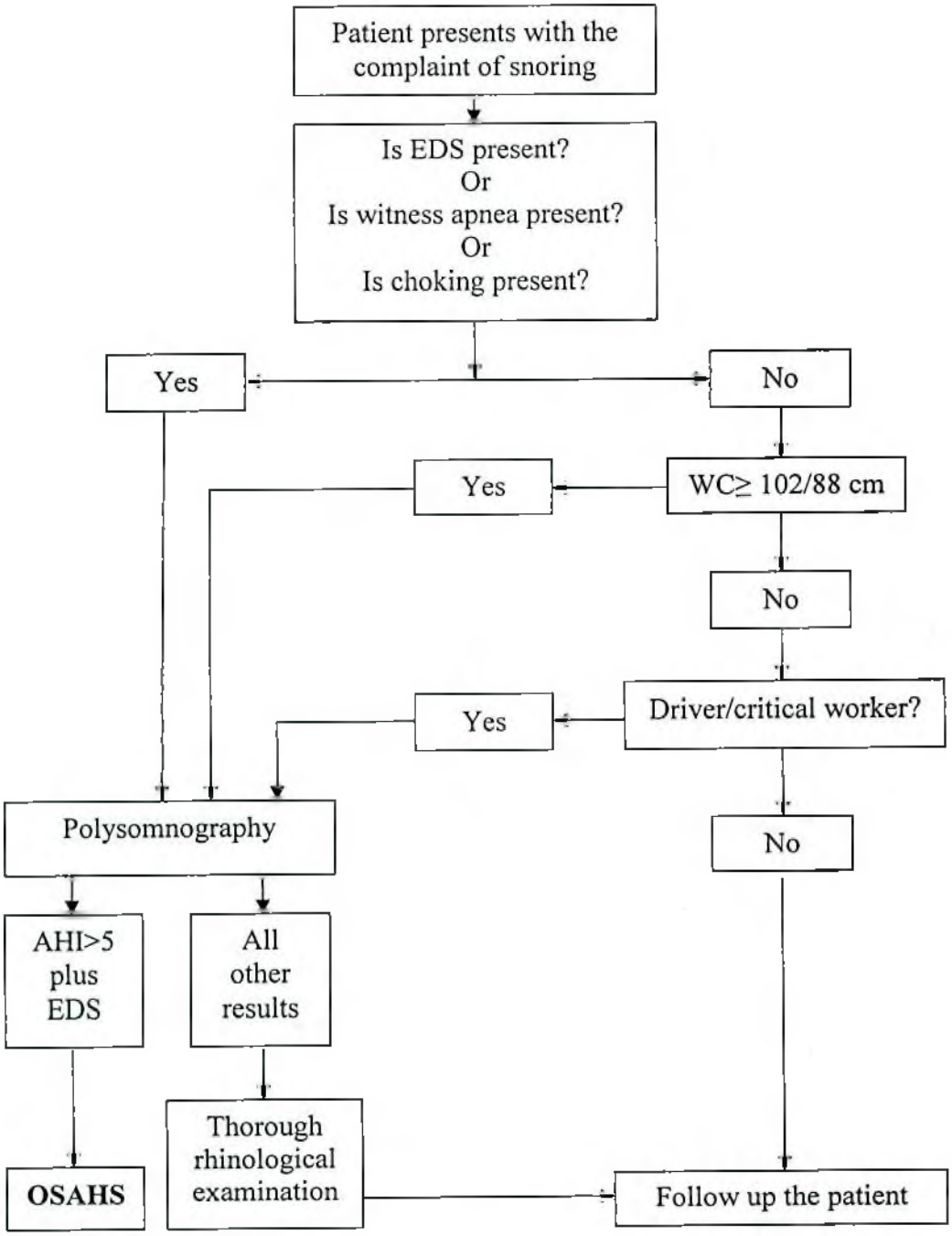

Figure 22: Proposed algorithm for diagnosis of OSAHS

5. Discussion

The burden of OSAHS is fairly high in the community. The delay in the diagnosis and treatment leads to prolonged morbidity.[125] It is remarkable that despite all of the clinical and scientific advancements regarding obstructive sleep apnea in the last two decades, a great majority (70–80%) of those affected remain undiagnosed.[126] The lack of an appropriate level of case identification is partially driven by the fact that patients are frequently unaware of the associated symptoms that are often identified either by a bed partner or family member. Compounding the lack of patient awareness, health care professionals in most medical specialties have not received the necessary training to help expedite case finding and institute early intervention for evaluation and treatment. Knowledge of OSAHS and especially its risk factors are therefore crucial for physicians to properly direct diagnostic attention at those with the highest risk. This study was aimed to identify risk factors of OSAHS among Bangladeshi adults to assist in early and appropriate referral for PSG study.

In this study, univariate analysis of variables including obesity parameter BMI≥25, habitual snoring, dry mouth, morning headache, impotence, presence of HTN, macroglossia, retrognathia were found to be associated with OSAHS, but none was proved to be independent predictor of OSAHS.

Similar to other study,[20] current study has shown an association between OSAHS and increased age. The mean age (±SD) was higher in OSAHS group compared to control group (46.60±9.41 vs. 41.09±7.06) and this difference was statistically significant ($P<0.001$). Using the younger age group (age < 45 years) as the reference category, the odds ratio (OR) for OSAHS for those in the older subjects (age ≥ 46 years) group was 3.6

(95% confidence interval, 1.92–6.79). Ip and colleagues[9] found that the prevalence of OSAHS tends to rise in the older population and that this was independent of obesity. However, some researchers [6,20] have concluded that this effect occurs only to middle age and that age ceases to be an independent risk factor for OSAHS beyond middle age. Similarly in this study, OSAHS was present in 27.7%, 24.6%, and 47.7% of the 30-39.9 year, 40-49.9 year and 50 and above age groups respectively. In male and female OSAHS was present in significantly differently in those age groups (37.5% vs.12%, 40% vs. 0% and 22.5% vs. 88% respectively, P<0.001). In this study, OSAHS prevalence was low in pre-menopausal women, the prevalence was relatively high in post-menopausal women as it was found in other study.[46] Mechanisms proposed for the age-related increase in prevalence include increased deposition of fat in the parapharyngeal area, lengthening of the soft palate, and changes in body structures surrounding the pharynx.[50] The question of whether obstructive sleep apnea in older adults represents a clinical entity distinct from that seen in middle-aged adults remains a controversial issue. Data on morbidity and mortality attributable to obstructive sleep apnea in older adults has been inconsistent, with some studies concluding increased risk of adverse outcomes whereas others report little or no association.[127] Undoubtedly, longitudinal data from representative population-based samples of older adults with adequate control for confounding covariates are needed to investigate whether obstructive sleep apnea portends excess medical risks in older people.

Earlier studies [6,9] have consistently reported a higher prevalence of OSAHS in men. In this study, the male to female ratio of OSAHS was 1.60; using female as the reference category, the odds ratio (OR) for OSAHS for male group was 1.30 (P=0.442,

95% confidence interval, 0.70–2.39). There are several reasons for the observed differences in the frequency between men and women. These include differences in the distribution of adipose tissue, upper-airway anatomy and muscle function, control of ventilation, and the effects of sex hormones and leptin.[128] The gender related protective effect decreases in postmenopausal women who are not receiving hormone replacement therapy.[129] On the contrary, this greater sleep-apnea prevalence in men has raised the concern that a selection bias for referral and identification of the diagnosis may favor men. The Wisconsin sleep cohort study estimated that sleep apnea was undiagnosed in more than 90% of women with moderate to severe sleep apnea.[126] However, the higher male preponderance shown in the current study could be due partly to the higher number of men among the subjects who underwent polysomnography studies or may be type II error.

Obesity has been an important modifiable risk factor in the occurrence of OSAHS.[30] Most Western studies have used a BMI of ≥ 30 kg/m2 as the upper limit for the definition of obesity. However, a different definition (*i.e.*, BMI ≥ 25 kg/m^2) as recommended by the World Health Organization was used in this study.[130] Other parameters of obesity were WC > 102 cm in men and > 88 cm in women, WHR of > 0.95 in men and > 0.8 in women, and NC>40 cm in men and >38 cm in women. Using parameters of BMI, WC, WHR and NC, obesity was found in 86.2% vs 24%, 70.8% vs 12%, 75.4% vs 19.2% and 69.2% vs 26.4% respectively. These obesity parameters were compared between OSAHS and control subjects and showed statistically significant association with OR as 19.70 (95% CI 8.72-44.50, P=<0.001), 17.75 (95% CI 8.31-37.94, P<0.001), 12.89 (95% CI 6.28-26.44, P<0.001) and 6.27 (95% CI 3.24-12.14, P<0.001). Among them BMI and

WC showed significant relation with increasing severity of OSAHS. Multiple logistic regression analysis revealed obesity parameter WC>102/88 as independent predictor of OSAHS subjects. Despite the unquestionable link between obesity and obstructive sleep apnea, controversy remains as to whether specific measures of body habitus (e.g., neck circumference, waist circumference) that reflect a central versus peripheral distribution of fat are associated with an increased risk for obstructive sleep apnea after controlling for BMI.[51] Receiver operating characteristic (ROC) curves showed comparison of different anthropometric parameters including BMI, WC, NC and WHR as a predictor of OSAHS. The area under curve values were 0.952, 0.899, 0.772 and 0.724 for BMI, WC, WHR and NC respectively.

Though snoring is the commonest symptom,[6] it definitely does not imply OSAHS.[131-2] Habitual snoring was categorized if the subject or bed partner complained of snoring in 4 or more nights per week[11] and was found in 52.6% of total subjects in this study. Habitual snoring was found in OSAHS group more frequently (98.5% vs. 28.8%, P<0.001) compared to normal group. Symptoms including witnessed apnea (81.5% vs.8%), choking or gasping (61.5% vs. 4.8%), brief awakening from sleep (57.8% vs. 14.4%), feeling unrefreshed after sleep (79.7% vs.41.6%), dry mouth during sleep (56.3% vs. 12%), morning headache (40.60% vs. 7.20%) and impotence (47.6% vs. 7.20%) were reported more frequently in OSAHS group and showed statistically significant differences between two groups (P<0.05). Symptoms like restlessness during sleep, sleep talking, excess sweating during sleep, nocturia and recent weight gain, if the subject gained ≥5% of weight of the previous year in 1 year were reported more frequently in case group, but not significant statistically. Among all these symptoms only witnessed

apnea and choking were revealed to be independent predictor (P<0.05). Another study reports similarly with witnessed apnea being the only predictor of OSA in severely obese subjects while choking and other OSAHS symptoms showed less correlation.[132]

EDS is a common condition, reported by 5% to 12% of adult subjects in a population survey.[133] In this study, ESS score was used to quantify the degree of sleepiness and a cut off score ≥11 was labeled as sleepy. EDS was reported more frequently in OSAHS group compared to control (100% vs. 29.6%, P<0.001), but it was not an independent predictor. In another study,[132] ESS score failed to predict OSA in severely obese, as daytime sleepiness measured by the ESS score were frequent both in those with and without sleep apnea. In a pilot study among Bangladeshi doctors and nurses in a hospital, about 41% subjects showed ESS score ≥11.[25] In this study, mean ESS score in the OSAHS group was significantly higher (15.29 ± 2.85 vs. 6.95 ± 2.76) than the non-OSAHS group (P <0.001) similar to other study.[134]

An interesting and unexpected observation that has emerged is that, while Asians are less obese than whites, disease prevalence in the East is no less than in the West. Moreover, for a given age, sex, and BMI, Asians have greater disease severity than whites.[66-7] It is established that differences in craniofacial features between Asians and Whites is the etiologic factors for the increased risk and greater severity of obstructive sleep apnea in Asians despite lesser degrees of obesity.[68] Retrognathia and macroglossia were reported more frequently in OSAHS group and this difference was significant (P<0.05). Tonsillar enlargement was reported more frequently in OSAHS group, but had no statistical significance. Posterior pharyngeal crowding as assessed by modified Mallampiti score (MS), was significantly more in OSAHS group (P<0.05). Additionally the effect of

increasing severity of posterior pharyngeal crowding as assessed by the modified MS on AHI showed to be significant (P=0.00), which was not found in tonsillar enlargement. Tsai and associates recently developed a decision rule for the diagnosis of OSA based on similar features of upper airway morphology including cricomental space (the perpendicular distance to the skin of the neck from the midpoint of a line joining the cricoid to the mentum); pharyngeal grade (similar to the MS); and overbite.[135] Use of the decision rule allowed these investigators to confidently confirm or exclude OSA in 44% of patients. These results strongly suggest that clinical measurements of craniofacial profile need inclusion in the development of algorithms for the diagnosis of OSA and the referral for polysomnography.

Increasing age, BMI, ESS score, NC, WC and WHR were compared in different categories of OSAHS severity; among them BMI, WC and ESS score showed statistically significant (P<0.05) positive correlation with increasing severity of OSAHS in this study, conflicting with other study where only NC and ESS score were significant.[134] Differences in clinical profile were compared between male and female OSAHS patients. Female patients were older and heavier, but not significant in this study. For the other sleep problems, women more frequently reported symptoms of restless legs, depression, and insomnia than male.[136] But in this study early morning or nocturnal headache was common in women.

PSG parameters were compared in OSAHS and control group. There was a significant difference in sleep efficiency. Sleep architecture revealed significantly higher light and low REM stages in OSAHS group compared to non-OSAHS group and the difference is significant; though no significant difference was noticed in SWS between groups, it was

low in OSAHS group. This study also showed that minimum SpO_2 (oxygen saturation) was significantly low and arousal index was significantly high in the OSAHS group similar to other study.[11]

In this study, association of HTN and DM were compared with OSAHS and control group. The prevalence of hypertension (HTN) and diabetes mellitus (DM) were greater in OSAHS subjects, though the difference was significant statistically in HTN. In this study, odd ratio for HTN was 2.91. In other studies both DM and HTN were found more frequently among OSAHS patients.[22,82] In a study among Asians, it was found that OSA patients were 3 times more likely to have HTN.[22]

Several limitations to the present study should be considered. The case-control study cannot estimate prevalence or incidence of the disease, nor the attributable or excess risk. The biggest weakness of case-control study was susceptibility to bias, mainly from two sources- separate sampling of cases and controls, and retrospective measurement of the predictor variables. Cases were not representative of the community OSAHS population as only available diagnosed cases were sampled due to limited resource and rarity of the disease. Population based nested case-control design could eliminate this sampling bias, which was not possible for poor record keeping. On the other hand, the subjects in the study were more urbanized and educated than most Bangladeshi.

Strength of this study was that a large number of predictors of OSAHS were investigated in a least expensive design, which is suitable in our setting. The assessment of EDS for the definition of OSAHS using the ESS score, which is a well-tested international instrument for the evaluation of EDS and the overnight in-laboratory attended polysomnography to diagnose OSAHS were strong component of this study.

Large population based cross-sectional study of OSAHS patients among Bangladeshi adults are scanty. These are necessary to identify predictors of OSAHS with less bias. Even considering the weakness of case–control design, in the absence of previous knowledge about this issue in the present study's setting, the observations found are helpful to generate new hypothesis. The clinical parameters of craniofacial profile including (a) thyromental distance (TMD)-the horizontal distance from the thyroid prominence to a perpendicular dropped from the soft tissue mentum, measured with a modified tape measure with a vertical attachment, (b) thyromental angle (TMA)- the angle between the soft tissue plane of the anterior neck and a plane running through the soft tissue mentum and the thyroid prominence, measured from a lateral photograph of the head and neck taken in the natural head position with the patient looking straight ahead were not included in this study. These craniofacial parameters are proved to be strong predictors of OSAHS among Asians.[68] Further study including these parameters will be more informative to predict OSAHS and prioritize patients for PSG.

In this study, stepwise multiple logistic regression were used to analyze variables of significant association including age ≥ 46, higher education, obesity parameters BMI≥25 and WC>102cm in men/WC>88 in women, habitual snoring, witnessed apnea, choking, dry mouth, morning headache, impotence, presence of HTN, macroglossia, retrognathia. Among those age≥46, higher education, WC, witnessed apnea, choking were revealed as independent clinical predictors of OSAHS. These results strongly suggest that parameters of obesity especially WC was very important predictor of OSASH in our study population. In addition, association of craniofacial features including macroglossia, retrognathia, oropharyngeal crowding that reflect structural narrowing of the upper

airway needs to be explored in further large population based studies in Bangladeshi population. As these are readily identified, can easily be incorporated into the routine physical examination of suspected OSAHS cases. Recognition of these abnormalities in the craniofacial profile should alert the physician to the possibility of OSAHS and prioritise patients for polysomnography.

In conclusion, similar to other Asians, the Bangladeshi are too will not be protected from the sweeping epidemic of obesity and the new kinds of health problems that it heralds. With the increasing problem of obesity, the impact of undetected OSAHS as a public health burden cannot be undermined and merits implementation of appropriate management and preventive strategies.

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Appendix-I

Questionnaire (Case/Control)

ID no: **Date:**

Address: **Tel:**

Sociodemographic:

1. Age in yrs(30-60):
2. Sex: male/female
3. Educational status: nil / primary /secondary / tertiary
4. Smoking: current smoker / current non-smoker / ex-smoker / non-smoker
5. Alcohol intake: yes/no
6. Snoring: Habitual / Non-habitual / Non-snoring
7. Duration of snoring:.....yrs
8. Family history of snoring: yes/no

Sleep history:

9. Excessive daytime sleepiness (EDS): yes/no

Daytime sleepiness will be assessed with four subjective questions. Using a 5-point scale (0 to 4), the subjects will be rated. The answer will be positive if the score was ≥ 2. Subjects will have excessive daytime sleepiness (EDS) if they give a positive response to three of the four questions:

Questions	Never	Rare	Sometimes	Often	Everytime
(1) felt excessively sleepy during the daytime	0	1	2	3	4
(2) felt unrefreshed or tired during the day, regardless of how long they had slept	0	1	2	3	4
(3) fell asleep or dozed off momentarily while watching TV, reading, or at meetings/mosque	0	1	2	3	4
(4)felt sleepy while driving/ working/ talking	0	1	2	3	4

9. **ESS score:** The following scale will be used for the appropriate number for each situation:

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

Sitting and reading	
Watching TV	
Sitting in active in a public place (e.g. a theater or meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the after noon When circumstances permit	
Sitting and talking to some one	
Sitting quietly after a lunch with out alcohol	
In a car while stopped for a few minutes in traffic	
Total	

10. Witnessed apnea: yes/no.
11. Choking or gasping or snorting sound during sleep : yes/no.
12. Excessive sweating: yes/no.
13. Restless sleep: yes/no.
14. Abnormal limb movements during sleep: yes/no.
15. Dry mouth during sleep: yes/no.
16. Sleep talking (somniloquy): yes/no.
17. Brief awakening from sleep: yes/no.
18. Bruxism: yes/no.
19. Nocturia: yes/no.
20. Enuresis: yes/no
21. Unrefreshed sleep: yes/no.

22. Morning or nocturnal headache: yes/no
23. Impotence or loss of libido: yes/no.
24. Impaired cognitive function: yes/no.
25. Memory impairment: short term/ long term/ nil
26. Automobile accidents in last 3 yrs : 0/1/2/3/4/do not drive

Comorbidities:

27. Hypertension: yes/no
28. Diabetes Mellitus (DM): yes/no

Anthropometric measurements:

29. Body mass index (BMI):
30. Waist circumference in cm:
31. Hip circumference in cm:
32. Waist hip ratio (WHR):
33. Neck circumference (NC) in cm:
34. Recent weight gain: yes/no

Examination of oronasal cavity:

35. Nasal cavity: normal / septal deviation / trauma or surgery /rhinitis / polyp / HIT
36. Dental problem: Dental overjet / malocclusion / overlapping / nil
37. Retrognathia: yes/no
38. Macroglossia: yes/no
39. Tonsils:grade 0/grade I/grade II/grade III/grade IV
40. Oropharyngeal crowding: class I/class II/class III/class IV

41. **PSG data :**

i. Total sleep time: .....hrs

ii. Snoring: yes / no

iii.Sleep efficiency (%):

iv.Sleep latency in mins:

v.AHI (%):

vi. stage 1 sleep (%):

vii. stage II sleep (%):

viii. slow wave sleep (%):

ix. REM sleep (%):

x. PLMI (%):

xi. Arousal index (%):

xii. Minimum oxygen saturation (%):

xiii. SpO2 < 90% in mins:

xix. PSG diagnosis: OSA / non-OSA / simple snoring / Normal sleep

(Signature of the interviewer & date)