Chapter

Diagnosis

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Abstract

Obstructive sleep apnea (OSA) is often confused with the clinical symptoms of other adult/pediatric medical conditions and neurological disorders. Since OSA affects all systems in the body, it is important to establish a correct diagnosis. The first step in the evaluation of a patient with a sleep disorder is to identify the primary symptom. A detailed history of the sleep and wakefulness cycles constitutes the second step. This is followed by the medical history of the patient; a list of previously used medications; family history; detailed information about school, work, family, and social life; and a physical exam of bodily systems. Relevant laboratory tests are performed for differential diagnosis. Polysomnography (PSG) is a golden standard diagnostic method that records electrophysiological signals used for sleep physiology and diseases. PSG is an indispensable method in the diagnosis of OSA.

Keywords: anamnesis, symptoms, physical examination, electrophysiology, PSG, sleep breathing disorders, snoring and OSA

1. Introduction

Although OSA is described as an upper airway disorder occurring during sleep; it should be regarded as a clinical syndrome by taking into consideration its adverse effects on bodily systems. In the presence of symptoms like snoring, sleepiness during daytime, not being able to lose weight, weight increase, apnea observed by close family members, arousal with a feeling of suffocation during the night, profuse sweating of the chest and the neck, nocturnal arrhythmias, nocturia, enuresis, sexual impotence, depression, anxiety, forgetfulness, attention deficit, difficulty in concentration, learning problems, personality changes, deterioration of decision-making ability, morning headaches, dry mouth in the morning, bruxism, gastric reflux symptoms, sleeplessness, abnormal motor activity during sleep, and somnambulance, we should keep OSA in mind. However, all these symptoms guide patients to apply to different medical disciplines, causing confusions of diagnosis and eventually leading to delays in correct diagnoses. When patients have OSA, they can go to "neurology, ear nose throat, dentistry, psychiatry, pulmonology, cardiology, pediatric neurology, pediatric cardiology, internal medicine, neurosurgery, and endocrinology" departments. Therefore, we can say that OSA is a multidisciplinary disease. When we consider the increased workload burden in these disciplines, we appreciate that there can be further delays in establishing an OSA diagnosis in the process. So, in hospitals the diagnosis of sleep physiology and diseases should be made by "clinical physiology, electrophysiology, neurophysiology, and sleep laboratories". Through these laboratories, all medical disciplines should be informed with reports for the correct diagnosis and treatment of these patients, and they should be followed up accordingly.

Despite the advances in the field of sleep medicine, neither the societies nor the physicians are sufficiently informed about sleep and sleep disorders. Among sleep disorders, OSA is very frequent in the population, and it leads to significant consequences. It can adversely influence the school and job success of an individual, his/her social life, marriage, and other relationships while resulting in traffic and occupational accidents. OSA can hinder the cognitive functioning of an individual while increasing the risk for psychiatric and other system-related diseases. Sleep apnea syndrome can play a role in the etiology of severe diseases, namely, hypertension, myocardial infarction, heart failure, stroke, and diabetes. Sleep deprivation brought forward by OSA can increase the number of seizure episodes in epilepsy patients.

This insidious disease has been affecting individuals and societies for many years; it can show itself during sleep, and its effects can deteriorate the performance of the individual during daytime. Complaints of snoring and feeling of suffocation that appear during sleep are mainly identified by the spouse and the close family members of the individual. This disease hinders respiration during sleep and influences all bodily systems and mainly the brain during nighttime. Thus, such patients need to be examined at a sleep and electrophysiology lab by obtaining electrophysiological signal recordings (EEG, EMG, ECG, etc.) throughout the night. This method is called PSG; it establishes the definitive diagnosis for OSA and discriminates it from other sleep disorders and general medical conditions.

Currently, PSG and snoring sound analysis are guiding the diagnosis and treatment of OSA while creating an innovative working field for engineering and medicine.

2. Diagnosis

2.1 Approach for an OSA patient and clinical signs

OSA patients generally experience their symptoms during nighttime, and first of all they need to be made aware as they are not aware of them. OSA has many symptoms; the major ones are snoring, apnea as observed by close family members, and excessive sleepiness during daytime. The presence of nocturnal symptoms is more valuable than daytime symptoms when establishing the diagnosis [1]. These patients are generally obese, and they have short and thick necks and narrow upper airways. This type of a body composition is not the rule as the disorder can even be seen in children.

Snoring is the most frequently seen symptom in the presence of sleep breathing disorders. Snoring is a medical and social complaint affecting both sleep and general well-being of children and their parents. When snoring is accompanied by air hunger, feeling of suffocation, or waking up, OSA should be considered. Snoring would not be sufficient by itself for diagnosis as OSA can also happen in the absence of significant snoring. Noisy breathing and increase in the respiratory effort in children during sleep can be the most significant sign. It is typical to have snoring disrupted by frequently repeating apnea in OSA patients. The patients deny snoring. Thus, information needs to be obtained from their partners or close family members. Despite intermissions in snoring and stopping of air exchange in the mouth and nose, abdomen and chest movements continue paradoxically; this results in a panic in people who are witnesses of this situation. Apnea usually ends with a deep breath. At the end of apnea, there can be a loud snoring, a sound of suffocation, coughing, or short arousals [1–6]. Sleep disruption caused by repetitive partial or total airway obstruction in OSA can result in sleepiness during

daytime. This situation is correlated with the severity of the disease; mild cases describe sleepiness only during sedentary circumstances, while in advanced cases, sleepiness can even be observed while eating food, talking, or driving. Patients turn and move in bed, and they describe sweating on the upper part of the chest including the neck [2–5, 7]. OSA patients need to breath from the mouth frequently; they talk about complaints like dryness of the mouth or drooling. Neurophysiological changes are weakening of memory and deteriorations in decision-making ability, attention, and concentration, personality changes include aggressiveness or depression, and decreased libido and impotence can as well be seen [1, 8]. There can be night and morning headaches due to decreases in oxygen concentration; these are blunt and widespread in nature. Increases in weight gain and inability to lose weight can be observed, and negative pressure within the chest and abdominal cavity increases because of obstruction resulting in esophageal reflux; patients usually wake up with a chest pain in the form of burning [1, 9]. These symptoms can make one consider several diseases like depression; hypothyroidism; stress; migraine; febrile diseases; metabolic syndrome; chest pain during nighttime due to coronary spasm; arrhythmias; iron deficiency anemia; Cushing syndrome; endocrine and metabolic diseases; heart, kidney, and liver failures; and enuresis nocturia; therefore, differential diagnosis needs to be made.

2.2 Physical examination findings in OSA

There is not any specific physical examination finding diagnostic for OSA. By approaching from a wider perspective, evaluation should be made for several disciplines (**Figure 1**). OSA is related to multiple anatomic risk factors. The most important one is central-type obesity with increased body mass index and increased neck circumference. On the other hand, many patients with OSA are not obese, yet they can demonstrate decreased oropharyngeal air space, retrognathia or

Figure 1.
The physician speaks with husband and wife. And he learns by the medical history of the patient, a list of previously used medications, family history, and detailed information about school, work, family, and social life. And he makes a physical exam of bodily systems.

micrognathia. Obesity mechanically obstructs pharyngeal soft tissues and results in pharyngeal compression. Also decreased lung volume through CNS-acting signaling proteins (adipokines) may alter airway neuromuscular control [10, 11]. Individuals with OSA have severe obesity due to sleep deprivation, hypersomnia, and altered metabolism. OSA is associated with endocrinopathies like hypothyroidism and acromegaly. Hypothyroidism is a known cause for secondary OSA. Myopathy of oropharyngeal airways, edema, and obesity lead to upper airway obstruction and collapse in these patients. Acromegaly is caused by excessive levels of growth hormones; there is enlargement of craniofacial bones, enlargement of the tongue (macroglossia), and thickening and widening of the laryngeal region. All these factors can contribute to the obstruction of the upper respiratory airways. In addition to acromegaly and hypothyroidism, goiter which is associated with a euthyroid state can as well contribute to OSA. Among factors contributing to the narrowing of upper airways, we can list Down syndrome and storage diseases like mucopolysaccharidosis and amyloidosis (deposition) [12–16].

2.2.1 Craniofacial factors

Cephalometric measurements demonstrate that when compared with controls, individuals with OSA have important changes in the size and position of soft palate and uvula, in the volume and position of the tongue, the position of the hyoid bone, and mandibulomaxillary protrusion. Mandibular retrognathia and micrognathia cause the tongue to stay at a higher position; these can be diagnosed during the examination by observing the patient from the side view. Racial differences in cephalometric features possibly play a role in the development of risks for OSA in the absence of obesity [17, 18].

2.2.2 Nasal factors

Examination of nasal airways should focus on the anatomical abnormalities that might contribute to nasal obstruction. These can be of congenital, traumatic, infectious, or neoplastic in nature [19].

2.2.3 Neck circumference

Increased neck circumference is an important risk factor for OSA. Patients with a neck circumference of more than 48 cm (19.2 inches) have a 20 fold increased risk for OSA [18].

2.2.4 Pharynx examination

There are two well-defined classifications to identify the relationship of the tongue with the pharynx. The Mallampati classification is a method first used by anesthesiology specialists to foresee difficult tracheal intubations. Friedman classification describes prognostic indicators for a successful surgery for sleep disorders by combining the position of the palate with the size of the tonsils [20, 21]. The Mallampati classification is as follows:

Class 1: Soft palate, fauces, uvula, and posterior and anterior pillars are visible.
Class 2: Soft palate, fauces, and uvula are visible.
Class 3: Soft palate, fauces, and only the base of uvula are visible.
Class 4: Soft palate is not visible.

2.2.5 Examination of the tonsils

Enlarged tonsils and adenoids are the primary causes of upper airway obstruction and sleep apnea in children, only a small portion of the adults can have an enlargement of these structures leading to obstruction of the airways. Adenoids cannot be visualized during a routine physical examination or the examination of tonsils, and a tongue depressor might be necessary. The size of the tonsils can be measured on a scale of 1–4 [22].

2.2.6 Neurological examination

During physical examination, the characteristics of the apparent neuromuscular disease can indicate OSA and hypoventilation. For example, progressive muscular atrophy and hand or tongue fasciculations can indicate amyotrophic lateral sclerosis. In amyotrophic lateral sclerosis, phrenic nerve dysfunction is common; during rapid eye movement sleep (REM) it leads to diaphragmatic paralysis due to significant hypoventilation. Furthermore, coexisting OSA can reveal itself during amyotrophic lateral sclerosis with bulbar involvement. In poliomyelitis, there is weakness of thoracoabdominal muscles and accessory muscles of respiration; this can frequently be accompanied with kyphoscoliosis. Postpolio syndrome demonstrated itself with muscular dystrophies; myasthenia gravis and metabolic myopathies exhibit themselves with weaknesses of chest wall muscles and the diaphragm. Myasthenia gravis can as well involve facial structures resulting in OSA. In myotonic dystrophy or muscular dystrophy, there can be craniofacial abnormalities; macroglossia can also be seen (e.g., in Duchenne muscular dystrophy). Lastly, obesity (e.g., steroid use or inactivity) and being overweight can contribute to sleep apnea during the course of a neuromuscular disease [23, 24].

2.2.7 Cardiopulmonary examination

Peripheral edema is a frequent finding in patients with obesity hypoventilation syndrome (as a manifestation of cor pulmonale) as well as in certain patients with obstructive apnea that have left ventricular heart failure. OSA can coexist with chronic obstructive pulmonary disease and asthma. Hypertension is associated with OSA. If a patient with OSA has chronic pulmonary disease, pulmonary hypertension can also be seen. Findings of polycythemia, arrhythmia, cyanosis, right heart failure, and chronic cor pulmonale can be identified [19, 25].

2.3 OSA diagnostic methods

2.3.1 Radiological diagnosis

Cephalometry: It is the standardized lateral radiographic imaging of the head and neck with which bone and soft tissue boundaries are evaluated in individuals with OSA. It is useful in diagnosing frequently encountered craniofacial and upper airway soft tissue anatomy-related anomalies like the hyoid, mandibular, tongue, soft palate, and facial anomalies. Maxillo-mandibular retrognathism has in patients with OSA and it has been accepted as an indicator of maxillary prognathism. Horizontal and vertical length of the mandibula affects the oral floor and the position of the tongue. The length of the horizontal ramus of the mandibula shortens in individuals with snoring and apnea, whereas vertical ramus only shortens in people who snore. Total facial height is found to have increased in OSA patients compared

to the normal population. Hyoid bone is the point where the dilator muscles of the upper airways attach; it is shown to have a lower location in OSA patients [26–28]. The distance between the root of the tongue and posterior pharyngeal wall (posterior airway space, PAS) is shortened in OSA patients. When PAS is measured by cephalometry in OSA patients, it is shown to have significantly narrowed in nasopharyngeal and oropharyngeal regions, gets larger towards the hypopharyngeal region, and gets within normal limits at the level of epiglottis. Computerized tomography (CT) is an imaging technique that provides detailed information about the size, cross-sectional area, and neighboring tissues of the upper respiratory system thanks to its superior bone and soft tissue resolution. It is not routinely used. Magnetic resonance (MR) is a noninvasive technique providing excellent views of all soft tissues of the upper respiratory system including the adipose tissues, and the images are obtained in the supine position by covering axial, sagittal, and coronal planes. It is superior to CT when evaluating PAS which is important for surgical treatment. Its biggest advantage is not having radiological exposure. MRI examinations of upper respiratory systems of individuals with OSA have been compared and significant increased have been shown in the adipose tissues of the supportive wall structures of soft palate, tongue and the pharynx. In another study, the narrowing of the upper airways was not due to adipose pads; it was reported to take place due to significant thickening of the lateral pharyngeal wall. Fluoroscopy is an imaging technique allowing for a dynamic evaluation of the upper airways when the patient is awake of sleeping. Tongue and pharyngeal regions are covered with barium, and for better visualization of the hypopharynx, the head is kept at an angle of 30 degrees. Its disadvantages are radiation exposure, not being able to obtain cross-sectional images, and not being able to perform bone structure measurements [28–30]. Acoustic reflection relies on the reflection of sound waves sent onto the upper respiratory tract, it does not utilize radiation, and it is a noninvasive imaging technique. In a study employing this technique, cross-sectional areas of the pharynx and glottis were found to have significantly reduced demonstrating a correlation between the degree of OSA and the horizontal cross-sectional area of the pharynx.

2.3.2 Endoscopic diagnosis

Nasopharyngolaryngoscopy is a diagnostic technique spanning the upper airways from the nose to the glottis to analyze the dynamic changes of the airways and to identify the level at which airways collapse. Fiberoptic nasopharyngoscopy only shows the open-closed status of the airways; it cannot measure and interpret the surrounding soft tissue areas. By having the patient perform Müller maneuver, the degree and the level of the collapse is diagnosed [29, 30].

2.3.3 Polysomnography (PSG)

The process of recording sleep with electrophysiological signals is called "polysomnography," ("PSG"). Sleep recordings that appear on computer screen or paper are called "polysomnogram." Electrophysiological signals recorded throughout one night during sleep and wakefulness are as follows: "Electroencephalogram (EEG), electromyogram (EMG; chin, arms and legs), electrooculogram (EOG), electrocardiogram (ECG), snoring, and oronasal air flow (L/s), chest and abdomen movements (respiratory effort recordings), oxygen saturation, and body position and real time-video-image recordings" [31].

PSG is a gold standard technique for OSA diagnosis. For this test, patients are prepared by sleep technicians (**Figure 2**).

Figure 2.
Patient is prepared for PSG by the sleep technician. She is wearing an airflow cannula which is very important for the diagnosis of OSA.

When defining respiratory events in PSG, we need to perform "scoring of sleep and scoring of respiratory events."

Scoring of sleep is done through staging of sleep. For staging sleep, polysomnography recordings are separated into 30 s intervals (epoch); each epoch is scored with a sleep stage. Sleep stages are as follows: "Stage N1, Stage N2, Stage N3, Stage R, and Stage W (wakefulness)." Every 30 s interval needs to be staged with one of these stages. Three main physiological signals are used when staging sleep: "EEG, EMG, and EOG." For each epoch, these three parameters are assessed, and a sleep stage name is assigned to each 30 s interval. Sleep staging is based on certain principles [31].

Electrophysiological signal recordings that are required for the interpretation of respiratory events in PSG are as follows: "oxygen saturation, nasal/oronasal air flow (nasal cannula, thermistor), thoracic respiratory effort, abdominal respiratory effort, EEG recordings (absolutely needed to identify arousal), body position, tracheal microphone, ECG, and leg EMG recordings." Measurement of thoracic and abdominal movements is the most frequently used technique in sleep laboratories in the identification of respiratory effort [31].

The American Academy of Sleep Medicine (AASM) has published the rules to be used when reporting sleep and sleep-associated events as well as respiratory event scoring based on [31, 32].

Apnea is the cessation of air flow in the mouth and nose for l0 seconds of longer. There are three types of apnea. (i) Obstructive apnea consists of the absence of air flow despite respiratory effort (**Figure 3**). (ii) Central apnea consists of the absence of airflow in the absence of respiratory effort (**Figure 4**). (iii) Mixed apnea consists of the absence of airflow in the absence of respiratory effort, followed by increase in respiratory effort despite the absence of airflow (**Figure 5**). Nowadays, mixed apneas are scored as obstructive apnea.

Hypopnea is a 50% reduction in air flow (currently this value is reduced down to 30%) for 10 s or longer together with a 3% decrease in oxygen saturation and arousal (**Figure 6**).

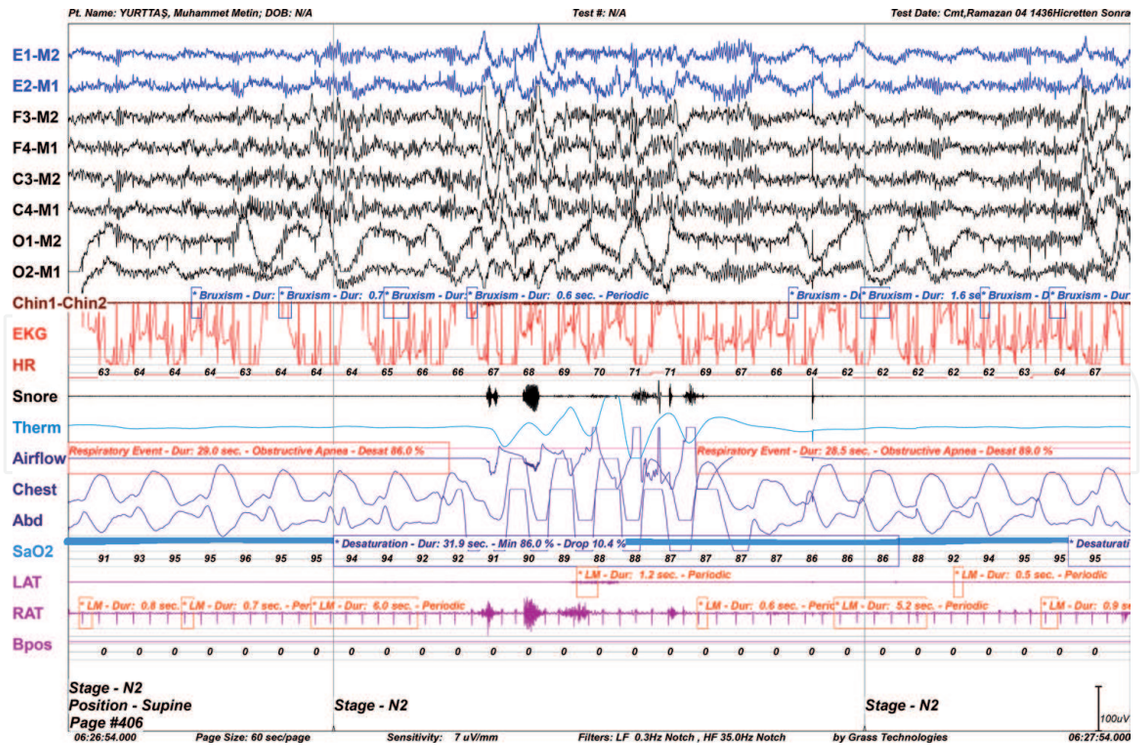

Figure 3.
Polysomnographic record image of obstructive apnea.

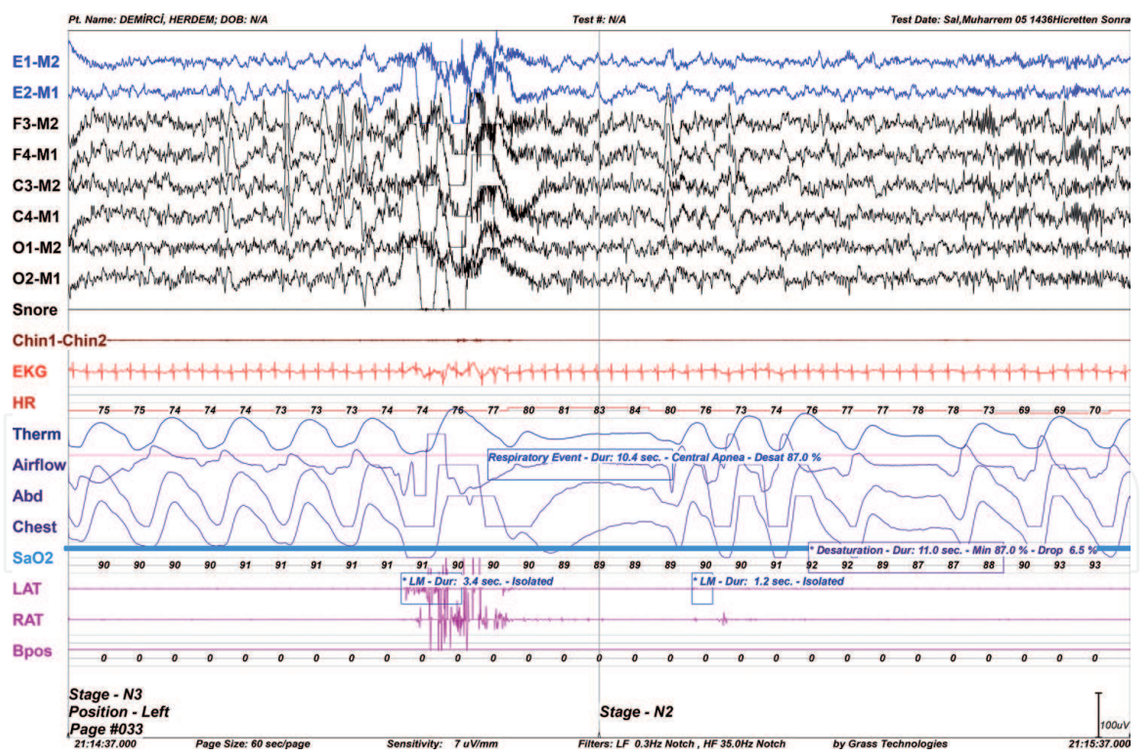

Figure 4.
Polysomnographic record image of central apnea.

Arousal is shifting to a more superficial level of sleep and wakefulness for short periods of time.

Respiratory effort-related arousals (RERA) are seen in the absence of cessation or reduction of air flow during the respiratory effort.

Apnea index (AI) defines the number of apneas that are seen during 1 h when sleeping.

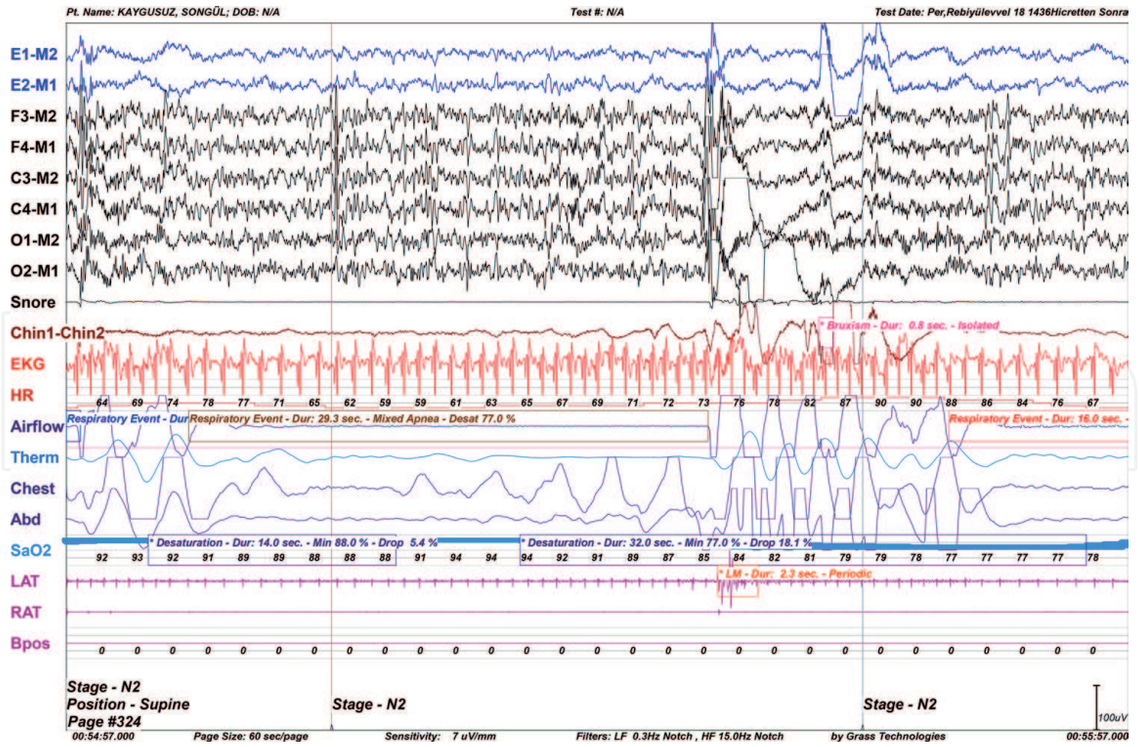

Figure 5.
Polysomnographic record image of mixed apnea.

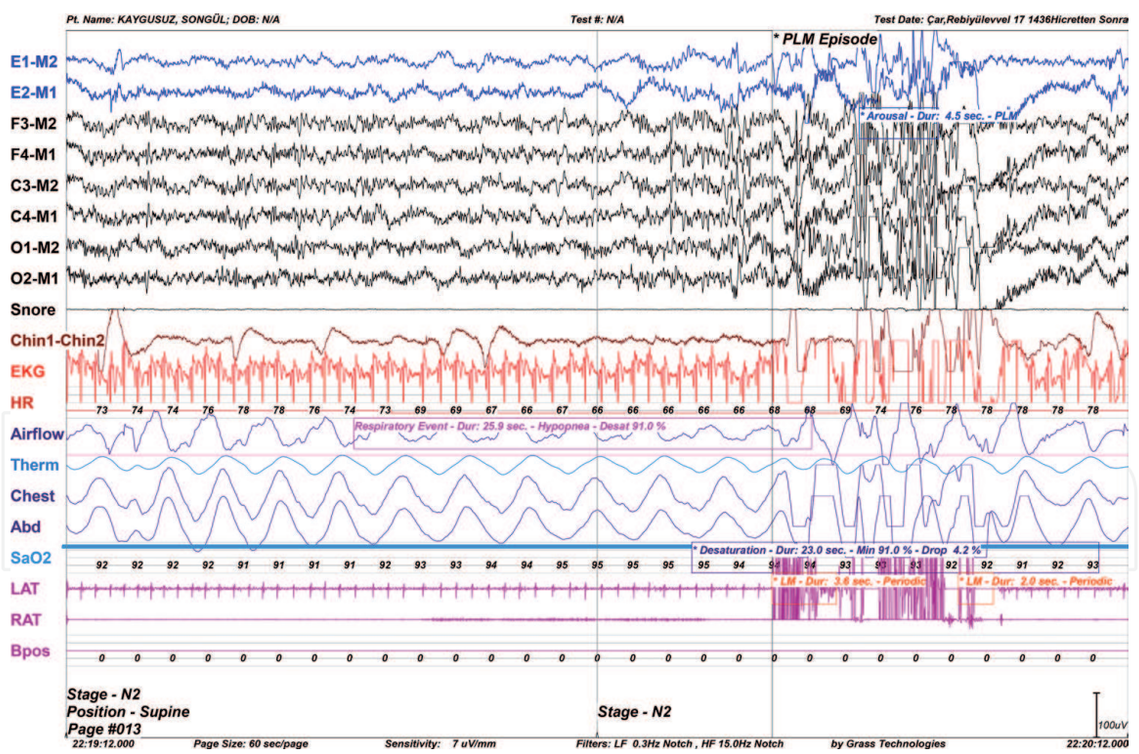

Figure 6.
Polysomnographic record image of hypopnea.

Apnea-hypopnea index (AHI) is calculated by the total number of apnea and hypopneas divided by the time spent while sleeping. When RERA is added to this number, the name of the index is respiratory disturbance index (RDI).

Characteristic PSG findings for OSA are as follows: (i) Increases in the duration of superficial sleep and decreases in the duration of deep sleep and REM. (ii) Apneas and hypopneas repeat frequently. (iii) Oxygen desaturation repeats frequently. (iv)

REM sleep can increase the frequency and duration of apneas and the degree and the duration of oxygen desaturation. Sleeping in supine position contributes to this increase. (v) It is typical to see paradoxical thoracic and abdominal movements during apnea. (vi) During apnea, the heart rate possibly slows down, and it increases in the period following the apnea; arrhythmias can be observed. (vii) In respiratory sound recordings, an irregular loud snoring that is interrupted by apneas is heard.

The degree of the disease is identified by AHI value calculated on the basis of PSG assessment: "AHI < 5, normal; AHI = 5–15, mild OSA; AHI = 16–30, moderate OSA; AHI > 30, severe OSA" [33].

2.3.4 Auxiliary diagnostic techniques

Several auxiliary tests are required to support the diagnosis, to identify the complications, and to aid in the differential diagnosis in OSA patients. Blood tests are helpful in identifying the diseases that might lead to OSA and their complications. Hemograms can play a role in idiopathic polycythemia when establishing a preliminary diagnosis of OSA. Thyroid hormone profile (T3, T4, TSH) is a routine test to discriminate between OSA and hypothyroidism [34, 35]. Lung X-rays can help identify certain lung diseases and their complications that accompany OSAS. OSA-related respiratory function tests have a ratio of greater than 1 for "forced expiratory flow 50% /forced inspiratory flow 50%" and saw tooth pattern in flow-volume curve. Individuals with OSA have normal arterial blood gas levels during daytime; in cases having chronic hypercapnia during daytime while they are awake, coexistence of chronic obstructive pulmonary diseases or diseases leading to alveolar hypoventilation like neuromuscular insufficiency should be considered [36]. In an obese patient who is hyper-somnolent and who snores, a diagnosis of OSA should be eliminated. In an individual having findings of right heart failure and pulmonary hypertension on echocardiogram, if these findings cannot be explained, possible coexistence of OSA should be considered [37, 38]. In OSA, sleep is interrupted due to apnea episodes frequently recurring during the night, and the patients are excessively sleepy the next day. In the identification of sleepiness, the most commonly used method is "Epworth Sleepiness Scale" [39]. A diagnostic method for objective demonstration of excessive sleepiness during daytime is "Multiple Sleep Latency Test (MSLT)". Despite the fact that it does not have a direct role in the diagnosis of OSA, it helps to differentiate diseases like central hypersomnia and narcolepsy that cause similar symptoms. Having short sleep latency is a non-specific sign for sleep pressure during daytime and is often seen for OSA patients [40].

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