A CRANIOFACIAL MORPHOLOGY STUDY OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

By

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DEDICATION

To my parents, for their unconditional love, support and encouragement during my work.

To my sisters, Aseel, Hadeel whose love and support made this possible.

To my in-law, Bashar, Raed, and **my sweet nieces**, Basma and Salim. Your smiles are all I need for encouragement.

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LIST OF ABBREVIATIONS

AHI	Apnea-Hypopnea Index
OSA	Obstructive Sleep Apnea
OSAS	Obstructive Sleep Apnea Syndrome
CSA	Central Sleep Apnea
AI	Apnea Index
HI	Hypopnea Index
RDI	Respiratory disturbance Index
UARS	Upper Airway Resistance Syndrome
SAHS	Sleep Apnea / Hypopnea Syndrome
BMI	Body Mass Index
NC	Neck Circumference
EDS	Excessive Daytime Sleepiness
HRQL	Health-Related Quality of Life
OSAHS	Obstructive Sleep Apnea – Hypopnea Syndrome
ICD	Inter canine Distance
1st IPD	Inter First Premolar Distance
2 nd IPD	Inter Second Premolar Distance
IMD	Inter Molar Distance
ANS	Anterior Nasal Spine
PNS	Posterior Nasal Spine
SPl	Length of Soft Palate
SPW	Width of Soft Palate

TI	Length of the base of tongue
TW	Width of tongue
SPAS	Upper Posterior Pharyngeal Space
MPAS	Middle Posterior Pharyngeal Space
IPAS	Inferior Posterior Pharyngeal Space
SNA	Position of Maxilla
SNB	Position of Mandible
Ba-S- N	Cranial Base Flexure Angle
PNS	Posterior Nasal Spine
ANS	Anterior Nasal Spine
NS	Anterior Cranial Base
SBa	Posterior Cranial Base
J-J	Maxillary Width
ZA-ZA	Facial Width
AG-AG	Mandibular Width
Kg	Kilogram
mm	Millimeter
NL	Nasopharyngeal Length
NW	Nasopharyngeal Width
OL	Oropharyngeal Length
OW	Oropharyngeal Width
HL	Hypopharyngeal Length
HW	Hypopharyngeal Width

GLOSSARY

1. Apnea: is the cessation of airflow at least 10 seconds.

2. Apnea index (AI): is the number of apneas per hour of sleep, with 5 or less considered normal.

3. Obstructive sleep apnea (OSA): is the cessation of airflow despite adequate effort to breathe.

4. Central sleep apnea (CSA): is the cessation of airflow from lack of respiratory effort.

5. Mixed sleep apnea (MSA): is the cessation of airflow starting as central followed by obstructive.

7. Hypopnea (H): is an abnormal reduction of airflow for at least 10 seconds.

8. Upper airway resistance syndrome (UARS): is an incomplete upper airway obstruction without apneas or hypopneas. Snoring, inadequate sleep, and daytime sleepiness characterize this condition.

9. Respiratory disturbance index (RDI): is another term for apnea-hypopnea index (AHI). The definition of slight OSA is RDI of 5 to 14 H, moderate OSA is RDI of 15 to 30 H, and severe OSA is RDI of >30 H.

A CRANIOFACIAL MORPHOLOGY STUDY OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

ABSTRACT

Obstructive sleep apnea (OSA) is defined as a repetitive cessations of breathing (apneas) lasting for at least 10 seconds or more for each event during sleep. The respiratory muscles attempt to inspire, but blockages in the upper airway prevent air from reaching the lungs. This will cause partial (hypopnea) or complete (apnea) closure of the upper airways with consequent adverse effects on sleep quality and gas exchange. The condition affects approximately 4% of men and 2% of women in their middle-ages. OSA is a potentially life-threatening condition in which a patient suffers periodic cessations of breathing during sleep. The aim of this study is to develop a data base on the craniofacial morphology of the upper airway morphology and skeletal patterns in patients with OSA and compare the findings with those of normal subjects in the control group. Twenty-five subjects as OSA patients and twenty-five as the control group were selected from the Sleep Laboratory by using Polysomnography. All the subjects of this study were adults age ranging 18-65 years. Methodologies include the measurements of the body mass index (BMI), neck circumference, lateral cephalometric X-ray, posterior-anterior X-ray, and upper and lower dental study models were taken. For severe OSA cases, the diameter of the pharynx was estimated by measuring the length and width of the pharynx at the level of nasopharynx, oropharynx, and hypopharynx, and compared with normal subjects by using CT scan. The results showed that there was a significant difference in BMI between OSA patients and control group (P value=.001), the BMI significantly increased in OSA patients, the neck circumference was also increased in OSA patients. The length of soft palate, width of soft

palate, width of tongue, upper posterior airway space, middle posterior airway space, lower posterior airway space, distance from hyoid bone to mandibular plane, distance from hyoid bone to posterior nasal spine, maxillary width, and cranial base flexure angle were statically significantly different in OSA patients compared to the control group. There were no significant differences between the two study groups in the inter-canine, inter-first and second premolar, inter-molar distances of upper and lower arches, maxillary protrusion, mandibular prognathism, lower face height, total face height, posterior facial height, facial width, mandibular width, anterior cranial base, and posterior cranial base. The CT scan shown that severe OSA patients have narrowing of pharynx at the level of nasopharynx, oropharynx, and hypopharynx. In conclusion, craniofacial morphological differences have been found in patients suffering from OSA as compared to control, and that a number of investigations and measurements are required to detect underlying deformities, to decide for the most suitable management methods.

Kajian Morfologi Kranofasial Pesakit- Pesakit Henti Dalam Tidur
(Bermasalah Tidur Obstruktif Apnea)

ABSTRAK

Masalah tidur obstruktif apnea (OSA) didefinisikan sebagai pemberhentian pernafasan berulang (apneas) yang berlaku sekurang-kurangnya selama sepuluh saat atau lebih pada sesuatu ketika semasa tidur. Otot pernafasan berusaha merangsang tetapi sekatan di bahagian atas saluran pernafasan menghalang udara dari sampai ke paru-paru. Ini akan menyebabkan penutupan separa atau penuh pada saluran pernafasan bahagian atas yang menyebabkan kesan mudarat keatas kualiti tidur dan pertukaran gas. Keaadaan ini memberi kesan kepada 4% lelaki dan 2% wanita pada peringkat umur pertengahan. OSA adalah satu keadaan yang membahayakan nyawa dimana pesakit mengalami pemberhentian pernafasan berkala ketika tidur. Tujuan kajian ini ialah untuk mengembangkan informasi pengkalan data morfologi kraniofasial tentang morfologi saluran pernafasan bahagian atas dan corak skeletal dalam pesakit OSA dengan membandingkan penemuan yang didapati dengan keputusan dari subjek yang normal dalam kumpulan kawalan. Oleh itu, dua puluh lima orang subjek diambil sebagai pesakit OSA dan dua puluh lima orang sebagai kumpulan kawalan yang dipilih dari Makmal beradu menggunakan polysomnografi. Semua subjek untuk kajian ini adalah orang dewasa berumur 18 tahun keatas. Metodologinya termasuklah mengira index jisim badan (BMI), lilitan leher setiap subjek, x-ray cefalometrik lateral, x-ray posterior –anterior, dan model kajian gigi bahagian atas dan bawah juga diambil. Diameter farinks ditentukan dengan mengukur kawasan saluran pernafasan yang paling minimal termasuk panjang dan lebar saluran pernafasan pada bahagian nasofarink, orofarink dan hypofarink, kemudian dibandingkan dengan subjek yang normal menggunakan imbasan CT . Imbasan CT hanya diambil untuk OSA yang

teruk. Usaha juga dilakukan untuk menentukan kekerapan pesakit untuk tidur dalam situasi yang berbeza menggunakan kajiselidik skala tidur Epsworth. Keputusan menunjukkan terdapat perbezaan signifikan BMI antara pesakit OSA dan kumpulan kawalan (nilai $P = .001$). BMI meningkat secara signifikan bagi pesakit OSA , lilitan leher pesakit OSA juga meningkat. Panjang lelangit lembut, lebar lelangit lembut, lebar lidah , ruang atas posterior saluran udara, ruang tengah posterior saluran udara, ruang bawah posterior, saluran udara, jarak antara tulang hioid ke plana madibular, jarak dari tulang hioid ke spina hidung, lebar maksilari, dan sudut fleksur tapak kranial berbeza secara signifikan bagi pesakit OSA dibandingkan dengan kumpulan kawalan. Tiada perbezaan yang signifikan antara dua kumpulan kajian dalam inter-kanin, inter-first dan premolar kedua, jarak inter – molar bahagian lengkungan atas dan bawah, protusi maksilari, pronatisma mandibular, ketinggian muka bawah, ketinggian keseluruhan muka, ketinggian muka posterior, lebar muka, lebar mandibular, tapak kranial anterior, dan tapak kranial posterior. Skala tidur Epsworth mempunyai perbezaan yang signifikan bagi pesakit OSA dan grade skala meningkat bagi pesakit OSA. Imbasan CT menunjukkan bahawa pesakit OSA peringkat teruk mempunyai farink yang sempit pada tahap nasofarink, orofarink dan hypofarink. Kesimpulannya, kelainan ukuran kraniofasial telah dikenal pasti dalam pesakit yang mengalami OSA, dan beberapa kajian dan pengukuran lain perlu untuk mengenal pasti kelainan yang berkaitan dan seterusnya menentukan kaedah yang paling sesuai untuk menguruskannya.

CHAPTER ONE

INTRODUCTION

1.1 Background

Over the past two decades, medicine and dentistry have increasingly focused on breathing disorders during sleep. The characteristics of obstructive apnea have been described in the medical and classical literatures for decades, in the 19th century Broadbent, who described the perfect silence during sleep through two, three, or four respiratory periods in which accompanied by ineffectual chest movements. Finally air enters with a loud snort, after which there are several compensatory deep inspiration (Jureyda and Shucard, 2004).

The understanding of sleep-disordered breathing has been evolved over the years. The first description of abnormal breathing with polygraphic demonstrations during sleep was first reported in France in 1955, in-patient with Pickwickian syndrome. Pickwickians patients had combination of obesity, edema, cardiac symptoms, and agitated sleep presented abnormal breathing patterns during sleep (Gilleminault and Quo, 2001).

Sleep apnea owes its name to Greek word apnea, meaning "want to breathe" (Yantis, 1999). Sleep apnea is a sleep disordered breathing characterized by repetitive cessation of breathing (apneas) lasting for at least 10 seconds, and occurring 30 times or more during 7 hours of nocturnal sleep (DePonte *et al.,* 1999).

Partial obstructive of the upper airway, termed hypopneas, also affects oxygen saturation, which led to sleep disturbances. These partial obstructions are defined as

polygraphic events with a reduction of airflow, as measured by thermistor, also lasting more than two breaths.

Investigations using specific polygraphic recordings of normal-weight patients with abnormal breathing during sleep led to the description of the (obstructive sleep apnea) OSA. The definition of the apnea syndrome came from studies that coxexist with excessive daytime sleepiness or related problems in daytime functions (Guilleminault and Quo, 2001).

The discovery of sleep apnea and its various forms and the subsequent elucidation of sleep disorder breathing (SDB) as a major mechanism of sleep pathology became a major impetus for the development of modern sleep medicine. The discovery obstructive sleep apnea (OSA) stimulated vigorous investigations in a new field of respiratory physiology focused on the control of upper airway function awake and in sleep (Nowara, 2001).

Sleep apnea is generally classified into obstructive sleep apnea (OSA), central sleep apnea (CSA) and mixed sleep apnea (MSA). OSA was recognized as the most common disorder with significant morbidity and potential mortality occurring in 2-4% of middle-aged adults. It was characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. These manifest as a decrease in airflow despite ongoing inspiratory efforts. The lack of adequate alveolar ventilation results in oxygen desaturation of at least 3%. Sleep-related obstructive breathing events are characterized by transient (10 seconds or longer) reduction in (hypopnea) or complete cessation of (apnea) respiratory flow. OSA is associated to snoring, obesity, systemic or pulmonary hypertension sleep

related cardiac dysrhythmias, nocturnal angina, gastroesophageal reflex, impaired quality of life, and insomnia.

CSA, it is less common which caused by some problems in the central nervous system and occur when the brain fail to send appropriate signals to the breathing muscle to initiate breathing causing cessation of all respiratory effort during sleep (Walter and Eliot, 2002).

MSA is the combination of both OSA and CSA. An episode of MSA usually starts with a central component and then becomes finally obstructive in nature (Jonas 2001).

Apnea refers to cessation of nasal and oral airflow. Hypopnea refers to a reduction in airflow to <50% of baseline in association with oxyhaemoglobin desaturation. Apnea – Hypopnea index (AHI) indicating the number of respiratory irregularities per sleep hour. AHI is calculated as (total number of apneas + hypopnoea) / (Total sleep time in minutes) x60 Obstructive sleep apnea may be mild (AHI < 15 events per hour), moderate (AHI = 15-30 events per hour), and sever (AHI = >30 events per hour).

1.2 Statement of the problem

OSA is a potentially life-threatening condition in the patient, who suffers periodic cessation of breathing during sleep, which impairs the quality of life (Ang *et al.,* 2004).

Sleep apnea patients appear to have at least twice as much hypertension, ischemic heart disease and cerebrovascular disease. The most serious potential consequence of sleepiness

is impaired preferences at the wheel while driving and there is convincing evidence that sleepiness is substantial risk factor for driving accidents (McNicholas *et al.,* 2002).

The National Traffic Safety Administration (NHTSA) estimated that the annual cost of motor vehicle accidents related to sleep deprivation totaled $12.4 billion. Other studies have shown that patients with sleep-disordered breathing who had been diagnosed with sleep apnea can have a seven- to 15-fold increase in accident frequency and an eightfold increase in the fault frequency (Bailey and Attanasio, 2001).

It is reported that 40 to 30 million Americans have some type of chronic sleep disturbance, and 20 to 30 million have intermittent sleep–related problem. A survey by the Gallup organization indicated that as many as 65 million Americans have sleep disorders and that 32% of the 65 million reported excessive daytime sleepiness that can interfere with their normal daytime routine (Bailey and Attanasio, 2001).

OBJECTIVES OF THE STUDY

3.1 General objective

The aim of this study is to obtain data base information of the craniofacial deformities in patients with obstructive sleep apnea.

3.2 Specific objective

1. To compare the dental morphometric data between OSA patients and a control group.

2. To compare the skeletal patterns observed in OSA patients and control group.

3. To compare the difference of the soft tissue patterns between OSA patients and control group.

4. To compare the length and width of the pharynx between OSA patients and control group at the levels of the nasopharynx, oropharynx, and hypopharynx.

3.3 Hypothesis

Abnormalities of craniofacial structure, including skeletal pattern and upper airway morphology, cause obstructive sleep apnea.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Obstructive sleep apnea (OSA) is the periodic reduction (hypopnea) or cessation (apnea) of breathing due to narrowing of the upper airways during sleep. The main symptom is daytime sleepiness, which may lead to premature death, hypertension, ischemic heart disease, stroke, and road traffic accidents. The high prevalence of the syndrome and the morbidity and mortality thought to be associated with it have led to the view that sleep apnea may be as big a public health hazard as smoking (Wright *et al.,* 1997).

The interaction between anatomy and muscle function of the upper airway is considerable importance to understanding the OSA (Ono *et al.,* 1996). The pathophysiologic etiology of OSA includes factors related to the upper airway, especially at the level of the soft palate and the base of the tongue. Other etiologies include, relative mandibular retrognathia, low position of the hyoid bone, decrease in posterior airway space, increased tongue volume, and enlargement of the palatine or adenoidal tissue (Gavish *et al.,* 2000).

Sleep arousal is an important defense mechanism, which was induced by internal stimuli activation of the autonomic nervous system, also called subcortical arousals, which are reflected by abrupt cardiac changes such as heart rate, arterial blood pressure, respiratory change, muscular or galvanic skin responses. The mechanoreceptor-triggered arousal

depends on the level of negative pressure during aggravated inspiration (Scholle and Zwacka, 2001).

The severity of sleep apnea is defined on the basis of the apnea – hypopnea index (AHI). OSA is defined by the presence of at least 5 obstructive apneas or hypopneas, or both happened per hour while the patient is a sleep. OSA is commonly divided into 3 levels of severity: mild AHI < 15 events per hour, moderate AHI are about 15-30 events per hour, and sever AHI >30 events per hour.

Recently, a survey of health care utilization among OSA patients showed that during the 10 years before diagnosis they had already been heavy users of health services for several years. The estimated cost of this care was twice as much as that of average patients. This finding reflected the underlying risk factors such as obesity, alcohol and tobacco consumption in OSA patients (Tangugsorn *et al.,* 2001).

The prevalence of OSA was 4% in men and 2% in women 30 to 60 years of age, and it may be much higher among elderly persons. A recent publication from The National Center on Sleep Disorders Research at the National Heart, Lung, and Blood Institute suggested that sleep apnea is common as asthma (Millman, 1999).

2.2 Sleep Apnea

Sleep apnea is defined as a repetitive cessation of breathing (apneas) lasting for at least 10 seconds, and occurring 30 times or more during 7 hours of nocturnal sleep (Francesco, 1999).

Sleep apnea is a potentially life-threatening condition in which the patient suffers periodic cessations of breathing during sleep, which impairs the quality of life. The main presentation is loud snoring which the individual is usually not aware, the irregular breathing patterns and restless movements in bed characterize of this disorder.

The sleep apnea syndrome represents something of a paradox in clinical medicine. On the one hand, this disorder has been recognized only in recent decades, and it is still regarded as a niche interest by many clinicians, particularly those from clinical disciplines other than respiratory medicine, neurology and otolaryngology. On the other hand, the syndrome is now recognized as being very common and current epidemiological data indicate that sleep apnea syndrome is second only to asthma in the prevalence league table of chronic respiratory disorders. Further more, there is increasing evidence that the sleep apnea syndrome is associated with a considerable number of adverse sequel in both behavioral and physical condition. Behavioral consequences include daytime sleepiness, impaired concentration and neuropsychological dysfunction, where as physical consequences include cardiovascular disorders, particularly hypertension (McNicholas *et al.*, 2002).

2.3. Classification of Sleep Apnea

2.3.1 Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway obstruction and increased upper airway resistance, leading to high negative intrathoracic pressure with consequent increased work of breathing, alveolar hypoventilation with hypoxemia, abnormal autonomic function, frequent arousal, movement of the legs or body, sleep fragmentation and derangement of sleep architecture (Lin *et al.,* 2003).

OSA is a common disorder affecting approximately 4% of men and 2% of women in the middle-aged workforce. Snoring is a precursor to OSA, which is more common affecting 40-60% of adults. These disorders result from sleep-related narrowing of the upper airway, which is though to be to varying combinations of anatomical and neuromuscular factors that culminate in an imbalance of forces acting on the airway. The respiratory muscles attempt to inspire, but a blockage in the upper airway prevents air from reaching to the lung (Figure 2.1). The figure show stop of nasal flow while the muscles of thorax and abdomen continue attempt to breath, also it show decrease in oxygen saturation. This will causes partial (hypopnea) or complete (apnea) closure of the upper airway, with consequent adverse effects on sleep quality and gas exchange.

Figure 2.1 Graph showing the attempt of the respiratory muscles to breath (Adapted from sleep science laboratory, Hospital Universiti Sains Malaysia)

OSA is an important widely prevalent public health problem. The typical symptoms during sleep are apnea, snoring, dyspnea, and choking episodes. Once apnea or hypopnea develops, recurrent arousal causes excessive sleepiness and cognitive decreases during the daytime. The combination of acute and chronic haemondynamic effects in obstructive sleep apnea have been associated with increased risk of myocardial infarction, cerebrovascular accidents, hypertension, and congestive heart failure.

2.3.2 Central Sleep Apnea (CSA)

Central apnea is defined as 10 seconds or more of no airflow without ventilatory effort (Figure 2.2). The figure show stop of nasal flow and the muscles of the thorax and abdomen also do not attempt to breath. Central sleep apnea (CSA) is diagnosed if the frequency of central apneas and hypopneas exceed 5 per hour and is accompanied by symptoms of daytime sleepiness. CSA is thought to develop when a stimulus by hypoxemia, arousals, and pulmonary congestion results in periods of increased ventilation and subsequent decline in CO_2 (Hahn and Staats, 2004).

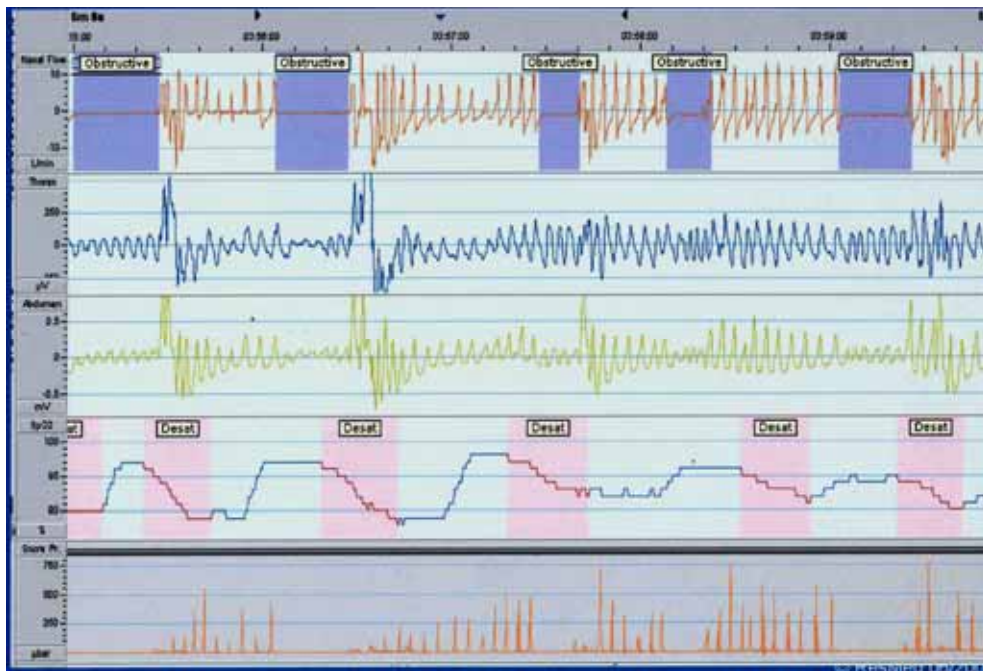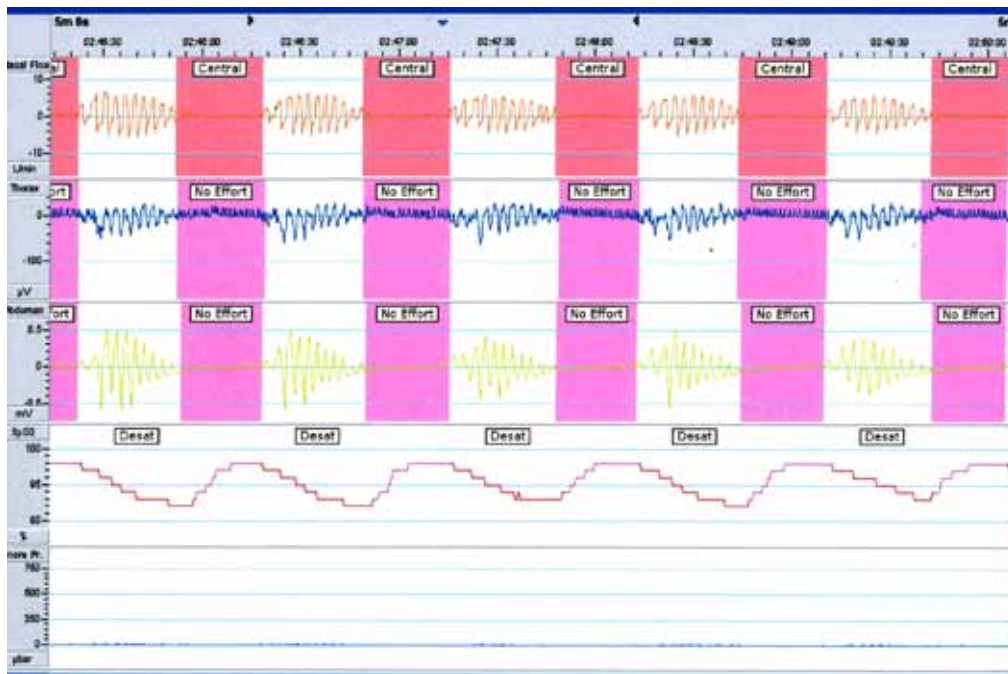**Figure 2.2 Graph showing no attempt of respiratory muscles to breath(Adapted from sleep science laboratory, Hospital Universiti Sains Malaysia)**

CSA constitutes a heterogeneous group of disorders whose common feature is a momentary cessation of breathing during sleep due to a transient withdrawal of central

respiratory drive to the muscles of respiration. Thus, in contrast to OSAS, in which respiratory drive continues during apnea, in CSA no respiratory efforts or intrathoracic pressure swings are generated.

The clinical evaluation and treatment of these disorders is challenging because they are relatively uncommon, which can arise from entirely different underlying causes, and have widely varying clinical presentations. Increases in CO_2 generally result from reductions in ventilation or outright apneas due to an underlying depression of respiratory drive (Walter and Eliot, 2002).

The CSA patient's having a loss of oxygen to the lung caused by the respiratory chest muscles make no attempt to breath as a result of central nervous system disorder. In patients with idiopathic central hypoventilation, pulmonary function test results typically are normal, unless there is coexisting lung disease, and tests of respiratory strength also are normal. The apnea and hypopnea that occur in association with central hypoventilation syndrome, the central feature of sleep hypoventilation is an abnormal increase in CO_2 during sleep (Walter and Eliot, 2002).

Since no airway obstruction is present in CSA, it seems that central and peripheral chemoreceptors play a more prominent role. It is generally accepted that the rapidly responding peripheral chemoreceptors are the most likely cause of feed-related respiratory instability (Verbraecken *et al.,* 1998).

2.3.3 Mixed sleep apnea (MSA)

MSA is due to an absent ventilatory effort (a 'central' pattern), and subsequently persists despite resumption of ventilatory efforts (an 'obstructive' pattern).

Central apneas can predispose to obstructive apneas. During central apnea, the central drive to the respiratory muscles is withdrawn and airflow ceases, thus the anatomically predisposed pharyngeal airway becomes compliant and is susceptible to collapse during the subsequent inspiration (Hahn and Staats, 2004).

Patients with OSA who also have prolonged central apnea should undergo imaging studies of the brainstem, most accurately performed by magnetic resonance imaging. Particular attention should be directed to the brainstem and cervico-medullary junction for evidence of a Chiari malformation or space-occupying lesion (Kirk *et al.,* 1998).

Mixed apneas contain polysomnographic characteristics consistent with a central and obstructive component. There is evidence, however, that the central compound of a mixed apnea is actually a prolongation of exhalation against an obstructed upper airway or a brief expiratory apnea before the resumption of cyclic respiratory efforts.

2.4 Hypopnea

Hypopnea is defined as an event which is characterized by disproportionate reduction of inspiratory airflow relative to inspiratory effort or metabolic needs. The American Academy of Sleep Medicine Task Force defined or characterized hypopnea as follows:' A clear decrease (>50%) from baseline in the amplitude of a valid measure of breathing during sleep or an amplitude reduction (<50%) associated with either an oxyhemoglobin desaturation (>3%) or an arousal, and the event should last at least 10 seconds. Hypopneas, like apneas, can be central or obstructive, although this distinction is infrequently made when reporting clinical sleep studies (Jonas *et al*., 2001).

Gould *et al. (*1987) have observed a number of patients with full clinical picture of the obstructive sleep apnea syndrome who have had no apnea at all but instead have had recurrent episodes of nocturnal hypoventilation. In the absence of apneas, these patients cannot be said to have the sleep apnea syndrome, which was originally defined purely in terms of nocturnal apnea frequency. Further confusion is caused by disagreement as to the definition of a hypopnoea, some describing them as a decrease in the airflow signal, some as a decrease in thoracoabdominal movement, and others as a decrease in the airflow in association with 4% drop in oxygen saturation.

2.5 Apnea, Hypopnea, and Apnea + Hypopnea Indices

Dividing the total number of apneas during a recording period by the total sleep time yields the average number of apneas per hour of sleep, or apnea index (AI). Similarly a variety of other indices, including hypopnea index (HI) and apnea + hypopnea index (AHI) (also termed the respiratory disturbance index RDI)) are usually employed to quantify OSAS severity. The concept of 'index' permits standardization of event frequency for the number of hours slept. This facilitates the comparison of individual patient data with normative as well as pre- and post – treatment values (Jonas *et al.*, 2001).

Alternatively, the AHI can be considered similar to blood pressure, with increasing values indicative of increasing disease severity. The advantages of using the AHI to classify disease status include its relative simplicity and high night-to-night reproducibility. The disadvantages of using AHI as a sole indicator of disease include the between-laboratory variability in measurement technique, its lack of informativeness regarding the severity of individual events (duration, associated hypoxemia and arousal) and its uninformativeness regarding the functional and physiological impact of the disorder (Redline and Tishler, 2000).

2.6 Upper Airway Resistance Syndrome

The upper airway resistance syndrome (UARS) is defined by repetitive and progressively increasing inspiratory efforts with subsequent transient arousals, but without associated reduction in airflow (Jonas *et al.*, 2001). Bader (2000), described the combination of habitual heavy snoring, increased upper-airway resistance, sleep

fragmentation, and daytime sleepiness is referred to as the upper-airway resistance syndrome.

Patients with UARS will go to sleep, then begin loud, crescendo snoring which leads to an arousal or awakening. This arousal is followed by the patient's falling back to sleep, resumption of snoring, and awakening again. These patients may exhibit all the clinical symptoms of OSA but without apneic or hypopneic events. Upper airway resistance syndrome is not a well-defined condition, and its diagnosis is therefore difficult. These patients are presently treated if they had OSA.

Patients with OSAS and UARS complain of day time tiredness, fatigue, and variable degrees of sleepiness. There was no difference in daytime sleepiness and daytime tiredness between the OSAS and UARS. Several hypotheses may be proposed to explain the differences in sleep electroencephalogram activity seen in OSAS and UARS patients. The differences suggest that both groups of patients have different cortical responses to abnormal respiratory challenges during sleep. There may be a different integration of messages from the periphery (i.e. respiratory apparatus) in the central nervous system (Gilleminault *et al.,* 2001). There are indications that the microstructure of nocturnal sleep is different in UARS and OSAS, and patients with OSAS present more important drops in oxygen saturation with their abnormal breathing events than UARS patients. But further research is needed to understand the exact relationship between the two clinical entities (Gilleminault *et al.,* 2000).

During nasal breathing the nasal passages constitute a relevant upstream inspiratory resistor whereas during mouth breathing the oral cavity is the potential site of upstream resistance. The resistance to airflow through the oral cavity is a major component of total upper airway resistance during oral and oronasal breathing. Mouth breathing occurs during sleep, even in normal subjects, and may be increased during sleep disordered breathing events (Lin *et al.,* 2003).

2.7 Upper Airway Anatomy

The anatomy of the upper airway, including the oral cavity, begins with intake of air through either the nose or the mouth. The critical component controlling the airway function are the muscles that control airway dimension or opening and are related to the primary structures of the airway, such as the tongue, soft palate, and uvula as well as the upper and lower pharynx. Some hard structures need to be considered, especially within the nose (Bailey, 2001).

The upper airway is generally divided into three regions based on midsagittal anatomy. These regions are first, the nasopharynx (the nasal turbinates to the hard palate). Second, the oropharynx, which is subdivided into a. retropalatal (the level of the hard palate to the caudal margin of the soft palate) and b. the retroglossal (the caudal margin of the soft palate to the base of the epiglottis) regions; and third, the hypopharynx, (the base of the tongue to the larynx) (Figure 2.3) (Schwab, 2001).

Upper airway dilator muscles play an important role in the determining the upper airway collapsibility. The dilating force developed by these muscles is only one that counterbalances the collapsing forces represented by the negative transmurul pharyngeal pressure and by the weight of upper airway structures.

At the pharyngeal level there is no bony or cartilaginous structure on maintain the aperture of the upper airway. Therefore, the maintenance of upper airway patency depends on the force developed by the contraction of upper airway dilators (Series, 2002). The pharynx extends superoinferiorly from the base of the cranium to the level of the inferior surface of the body of the 6th cervical vertebra. The pharynx lies dorsal to the nasal cavity, the oral cavity, and the larynx.

The contraction of the diaphragm against the high resistance offered by the nose during inspiration creates a subatmospheric intra-airway pressure which may narrow the collapsible pharyngeal segments in the pharynx. There are three collapsible pharyngeal segment which include the retropalatal pharynx as a velo- or nasopharynx, posterior to the soft palate, the retroglossal pharynx where oropharynx, posterior to the tongue from the tip of the uvula to the tip of the epiglottis) and the retroepiglottic pharynx (laryngo- or hypopharynx, posterior to the epiglottis). These pharyngeal segments are collapsible because the anterior and lateral walls lack bony support. The adult human is the only mammal to have an oropharynx (in all other mammals the tip of the uvula touches the tip of the epiglottis) and to suffer from OSA (Benumof, 2001).
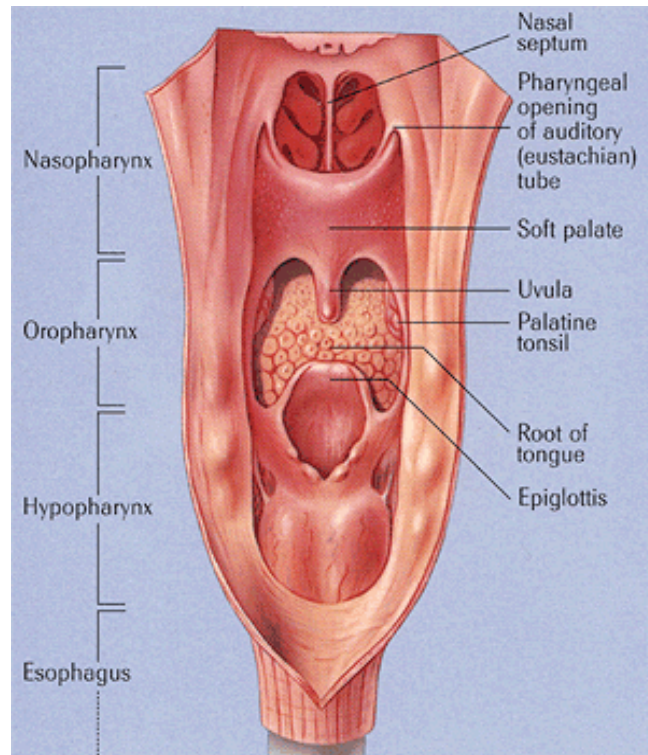
**Figure 2.3 Diagram showing nasopharynx, oropharynx and
hypopharynx (Adapted from www.dentalresource.com)**

2.8 Normal Physiology of Upper Airway

The upper airway is basically a soft tissue tube, the patency of which is maintained in part by the activity of muscular groups of which the tensor veli and genioglossus muscles are highly important members. The action of these muscle groups has an important influence on the physiology of sleep disorders.

The upper airway is a complex structure with many competing physiological functions, including swallowing, speech and breathing. It is richly innervated and its mechanical behavior is influenced by a multitude of neural controls and reflexes (Ayappa and Rapoport, 2002).

According to the "balance of the pressures" concept, the size and the resistance of the airway depends on the balance between collapsing intraluminal pressures generated during inspiration by subatmospheric pressures in the thorax and outward contraction forces of the upper airway dilator muscles. Patency of the airway depends on transmurul pressure (Ptm), which is the different between the negative intraluminal pressure caused by inspiratory efforts and the positive pressure from the upper airway musculature (Ayappa & Rapoport, 2002).

The influence of upper airway compliance on upper airway muscle characteristics can be accounted for by the influence of negative airway pressure on the activity of these muscles; the more compliant the upper airway tissues, the greater the decrease in the pharyngeal cross-sectional area with decreasing upper airway pressure, the greater the increase in airflow velocity with decreasing upper airway patency, with a further increase transmurul pressure gradient in a self-aggravating phenomenon. Therefore, the maintenance of upper airway patency during wakefulness requires a constant adaptation of upper airway dilator activity to counterbalance the destabilizing effect of the increase in upper airway collapsibility in Sleep apnea / hypopnoea syndrome (SAHS) (Series, 2002).

2.9 Pathophysiology of the Upper Airway

Anatomic abnormalities of the pharynx are thought to play a role in the pathogenesis of obstructive sleep apnea. One key feature of sleep is suppression of upper airway muscle activity, and a sleep-related decrease in upper airway dilator muscle force is thought to lead pharyngeal narrowing or closure in patients with obstructive sleep apnea or hypopnea (Isono *et al*., 1997).

There is structural narrowing between either the area behind the soft palate and the posterior pharyngeal wall; including the uvula and the tonsils, or the area between the base of the tongue the posterior pharyngeal wall, or both sometimes, although not as frequently, the hypopharynx is also narrowed. What appears to happen is that the muscles, particularly the genioglossus, that keep the airway open in the waking state and are phasic inspiratory in nature become somewhat blunted in their response during sleep, allowing a narrowed airway to collapse. Then, the increased effort of the chest wall muscles builds up negative pressure in the lungs, and an arousal take place to break the cycle (Cartwright, 2001).

OSA occurs when the dilator muscles of the upper airway (geniohyiod, genioglossus, tensor veli palatine) lose their tone and are unable to offset the negative pressure of the inspiration which draws the base of tongue (including the epiglottis) and soft palate posteriorly against the pharyngeal walls (Friedlander *et al.,* 2000). The inspiratory patency of the retropalatal, retroglossal, and retroepiglottic pharynx is caused by contraction of the

tensor palatine, the genioglossus, and the hyoid bone muscles, respectively (Benumof, 2001).

The pharynx is patent at atmospheric intraluminal pressure in normal subjects, and requires negative intraluminal pressure for closure. In contrast, patients with obstructive sleep apnea had positive closing pressure, ie, the pharynx was closed at atmospheric intraluminal pressure. Hence, the surrounding extraluminal pressure is an important contributor to the collapsing transmurul pressure during sleep (Badr *et al.*, 1999).

Upper-airway dysfunction and the specific sites of narrowing or closure are influenced by the underlying neuromuscular tone. Upper-airway size is determined by soft-tissue and skeletal factors that are also the major determinants of upper-airway patency during sleep. In obese patients, increased adipose tissue in the neck may predispose the airway narrowing.

During sleep the neural impulses to pharyngeal dilator muscle are diminished, allowing the anatomical forces to increase pharyngeal collapsibility. Two hypotheses have been proposed to explain the maintenance of pharyngeal airway during sleep. The neural hypothesis proposes the loss of wakefulness stimulus and diminished neural drive to pharyngeal dilator muscles during sleep, promoting the highly compliant pharynx to narrow or collapse. The second hypothesis implicates the role of mechanical factors inherent in the pharynx as the mechanism of airway collapse (Mohesinin, 2003).

The size of the pharyngeal lumen is determined by balance between outward forces developed by active contraction of upper airway muscles and inward forces resulting from subatmospheric luminal pressure during inspiration (Isono *et al*., 1997). The upper airway obstructions are classified for purpose of treatment: type I, an upper pharynx obstruction, involves the palate, uvula, and tonsils; type III, a lower pharynx obstruction, involves the tongue base and supraglottic structures; and type II is a combination of upper and lower obstructions (Waite, 1998).

2.9.1 Shape and Position of the Tongue

The tongue plays an important role in OSAS, in the supine position the tongue projects posteriorly by gravity, only counteracted by the tone of the genioglossal muscle (Figure 2.4). Herper (1976) and Sauerland (1978) have documented loss of tone in the genioglossal muscle during apnoeic periods and suggested that the posterior projection of the tongue onto the posterior pharyngeal wall accounts for the obstruction. Both the size and position of the tongue are important determinators wherther apnoeic periods are precipitated (Lyberg, 1989).
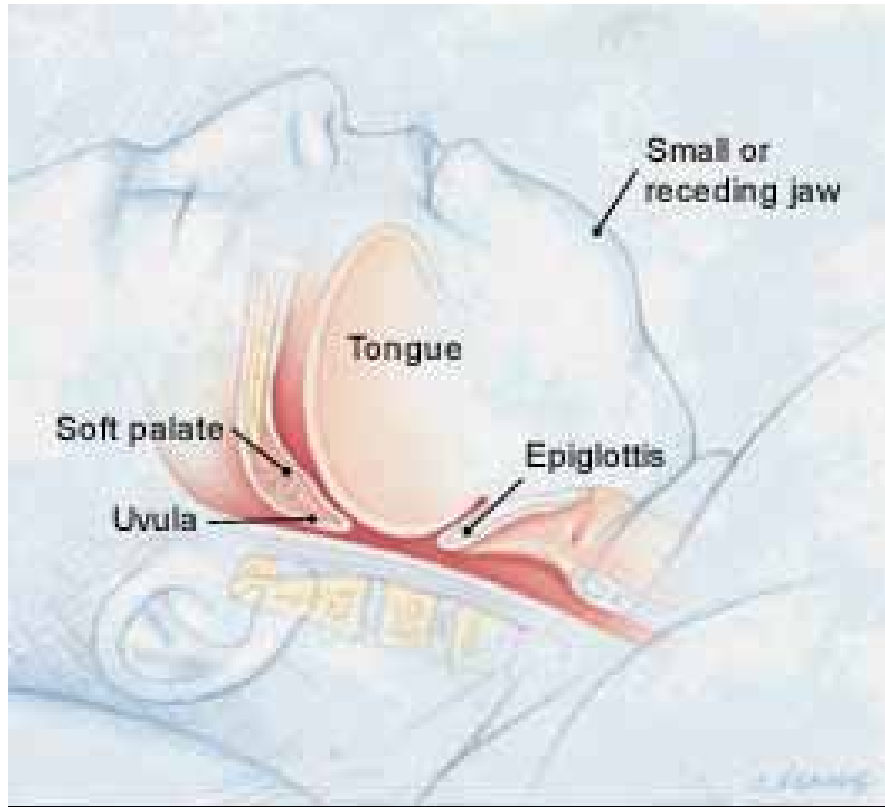
Figure 2.4 Abnormal airway during sleep (Adapted from American Academy of Family Physion, 1999)

The important role of the tongue in the pathogenesis of OSA has been confirmed in several studies. There is evidence that phasic respiratory activity of the phasic genioglossus is diminished in patients with OSA. This relaxation of the genioglossus during sleep would cause posterior displacement of the tongue, thus further occluding an already narrow airway it must be stressed that the genioglossus is only one of the muscles that are important in maintaining airway patency. Other muscle, such as the tensor palatine, which holds the soft palate up, and the masseter, which prevents the recession and rotation of the mandible during sleep, may also play an important role in the pathogenesis of OSA (Rivlin *et al.*, 1983).

Electromyogram of the genioglossus during sleep has shown decreased activity in response to airway occlusion in nine premature infants with mixed obstructive and central apnea. A similar study in older children who had OSA secondary to tonsillar hypertrophy showed no decrease in genioglossus electromyogram activity at the onset of an obstructed breath however, there was an in increase in activity of the electromyogram at the end of the obstructive (Singer and Saenger, 1990).

Enlargement of the tongue as defined by the tongue extending about the level of the mandibular occlusal plane was associated with increased risk for OSA when controlled for other variables within the model but was not significant after controlling for body mass index and neck circumference (Figure 2.5). Macroglossia is a common feature in individuals with Down syndrome and is likely to be a major factor in the increased prevalence of obstructive sleep apnea observed in this population.

There is a trend for patients with sleep disordered breathing to have larger tongue size compared with people without sleep disorder breathing, but tongue size is independent of AHI. Tongue size positively correlates with body mass index and neck circumference (Do *et al.,* 2000).