Obesity Hypoventilation Syndrome (Pickwickian Syndrome) — Definition and Pathophysiology

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The problem of obesity has already affected almost all corners of the world, thus causing emergence of syndromes and symptoms in all known diseases creating new comorbidities as well as separate ailments. Therefore, innovations and alterations in medical management of various illnesses are required. In 2015, approximately 1 in 3 adults on the planet were predicted to suffer from excess body mass (BMI>25kg/m²) and 10% of the world population was diagnosed as having obesity (BMI>30kg/m²). One of the syndromes that come with being obese is obesity hypoventilation syndrome (OHS) stipulated by a quotidian alveolar hypoventilation (PCO₂ >45mm Hg), while other conventional reasons for the condition are absent. OHS is the causative factor of intensive usage of hospital beds nowadays. In addition, it is a leading factor in the development of cardiorespiratory diseases.

Definition

Obesity hypoventilation syndrome (OHS) is a clinical combination of obesity/body mass index > 30 kg/m² and awake chronic hypercapnia (paCO₂ > 45 mmhg) in the absence of
other causes of hypercapnia. Close to 90 % of these patients will have obstructive sleep apnea.

**Epidemiology of Obesity Hypoventilation Syndrome**

According to the US Centers of Disease Control and Prevention (CDC), the occurrence of OHS ranges from 10 % to 20 % because 30 % of American citizens are obese. The figures characterizing the disorder tend to **elevate as obesity rate grows** from year to year at an alarming rate.

OHS often remains **undiagnosed**; the prevalence of OHS is 10—20 % in patients with **obstructive sleep apnea** and 0.15—0.3 % in the adult population. OHS is more **common in males**, with a ratio of 2:1 male-to-female. Also, patients **older than 50 years** tend to have OHS.

**Background of Obesity Hypoventilation Syndrome**

Alveolar hypoventilation is defined as **insufficient ventilation** leading to **hypercapnia**. The severity can be determined by measurement of the increase in the partial pressure of carbon dioxide by **arterial blood gas analysis** (PaCO₂).

**Alveolar hypoventilation** occurs due to several disorders that are referred to as **hypoventilation syndromes**. They include:

- Obesity hypoventilation syndrome (OHS)
- Central alveolar hypoventilation
- Chest wall deformities
- Neuromuscular disorders
- Respiratory diseases such as COPD

Therefore, obesity hypoventilation syndrome (OHS) manifests as the development of pronounced **hypoxemia**, **lack of oxygen in the blood** affecting all parts of the body.

OHS may be **acute or chronic**; there are a number of mechanisms that affect the development of both conditions. First of all, the main triggers of OHS are the **disturbance of the central ventilator drive** and an **increased body weight**.

OHS encompasses obesity itself accompanied by **disordered breathing during sleep**, **BMI > 30 kg/m²**, and **hypercapnia PaCO2 > 45 mm Hg**. The majority of patients with OHS (90%) suffer from **obstructive sleep apnea** (OSA) respectively.

**Etiology of Obesity Hypoventilation Syndrome**

Owing to the **increased energy needed for breathing**, a **weakening of the inspiratory muscles occurs** accompanied by **low resting tidal volumes** in patients with OHS, leading to **respiratory and cardiovascular disorders**.
Patients with OHS tend to have **20 % decreased lung capacity, 40 % lower maximal voluntary ventilation** and **lower pulmonary compliance** than people with obesity who do not suffer from hypoventilation. OHS triggers **intensive breathing**, as the lack of oxygen in the blood elevates the quantity of carbon dioxide, thus stimulating the respiratory center in the brain leading to additional breathing in.

**Carbon dioxide retention** may be stipulated by the **scarcity of leptin** or its resistance in the case of OHS patients.

Nevertheless, the **central respiratory control disorder** remains the most contributing factor in the development of OHS, as overweight individuals that hyperventilate tend to have **abnormal body reaction to hypoxia** and are less responsive to CO$_2$ rebreathing.

## Presentation of Obesity Hypoventilation Syndrome

### History

OHS is usually a **secondary syndrome** for the main condition, of which the flow is characterized by the stage of hypoventilation and hypercapnia as well as the body’s ability to recover from respiratory acidosis.

OHS sufferers tend to develop **signs of OSA**, namely, hypersomnolence, daytime sleepiness, tiredness, especially during daytime even after minimal physical activity, disturbing snoring, poor sleeping patterns, night choking – sleep apnea, frequent depression attacks, and **headaches**, especially in the morning. **Fatigue** usually follows **shortness of breath** which is a symptom of **low blood oxygen levels** *(chronic hypoxia)*.

**Pulmonary hypertension** and **chronic right-sided heart failure** *(cor pulmonale)* are some of the major complications of OHS in obese patients, further aggravated by **peripheral edema**, leading to the emergence of swellings in the limbs. Also, there can be the presence of **cyanosis-bluish color** on the lips, fingers, toes, or skin.
Physical examination

Physical examinations are not clinically articulate, are non-specific, and are characterized by comorbidities:

**Thoracic examination**

During thoracic examination, patients who are at different stages of OHS have **diffuse wheezing**, **hyperinflation**, a specific appearance of the chest, “**barrel chest**”, percussion produces **hyperresonance**; there is **prolonged expiration** and breath sounds are diffusely decreased.

Also, there are **coarse crackles** during inspiration, followed by **wheezes during expiration**. In addition to thoracic examination, there may be **clubbing** and **cyanosis** indicating the rate of hypoxia.

**Pulmonary hypertension**

**While auscultating:**

- Second heart sound has a characteristic split and pronounced pulmonary component (P2)
- Left parasternal (right ventricular) heave has an S4 of right ventricular origin
- Jugular venous pulse has a large a-wave component
- Pulmonic valve regurgitation is reflected by a diastolic murmur

**Advanced stages of the disease**

- There are usually signs of **right ventricular failure** (cor pulmonale) coupled with **V wave upon increased jugular venous pressure**
- **Swelling of the limbs** aggravates
- There is **severe tricuspid regurgitation** that manifests as a systolic murmur as a result of a pulsatile liver
- **Hepatosplenomegaly**
### Differential Diagnosis

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### Diagnosis of Obesity Hypoventilation Syndrome

Diagnosis is established based on the results of physical, laboratory and imaging examinations, namely:

- **Arterial blood gas** is compulsory while conducting OHS diagnosis
- **CT scan/chest x-ray** either of them are conducted in order to exclude comorbidities and other ailments
- **MRI**
- **ECG** helps to detect signs of right heart strain, right atrial enlargement and right ventricular hypertrophy
- **Echocardiography** looks for evidence of *pulmonary hypertension* and right ventricular enlargement
- **Electromyography** and **nerve conduction velocity** is informative in neuromuscular disorders, such as myasthenia gravis, *Guillain-Barré syndrome*, and amyotrophic lateral sclerosis, this method allows differentiation of neuropathic and myopathic patterns of the disorders
- **Lung function tests** (pulmonary function tests)
- **Polysomnography** is sleep pattern study, which is often disordered in OHS followed by OSA

### Laboratory studies

**Serum biochemical examination**: elevated concentration of serum bicarbonate (HCO$_3^-$) as a response to respiratory acidosis, as well as high volumes of serum Ca and K, hypercalcemia and hyperkalemia

**Complete blood cell count**: due to hypoxia, there may be polycythemia and an increased level of hematocrit

**Thyroid function studies**: Decline in the functioning of the thyroid gland, *hypothyroidism*, leads to development of obesity and OHS. Those who are suspected to have developed OSA have to undergo thyroid function examination

**Arterial blood gas analysis**: OHS is represented by hypercapnia/high PaCO$_2$ $>$45mmHg.

The development of acute and chronic acidosis as well as the rate of their compensation are determined via **estimation of HCO$_3^-$ and PH**
Transdiaphragmatic pressure is informative while monitoring muscular weakness; it helps to distinguish the etiology of the disorder (diaphragmatic dysfunction and paralysis).

Imaging studies

- **Chest radiography** is administered in order to exclude pulmonary diseases; it helps to determine the etiology of hypoventilation.
- **Fluoroscopy** is informative while looking for unilateral diaphragmatic paralysis, and is used as an additional measure of chest radiography.
- **Chest CT scanning** has better sensitivity and may detect abnormalities that are not found on a chest radiography (emphysema, diaphragm and skeletal thoracic abnormalities).
- **Brain CT scanning** is indicated if a physician suspects a central cause of hypoventilation; it may also help to rule out cerebrovascular accidents and CNS tumors or trauma, various lesions of the brainstem in the area of the pons and medulla.
- **Brain MRI** is useful when a CT scan of the brain is negative but a central etiology of OHS has not yet been ruled out.

Management of Obesity Hypoventilation Syndrome

Management of OHS includes a combination of different medical and surgical methods. The sufferers require the intervention of different specialists:

Physicians and endocrinologists regarding probability of diabetes mellitus, hypertension, elevated blood pressure, hyperlipidemia, heart failure and hypothyroidism therapy. Dietician for the correction of daily nutrition in order to lose weight.

Respiratory therapist for the management of respiratory failure. Surgeon considering potential bariatric surgery.

*Image:* “Figure A shows a side view of the neck and the correct placement of a tracheostomy tube in the trachea, or windpipe. Figure B shows an external view of a patient who has a tracheostomy.” by National Heart Lung and Blood Institute (NIH). License: Public Domain

Based on the severity of OHS there are certain steps required:
1. Correction of weight gain towards reduction
2. Therapy with oxygen
3. Positive pressure ventilation
4. Medication
5. Tracheostomy
6. OHS complications and comorbid illnesses management

**Advanced cases** of OHS require **ICU admission**. Such cases include: If the patient is confused and lethargic, respiratory acidosis reflected by a pH of less than 7.3, there is fatigue of the respiratory muscles, aggravation of hypoxia in the form of hypercapnia.

**Non-invasive positive airway pressure**

This is the first line method of management that can be used even on patients who are planning to lose weight. It is indicated in all patients with all forms of sleep-related hypoventilation. It may be continuous (CPAP) or bivalve (BPAP).

**Dietary modification**

Weight loss is part of the first line method of management for OHS since it improves normal daytime physiology of gaseous exchange. It has been shown to reduce the number of sleep disordered breathing events and the severity of hypoxemia.

**Pharmacotherapy**

**Medroxyprogesterone acetate**, a synthetic progesterone, a breathing stimulator: This remedy has been efficiently used in patients with OHS, and elevates ventilatory response to hypercapnia. Administration of medroxyprogesterone acetate leads to a decrease in PaCO$_2$ and an elevation in PaO$_2$. A possible side effect is hypercoagulation, especially in those who are predisposed to this condition.

**Acetazolamide** is the carbonic anhydrase inhibitor; a moderate diuretic may become the reason for metabolic acidosis leading to an increase in minute ventilation, thus reducing PaCO$_2$ level. In addition, acetazolamide stipulates decline of serum bicarbonate level.

**Beta-2 agonists**: albuterol, metaproterenol, atrovent affect beta-2 receptors in the bronchial smooth muscle, bronchospasm relief.

**Surgical intervention**

- **Vertical banded gastroplasty** (VBG) allows restriction of the volume of the stomach.
- **Adjustable gastric banding** (AGB)
- **Roux-en-Y gastric bypass** (RYGB) is the most common procedure that provides short- and long-term after-effects regarding safety, efficiency, and durability; it is performed laparoscopically
- **Biliopancreatic diversion** (BPD) and **biliopancreatic diversion with duodenal switch** (BPD-DS) leading to malabsorption

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